

RAPID FIRE 1 – ACUTE HEART FAILURE

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Location: Agora

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Prognostic value and kinetics of soluble neprilysin in acute heart failure. A pilot study

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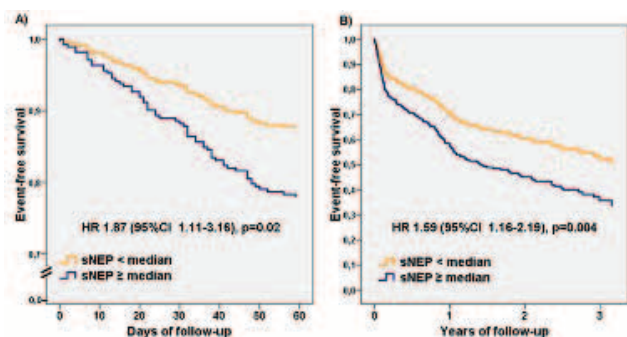
Background: The soluble form of neprilysin (sNEP) was recently identified in chronic heart failure (HF) and associated with cardiovascular outcomes.

Objectives: To examine the prognostic value of sNEP in acute HF (AHF) and sNEP kinetics during hospital admission.

Methods: A total of 350 patients (53% women, mean age 72.6 ± 10.7 years) were included in the study. Primary endpoints were a composite of cardiovascular death or heart failure hospitalizations at short-term (2 months) and long-term (mean 1.8 ± 1.2 years) follow-up. sNEP was measured using an ad hoc modified ELISA assay and its prognostic value assessed using Cox regression analyses. In a subgroup of patients sNEP was measured both at admission and discharge ($n = 92$).

Results: Median admission sNEP levels were 0.67 ng/ml (Q1-Q3 0.37-1.29), and sNEP was significantly associated, in age-adjusted Cox regression analyses, with the composite endpoint at short-term (hazard ratio [HR] 1.29, 95% confidence interval [CI] 1.04-1.61, $p = 0.02$) and long-term follow-up (HR 1.23, 95% CI 1.01-1.05, $p = 0.003$). In multivariable Cox analyses that included clinical variables and NTproBNP, admission sNEP showed a clear trend towards significance for the composite endpoint at 2 months (HR 1.22, 95% CI 0.97-1.53, $p = 0.09$) and remained significant at the end of follow-up (HR 1.21, 95% CI 1.04-1.40, $p = 0.01$). At discharge, sNEP levels decreased from 0.70 to 0.52 ng/ml ($p = 0.06$).

Conclusions: Admission sNEP was associated with short- and long-term outcomes in AHF and dynamic sNEP concentrations were observed during hospital admission. These preliminary data may be proof-of-principle for the use of NEP inhibitors in AHF.



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Mortality in takotsubo syndrome is similar to mortality in myocardial infarction

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Background: Takotsubo syndrome is an acute cardiovascular condition that predominantly affects women. In this study, we compared patients with takotsubo syndrome and those with acute myocardial infarction with respect to patient characteristics, angiographic findings, and short- and long-term mortality.

Methods: From the Swedish Coronary Angiography and Angioplasty Registry (SCAAR) and the Register of Information and Knowledge about Swedish Heart Intensive Care Admissions (RIKS-HIA), we obtained and merged data on patients undergoing coronary angiography in a County in western Sweden between January 2005 and May 2013. Short- and long-term mortality in patients with takotsubo ($n = 302$) and patients with ST-elevation myocardial infarction (STEMI, $n = 6595$) and non-ST-elevation myocardial infarction (NSTEMI, $n = 8207$) were compared by modeling unadjusted and propensity score-adjusted logistic and Cox proportional-hazards regression.

Results: The proportion of the patients diagnosed with takotsubo increased from 0.16% in 2005 to 2.2% in 2012 ($P < 0.05$); 14% of these patients also had significant coronary artery disease. Cardiogenic shock developed more frequently in patients with takotsubo than NSTEMI (adjusted OR 3.08, 95%CI 1.80 - 5.28, $P < 0.001$). Thirty-day mortality was 4.1% and was comparable to STEMI and NSTEMI. The long-term risk of dying in takotsubo (median follow-up 25 months) was also comparable to NSTEMI (adjusted HR 1.01, 95%CI 0.70 - 1.46, $P = 0.955$) STEMI (adjusted HR 0.83, 95%CI 0.57 - 1.20, $P = 0.328$).

Conclusions: The proportion of acute coronary syndromes attributed to takotsubo syndrome in Western Sweden has increased over the last decade. The prognosis of takotsubo syndrome is poor, with similar early and late mortality as STEMI and NSTEMI.

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Short and long-term prognostic implications of jugular venous distension among patients hospitalized with acute heart failure

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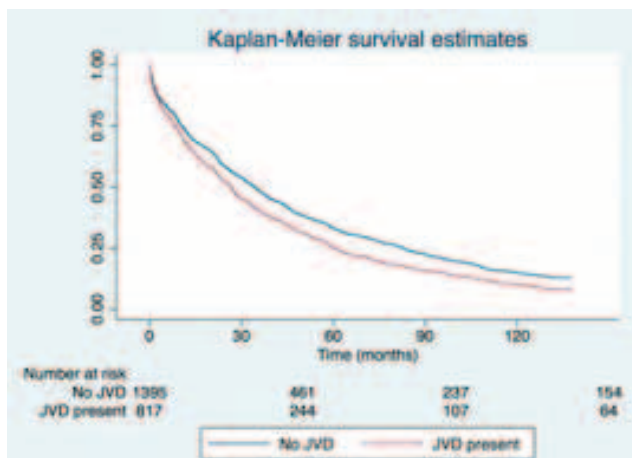
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Purpose: The present study was designed to assess the role of jugular venous distension (JVD) as a predictor of short term and long term mortality in a 'real-life' setting.

Methods: The independent association between the presence of admission JVD and the 30-day and 10-year mortality was assessed among 2,212 patients hospitalized with acute HF who were enrolled in the Heart Failure Survey in Israel (HFSIS 2003).

Results: Independent predictors of JVD finding among study patients included: the presence of significant hyponatraemia (OR 1.48; $p=0.03$), reduced LV function (OR 1.24; $p=0.03$), anaemia (OR 1.3; $p=0.01$), NYHA III-IV functional class (OR 1.34; $p<0.01$) and age >75 years (OR 1.32; $p=0.01$). The presence of JVD vs. its absence at the time of HF hospitalization was associated with increased 30-day mortality (7.2% vs. 4.9%, respectively; $P=0.02$) and greater 10-year mortality (91.8% vs. 87.2% respectively; $p<0.001$, graph 1). Consistently, multivariate analysis demonstrated that presence of JVD at the time of the index HF hospitalization was independently associated with a significant 15% increased risk for 10-year mortality ($p<0.01$), with a more pronounced effect among patients 75 years of age or younger (75% higher risk of 10-year all-cause mortality [p -value for age-by-JVD interaction = 0.03]).

Conclusions: In patients admitted with HF, JVD is associated with specific risk factors, and is independently associated with increased risk of both short and long-term mortality. These findings can be used for improved risk assessment and management of this high-risk population.



Graph 1

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Prognostic implications of pericardial effusion in acute heart failure

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Purpose: Some authors have reported that in chronic heart failure, even hemodynamically irrelevant PE is associated with an increased risk of adverse events. Nevertheless, the prognostic relevance of PE in patients with acute heart failure (AHF) remains to be determined. We aimed to evaluate the association between PE and 1-year mortality.

Methods: We included 1827 consecutive patients admitted for AHF in a single teaching-center from January 2004 to July 2013. Patients presenting with a hemodynamically relevant PE at baseline echocardiography were excluded. A two-dimensional echocardiogram was performed during index hospitalization. PE was categorized in non-PE, mild (I) and moderate-severe (III-IV). Cox regression analysis was used to evaluate the association among PE severity and the risk of 1-year death.

Results: Mean age was 72.8 ± 11.4 years, 51% were females, 35.5% and 54.5% showed LVEF $\geq 50\%$. Any grade of PE was found in 262 patients (14.2%), most of them displaying grade I (11.6%), whereas PE grade II or III/IV was relatively infrequent (1.9% and 0.9%, respectively). At 1-year, 370 (20.3%) deaths were registered. Rates of mortality were lower rates those with no-PE and grade I and higher for those exhibiting grade II and III/IV as is depicted in the figure below. In multivariate analysis, adjusting for well-established risk factors (including natriuretic peptides), only patients with grade II and III-IV showed and increased risk of mortality compared to those with no-PE (HR=1.90; CI 95%:1.09-3.32, $p=0.024$ and HR=3.16; 95% CI: 1.37-7.34, $p=0.007$, respectively).

Conclusion: Moderate to severe PE is an infrequent finding in patients with AHF. However, when it is present is associated with a striking increase of 1-year mortality risk.

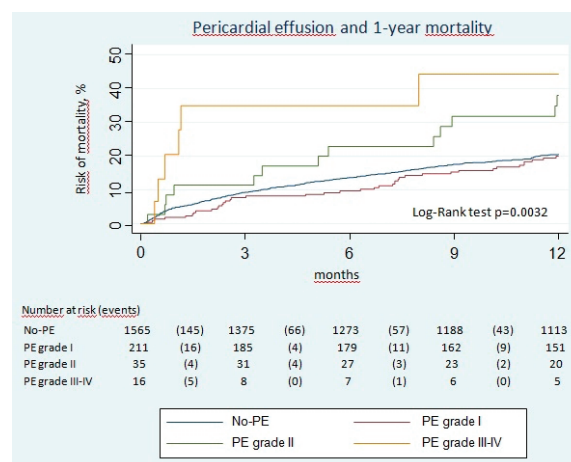


Figure 1

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The influence of gender on epidemiology, precipitating Factors, management and prognosis of the patients with acute decompensated heart failure: insights from KorHF Registry

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Background: Because relatively little attention has focused on the gender related differences in heart failure (HF), women have been underrepresented in clinical trials. We aimed to determine the influences of the gender on baseline characteristics, management, and prognosis in patients with acute decompensated heart failure (ADHF).

Methods: The influences of the gender were evaluated in the Korean acute heart failure (KorHF) registry including hospitalized patients with ADHF. The patients were enrolled at 32 university grade hospitals in Korea from November 2005 to April 2009 and followed up until November 2009.

Results: We evaluated 3200 patients (1600 women) with HF whose mean age was 67.6 ± 14.3 and mean follow up duration was 3.8 years. Women were older and had lower BMI. They showed higher prevalence of hypertension and valvular heart disease and lower prevalence of previous MI and coronary revascularization. At the baseline echocardiography women had higher LA volume index, E/E' ratio and LV ejection fraction (EF). Despite the higher EF, mean NYHA functional class of women was worse at baseline. Women also had higher serum level of total cholesterol, triglyceride and relatively lower HDL cholesterol and showed higher level of NT-proBNP at the initial presentation. The use of inotropics was more common in men and the use of ACE inhibitor, beta adrenergic blocker and aldosterone antagonist in women during hospitalization was less than men. Improvement in mean NYHA functional class after treatment and during follow-up was significant in both groups, even more significant change was observed in women shortly after discharge whereas the degree of improvement had similar significance between both groups at 12months later. There were significant improvements in LV EF and E/E' ratio for both gender and those were more apparent in men. There were no significant differences in mortality, rehospitalization rate and the composite outcome.

Conclusions: Women tend to have worse baseline characteristics and be treated less aggressively than men despite of comparable outcome. The differences of gender can affect the prognosis variously, so we emphasize the importance of the approach concerning these differences.

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ST2 kinetics during hospitalization for heart failure: implications for readmission and mortality

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Background: ST2 has been identified as a novel biomarker involved in three pathophysiological pathways: cardiac stretch, fibrosis and remodelling, and inflammation. Soluble ST2 provides important prognostic information in different cardiovascular settings, mainly in chronic heart failure (HF). ST2 kinetics and prognostic value at different points in acute HF (AHF) is less established.

Aim: To examine the prognostic value of ST2 levels in AHF during admission (median 2 days [Q1-Q3 1-4] of hospital entrance and soon after discharge (from discharge up to one month; median 0 days [Q1-Q3 0-14]).

Patients and Methods: 182 patients (65.9% men, mean age 69.2 ± 12.8 years) were studied. Admission ST2 levels were available in all patients and a post-discharge sample was available in 85 patients. Median time between samples was 13 days [Q1-Q3 7-17]. Prognostic role of ST2 concentrations were assessed using Cox regression analysis after logarithmic transformation. LST2 (relative change between admission and post-discharge) was also evaluated with Cox regression analysis, adjusting for initial ST2 levels. Primary endpoint was the composite of all-cause death and HF rehospitalisation at one year.

Results: ST2 upon admission (HR 1.44 [95% 1.08-1.92], p=0.01) and post-discharge (HR 2.64 [95% 1.60-4.39], p<0.001), as well as LST2 (HR 1.02 [95% 1.01-1.03; p=0.006] were significantly associated with the primary endpoint. Similar results were observed for the individual endpoint of all-cause death (HR 1.58 [95% 1.12-2.24], p=0.01 for admission ST2; HR 2.32 [95% 1.21-4.46], p=0.01) for post-discharge ST2; and HR 1.02 [95% 1-1.03], p=0.02 for LST2). In multivariable analysis including admission ST2, age, sex and concomitant NTproBNP levels, only age remained associated with primary end-point (p=0.005) and all-cause death (p=0.03). By contrast, when post-discharge ST2 was included in the multivariable analysis, ST2 emerged as an independent prognosticator with both the primary endpoint and all-cause death (p=0.004 and p=0.03, respectively). LST2 also remained associated with both the composite primary endpoint (p=0.02) and all-cause death (p=0.01) in the multivariable analysis.

Conclusions: ST2 concentrations during admission and soon after discharge and ST2 kinetics provide valuable one-year risk stratification. After adjustment by age, sex and concomitant NTproBNP levels ST2 at discharge and ST2 kinetics provide the most valuable information.

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Predictors of progression to severe heart failure in non-ST-segment elevation acute coronary syndrome. Results from the ARIAM registry

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Purpose: Acute heart failure (AHF) is a common complication of acute coronary syndromes, and increases mortality rate. We propose to identify clinical features, easily measurable at admission, for the development of AHF throughout the course of non-ST-segment elevation acute coronary syndrome (NSTEMI).

Methods: Retrospective analysis of ARIAM registry data, collected from Intensive Care Units (ICU) of Andalusian hospitals from January 2001 to January 2012. We analyzed 10160 patients admitted for NSTEMI categorized as Killip I class at admission, and predictors for the progression to Killip class III or IV (AHF group).

Results: A total of 210 patients (2.1%) had AHF. These patients were older (mean age 64.44 vs 70.74, p<0.001), without differences according to gender. AHF group showed a larger proportion of non-smokers, ex-smokers, diabetes, hypertension, previous myocardial infarction, previous heart failure, stroke, previous arrhythmia, peripheral artery disease (PAD), chronic obstructive pulmonary disease or chronic renal failure. AHF patients were more often previously treated with antiplatelet agents, beta-blockers, renin-angiotensin system inhibitors, antiarrhythmic drugs, nitrates, anticoagulant therapy and diuretics. Atrial fibrillation at admission was more frequent in AHF group (6.7% vs 3.4%, p<0.05). AHF patients had greater mortality, both in ICU (0.5% vs 31.4%, p<0.001) and in-hospital (1.0 vs 33.8%, p<0.001). On multivariate analysis, age, diabetes, PAD, diuretics and heart rate at admission were independent predictive factors for AHF (table 1).

Conclusions: AHF complicating NSTEMI carries a much worse prognosis. According to the ARIAM registry data, age, diabetes, previous PAD, previous diuretics treatment and tachycardia at admission, are independent predictors for the progression to Killip class III or IV. Identifying these factors at admission may be useful in the management NSTEMI patients.

Table 1

	Odds Ratio	95% CI	P Value
Age	1.043	1.026-1.061	<0.001
Diabetes	1.504	1.106-2.046	0.009
Peripheral artery disease	1.703	1.077-2.695	0.023
Diuretics	1.479	1.038-2.107	0.030
High heart rate at admission	1.009	1.001-1.016	0.032

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Is hemoconcentration a reliable marker of decongestion in acute heart failure?

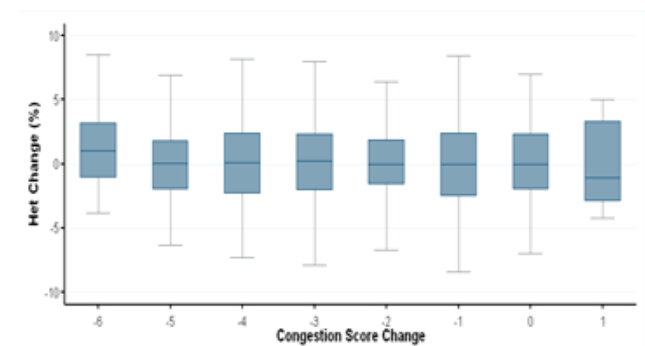
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Introduction: The principal cause for hospitalization due to worsening acute heart failure (AHF) is related to congestion. Persistent congestion at hospital discharge is associated with increased risk for mortality and rehospitalizations for HF. Recently, hemoconcentration (HC) has been suggested as a surrogate for successful decongestion during fluid removal in AHF.

Methods: We studied 660 patients with AHF and volume overload. Congestion was assessed at admission and discharge using A 9-point scale (0 to 8) as follows: JVP ≥8 cm water (1 point), hepatomegaly (1 point), peripheral edema (Absent/trace, 0 points; slight 1 point; moderate, 2 points; marked, 3 points; and anasarca, 4 points), pulmonary rales (1 point), and third heart sound (1 point). A composite score was calculated by summing the individual scores, with a score >1 denoting congestion. HC was defined as any increase in hematocrit and hemoglobin levels between baseline and discharge. The association between HC and congestion and mortality (mean follow-up 1.5 y) was determined by Cox regression.

Results: At discharge, of 475 patients without persistent congestion, only 199 were with HC (42%). There was weak correlation between the decline in congestion score and changes in hematocrit levels (Figure; P=0.85). Compared with patients with HC and no congestion (lowest mortality group) the adjusted HR for mortality was 1.5 (95% CI, 1.1-2.1) with no HC and no congestion, 1.7 (95% CI 1.1-2.7) with HC but with persistent congestion and 2.1 (95% CI 1.4-3.0) with no HC and congestion.

Conclusion: Persistent clinical congestion at hospital discharge is associated with increased risk for mortality even when HC occurs. There is a weak correlation between HC and the improvement in congestion as assessed by clinical examination.



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A phase III, multicenter, randomized, double-blind, placebo-controlled study for efficacy and safety of short-term tolvaptan usage in patients with acute decompensated heart failure

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Background and Purpose: Admission with acute decompensated heart failure (ADHF) carries a grim prognosis and poor quality of life due to dyspnea and edema. Tolvapan, a vasopressin V2 receptor antagonist, is effective on water diuresis. This study aimed to evaluate the efficacy and safety of a short course tolvapan to treat volume overload in patients with ADHF.

Methods: A phase III, multicenter, randomized, double-blind, placebo-controlled study was performed to evaluate the efficacy and safety of a short course Tolvaptan (15mg/day for four days) in hospitalized ADHF patients with volume overload despite the use of conventional diuretics. The primary end-point was the change in body weight after 4 days of treatment. The secondary end-points were the change in intake/output balance, change in serum sodium/potassium concentrations, treatment failure, physician/patient assessed signs and symptoms of heart failure after 4 days of treatment and all-cause mortality in one month.

Result: A total of 110 subjects were screened, and 91 were randomized to receive study treatment for 4 days (15mg/day of tolvaptan (n=46) or matching placebo (n=45). Compared to placebo treated subjects, tolvaptan significantly reduced body weight (-1.36 ± 2.13 kg in tolvapan group vs. -0.59 ± 1.27 kg in placebo group,

$p = 0.044$). Subjects in the tolvaptan group also experienced a negative intake/urine volume balance compared to subjects on placebo (-509 ± 2788 vs $+976 \pm 1903$ ml, $p = 0.006$). The safety profile of tolvaptan was acceptable with minimal adverse effects.

Conclusion: Tolvaptan significantly reduced volume overload in hospitalized ADHF subjects with volume overload despite the use of conventional diuretics.

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Red cell distribution width and mortality in patients with acute heart failure and preserved or reduced left ventricular ejection fraction

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Background: Red cell distribution width (RDW) increases with inflammatory stress, decrease in hemoglobin, and impaired iron mobilization. Elevated RDW thus reflects interaction of various pathophysiological mechanisms active in HF which can explain why elevated RDW is a valid predictor. It remains unknown whether outcome is different in AHF with preserved or reduced left ventricular ejection fraction (LVEF $<50\%$ or $\geq 50\%$) and elevated RDW.

Methods and Results: Prospective single-center registry following 402 consecutive patients hospitalized for AHF. Patients with AHF due to acute coronary syndrome or cardiogenic shock necessitating intensive care were excluded. The primary outcome is all-cause mortality (ACM) within the first year after hospitalization. Demographic, clinical, and laboratory data were obtained at admission. Echocardiographic data derive from standard transthoracic exams during hospitalization ($n = 269/402$).

Patients were separated into quartiles of RDW; high RDW was associated with elder age and known HF, as well as higher creatinine, CRP, and NT-proBNP, whereas systolic and diastolic blood pressure, hemoglobin, and glucose were lower. Furthermore, high RDW was associated with increased use of loop diuretics and oral anticoagulation.

The Cox proportional hazard model including all patients (maximal logistical likelihood -614.37 ; LR test statistic: 79.74 ; $p < 0.001$) and adjusted for age, gender, and RDW quartiles showed an increased hazard of 1-year death with cardiogenic shock (HR 2.86), male sex (HR 1.9), highest RDW quartile (HR 1.66), known HF (HR 1.61), valvular cardiomyopathy (HR 1.61), diastolic blood pressure (HR 1.02), age (HR 1.04), platelets (HR 1.002). Variables with a decreased hazard were intermediate quartiles of RDW (HR <0.88), weight (HR 0.98), and systolic blood pressure (HR 0.99).

During follow-up 114 patients died. The Kaplan-Meier analysis of the 402 study patients showed a graded increased probability of mortality during follow-up with increasing quartile of RDW (chi-square 18; $P < 0.001$). ACM was not different between RDW quartiles in patients with LVEF $<50\%$ ($n = 153$; chi-square 6.6; $p = 0.084$) while the probability of ACM increased with increasing quartile of RDW (chi-square 9.9; $p = 0.0195$) in patients with preserved LVEF ($n = 116$).

Conclusion: High RDW was associated with an increased hazard of 1-year ACM in AHF patients similar to previous studies. High RDW was associated with increased ACM in AHF with preserved LVEF suggesting that pathophysiological mechanisms inducing in high RDW also promote progression of HF disease.

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Right bundle branch block predicts mortality in acute heart failure caused by acute coronary syndrome

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Purpose: The prognostic role of right bundle branch block (RBBB) has been controversial in both acute coronary syndrome (ACS) and acute heart failure (AHF). The aim was to investigate the effect of RBBB on survival in AHF with and without concomitant ACS (ACS-AHF and non-ACS-AHF).

Methods: We analysed the admission ECG of 2493 patients hospitalised for AHF from three prospectively collected European cohort studies. The end-point was all-cause mortality and the mean follow-up time was 5.1 years. The mortality models were adjusted for age, gender, medical history, renal function, and ejection fraction.

Results: AHF was precipitated by ACS in 977 (39.2%) patients. Male gender,

new-onset AHF, and diabetes were more common in the ACS-AHF group compared to the non-ACS-AHF group (Table 1). Mortality rate during the follow-up period was 63.8% in the ACS-AHF group and 70.1% in the non-ACS-AHF group ($p = 0.5$). RBBB was present in 86 (8.8%) in the ACS-AHF and in 118 (7.8%) in the non-ACS-AHF patients ($p = 0.4$). The presence of RBBB was associated with increased risk of death in those with concomitant ACS (adjusted HR 1.41, 95% CI 1.06-1.88, $p = 0.019$), but not in those without ACS (adjusted HR 1.03 (95% CI 0.78-1.36, $p = 0.3$). The increased risk of mortality was more pronounced in those ACS-AHF patients with new-onset AHF (adjusted HR 1.66, 95% CI 1.20-2.30 $p = 0.002$).

Conclusions: RBBB is an independent predictor of death in patients with AHF and concomitant ACS, and should be considered in the risk assessment of these patients.

Baseline characteristics; mean(SD), n(%)

	All (N = 2493)	ACS-AHF (n = 977)	non-ACS-AHF (n = 1516)	P-value
Age	72.5 (12.0)	71.3 (11.0)	71.2 (12.4)	0.17
Men	1383 (55)	568 (58)	815 (54)	0.02
History of heart failure	1009 (41)	202 (21)	807 (53)	<0.001
History of coronary artery disease	958 (39)	378 (39)	580 (39)	0.8
Hypertension	1659 (68)	634 (67)	1025 (68)	0.4
Diabetes	930 (38)	387 (40)	543 (36)	0.03
LVEF $< 40\%$	908 (44)	381 (44)	527 (44)	0.99
Sinus rhythm	1609 (65)	784 (80)	825 (55)	<0.001
Any ventricular block	823 (33)	282 (29)	541 (36)	<0.001
RBBB	204 (8)	86 (9)	118 (8)	0.4

LVEF=left ventricular ejection fraction, RBBB=right bundle branch block

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Usefulness of ultrasonography of inferior vena cava and bioelectrical impedance against NT-proBNP for the diagnosis of acute decompensated heart failure in an emergency department

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Purpose: the aim of this study is to evaluate the utility of inferior vena cava (IVC) ultrasound and bioelectrical impedance analysis (BIA) for diagnosis of acute decompensated heart failure (ADHF) and compare it with proBNP levels.

Methods: We performed proBNP determination, IVC ultrasonography and BIA of 96 patients who presented to our Emergency Department referring dyspnea, between November 2012 and December 2013. Maximal and minimal IVC diameter as well as collapse index (CI) were measured. Volume overload was estimated by resistance (Rz) and reactance data obtained from BIA. After discharge, patients were classified as ADHF or non-ADHF attending to the responsible doctor judgement and Framingham Criteria.

Results: 59.4% (57) of patients had ADHF, whereas 40.6% were non-ADHF. ADHF patients were older (82 vs 76 years) and had more frequently chronic kidney disease (35.1 vs 10.3%) and known heart disease (75.4 vs 30.8%). ADHF patients showed significantly higher proBNP values (5801 vs 598 pg/mL), lower Rz (458.8 vs 627.1 Ohm), and lower CI (27 vs 59%) ($p < 0.001$). The area under the curve (AUC) for proBNP was 0.84 and the optimal cutoff point was 1825 pg/ml with an 81.5% sensitivity and a 76.5% specificity. The AUC for Rz was 0.83 and the optimal cutoff point was 304 mOhm/m with a 68.5% sensitivity and an 88.9% specificity. Finally, AUC for CI was 0.90, and the optimal cutoff point was 36%, with 80.7 and 92.3% sensitivity and specificity, respectively.

Age, glomerular filtration (GFR) and body mass index (BMI) were statistically influential variables in a multivariate analysis with predictive purpose for proBNP levels. In patients older than 80 years the power of the proposed diagnostic cutoff proBNP obtained an 88.6% sensitivity and a 67% specificity. However, resistance had a 65.8% sensitivity and an 88.9% specificity. In the case of the cutoff CI sensitivity was 84.2% and specificity was 88.9%. In patients with GFR less than 60 ml/min sensitivity of proBNP was 84.9% but specificity was 37.5%. However, data sensitivity and specificity were respectively 72.2% and 77.8% for Rz, and 86.1% and 88.9% for CI. Finally, for patients with BMI greater than 25 kg/m² sensitivity of proBNP was 66.7% and specificity was 64.5%. However, data sensitivity and specificity were 92.3% and 78.6% for Rz, and 84.6% and 100% for the CI.

Conclusions: all tests referred had an adequate diagnostic power in our study population. But in cases of advanced age, kidney disease or overweight, diagnostic power of BIA and, specially, IVC ultrasonography is more robust and do not require cutoff points adjustment, unlike proBNP.

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Hypercapnia in patients with acute heart failure

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Purpose: Noninvasive ventilation rapidly improves the symptoms of acute heart failure (AHF). Some patients, however, are forced to be intubated due to unconsciousness or other reasons even though intubation is associated with serious complications. Although hypercapnia is often observed in AHF requiring intubation, clinical characteristics of hypercapnia are uncertain because blood gas data in unselected consecutive AHF patients has been lacking. The purpose of this study is to examine the clinical profile and management of hypercapnia in AHF patients.

Methods: We examined the arterial blood gas analysis at admission in consecutive 159 AHF patients (74 ± 11 years, 63 % men), including 131 patients (82.3%) who had already treated with oxygen by the ambulance staffs.

Results: Hypercapnia, defined as pCO₂ at admission >45 mmHg, was observed in 59 patients (37.1%) and one of the strong predictors of immediate airway intervention (univariate odds ratio (OR) for non-invasive positive pressure ventilation: 9.35; 95% confidence interval (CI): 4.22 to 20.41, p < 0.001 and OR for intubation: 16.67; 95% CI 3.66 to 76.92, p < 0.001). Patients with hypercapnia are more likely to be in New York Heart Association class IV (96.6% vs 79.0%, p < 0.01), acute onset within 6h (49.1% vs 24.5%, p < 0.01), to have pulmonary edema in X-ray (84.8% vs 58.0%, p < 0.001), disturbance of consciousness (45.8% vs 9.0%, p < 0.001) than those without hypercapnia. Other baseline characteristics including age, sex, hypertension, diabetes, ejection fraction, ischemic etiology, and smoking status were comparable between two groups. Acute cardiogenic pulmonary edema (APE), defined as acute onset within 6h and pulmonary edema in X-ray, was observed in 42 (26.4%) patients. Hypercapnia was more frequent in APE patients than non-APE patients (59.5% vs 29.1%, p < 0.001 and pCO₂ of 63 ± 29 vs 44 ± 20 mmHg, p < 0.001). At discharge, hypercapnia was observed only 3.1 % of patients.

Conclusion: Hypercapnia emerged in AHF acutely and transiently, was associated with immediate airway intervention, and possibly involved in the pathophysiology of APE. Patients with acute onset should be carefully managed about their respiratory status. These pathophysiological findings are expected to be utilized in treating or preventing AHF.

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Fluid balance and diuresis in cardiogenic shock

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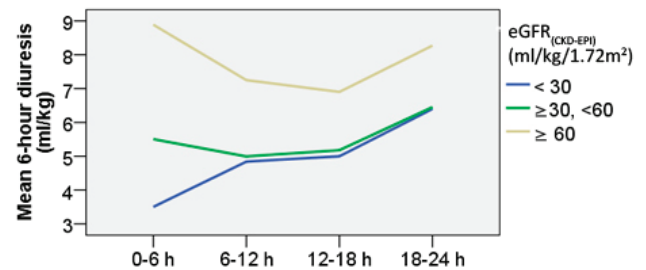
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Purpose: To assess fluid balance in relation to clinical variables and mortality in cardiogenic shock (CS).

Methods: We analyzed the first 24-h diuresis and fluid administration in relation to baseline variables and survival from 220 patients with CS of various etiologies from the prospective European multicenter CardShock study. We performed analyses of 90-day all-cause mortality with multivariable logistic regression adjusting for potential confounders.

Results: Final analyses included 184 patients at 24 h; patients were 66 (±12) years and 26% were women. Median baseline eGFR was 62 (IQR 44-85) ml/min/1.73m². At 24 h, median cumulative diuresis was 25 (IQR 14-38) ml/kg; 20% of patients had an average diuresis below 0.5 ml/kg/min. Median amount of fluids administered was 34 (IQR 22-48) ml/kg, and 65% of patients received IV furosemide with a median cumulative dose of 120 (IQR 40-300) mg. The amount of diuresis was associated with baseline eGFR (figure 1), and inversely associated with age, history of diabetes mellitus, resuscitation prior to enrolment, rhythm other than sinus, and baseline blood lactate. Use of IV furosemide was positively associated with cumulative diuresis and inversely with amount of fluids administered. Amount of fluids administered, however, had no associations with baseline eGFR, diuresis or mortality. Lowest quartile of cumulative diuresis at 24 h (<14 ml/kg; <0.58 ml/kg/h on avg.) was independently associated with higher 90-day mortality (adjusted OR 4.5, 95% CI 1.6-13.0, p = 0.005).

Conclusions: Cumulative diuresis below 14 ml/kg (<0.58 ml/kg/h on avg.) at 24 h independently predicted higher 90-day mortality in CS. Whereas baseline variables predicted the amount of diuresis, the amount of fluids administered, however, had no associations with eGFR, diuresis or mortality.



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A combined clinical and biomarker approach to predict diuretic response in acute heart failure

MerckJ M Jozine Ter Maaten¹; MAE Valente¹; M Metra²; CM O'connor³; MM Givertz⁴; DM Bloomfield⁵; DJ Van Veldhuisen¹; HL Hillege¹; K Damman¹; AA Voors¹

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Purpose: Diuretic resistance in acute heart failure is related to poor clinical outcome, and is associated with an increased risk for early rehospitalization. To better identify patients at risk and to gain insight in the pathophysiological mechanisms behind diuretic resistance we combined clinical characteristics and biomarkers to predict diuretic response in acute heart failure

Methods: We investigated explanatory (based on significance) and predictive models (based on best fit) for diuretic response - weight loss at day 4 per 40 mg of furosemide - in 960 patients with acute heart failure included in the PROTECT trial. Biomarkers, addressing multiple pathophysiological pathways, were determined at baseline and on after 24 hours.

Results: A poor diuretic response was associated with impaired renal function and an atherosclerotic profile. A baseline explanatory biomarker model of a poor response includes low potassium, chloride, red blood cell count, myeloperoxidase, and high blood urea nitrogen, albumin, triglycerides, tumor necrosis factor alpha receptor 1 and white blood cell count levels (r² = 0.092). Addition of diuretic response after 24 hours (β = 0.468, P < 0.001; r² = 0.523) to biomarkers and clinical characteristics significantly improves the predictive model (r² = 0.585, P < 0.001).

Conclusions: Clinical characteristics and biomarkers indicate that diuretic response is associated with an atherosclerotic, renal and abnormal electrolyte profile. These markers only modestly predicted diuretic response. Patients at risk of diuretic resistance can be identified by measuring diuretic response after 24 hours.

Explanatory biomarker baseline model

Variable	Beta Coefficient	95% Confidence Interval	T-value	P-value
Albumin	0.160	0.05-0.27	2.930	0.003
Log Blood Urea Nitrogen	0.177	0.06-0.30	2.882	0.004
Chloride	-0.013	-0.02-0.00	-2.604	0.009
Myeloperoxidase	-0.001	0.00-0.00	-2.426	0.015
Potassium	-0.176	-0.26-0.10	-4.294	<0.001
Red Blood cell Count	-0.102	-0.18-0.03	-2.682	0.007
Tumor Necrosis Factor Alpha Receptor 1	0.025	0.00-0.05	2.052	0.040
Triglycerides	0.001	0.00-0.00	2.635	0.009
White Blood cell Count	0.022	0.01-0.04	2.840	0.005

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Tricuspid regurgitation and mortality risk across left ventricular systolic function in acute heart failure

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¹Hospital Clinico Universitario. INCLIVA. Universitat de Valencia, Valencia, Spain; ²Hospital de Manises, Valencia, Spain

Tricuspid regurgitation (TR) is a common echocardiographic finding that has been related to adverse outcomes under various clinical scenarios. Nevertheless, evidence supporting its prognostic value in heart failure (HF) is scarce, and in most cases, contradictory. We sought to evaluate the association of TR grade with 1-year all-cause mortality in acute heart failure (AHF).

We included 1842 consecutive patients admitted for AHF to the cardiology department of a tertiary-care teaching hospital from January 2004 to August 2013. In all patients a 2-dimensional echocardiogram was performed during index hospitalization. According to current recommendations, the severity of TR was graded in non-TR, mild (1), moderate (2), moderate-to-severe (3), and severe (4), using an integrated multi-parametric score that included qualitative and semi-quantitative parameters. HF with reduced ejection fraction (HFrEF) and HF with preserved ejection fraction (HFpEF) were defined as left ventricular ejection fraction (LVEF) <50% or ≥50%, respectively. The association between TR grade with 1-year all-cause mortality was evaluated using a Cox regression analysis. The Harrel's C-statistics and the Groennesby and Borgan test of the final multivariate analysis were 0.742 and 0.391, respectively.

At 1-year follow-up, 370 (20.1%) patients died. Mean age was 72.8 ± 11.3 years, 51% were females and 45.5% showed LVEF <50%. Of note, the distribution of TR severity was similar among the 2 groups defined by LVEF (HFrEF vs. HFpEF, $p = 0.826$). In patients with LVEF ≥50%, a significant and positive association between TR severity and mortality was documented. Indeed, the hazard ratios (HR) for mortality of the comparison between TR-3 and TR-4 versus no-TR/TR-1 were HR: 1.68, CI 95%: 1.08-2.60, $p = 0.02$, and HR: 2.87, CI 95%: 1.61-5.09, $p < 0.001$, respectively. On the contrary, no association between TR-grade and mortality ($p = 0.650$) was observed in patients with LVEF <50%. The P-value for interaction was 0.033.

In conclusion, a differential prognostic effect of TR severity on 1-year mortality was observed among LVEF HF-status. Indeed, only in patients with HFpEF this association was significant, with increasing mortality risk as TR becomes more severe, whereas in HFrEF patients it did not provide additive prognostic value to established risk factors.

Clinical Case 1 – Have you ever thought of that? Unusual causes of heart failure

Saturday 23 May 2015 10:30–12:00

Location: Agora

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Hypoxia, platypnea-orthodeoxia and transient ischemic attacks in a patient with carcinoid heart disease and patent foramen ovale corrected by closure

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In 2010, a 43-year-old man presented with dyspnoea, fatigue, flushing, diaphoresis and diarrhoea. Echocardiographic evaluation revealed a severe tricuspid regurgitation as well as a marked right sections enlargement with right ventricular dysfunction, without any left-side heart disease and with a preserved left ventricular systolic function. The whole picture arose the suspicion of carcinoid syndrome, confirmed by serial neurohormonal assays (serum serotonin 6250 ng/ml, urinary serotonin 2367 mcg/24h, serum chromogranin A 2752 ng/ml) and octreoscan, with the primitive lesion located at ileum and with metastatic diffusions at liver, at CT scan. The patient was treated with low dose of furosemide and beta-blockers, obtaining a weak hemodynamic and symptom balance. After oncologist advice, he underwent the resection of ileum and metastasis of V hepatic segment, and was addressed to radioimmunotherapy. After surgery, he complained of left hemiparesis, and a brain TC scan revealed signs of recent brain ischemic lesions, and worsening dyspnoea. Re-admitted to our Institution, he was diagnosed with a severe interatrial shunt through patent foramen ovale (PFO), at a contrast, transesophageal echocardiography, confirmed by a cardiac magnetic resonance imaging (Qp/Qs 0,62), and by transcranial Doppler evaluation of a massive right to left shunt. At hyperoxemic stimulus, platypnea-orthodeoxia was found with severe hypoxemia not corrected by oxygen administration. The patient underwent the PFO device closure with an improvement of dyspnoea and exercise tolerance, as well as normalization of arterial gasanalysis. During the next three years patient preserved a good haemodynamic balance without symptoms of dyspnoea, and was readmitted once for atrial flutter catheter ablation. The patient is now doing well on treatment with furosemide, bisoprolol and cardioaspirin with a stable carcinoid disease (regular oncological follow-up).

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Dilated cardiomyopathy due to acromegaly: a review of one case

C D'amore¹; P Gargiulo¹; P Perrone Filardi¹

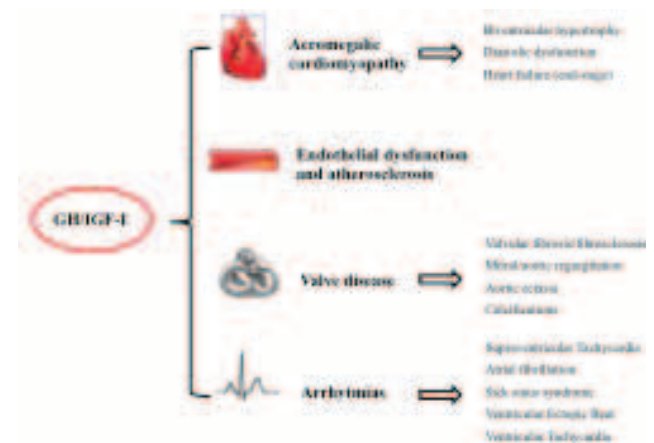
¹Federico II University Hospital, Department of Advanced Biomedical Sciences, Naples, Italy

Dilated cardiomyopathy is a rare cardiovascular expression of acromegaly, characterized by specific structural and functional changes of myocardium due to chronic increased growth hormone (GH) and insulin-like growth factor-1 (IGF-I) levels (Figure 1). Usually, the coexistence of cardiovascular risk factors makes the diagnosis of acromegaly difficult. A 52-year-old woman patient with history of hypertension was admitted in the Department of Cardiology due to progressive dyspnoea and palpitations. The patient reported no history of ischaemic heart disease, infective disease or other cases of cardiovascular disease or sudden death in her family. At the admission, blood pressure levels were 150/100 mmHg at both upper limbs and heart rate was 95 beats per minute. Heart rhythm was not regular and there were a systolic murmur at the mitral valve area and accentuation of second heart sound at the aortic valve area. General examination reported prominent forehead, anterior mandibular protrusion and large hands. The laboratory finding showed only increased serum cholesterol and LDL-C levels. The echocardiographic exam showed dilated left ventricle with global and uniform reduction of contractility (Ejection Fraction: 25%). Patient performed ergometric stress test that did not exclude inducible ischemia. Thus, coronary angiography was performed that showed normal major epicardial vessels and only not significant stenosis of the branch I diagonal artery. Once coronary artery disease was excluded, GH and IGF-I serum levels were analysed and they resulted increased. Consequently a brain magnetic resonance

imaging (MRI) was performed and it showed a pituitary macroadenoma. Thus, acromegaly was diagnosed and therapy with somatostatin analogues was started. At the follow-up, MRI showed a reduction of pituitary macroadenoma, while the echocardiographic exam confirmed a severe reduction of ejection fraction, so an implantable cardioverter-defibrillator was implanted.

Discussion: In the patient described in this case report, acromegaly coexisted with several cardiovascular risk factors such as hypertension and dyslipidaemia, that were an important confounding since it led to suspect myocardial ischemia as cardiomyopathy aetiology. However, coronary angiography showed no significant coronary stenoses so an ischaemic aetiology of heart failure was excluded. Another possible cause of cardiomyopathy was hypertension, but the good blood pressure control during the observation and the mild grade of ventricular hypertrophy did not justify the acute heart failure. In fact, acromegalic patients show a pharmacological good control of blood pressure and hypertension is due to expansion of plasma volume by GH related sodium-retaining and to hypertrophy and fibrosis of smooth muscle cells in the myocardial tissue and in the peripheral arterioles. Dilative cardiomyopathy with systolic left ventricular dysfunction might have been also caused by prolonged supraventricular or ventricular tachycardia. However, tachycardiomyopathy usually develops after long time (from few weeks to more than twenty years) from the first report of arrhythmia, so it was not compatible with our patient who had showed a recent onset of (about ten days). Probably, premature ventricular complexes were due to areas of myocardial fibrosis responsible for the slowing and non-homogeneous conduction of action potential.

Conclusions: The reported case shows that in the management of patients is necessary a holistic approach and not a purely specialist one. In the patient described, the clinical picture was dominated by dyspnoea that could have had cardiac (frequent BEVs and heart failure) or extracardiac causes (acromegaly).



Cardiac involvement in acromegaly

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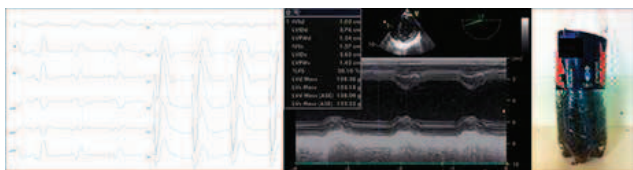
Breaking bad: acute heart failure in a 24 year old maleP Timmermans¹; P Dewolf²; L Desmet³; E Pihadi¹; P Rega⁴; P Sinnaeve⁵¹University Hospitals (UZ) Leuven, cardiology, department of heart failure and transplantation, Leuven, Belgium; ²University Hospitals (UZ) Leuven, emergency medicine, Leuven, Belgium; ³University Hospitals (UZ) Leuven, intensive care medicine, Leuven, Belgium; ⁴University Hospitals (UZ) Leuven, cardiac surgery, Leuven, Belgium; ⁵University Hospitals (UZ) Leuven, cardiology, department of interventional cardiology, Leuven, Belgium

Case description: A 24 year old male patient was rushed into the hospital after collapsing at home. He regained consciousness and was alert before he got into the ambulance, but collapsed again on admission in the ER due to broad QRS tachycardia. Advanced life support was immediately started. After 15 minutes, restoration of spontaneous circulation (ROSC) was achieved, but the patient remained in critical condition.

Diagnostic and treatment procedures: After ROSC, a bradycardia was present at around 40 bpm. The ECG showed a non-determined slow rhythm with very wide and distorted complexes (see figure, left). Neither transcutaneous nor endomyocardial pacing was successful. Transesophageal echocardiography showed a structurally normal heart (see figure, middle). Severe metabolic acidosis (pH 7.07, pCO₂ 38.7 mmHg, lactate 10.7 mmol/L) and normokalemia was seen on blood gas analysis. The patient was urgently placed on a peripheral veno-arterial ECMO in the ER. On day 3 and 4, he was successfully weaned from the ECMO and ventilator respectively. His ECG returned to normal. The toxicology came back negative.

Outcome & discussion: In very young patients with a structurally normal heart who present with acute heart failure and arrhythmias, the differential diagnosis of a cardiac channelopathy or intoxication needs to be made. The patient's ECG did not resemble any "typical" abnormality compatible with a channelopathy. Meanwhile, we learned more about our patient: he was a chemistry student, believed (by his parents) to be in the middle of his exams, but who dropped out of school a few months earlier. His parents found several strange bottles in his room, containing branches and leaves, and brought one to the hospital (see picture, right). After extubation, a more profound history was taken: he admitted attempting suicide by drinking large quantities of yew leaves extract (*Taxus Baccata*), a recipe he found on the internet. After full physical recovery and counseling, he was admitted on the psychiatry ward.

Conclusion: Taxine alkaloids are very potent cardiovascular toxins. The combination of tachycardia evolving to therapy-refractory bradycardia with extreme distorted QRS complexes in a previously healthy patient with a structurally normal heart may urge the clinician to include taxine alkaloid poisoning in his differential diagnosis of acute heart failure. Unless there is direct evidence of auto-intoxication with yew leaves on admission, the diagnosis can only be made by history taking. By lack of specific therapies, the treatment of taxine alkaloid poisoning is supportive. In this case, we successfully used a VA-ECMO to treat this extreme case of acute heart failure.



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An unusual case of advanced heart failure. Family mattersF Macaya Ten¹; J Pons¹; L Asmarats¹; A Grau¹; P Pericas¹; A Bethencourt¹¹University Hospital Son Espases, cardiology, Palma de Mallorca, Spain

Introduction and case report description: A 45-year-old woman who received an implantable pacemaker in 1996 for a congenital complete AV block presented symptomatic atrial flutter in 2008. Cardioversion was not attempted because transthoracic echocardiogram detected a thrombus image surrounding the pacemaker lead. Oral anticoagulation was started but the thrombus persisted within the following months, thus atrial flutter was managed as permanent. In July 2012 she was admitted in the gastroenterology department because of ascites, which was finally diagnosed as pure right-sided congestive heart failure.

Description of the problem, procedures, techniques and/or equipment used: Transthoracic echocardiogram showed normal left ventricular ejection fraction and a restrictive filling pattern with severely dilation of atria and inferior cava vein. Left- and right-sided heart catheterizations were performed showing findings more consistent with a restrictive physiology. Cardiac magnetic resonance could not be performed due to incompatibility of the pacemaker. The patient evolved well under medical treatment, which resolved congestive signs. Anamnesis looking for familial cardiologic precedents yielded the following data: Her father, one uncle, and 3 aunts (5 of the 7 siblings), and her paternal grandfather were deceased of unknown causes

between 45 and 65 years, all of them needing pacemaker therapy at younger ages. Four of her 6 cousins presented probable sudden death at ages between 25 and 48 years.

Questions, problems or possible differential diagnosis: At this point, we had a young female patient, with a pacemaker for AV block catalogued as congenital, atrial flutter and hospitalization for acute decompensated right-sided congestive heart failure with a ventricular restrictive physiology as well as a remarked familiar history of bradiarrhythmias and sudden death. Amyloidotic and desmin cardiomyopathies were considered.

Answers and discussion:

Genetic testing revealed a mutation in I367F for desmin codification. Considering relevant family history of sudden death, a cardioverter defibrillator was implanted. Neurologic evaluation ruled out skeletal muscle affection. Despite optimal medical treatment the patient developed increasing dyspnea and congestion and was considered for heart transplant. She is currently on the waiting list.

Conclusions and implications for clinical practice: Several considerations and important discussion derive from the present case. First of all, AV block and/or heart failure with restrictive cardiomyopathy presented in a young patient should raise suspicion and lead to investigation for a primary disorder or genetic disease. Family history and anamnesis could yield critical hints leading to diagnosis and eventual treatments. The most sophisticated, expensive or invasive examinations are not necessarily the most informative. Importantly, cardiac transplantation for young patients suffering desminopathies with pure cardiac affection should be considered.

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Cardiac and thrombotic complications in the peripartum period of a patient affected by beta-thalassemia intermediaD Giulio Binaghi¹; GM Argiolas²; D Congia¹; C Dessi³; G Matta²; S Mura⁴; A Pani¹; G Pasqualucci¹; E Serra¹; M Porcu¹¹G. Brotzu Hospital, Department of Cardiology, Cagliari, Italy; ²G. Brotzu Hospital, Department of Radiology, Cagliari, Italy; ³Microcitemico Hospital, Thalassaemic Day Hospital, Cagliari, Italy; ⁴G. Brotzu Hospital, Department of Obstetrics & Gynaecology, Cagliari, Italy

Thalassemia (T) is a heterogeneous group of genetic diseases, due to the imbalance of production of α - and β -chains, resulting in chronic hemolysis, ineffective erythropoiesis and iron overload and whose complications include bone changes, hypercoagulable and organ damage. Advances in management of β -T have significantly improved the expectancy and quality of life of these patients increasing their reproductive potential. A 33 year-old woman affected by β -T intermedia, HCV positive, underwent splenectomy at 25 years-old, following regular transfusion regimen from 4 years, with inconstant iron-chelation treatment (ICT) due to poor tolerance and compliance, began a twin pregnancy after in-vitro fertilization. Because of teratogen risk ICT was suspended. At the pre-conception period and at 21 weeks of pregnancy she had not cardiac signs or symptoms, ECG and echocardiography were normal. Pre-conception ferritin was 2234 ng/ml and the last T2* cardiovascular magnetic resonance (CMR) known was 37.2 ms in 2007. As result of a superior consumption of haemoglobin during pregnancy, the rate of transfusions was increased up to a bi-weekly regimen. At 33 weeks, due to a foetal growth restriction, a caesarean section was performed with good result for unborns. During the procedure the patient had a transitory severe hypotension (SBp < 90 mmHg). The physical examination showed signs of acute heart failure (sinus tachycardia; T3; peripheral oedema) and echocardiogram revealed a severe left ventricular systolic dysfunction (EF: 25%) due to a global hypokinesia. After continuous diuretic infusion therapy, a clinical and hemodynamic improvement is achieved. Thus, β -blocker, ACE-inhibitor and anti-aldosterone treatment was introduced and, after hematologic consult, a double ICT is started (deferioxamine iv and oral deferiprone). Then she presented recurrent episodes of supra-ventricular tachycardia, so amiodarone was added. Because of abdominal pain, an ultrasound exam was performed showing bilateral ovarian veins thrombosis, despite prophylaxis with LMWH. Thus an anticoagulant therapeutic regimen was established, initially with heparin iv, then with vitamin K antagonists (VKA), but due to difficulty to reach a stable therapeutic PT-INR and the persistence of thrombosis at the echo check, a switch from VKA to rivaroxaban was decided. A CMR was performed a week after delivery; showing a reduced left ventricle function and a severe iron overload (T2*: 10.2 ms). After 22 days of hospitalization, the hemodynamic was stable and echocardiography revealed a mild recovery of EF (42%). At laboratory tests a hypothyroidism were detected, so L-thyroxine was started. In the following weeks, because of hypotension and bradycardia, the β -blocker and amiodarone were discontinued. At 6 months, a clinical visit confirmed a discrete well-being and the echocardiogram showed a normal EF (\approx 55%), besides, due to lack of certain efficacy and safety of dual prolonged ICT, haematologist discontinued deferioxamine, keeping only deferiprone. Nowadays patient has a stable clinical and hemodynamic status, despite ferritin is still high (1694 ng/ml). CMR confirms a severe iron overload of heart (T2*: 9.46 ms); so a dual-ICT is restarted. In literature are reported more than 500 pregnancies in β -T and recent data from North America and UK Registry demonstrate a rate of pregnancy of 27.3%, where β -T intermedia is the condition with higher probability, but is also characterized by high

rate of thrombo-embolic event. The rate of cardiac complications reported is variable (1.1%-15.6%). Our case underlines these data and the need for close follow-up of these patients, especially in a particular condition such as pregnancy.

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An uncommon cause of reversible dilated cardiomyopathy: chronic hypocalcaemia

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Introduction: serum calcium levels, particularly in its ionized form, are key determinants in the maintenance of myocardial contractility and neuromuscular excitability. Chronic hypocalcaemia has been reported as a rare cause of reversible dilated cardiomyopathy. Case report description: a 56 year old Indian woman was admitted to our hospital for progressive dyspnea with orthopnea, which started about one week before. She had a subtotal thyroidectomy several years before and she was euthyroid. She had no previous history of cardiac disease and was not taking any drug. On admission she had bilateral lung rales and heart auscultation was substantially unremarkable. The ECG showed sinus rhythm, left ventricular hypertrophy, negative T waves and a quite long QT interval (QTc 580 msec). The echocardiogram revealed a moderate left ventricular dilatation with severe global hypokinesia (EF about 30%, septal S' 4 cm/s), the right ventricle was normal. Chest X-ray showed pulmonary congestion and cardiac enlargement. Blood tests revealed severe hypocalcaemia (5,1 mg/dl, normal values 8,3-10,5 mg/dl), normal

albumin levels, hyperphosphoremia (6,8 mg/dl, normal values 2,5-4,8 mg/dl) and mild hypokaliemia (3,2 mEq/l). BNP was increased (1061 pg/ml). Troponin I, CK MB, creatinine and TSH were within normal range. Serum parathormone levels were at the lower edge of normal values (18 pg/ml, normal values 10-60 pg/ml), which, in presence of very low calcium levels, confirmed the diagnosis of hypoparathyroidism, probably caused by previous thyroid surgery. The patient was first treated with oxygen, furosemide and ACE- inhibitors. She was also given calcium supplements, calcitriol and, later, a low dose of hydrochlorothiazide to reduce calciuria. A rapid clinical improvement was observed. Coronary angiography showed normal coronary arteries and left ventriculography confirmed echocardiographic data of severe LV systolic dysfunction. After discharge calcium and vitamin D were continued, along with furosemide and ACE inhibitors, and the patient remained asymptomatic. Serial echocardiograms showed a reversal of left ventricular dilatation and systolic dysfunction already by three months (EF 59 %, septal S' 6 cm/s), but interestingly left ventricular mass remained fairly stable, as volume reduction was accompanied by an increase in wall thickness (in a similar way to post-surgical remodeling in aortic regurgitation), and decreased only by six months. QT interval returned to almost normal values (440 msec) already at one month and T abnormalities completely reversed too in about three months. Discussion: hypoparathyroidism induced a severe hypocalcaemia, which caused a reversible dilated cardiomyopathy. Hypoparathyroidism may develop late after thyroid surgery and neurologic symptoms may be mild, thus making the diagnosis difficult. Even though hypocalcaemia is a rare cause of dilated cardiomyopathy, it should be considered in the differential diagnosis in the presence of a long QTc interval, particularly if thyroid surgery has been previously performed.

Moderated Poster Session 1 – Diversified acute heart failure management strategies

Saturday 23 May 2015 12:00–13:00

Location: Poster Area

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Clinical presentation, management, and in-hospital outcomes of patients admitted with decompensated heart failure in a tertiary care center in india

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Introduction: Heart failure (HF) is emerging as a leading cause of hospitalization in India. There is hardly any data regarding HF from India. We retrospectively analysed the data of patients admitted over a 10 year period with decompensated HF in SCTIMST, a tertiary care center in India.

Objective: Was to collect data regarding consecutive HF admissions and outcomes in a tertiary care center over a period of 10 years (2003-12).

Methods: The data of consecutive patients who were admitted with a diagnosis of HF (satisfying European Society of Cardiology 2012 Criteria) were retrospectively collected. Data regarding diagnosis, risk factors, treatment and in-hospital outcomes were captured.

Results: The data of 1985 patients (1228, 61.9% males, mean age 49.2 +/- 14.2 years) were collected. The most common etiology were rheumatic heart disease (RHD) (37.1%) followed by coronary artery disease (33.4%), non-RHD valve disease (8.2%), cardiomyopathies (dilated, restrictive, hypertrophic and endomyocardial fibrosis - which is unique to the region) - 7.8% and GUCH - grown-up congenital heart disease (4%). Pure diastolic heart failure constituted 4.3% of the population. 33 % of patients were in atrial fibrillation or atrial flutter(AF).

Risk factor profile was as follows - diabetes - 18.9%, hypertension - 21.1%, history of tobacco use - 44% and presence of renal dysfunction during admission (by creatinine clearance) - 34.5%

The mean duration of hospitalization was 8.2+9.5 days. The total in-hospital mortality was 15.9%. The major cause of death was as follows - pump failure 61.6%, sepsis 26% and arrhythmia related - 12.4%.

In-hospital mortality was higher among males than females (16.7% vs 14.7%). Discharge medications were as follows - beta-blockers 79%, ACEI/ARB (52%), aldosterone blockers (48%) and diuretics - 77%.

Conclusions: Compared to data from the west, this data from a tertiary referral center shows that Indian patients are younger and have male predominance. RHD is still a major problem while CAD is also contributing to HF burden. Prevalence of hypertension, AF and CKD were less. In-hospital stay was longer and mortality was higher. Usage of evidenced based therapy was not very different. This has implications in control of HF in a developing country like India.

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Predicting value of biomarkers for short-Term outcomes in acute heart failure

This study was supported by the Twelve-Fifth National Key Technology R&D Program (2011BAI11B08)R Rongrong Gao¹; YL Zhou¹; MC Jin¹; K Wang¹; XY Kong¹; WM Yao¹; F Zhou¹; DJ Xu¹; HF Zhang¹; XL Li¹

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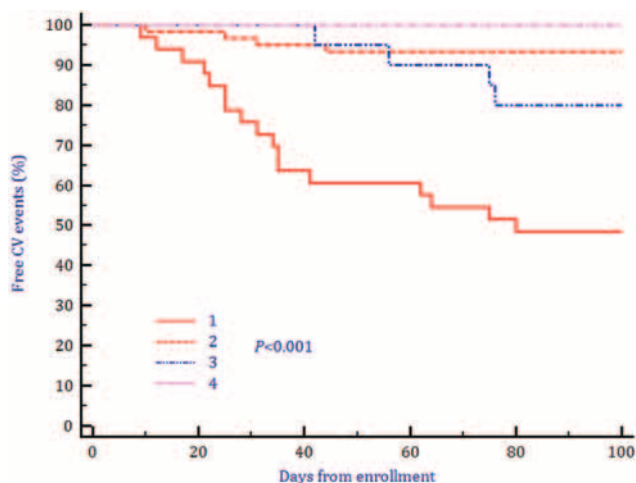
Purpose: B-type natriuretic peptide(BNP) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) are increasingly being used to guide the management of acute heart failure (AHF) patients. This study aims to explore some new biomarkers providing predicting values for short term prognosis in patients with AHF.

Methods and Results: A total of 206 patients with AHF were enrolled and followed for 3 months. Baseline level of complete blood count, complete biochemistry, D-dimer and NT-proBNP were measured at admission or the following morning. Primary endpoints of the study were cardiovascular (CV) events, defined as cardiac death and/or readmission for AHF. During the 90-day follow-up period, 15 patients died and 10 patients were re-hospitalized due to worsening of heart failure(12.14%).

Red cell distribution width (RDW), D-dimer and NT-proBNP were significantly higher in the patients who had a CV events at the 90-day (p 1.1mg/dl and NT-proBNP >2262.0pg/ml were at high risk (p < 0.001) for short-term outcomes of AHF.

Conclusions: D-dimer could be as a new biomarker combined with NT-proBNP for predicting early prognostic value to cardiovascular events of AHF.

The study and its protocol were reviewed, approved, and registered by an independent ethics committee associated with the hospital. Written documentation and informed consent was provided to all of the participants in accordance with the principles of Good Clinical Practice and the Declaration of Helsinki.



Kaplan-Meier survival curve

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The impact of rapid access heart failure clinic on mortality and subsequent heart failure admissions, and predictors of these outcomes in patients seen in this clinic

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Background: Recent guidelines advise early diagnosis and review of patients with suspected or confirmed heart failure by a heart failure specialist team. Although many hospitals across the United Kingdom are providing rapid access heart failure services, the impact of these services on hard clinical endpoints as well as predictors of poor outcomes in patients seen in these services remain fairly uncertain.

Aim: The aim of our study was to determine the impact of Rapid Access Heart Failure Clinic on mortality and subsequent hospital admissions for heart failure and to determine the predictors of these outcomes.

Methods: Patients were seen at the University Hospitals of Leicester within two weeks of initial referral by their primary care physician. The county of Leicestershire in the United Kingdom has three main National Health Service clinical commissioning groups (CCGs). Only one of these CCGs referred patients to the Rapid Access Heart Failure Clinic (Group 1), while the others did not (Group 2) and were therefore used for comparison. We compared hospital admission rates, hospitalisation bed occupation days and mortality rates for heart failure between the two groups. The clinic started running from 1st of October 2012 and included in these analyses are

patients seen till 30th of September 2014 and followed-up to the 31st of December 2014. The median follow time was 11.2 months.

Results: Heart failure hospital admission rates were lower at 3.7/1000 population in Group 1 compared to 4.1/1000 in Group 2. The hospitalisation bed occupation days for heart failure were lower in Group 1 at 47.4/1000 population compared to 52.3/1000 in Group 2, while mortality rate was 0.4/1000 in Group 1 compared to 0.5/1000 in Group 2. There was a significant reduction of 4.4 % in average monthly heart failure hospitalisations from 2013/2014 to 2014/2015 in the Group 1 compared to 9.6% for Group 2. There were 312 patients who attended the clinic, of which 265 (84.6%) had confirmed diagnosis of heart failure. During follow-up, a total of 67 (21.5%) died or were subsequently admitted to hospital for heart failure. The independent predictors of death and subsequent heart failure admission were age, male gender, orthopnoea, smoking history, atrial fibrillation/flutter, and history of coronary artery disease.

Conclusion: There is a trend towards a positive impact of the rapid access heart failure clinic on hard clinical outcomes and a palpable cost-effectiveness of such a service, although robust data from randomized controlled trials are warranted.

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Current management of acute heart failure in spanish hospitals: preliminary results of a survey of the spanish society of cardiology

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Purpose: Current management of patients with acute heart failure (AHF) is not well known and it could account for worse quality of clinical results and regional differences. The Spanish Society of Cardiology aimed to know current management of patients with AHF.

Methods: A total of 159 Spanish hospitals (83% university hospitals), which attend a total population of 40.773.490 people across the entire national territory, participated in a voluntary survey from september to december 2014. The services involved were 87% cardiology and 13% internal medicine services.

Results: The role of cardiologists in the management of AHF patients was: 57% emergency units, 41% coronary units, 92% hospitalization wards. In the emergency unit, 57% of the hospitals had 24 hours availability to perform echocardiography and 68% to measure natriuretic peptides. At discharge, 45% of the hospitals had specific discharge protocols and 95% received specific medical education, but only 41% was written or supported by a specific medical document. After discharge, the first scheduled follow-up appointment was in 77% with general cardiologists and 33% with cardiologists specialized in HF, even when 62% of hospitals had outpatient HF clinic including HF nurse able to administer intravenous treatment in 30%.

Conclusions: Further efforts are necessary to improve the management of AHF, through the participation of cardiologists in acute settings and especially by the participation of HF units in the transition from the hospital to the out-patient setting.

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Reasons for admitting a patient for heart failure: where did we go wrong?

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Introduction: There is a widely held belief that most patients admitted with heart failure have severe shortness of breath at rest but large registries and surveys report that many patients were comfortable at rest with little sign of acute cardiac or respiratory distress. However, information was collected across many centres and by a variety of staff using survey questions that might have been misinterpreted.

Methods: We conducted a retrospective case-note review of patients with a primary death or discharge diagnosis of heart failure already reported to the National Heart Failure Audit for England & Wales to determine what proportions were Short Of Breath At Rest (SOBAR) or Comfortable At Rest but Breathless On Slight Exertion (CARBOSE). We collected blood pressure (BP) and heart (HR) and respiratory rate (RR) at initial presentation and frequently thereafter for the first 24 hours and tracked mortality for 180 days.

Results: Of 701 patients (311 from Hull and 390 from London), the median age was 76 (IQR 65-73) years, 38% were women, 46% were in atrial fibrillation and median NT-proBNP was 4082 ng/l (IQR: 1895-10279ng/L); 45% had SOBAR and 55% had CARBOSE. Compared to patients with CARBOSE, patients with SOBAR were of similar age but had higher HR (100 v 84bpm); systolic BP (142 v 125 mmHg); and RR (26 v 19 rpm). Vital readings changed little amongst patients with CARBOSE in

the first 4-6 hours but declined steeply in those with SOBAR (BP: 142 to 127 mmHg, HR: 100 to 90bpm, and RR: 26 to 21 rpm at presentation and 4-6 hours respectively). At presentation, systolic BP was >125mmHg in 71% patients with SOBAR and 50% with CARBOSE, dropping to 52% and 43% respectively by 4-6 hours. By 180 days after presentation 15% of SOBAR and 35% of CARBOSE patients had died (OR 1.92, p-value=0.001, CI 1.30-2.84). This difference in mortality remained significant in multi variable analysis.

Conclusion: Contrary to popular belief, most patients admitted with a primary diagnosis of heart failure don't have breathlessness at rest although they do report breathlessness on slight exertion. Patients presenting with SOBAR have higher heart rates, respiratory rates and systolic blood pressures and often respond quickly to conventional treatments. Although patients with SOBAR have more alarming initial symptoms and signs, patients with CARBOSE have a worse prognosis, perhaps reflecting more severe cardiac (right heart) dysfunction.

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The role of copeptin and NT-proBNP levels in the prognosis of acute decompensated chronic heart failure: results from the MOLITOR trial

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Purpose: Disease progression in acute and decompensated chronic heart failure (ADHF) reflects disorders in neurohormonal systems. It was shown that certain biomarkers may help with the diagnosis and prognosis in many cardiovascular patient population. In a pilot study, we aimed at determining the best time point for measuring biomarkers to predict primary clinical outcomes of mortality, rehospitalization and quality of life (QoL). A first inspection revealed that serial measurements of the precursor peptides of the natriuretic and vasopressin systems (NT-proBNP and copeptin) add incremental value to risk stratification in patients. The present analyses focus on relevance of those data for QoL.

Methods: MOLITOR is the first observational trial to explore biomarker trajectories in patients with ADHF (NYHA III-IV). Out of 168 patients, who were followed for 2 years, 113 were available for statistical analyses. Their NT-proBNP and copeptin levels were used as predictors for physical and psychosocial aspects of QoL (short-form health survey, SF36). Hierarchical multiple linear regression analyses were used to investigate whether log10 transformed NT-proBNP and copeptin at baseline, discharge, 3 months after discharge predicted psychological and physical functioning at follow-up above socio-demographic data (age, marital status, education), additional treatment with benzodiazepines or antidepressants and NYHA-classification at discharge. We also evaluated if those effects of NT-proBNP on QoL are due to its anxiolytic impact (assessed with the Hospital Anxiety and Depression).

Results: Copeptin levels were highly predictive for survival, but they did not have any incremental value for QoL (all ps > .13). In contrast, NT-proBNP levels 3-months after discharge significantly predicted psychosocial ($\beta = -.25$, p < .015) and physical ($\beta = -.28$, ps < .05) QoL at follow up: Higher levels of NT-proBNP were associated with worse QoL. Also, elevated NT-proBNP at admission predicted reduced HADS-anxiety at discharge, $\beta = -.16$, p < .05, but not QoL at discharge or follow up.

Conclusions: First results showed that copeptin levels are not relevant for QoL prediction. On the contrary, NT-proBNP levels measured at different time points may differentially predict QoL, especially the physical component and anxiety. It is known that higher levels of NT-proBNP at baseline hospitalization predict less anxiety at discharge, whereas NTproBNP 3-months after discharge predict worse physical QoL but doesn't associate to anxiety. Current analyses now probe whether ongoing cardiovascular medication can affect NT-proBNP, QoL and anxiety.

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Diuretic strategies in acute heart failure: data from a web survey among members of the italian association of hospital cardiologists (ANMCO)

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Purpose: Diuretics are the cornerstone of volume overload treatment in patients with acute heart failure (AHF). Despite their widespread use in this setting, limited evidence is available to guide clinicians on the appropriate management of diuretic therapy and on the identification and treatment of diuretic resistance (DR), a common, complex clinical issue. We conducted a web-based Survey direct to members of a national cardiology society to investigate strategies of diuretic management in AHF.

Methods: The survey consisted of a demographic section and 30 multiple choice questions concerning diuretic strategy, definition and treatment of DR, methods of

non-pharmacological decongestion. Anonymous answers were directly transferred via web to an electronic secure database.

Results: 601 hospital cardiologist (age 52 ± 11 years, clinical practice 22 ± 11 years, 72.3% men). Furosemide was the preferred diuretic for 98%, but only 30.3% of respondents used a predefined therapeutic protocol. Bolus, continuous infusion alone or preceded by bolus were used by 36%, 23% and 41%, respectively, 93% used a loading dose \geq the chronic oral dose, but only 23% adjusted dosage according to patients' baseline renal function. Clinical criteria (signs, symptoms, weight loss) ranked first in respondents' definition of diuretic effectiveness, followed by urinary output. DR was identified by 48% using a multiparametric evaluation, while 24% considered only urinary output $< 1000/24h$ in isolation. Sequential nephron blockade is used by 80% only in case of loop diuretics failure, metolazone being the commonest agent added (32%). Mineralocorticoid receptor antagonists are used by 54% as initial treatment. In the setting of DR, 60% of respondents considered fluid restriction a priority and 77% add low-dose dopamine. Switching to ultrafiltration is considered in case of clinical DR by 23% of respondents, 22% routinely rule out pseudo-resistance with worsening renal function by 5% of worsened renal function and in the presence of severe diuresis contraction in 14%. Finally, we calculated the proportion of respondents who complied with a guideline-derived appropriateness profile, defined as $>75\%$ answers fitting using a set of multiple criteria: only 23% of respondents met this predefined target. No demographic variables were predictive of a guideline-compliant behavior.

Conclusions: We observed a wide variance in diuretic therapy management in a large cohort of Italian hospital cardiologists. This finding underscores a compelling need to standardize the criteria for appropriate diuretic strategies in AHF.

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Lung impedance-guided therapy of patients with chronic heart failure improves clinical outcome

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Background decompensation of patients with chronic heart failure (CHF) leading to re-hospitalizations for pulmonary congestion or edema (PCE) is an unresolved problem. At the initial stages of decompensation, patients have neither complaints nor overt signs of PCE. Current methods for PCE monitoring such as implantable devices, are invasive and of low sensitivity (35-76%) and monitoring by chest x-rays is both impractical and detrimental due to radiation exposure. Decreasing lung impedance (LI) is the result of an increase in pulmonary congestion. PCE monitoring was done by device which is 25-fold more sensitive for small changes in lung fluid content than current ones due to measurement LI instead widely used transthoracic impedance.

Aim: To evaluate the effectiveness of treatment guided by the new LI device of patients with CHF.

Methods and Results: We have shown previously that an LI decrease of more than 24% from dry (baseline) LI reflects the clinical threshold of lung fluid accumulation that signifies the evolution to PCE and hospitalization for $>90\%$ probability. We recruited 250 patients during the first month after hospitalization for PCE (age 68 ± 11 years, male 80%, LVEF $28 \pm 7\%$) at NYHA II/III/IV (107/100/43, respectively) and followed them in an outpatient clinic for 36 ± 22 months on a monthly basis. Initial NT-proBNP level was 3594 ± 5114 pg/ml. Patients were randomized (1:1) into 2 well-matched groups according to treatment policy. Group 1 included patients treated according to measured LI while group 2 patients were treated by clinical assessment alone. There were 23 cardiovascular deaths and 15 non-cardiovascular deaths in group 1 and 40 and 10 in group 2, respectively ($p=0.006$). The average annual number of hospitalizations for PCE in groups 1 and 2 were 63 and 140, respectively ($p < 0.001$). In patients whose treatment was LI-guided (group 1) pre-emptive therapy was intensified 3.2 times more frequently than in group 2 ($p < 0.001$). The average annual non PCE hospitalizations were 84 and 104 in group 1 and 2 respectively ($p < 0.05$).

Conclusion: Preemptive LI-guided treatment in CHF patients reduced recurrent hospitalizations due to PCE and improved survival.

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Intravenous inotropes and short-term mortality in acute heart failure: a propensity-score matching secondary analysis of the ALARM-HF registry

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²Hospital Lariboisiere, Department of Anesthesiology and Critical Care Medicine, Paris, France; ³University Hospital Zurich, Department of Internal Medicine, Zurich, Switzerland

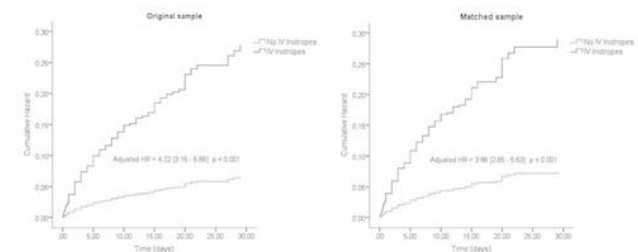
Aims: Despite improving symptoms and hemodynamics, intravenous (iv) inotropes have not demonstrated improved prognosis in patients with acute heart failure

(AHF). We sought to evaluate the effect of iv inotropes on short-term mortality in a large group of AHF patients using propensity-score matching.

Methods: We perform a secondary analysis of the Acute Heart Failure Global Survey of Standard Treatment (ALARM-HF) registry, a survey of 4953 AHF patients from 9 countries. The primary endpoint was death during hospitalization or within 30 days. We applied propensity-score nearest neighbor matching to produce a balanced sample of treated and non-treated with iv inotropes patient pairs. Mortality was assessed using Cox regression with adjustment for age, gender, systolic blood pressure (SBP), atrial fibrillation (AF), NYHA class, renal function and acute coronary syndrome (ACS) as the cause of AHF.

Results: Data on inotropic therapy were available in 4944 patients; 1775 of them had received iv inotropes and 3169 had not. After propensity-score matching, we selected a sample of 1836 patients, 918 in each treatment group. Inotropes had a negative unadjusted effect on mortality both before matching (HR: 6.70, 95%CI:[5.40, 8.32]) and after matching (HR: 5.63, 95%CI:[3.93, 8.06]). Mortality remained consistently higher after adjustment in both samples (HR: 4.22, 95%CI:[3.15, 5.66] and HR: 3.86, 95%CI:[2.65, 5.63] respectively; Figure). Among those treated, age >70 years, female gender, SBP < 100 mmHg, ACS and sinus rhythm years were associated with greater mortality.

Conclusions: In AHF patients, iv inotropes are associated with a significantly higher short-term mortality, especially among elderly, females and those with ACS as the cause of AHF.



Figure

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Extracorporeal life support combined with left-ventricular decompression enhances outcome of cardiogenic shock with concomitant lung failure - challenges to the interdisciplinary heart team

B Schmack¹; P Seppelt¹; A Weymann¹; C Alt¹; R Arif¹; AO Doesch²; P Raake²; K Kallenbach¹; M Karck¹; A Ruhparwar¹

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Purpose: Cardiogenic shock (CS) has a poor survival. Extracorporeal life support (ECLS) remains the only option in INTERMACS level 1 & 2 to instantly save life and attain a time frame for decision. ECLS approach can be central (c) or peripheral (p). While pECLS is simple and fast, vessel injury or limb ischemia remain severe complications, while cECLS is invasive and needs a surgical setting with thoracotomy, but establishes a physiologically flow. Despite techniques are highly standardized in modern AHFs, lung failure following ECLS remains a crucial limitation, caused by a lack of decompressing the failing left ventricle (LV) with blood backlog into the lung and subsequent congestion while the persistent distension impedes LV recovery. Both can be obviated by LV decompression to better lung and end organ function retaining the ability to wean ECLS or bridge to VAD/HTX. However, comparative data about the outcome of ECLS w/ or w/o LV vent are not available yet. The purpose of this single center study was to identify influence of LV decompression during ECLS on patient's outcome under consideration of the ECLS approach.

Methods: 70 patients were collectively evaluated (mean age 34.9 ± 27.3 y) with INTERMACS 1 CS obtained ECLS (pECLS 14.3%, cECLS + vent 47.1% and cECLS w/o vent 38.0%) from 2004-2014. Most common cause for CS was DCMP (15.7%), myocarditis (15.7%) and acute MI (8.6%). Infants (≤ 10 years) were assessed separately.

Results: FU was 100% with a mean survival of 1.9 y (± 0.49) for adults and 2.64 y (± 0.55) for infants. Bridge to recovery was feasible in 21.4%, bridge to transplant in 8.8% and 20% were bridged to VAD. 48 (68.5%) Patients died, mostly ($n=39$) within 30d (overall 30d mortality 55.7%). In total, 1y and 30d survival was superior with cECLS and vent compared to pECLS ($p=0.047$; $p=0.007$). 30d survival of adults with cECLS plus vent was superior to pECLS ($p=0.019$). cECLS had a better 30d survival ($p=0.041$) and horowitz index was significantly greater (214.21 vs. 109.38, $p=0.015$) with LV vent. Estimated survival did not differ within pediatric groups, but infants w/o vent presented late postoperative significantly more often with a reduced EF ($p=0.013$).

Conclusion: Acute therapy of CS remains challenging. Conservatively treated CS has a poor survival, while ECLS can remain the last opportunity leading to an acceptable overall outcome in adults. Patients who underwent cECLS with LV vent

had a superior survival after 30d and 1y. We postulate LV decompression, while the technique may vary. Urgent interdisciplinary discussion and interaction among the Heart Team is mandatory.

Clinical Case Corner 1 – Do not break the woman's heart

Saturday 23 May 2015 12:15–14:00

Location: Poster Area

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A case of reversed Takotsubo cardiomyopathy associated with vertebral artery dissection

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Background: Reversed (Inverted) Takotsubo cardiomyopathy, first described in 2010, is an atypical variant form of Takotsubo cardiomyopathy characterized by a basal and mid ventricular segment akinesis and apical hyperkinesis. It typically occurs in young females with neurological disorders. It is usually reversible with supportive management. To the best of our knowledge, there are no recorded cases of Inverted Takotsubo cardiomyopathy associated with vertebral artery dissection.

Case: We present to you a case of a 29 year old female with a background history of multiple sclerosis on interferon therapy for two months. She presented with history of sudden onset headache, nausea and vomiting and was found to have vertebral artery dissection. She reported atypical chest pain for which cardiac biomarkers and ECGs were requested. Her serial ECGs showed diffuse dynamic ST-T changes with poor progression of R waves anteriorly. Her serial cardiac biomarkers revealed an elevated high sensitivity troponin with an initial value of 300ng/L (normal The main clinical delimitas that were encountered in this case include the following:

Need for angiography, especially given the fact that the patient is young with a low pretest probability of CAD and the unusual wall motion abnormalities not in keeping with a coronary artery territory.

The need of initiation of dual antiplatelets especially in the presence of multiple enhanced lesions in the brain and initially a question of a neurological bleed was present.

What medications to continue seeing that the patient was symptom free with complete resolution of LV function within 72 hours.

From a management standpoint, she was initially instituted on acute coronary syndrome treatment in the form of heparin, aspirin, clopidogrel, statin, beta blockers and nitrates and risks of bleeding was explained to the patient. She was planned to go for coronary angiography once stable from the neurological point of view. However, as was mentioned earlier, the patient's symptoms remarkably improved and her cardiac biomarkers normalized within the subsequent two days. Given that the regional wall motion was not consistent with a coronary artery territory, a repeat echocardiogram was requested. It showed significant improvement with normalization of her left ventricular systolic function. The wall thickness of the septum recovered with normal thickening of all of the proximal segments with no residual regional wall motion abnormalities detected. (See attached echo) She was maintained on beta blockers to block any excessive catecholamine surge and all other cardiac treatments were discontinued. She was seen in 6 weeks with a repeat echo which remained normal.

Conclusion: We present to you a case of Inverted (Reversed) Takotsubo cardiomyopathy associated with vertebral artery dissection.

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Reverse takotsubo cardiomyopathy following inadvertent intrathecal injection during percutaneous epidural neuroplasty

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Introduction: Reverse takotsubo cardiomyopathy (RTC) is a variant of Stress induced cardiomyopathy (SIC) involving basal and mid-ventricular segments, but while preserving the contractility of apical segments, and thus, differs from the classic subtype of SIC.

Case description: A 34-year-old woman was transferred to our emergency room due to dyspnea. One day before, she was meant to receive percutaneous epidural neuroplasty due to herniated nucleus pulposus (L4/L5 level), however, the anesthetics were inadvertently injected into the intrathecal space instead of the epidural space. Five hours after the procedure, respiratory failure with tachycardia and low blood pressure (60/40 mmHg) were documented. Chest radiography showed

diffuse consolidation consistent with pulmonary edema, and electrocardiography (ECG) revealed sinus tachycardia with ST segment depression in II, III, aVF, and V3-6 leads. Transthoracic echocardiography revealed severe LV dysfunction (ejection fraction [EF] 18%) and contractile abnormality consisting of akinesis of the basal and upper mid-ventricular segments with sparing of apical segment. Myocardial contrast echocardiography also showed akinesis of the basal to upper mid-ventricular segments without definite myocardial perfusion defect. Coronary angiography revealed normal epicardial coronary arteries without luminal stenosis. Positron emission tomography/magnetic resonance imaging (PET/MRI) revealed akinetic segments of the LV with diminished F-18 fluorodeoxyglucose (FDG) uptake and subendocardial edema in the basal lateral segment. The patient was diagnosed to have RTC and managed conservatively using diuretics, digoxin, angiotensin converting enzyme inhibitors, and beta-blocker. A repeated echocardiography taken eight days after admission revealed partial improvement of LVEF from 18% to 48%. She was discharged on hospital day 12. At one week after discharge, repeated echocardiography showed a fully improved LV function (EF 59%) with no significant contractile abnormality. Repeated PET/MRI conducted at 2-month follow-up showed normalized FDG uptake of the LV basal wall without myocardial edema or fibrotic change.

Conclusion: We present a rare case of RTC, following an unexpected intrathecal injection during percutaneous epidural neuroplasty. Although the precise mechanism involved remains unclear, the direct neurohumoral effects of hyperbaric anesthetics and adhesiolytic appear to result in a catecholamine surge and myocardial stunning that precipitate SIC.

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Cardiac sarcoidosis- the dilemma

MNUM Meah¹; JH Hasleton²; JDS Somauroo¹

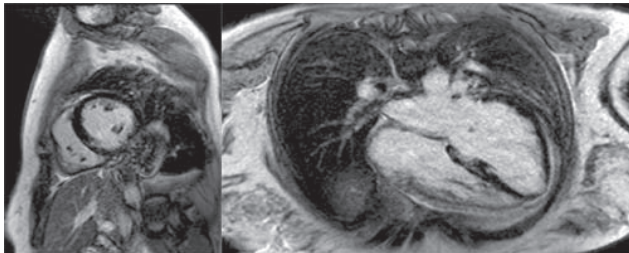
¹Countess of Chester Hospital, Chester, United Kingdom; ²Liverpool Heart and Chest Hospital, Liverpool, United Kingdom

Background: Sarcoidosis is a granulomatous disease of unknown aetiology, it can affect any organ in the body. Cardiac sarcoidosis (CS) can occur alone or concurrently with multiple organ involvement. It is difficult to diagnose, as often stays clinically silent, though its presence is more common in those with cardiac symptoms. It is thought to affect at least 25% of patients with sarcoidosis and contributes significantly to mortality and morbidity statistics. Despite this there is no screening process or guidelines available on the diagnosis and long-term management of cardiac sarcoidosis.

Case Description: A 43-year-old was readmitted with respiratory failure one month after being diagnosed with pulmonary sarcoidosis. Arterial blood gases showed type I respiratory failure, troponin-I came back elevated at 3.6 ng/mL and CXR confirmed pulmonary oedema. ECG showed sinus rhythm with right axis deviation and Q-waves anteriorly. The patient required intubation and was treated with diuretics, nitrates and steroids. Echocardiography showed hypokinesis of the infero-posterior walls (EF 45%). Once she had stabilised we performed coronary angiography that showed normal vessels. Magnetic resonance imaging however revealed a dilated left ventricle with mild-moderate systolic impairment and hypokinesis of the basal-mid inferior wall. T2-weighted imaging demonstrated increased signal in the basal to mid infero-septum with late gadolinium enhancement showing patchy hyperenhancement in the basal to mid infero-septum and inferior walls. The patient was discharged with a diagnosis of cardiac sarcoidosis and treatment including prednisolone and standard heart failure medication. Outpatient holter monitoring revealed two salvos of monomorphic, non-sustained (10 beats) ventricular tachycardia. A repeat echocardiogram 3 months later revealed a significant improvement in both systolic (EF 56%) and diastolic function. In view of this, it was decided to continue her treatments rather than implanting an ICD.

Discussion: Ventricular arrhythmias and conduction defects such as complete heart block are a significant source of mortality in patients with cardiac sarcoid. Figures for sudden death range between 30-65%. Despite this, there is a lack of consensus on the place of Implantable Cardioverter Defibrillator (ICD) therapy in patients with cardiac sarcoidosis. Whilst NICE guidance fails to mention the

use of ICDs in cardiac sarcoid specifically the AHA/ACC guidelines suggests that ICD implantation is reasonable in patients with cardiac sarcoid but fails to provide more details as to exact situations, leaving the problem open to clinician's interpretation. Prospective and anecdotal evidence exists showing ICD insertion improves mortality for secondary prevention of sudden death; indeed it is deemed mandatory in cases of "refractory" ventricular tachyarrhythmias. Its use in primary prevention is less well delineated leading to clinical dilemmas over what to do with patients who do not fully fit into the typical "sudden death" stereotype. Through this case we hope to highlight the importance of screening for cardiac sarcoidosis and the need for studies to delineate guidance on when to use ICDs in this patient group.



MRI- Cardiac Sarcoid

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Takotsubo cardiomyopathy of mid-ventricular type after iatrogenic intravenous epinephrine injection

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Takotsubo cardiomyopathy (TCMP) is an increasingly recognized disorder characterized by acute reversible apical ventricular dysfunction in the absence of epicardial coronary disease. The precise mechanisms of TCMP have not been fully elucidated. Direct catecholamine-induced myocyte injury may be a mechanism of TCMP. We report a variant type of TCMP with isolated mid-ventricular dysfunction after inadvertent epinephrine injection.

A 43-year-old female presented with abrupt chest discomfort and shortness of breath after inadvertent intravenous epinephrine injection of 1mg during hospitalization for removal of colon polyp. The patient had a blood pressure of 160/100 mmHg, pulse rate of 110 beats per minute, respiration rate of 24 per minute and body temperature of 37.0°C. Troponin T was raised, electrocardiogram showed sinus tachycardia with low voltage, chest X-ray showed pulmonary congestion, ejection fraction was reduced to 40% calculated by Simpson's method, transthoracic echocardiography showed severe hypokinesia of all the middle segments of the left ventricle with normal basal and apical segments. In addition contrast echocardiography was performed in order to enhance endocardial definition more exactly myocardial motion. Diuretics and ACE inhibitor was administered. By day 3, follow-up echocardiography showed left ventricular ejection fraction of 45% persisting hypokinesia only in the middle segment. She was discharged the next day in good clinical condition on perindopril 2mg once daily and spironolactone 12.5mg once daily. On follow-up, the impaired contractility resolved completely, with no residual deficits found in an echocardiography 30 days after inadvertent epinephrine injection.

Epinephrine is widely used to treat a number of conditions including: cardiac arrest, anaphylaxis, and superficial bleeding. In our case, submucosal epinephrine of 0.5mg was already injected during endoscopic polypectomy. And additional inadvertent intravenous epinephrine injection induced myocardial stunning of the mid-ventricular TCMP type. Fortunately, recovery was fast and without complications. Our case suggests that submucosal and/or intravenous epinephrine injections can cause TCMP and lead to life-threatening condition. Cautious catecholamine administration is required for physicians to use catecholamine including epinephrine under the various medical conditions.

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Severe preeclampsia complicated with acute pulmonary oedema

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A48-year-old woman was admitted to our Institution after developing a sudden-onset dyspnoea. Relevant medical background included a cutaneous allergic reaction to Penicillin and chronic gastropathy related to *Helicobacter pylori* infection. Cardiovascular risk factors were not present. She was primigravida with current gemelar gravidity at the 30th week of gestation. During outpatient follow-up,

severe preeclampsia was identified, with a gestational hypertension beyond 160/110 mmHg and 24-hour proteinuria of 1.5 grammes. Patient was admitted to hospital in two occasions and alfa-metildopa and steroids were started in order to lower blood pressure and induce fetal pulmonary maturing. Neither cerebral nor cardiac symptoms were present at this point. Few days after discharge, she was re-hospitalized with the diagnosis of acute pulmonary oedema. An echocardiogram at the bedside showed severe left ventricle systolic dysfunction. The patient underwent a caesarean delivery under general anaesthesia, and both male and female newborns were healthy according to Apgar test. In the early postoperative period, a new heart failure episode developed, which responded to diuretic and vasodilator therapy. At discharge, treatment with diuretics, angiotensin-converting enzyme inhibitors and beta-blockers was prescribed and maintained for several weeks. In a subsequent outpatient clinic visit, recovery of systolic function and resolution of symptoms were proved, and normal blood pressure was noted. Nevertheless, in these cases long-term follow-up is paramount. This is related to the fact that not only can preeclampsia acutely impair cardiac function, but it also might identify women at high risk for future cardiovascular events, even in the absence of other concomitant risk factors.



Chest X-ray: lung alveolar edema

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Stress cardiomyopathy after heart valve surgery

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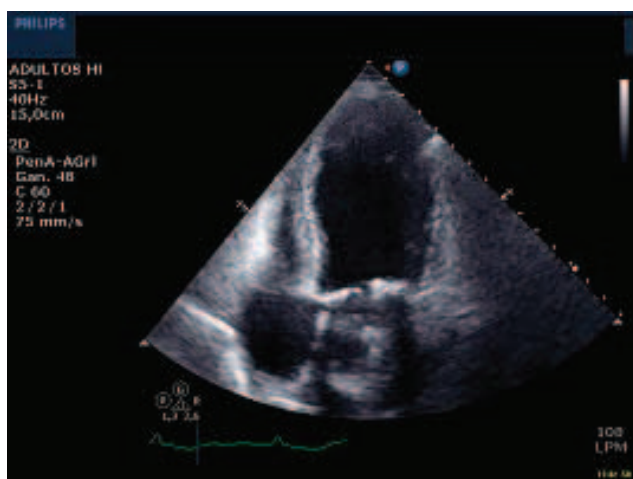
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Introduction and case report description: A 68-year-old woman came to the Emergency Department complaining of palpitations and a 3 days progressive dyspnea becoming rest dyspnea. She denied chest pain, dizziness, syncope, fever or other symptoms. The patient had no known allergies and a prior history of dyslipidemia, chronic renal failure, secondary hypothyroidism and rheumatic heart disease, in treatment with atorvastatin, aspirin, levothyroxine, Candesartan/Hydrochlorothiazide and warfarin. She had undergone cardiac surgery a month before (double valve replacement was performed with Carbomedics reduced metallic prosthesis number 21 in aortic position and Carbomedics Optiform number 27 in mitral position). She had been discharged ten days after cardiac surgery without any complications and with an echocardiography showing normal left ventricle ejection fraction and normal function of both prosthesis. On physical examination, she had no fever, blood pressure was 104/60 mmHg, heart rate 130 beats per min, respiratory rate of 30 breaths per minute and normal oxygen saturation with nasal cannula delivering oxygen at a rate of 2 liters per minute. The cardiac auscultation was arrhythmic with no murmurs or pericardial rub. Pulmonary crackles were heard at both lower lungs. The rest of the physical exam was normal. Description of procedures and techniques: Biochemistry and blood cell count showed stable Creatinine and Hemoglobin (9.8 gr/dl) levels.

Coagulation: INR 2.5. Liver function, C-reactive protein and ultrasensitive troponin were normal. ECG showed a new atrial fibrillation at a rate of 130 and developed inverted T waves in precordial leads (V2-V6), not described in prior ECGs. Echocardiography showed a mild dilated and hypertrophic left ventricle with akinesis of

the apex, apical segments and midsegments of the left ventricle and 35% ejection fraction (biplane Simpson). Both prosthetic valves were normal in function and structure. The coronariography showed no significant stenosis and a TIMI 3 flow over the coronary arteries. Discussion: according to Framingham criteria, our patient was admitted with the initial diagnosis of acute heart failure. Firstly, due to the recent heart valve surgery, a prosthetic valve dysfunction was the first option to rule out. After dismissing valve complications, considering echocardiographic contractility alterations and ECGs repolarization changes, an ischemic entity was the next possible differential diagnosis. However, coronary arteries were normal. Finally, after intensive treatment with loop diuretics, beta-blockers and renin-angiotensin enzyme inhibitors, the patient showed a great clinical improvement. Echocardiography before discharge showed no contractility alterations with a mild left ventricle dysfunction. Moreover, two months after discharge, another echocardiography was performed, confirming full left ventricle function. Therefore, stress induced cardiomyopathy was the final diagnosis.

Conclusions and implications for clinical practice: Clinical cases of stress cardiomyopathy induced by invasive procedures have been reported. Only a few cases are reported after surgery, commonly taking place during surgery or in the first 48 postoperative hours. However, we present a rare case of stress cardiomyopathy, interestingly a month later, after a cardiac surgery that had undergone without any intra/postoperative complications.



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A case of trastuzumab induced cardiomyopathy

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Introduction: Chemotherapy presents a vast array of adverse effects which sometimes include the cardiovascular system. Heart failure, ischemia, venous thrombosis or arrhythmias can occur during treatment and as the survival and age of cancer population increases so does the incidence of such adverse effects.

Case presentation. We present the case of a young woman, with no known prior heart disease, diagnosed in the ER with acute heart failure after trastuzumab treatment for metastatic breast cancer. Female, 39 years old, with a history of breast cancer and multiple secondary bone lesions, currently under palliative chemotherapy, who presents herself to the emergency room of our Hospital with shortness of breath, orthopnea and atypical thoracic pain. The symptoms began three days prior with progressive worsening. Transthoracic echocardiography shows dilatation of all four chambers, an ejection fraction of 32%. The patient had been previously diagnosed with locally advanced, stage IV breast carcinoma with multiple bone secondary lesions. She followed a palliative chemotherapy regime with Docetaxel and Trastuzumab for the first 4 months followed by Trastuzumab in association an aromatase inhibitor for the next 6 months. CT scans at 4 and 10 months after therapy initiation showed partial remission and stationary disease respectively. Considering the history of cytostatic medication, the clinical and paraclinical findings and by excluding other causes for cardiomyopathy, the final diagnostic can be established: Iatrogenic dilated cardiomyopathy, Second degree mitral regurgitation, Second degree tricuspid regurgitation, Heart failure NYHA II, Small bilateral hydrothorax, Locally advanced, metastatic breast carcinoma with secondary bone lesions, Mild normochromic normocytic secondary anemia. Treatment with betablocker, ivabradine, diuretics and deep venous thrombosis prophylaxis with enoxaparine was initiated. Although angiotensin converting enzyme inhibitors are strongly indicated

they could not be introduced due to low blood pressure values. During hospitalisation the evolution was favorable with gradual remission of symptoms, patient was asymptomatic at discharge. First checkup was appointed at one month. Oncological reevaluation was also indicated. The patient was reevaluated monthly. At one and two months the patient was asymptomatic, but without an observable improvement in ejection fraction. At three months the ejection fraction was 43%. The patient was taken off trastuzumab treatment during the follow-up period.

Discussion. It has been known since the 1960s that some cancer treatment regimes can be cardiotoxic both on the short and long term. The introduction of trastuzumab as an anticancer treatment in HER2-positive breast cancer meant an improvement in both early and metastatic disease. However it also brought into perspective a new type of cardiac toxicity. Trastuzumab does not cause myocyte loss and is referred to as type II cardiotoxicity. The damage done to the myocardium can only be seen in electron microscopy. By binding to the HER2 protein on the cell surface, trastuzumab inhibits ErbB2-ErbB4 signaling. This blocks important myocyte protective and growth-promoting pathways leaving the cardiac tissue vulnerable to injury via hemodynamic or other stress. The blockage is reversible once the treatment is discontinued.

The management of trastuzumab ventricular dysfunction consists of standard heart failure medication. The particularity of this case is represented by an asymptomatic evolution of both the breast carcinoma and the cardiomyopathy which became clinically evident at a very late stage. Also the systolic functions recovery period was longer than expected.

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Peripartum cardiomyopathy with non-response to bromocriptin

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Introduction and case report description: 11 days after delivery of her first child by Caesarian section, a 26-year old female patient was presenting to the emergency department with sinus tachycardia of 144 bpm and symptoms of heart failure NYHA functional class IV. Chest x-ray showed signs of congestion and echocardiography revealed a dilated left ventricle (LVEDD 58 mm) and severe LV dysfunction with a reduced ejection fraction of approximately 15%. 8 years ago, the patient suffered from viral myocarditis with slightly impaired left ventricular ejection fraction (LVEF) but complete remission after a few months. A normal LVEF was confirmed by echocardiographic examination in the first trimester of pregnancy. Upon the initial findings, the patient was admitted to the intensive care unit.

Medical treatment and in-hospital stay: Standard heart failure therapy and ablation were initiated. Because of increasing signs of congestion, levosimendan (0,35 µg/kg/min) was administered from day 5 to 7. Bromocriptin was continued according to available data and current local opinion. Myocarditis and left ventricular thrombi were ruled out by cardiac MRT. Because of non sustained ventricular tachycardia, the patient was supplied with a wearable defibrillator prior to transfer to the ward. After 5 weeks of slow but steady recovery, the patient was discharged with optimal medical treatment.

Outpatient follow-up: During a 6-month period, follow-ups were initially arranged every 2 weeks and every 4 weeks later on. NYHA class, echocardiographic assessment of LV function and proBNP were evaluated. The patient improved to NYHA class I, consistent with a continuous decline of proBNP levels from an in-hospital peak of 10223 pg/ml to 781 pg/ml. LVEF did improve from 15% to 30%, but definitely not significantly above 35%. Even though no cardiac events due to arrhythmias were reported, re-admission for final assessment was arranged and implantable cardioverter defibrillator (ICD) treatment advised.

Problems and possible differential diagnosis: Sinus tachycardia was noticed shortly after delivery, but the potentially life-threatening underlying cause of peripartum cardiomyopathy (PPCM) was overlooked due to lack of awareness and failure to perform echocardiography. Instead, the patients signs and symptoms were attributed to having given birth recently.

Upon initial presentation to the emergency department and before there was echocardiographic evidence of severe LV dysfunction, the initial work-up focussed on pathologic causes of sinus tachycardia. Postoperative anaemia after Caesarian section seemed to be among the most likely but could be ruled out easily.

Pre-existing dilated cardiomyopathy (DCM) is sometimes not distinguishable from PPCM but usually presents during pregnancy, with larger cardiac dimensions and a positive family history. A normal echocardiographic examination in the first trimester ruled out pre-existing DCM.

Discussion: Despite promising data concerning the use of bromocriptin in PPCM, it is not recommended as a standard therapy yet. No events of thrombo-embolism occurred under frequent echocardiographic assessment, which was used as an alternative strategy to oral anticoagulation, which is generally recommended in severe LV dysfunction and the use of bromocriptin.

Conclusion: PPCM is a rare, but potentially life-threatening complication of uneventful pregnancy that can easily be overlooked at an early stage. Despite early presentation, optimal medical treatment plus bromocriptin, improvement to NYHA class I and low levels of proBNP, there was no significant improvement of LVEF above

35% on 6-month follow-up. The patient was advised to ICD treatment and against subsequent pregnancy.

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Cardiomyopathy of takotsubo

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Patient T., 80 years old, was admitted 23.12.2014 in 21:50 complaining of intense pain in the chest and pressing nature emerged for the first time after natureline. An ambulance was called due to changes on ECG diagnosis non- STEMI, the patient was taken by ambulance to the hospital. When you receive a state of moderate severity, the respiratory rate of 16 per minute. Auscultation of breath vesicular weakened right in the projection of the lower lobe. The borders of cardiac dullness is not extended. Heart sounds auscultation muted, with regular rhythm. Heart rate of 100 per minute. Blood pressure 140/90 mm. The abdomen is soft, painless. ECG at admission: Sinus tachycardia with a heart rate of 100 per minute. rS V1-V5. The ST segment on the contour. Preliminary diagnosis: non- STEMI. The GRACE risk calculated as high (140 points). Clinical analysis of blood: Leucocytes-10,2*10⁹/l, Hemoglobin-148 g/l, Hematocrit-42,4%, Erythrocytes-4,78*10¹²/l, platelets-194*10⁹/l. Biochemical blood analysis: serum Potassium 3.3 mmol/l, serum sodium 135 mmol/l, ALT - 22 U/l, AST 35 U/l, CPK 190 U/l, MB KLF - 29 U/l, urea - 5.9 mmol/l, creatinine - 54 μmol/l, APTT s, blood sugar 6.0 mmol/L. review Radiography of the chest: Pulmonary pattern is reinforced deformed due to the pneumosclerosis, more in the lower right. Roots fibrous changed. The sinuses are free. Heart shadow enlarged in cross-section. Coronary angiography, aortography: type of blood supply to myocardium right. Coronary artery without pathology. Estimated probability of acute pulmonary embolism (PE) on scales Well's, Geneva. The intermediate risk. Taken D-dimer - 3600 ng/ml (N up to 600 ng/ml). Assigned anticoagulant therapy. According to ECHOCARDIOGRAPHY revealed aneurysm of the top and middle segments of the interventricular septum and the anterior wall, the ejection fraction on Teicholz 45 %. Markers of necrosis of the myocardium in the dynamics (table 1).

Pain not had anticipated. On the basis of complaints, anamnesis, results of additional laboratory and instrumental methods of examination Diagnosed with Cardiomyopathy "Takotsubo"- stressinducing.

Treatment: bisoprolol 2.5 mg * 1 time per day, aspirin 100 mg * 1 time per day/, ACE Inhibitors

ECG 28.12.2014: Sinus rhythm with heart rate of 68 per minute. EOS horizontally. The increase in R in the dynamics from the previous violation of repolarization on the anterior-lateral wall of the left ventricle. ECHOCARDIOGRAPHY in the dynamics after 7 days. PV on Teicholz - 68,98%. Disorders of contractility is not revealed. ECG at discharge: Sinus rhythm with heart rate of 70 per minute. The improvement phase of repolarization on the anterolateral wall of the left ventricle. The patient was discharged from hospital in a stable, satisfactory condition.

Final diagnosis : Cardiomyopathy "Takotsubo"- stressinducing.

Markers of myocardial damage

Date	Figure	result	Norm
24.12.2014, 12:00	Troponin I	1,14 ng/ml	0,00-0,4 HΛ/Mπ
24.12.2014, 21:30	Troponin I	1,55 ng/ml	0,00-0,4 HΛ/Mπ
29.12.2014	Troponin I	0,2 ng/ml	0,00-0,4 HΛ/Mπ

A slight increase and rapid decrease in the level of troponin

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Cancer as a cause of heart failure

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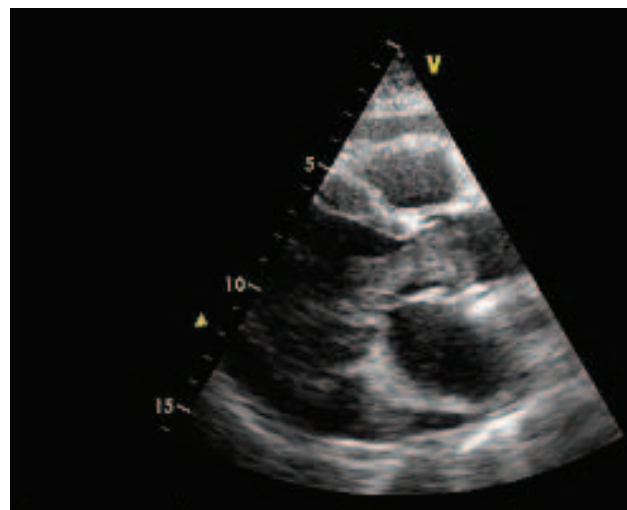
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Background: Patients with cancer can develop heart failure either as a result of locally invasive disease, cancer dissemination, or as a chemo/radiotherapy induced cardiac toxicity. In patients with suspected heart failure, echocardiography is a diagnostic method of choice.

Clinical report: A 68-year old woman was referred as suspected heart failure due to 1-week history of dyspnoea and chest pain on exertion. In 2010, she was diagnosed with monophasic synovial sarcoma of her right foot, which was amputated below knee. In March 2014, metastases in left thoracic wall and left iliac muscle were surgically removed. Adjuvant chemo- and radiotherapy was completed in September 2014, when she first experienced dyspnoea on exertion after walking one set of stairs. Symptoms progressed and on admission she reported orthopnoea as well as dyspnoea and chest pain with minimal exertion. On examination, she was well, with blood pressure 185/80 mmHg, pulse rate 77bpm, without peripheral oedema, and her jugular venous pressure was estimated at 20 cm of water. On auscultation,

lungs were clean, heart apex was not displaced, she had no evident heart murmur, but a 4th heart sound was heard. Laboratory results were, except for elevated CRP (17,5 mg/L) and NT-proBNP (873 ng/L), unremarkable. On echocardiography, a large tumour mass (4x3 cm) in the left ventricular cavity was detected (Figure). Tumour had a broad base originating from inferior and inferolateral wall, and protruded through left ventricular outflow tract (LVOT) into the aorta, causing dynamic LVOT obstruction. Additionally, pericardial effusion without tamponade criteria was present. Computerized tomography of the chest and abdomen showed progress of underlying malignant disease with multiple metastases in several organs, including heart. Given the clinical scenario the left ventricular mass was thought to be most likely consistent with a metastatic tumour. A multi-disciplinary team of cardiologist, cardiovascular surgeon, oncologist and radiologist discussed heart tumour aetiology and therapeutic options. After careful evaluation of patient status, stage of malignant disease and comorbidity, only palliative measures were advised. Within one month after first hospitalization, pericardial effusion progressed and she presented with severe dyspnoea caused by cardiac tamponade. Emergency pericardiocentesis was performed to relieve the patient symptoms, and supportive measures, including opioid analgesics were started. Patient recovered and was discharged in stable condition. 5 months after initial presentation, she has clinical symptoms and signs of heart failure with some limitations in her activities of daily living. Regular ambulatory visits are scheduled to follow pericardial effusion and tumour size.

Conclusion: Metastatic cardiac tumours are a rare cause of heart failure but should be considered in patients with malignant disease. A multidisciplinary approach to evaluate patient condition and to individually tailor therapeutic options is warranted.



Parasternal long axis view

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Tachycardia induced cardiomyopathy as first manifestation of congenital atrial septal defect

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Background: Tachycardia Induced Cardiomyopathy (TIC) is systolic left ventricular (LV) or biventricular heart failure secondary to long standing tachyarrhythmia. We describe an unusual case of reversible TIC after cardioversion of rapid atrial flutter in previously asymptomatic woman. Further investigation revealed Right Ventricular (RV) Enlargement on Transthoracic echocardiography (TTE) and significant left to right shunt on right heart catheterization (RHC). Case report: A 51 year old woman with history of hypertension and chronic hepatitis B was admitted to the hospital due to weakness and dyspnea. On physical examination she was tachypneic with bilateral leg edema. ECG tracing showed rapid atrial flutter of 140 per minute, right bundle branch block and low voltage QRS complexes. TTE showed severely reduced LV function with estimated ejection fraction (EF) of 25% , RV enlargement with severe systolic dysfunction, severe Tricuspid Regurgitation (TR), moderate pulmonary hypertension (PH) and moderate pericardial effusion without signs of tamponade. The working diagnosis at this point was possible TIC . Further workup ruled out ischemic heart disease, autoimmune myocarditis and pulmonary embolism. Treatment of acute heart failure was started with furosemide, ramipril and carvedilol. Electrical cardioversion was successfully performed after ruling out Left Atrial Thrombus by Transesophageal Echocardiography (TEE). Follow up TTE on one month revealed significant improvement of LV Function (EF 50%) and RV systolic

function but still enlarged RV, severe TR and severe PH. Due to the TTE findings at follow up visit which are not explained by TIC, a RHC was performed. The findings on RHC showed significant left to right shunt at the atrial level (Qp/Qs=1.9:1.0) and PH (mean pulmonary pressure =32mmHg) These findings suggested the diagnosis of Atrial Septal Defect(ASD) but the previous TEE that was performed before cardioversion showed intact interatrial septum. On further investigation of this shunt a Cardiac Magnetic Resonance Imaging was performed and a diagnosis of Sinus venous ASD with partial anomalous drainage of right upper pulmonary vein to superior vena cava was confirmed. The patient was sent to cardiac surgery.

Conclusion: We have described an unusual case of undiagnosed congenital heart disease that presented as acute decompensated heart failure in a middle aged woman. Despite the suspicion of heart failure caused by TIC the continued investigation of enlarged RV on follow up TTE led us to the correct diagnosis. This case showed us that the first impression is not always the right diagnosis and fully comprehensive workout should be performed when the tests do not align with the diagnosis.

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Severe course of peripartum cardiomyopathy- management and outcome

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Introduction. A 25-year-old nulliparous woman, 36 week pregnant, with no history of heart disease, was admitted to the hospital due to unspecific chest pain and dyspnea from 2 days. The patient presented symptoms of severe heart failure (HF) NYHA class III/IV, tachycardia 135 bpm, systolic apical murmur, BP 105/75mmHg and pulmonary congestion. Description of the problem. HF is a particularly dangerous condition in pregnancy. A significant cause of HF occurring at the end of pregnancy or in first months after delivery is peripartum cardiomyopathy (PPCM). The rate of recovery is very low in severe insufficiency and dilatation of left ventricle (LV). Problems and possible differential diagnosis. Differential diagnosis included different etiologies of cardiomyopathy, pulmonary embolism (PE), aorta dissection. Choosing a proper management of severe HF was crucial for the outcome. A very important step was to decide about timing and mode of delivery. Discussion. Transthoracic echocardiography (TTE) revealed dilated LV 6.3cm, LVEF 25%, significant mitral insufficiency, pulmonary hypertension, no signs of aorta dissection. NT-proBNP 4378pg/ml was observed. In a life-threatening condition cesarean section under general anesthesia in a cardiac surgery operating theatre was performed. A male healthy infant was delivered. The patient was admitted to CICU. Pharmacological treatment of HF and bromocriptine 2.5mg twice daily were introduced. Because HF exacerbated, dobutamine was introduced. CMR revealed dilated cardiomyopathy of a different than ischemic origin and severe impairment of LV and RV function. PE and aorta dissection were excluded in CT-angiography. Cardiac catheterization was performed and the patient was listed for heart transplant. Fortunately, patient's condition improved and she was admitted to cardiology ward where treatment was optimized and simvastatin 10mg was introduced. Bromocriptin in dose 2.5mg daily was continued for 10 months due to high level of serum prolactin. The patient was discharged home in 10th week in NYHA class II/III, with LVEF 32%. In 4th month postpartum thyroiditis occurred, requiring thyrostatic and prednisolone treatment. Due to increasing number of VT episodes, RF ablation was performed in 6th and 12th month with good outcome. TTE in 1 year follow-up revealed LVEDd 6cm and LVEF 54%. Conclusions. A multimodal care was crucial for a satisfactory outcome of the patient with PPCM. Treatment with bromocriptine was safely continued for a longer time, guided by serum prolactin levels. Strict ambulatory monitoring is important in case other conditions occur.

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Acute dyspnea after giving birth

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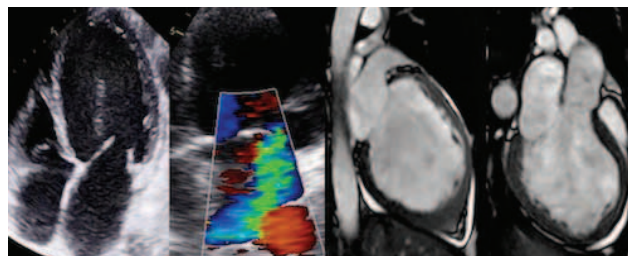
We present the case of a primiparous 37 year-old woman without known cardiovascular risk factors or family history of sudden death or premature cardiomyopathy who was referred to our Cardiology Department after presenting progressive dyspnea at rest 24 hours after an uncomplicated cesarean delivery. Pregnancy evolved normally, without evidence of elevated arterial pressure or fetal distress, and patient was previously asymptomatic developing slight fatigue and shortness of breath in the last month of gestation.

On admission in the cardiac intensive care unit, the patient had acute pulmonary edema, with significant respiratory work, bilateral crackles and a holosystolic

murmur at the apex. High flow oxygen and intravenous diuretic therapy and vasodilators were initiated with good response. The ECG showed sinus tachycardia with a narrow QRS and without significant repolarization abnormalities. Transthoracic echocardiogram revealed a severely enlarged left ventricle (LVEDD 70 mm) with severe systolic dysfunction (EF 25 %) due to generalized hypokinesia and severe functional mitral regurgitation with increased pulmonary pressures. Right ventricle had normal size and function. Cardiac MRI during hospitalization demonstrated a dilated cardiomyopathy with myocardial delayed enhancement in posterior, lateral and septal walls with a non-coronary artery distribution. No perfusion defects were observed.

Pharmacological treatment for heart failure was gradually titrated and Bromocriptine therapy was given at a dose of 2.5 mg / 2 times a day for 2 weeks followed by 2.5 mg daily for 4 weeks. Anticoagulation with low molecular weight heparin was also administered to prevent embolic events. Clinical outcome was favorable and the patient could be discharged. During over one year follow-up she remained in functional class II of NYHA classification, with chronic mild elevation of NTproBNP, and repeated imaging tests showed persistent severe ventricular dysfunction due to a highly remodeled left ventricle with little improvement despite optimal medical treatment and mild to moderate mitral regurgitation caused by valve tenting. Due to these findings, an implantable cardioverter defibrillator was recently implanted for primary prevention.

Peripartum cardiomyopathy is a fairly rare cause of heart failure associated with pregnancy and related with high mortality and morbidity. It typically presents during the third trimester of pregnancy or postpartum in women without known cardiovascular disease. Up to around a third of patients have partial or complete recovery of ventricular function during first months of follow up. However, many patients may require long term treatment of advanced heart failure. The pathophysiology of this disease is not exactly known but probably multiple mechanisms are involved including oxidative stress of prolactin. Severely dilated left ventricle and an ejection fraction below 30% are predictors of poor recovery as it was in our patient.



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Rapid onset cardiogenic shock secondary to a case of peripartum cardiomyopathy

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A 23 year old pregnant lady had initially presented to her local accident and emergency department complaining of breathlessness. She had no past medical history, was diagnosed with asthma and sent home. She reported her ongoing breathlessness to the midwife who advised the patient to come to hospital, however the patient declined.

Soon after, 35 weeks into her pregnancy she re-presented to the same hospital with worsening epigastric pain and breathlessness. On examination it was clear that she was in heart failure and her ECG showed sinus rhythm with frequent ventricular ectopics.

An echocardiogram performed at the time revealed a severely dilated left ventricle with an ejection fraction of 15%. The patient subsequently deteriorated further, requiring intensive care admission and transfer to a tertiary unit for venous-arterial extracorporeal membrane oxygenation (VA-ECMO) and caesarean section.

Investigation revealed normal coronary arteries and myocarditis screen, and she had no family history of cardiomyopathy. A diagnosis of peripartum cardiomyopathy (PPCM) was made and in addition to VA-ECMO, she was started on optimal medical heart failure therapy. Her ejection fraction remained at 5% and she ultimately died as a result of major haemorrhage and multi-organ failure. The drainage of a haemothorax, resulted in rapid mediastinal shift and dislodged her central ECMO canula.

This was an extreme case of peripartum cardiomyopathy with an especially rapid onset and rate of deterioration. Heart disease in pregnancy is becoming increasingly common and is a significant overall cause of death. Symptoms are occasionally dismissed by doctors and patients because they can be non specific and are deemed to be typical of normal pregnancy. Early detection of PPCM with an ejection fraction of greater than 30% is associated with higher survival rates and

recovery, hence promoting patient symptom awareness, and having a high index of clinical suspicion leading to prompt disease recognition/treatment can improve outcome. This case also highlights the challenges of VA ECMO as a form of organ support in these critically ill patients with bleeding being a frequently occurring and occasionally fatal complication.

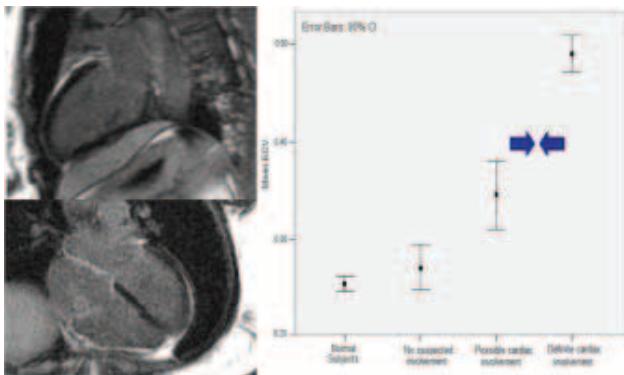
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Familial amyloid polyneuropathy: the importance of cardiac involvement

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Introduction: Cardiac involvement is frequent in familial amyloid polyneuropathy (FAP). Liver transplantation slows disease progression by removing the abnormal precursor protein, but if there is cardiac amyloid involvement, paradoxical acceleration of the disease is frequent following transplantation. The exclusion of cardiac involvement is therefore essential in FAP before liver transplantation. Current assessment of cardiac involvement uses echocardiography. Cardiac MR imaging (CMR) with gadolinium contrast administration is a candidate "gold standard", however late gadolinium enhancement can be difficult to assess in amyloidosis, particularly for the exclusion of early disease. We present a case where T1 mapping was used with ECV (extracellular volume) calculation in early cardiac amyloid detection. Case description: A 53 year-old female carrier of the FAP mutation (Transthyretin, TTR mutation G47V) was found through cascade screening. In her family, carriers had sufficiently high risk of severe neuropathy leading to death at a young age that liver transplantation was considered even in asymptomatic carriers. Accordingly, the patient was worked up for transplantation despite the absence of symptoms, and hence exclusion of cardiac involvement was necessary. Echocardiography was normal (including strain and strain rate). A new test for TTR cardiac amyloid: Tc 99m-DPD scintigraphy was of "uncertain significance" - a small amount of cardiac uptake - Perugini grade I. CMR demonstrated normal morphology, function and mass with no focal fibrosis or scar (Figure 1, left panels). T1 mapping precontrast was normal, however the calculated ECV was elevated at 0.39 (normal values 0.27±0.03) - indicating significant interstitial expansion (Figure 1: right panel). As a result, cardiac biopsy was performed which confirmed significant amyloid infiltration. Outcome: Here, early cardiac involvement was detected non-invasively using ECV mapping and confirmed by biopsy. After discussion with the patient, the difficult decision was made to proceed with liver transplantation and she is currently listed. Conclusion and implication for clinical practice: Further work on ECV calculation is likely to facilitate the early detection of cardiac involvement in amyloidosis, enabling targeted therapy to be given to potentially prevent progression to end-stage heart failure. Figure 1. Left panels: late gadolinium images showing normal myocardium with no focal fibrosis or scar. Right panel: mean extracellular volume (ECV) ± 2SD in healthy controls versus systemic AL amyloidosis patients with 3 grades of cardiac involvement by conventional testing: no suspected involvement, possible and definite involvement. Arrows show the ECV value of the patient.



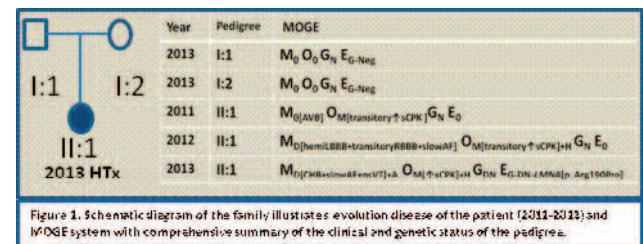
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Overlapping phenotype of cardiomyopathy associated with lamine (LMNA AIC) gene mutation

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Lamin A/C (LMNA) mutations are amongst the most important causes of dilated cardiomyopathy (DCM) associated with conduction disorders, cardiac arrhythmias and with or without discrete muscle disruption. DCM may form part of overlapping syndromes, which include arrhythmogenic right ventricular cardiomyopathy (ARVC). The most cause of ARVC is desmosomal pathology which characterized by fibro-fatty replacement and dysfunction of right ventricle (RV). ARVC may appear very similar to other mimics such as DCM have desmosomal abnormalities. We describe a case overlapping of DCM and ARVC phenotypes with mutation of Lamin A/C gene in patient with a severe cardiomyopathy affecting primarily the right side of the heart. DCM lamine phenotype manifested as follows: conduction disorders, cardiac arrhythmias, muscular disturbance and biventricular dysfunction. ARVC manifested by clinical phenotype affecting primarily the right side of the heart and atrial fibrillation (AF) with an alternating right bundle branch block (RBBB). A 23-year-old patient (pt) without a history of family DCM was admitted with progressive heart failure (HF). The clinical signs of HF associated with NYHA III developed after 17 months after her first complaints of dyspnea (electrocardiogram showed 1 degree AV-block and SVEc, echocardiography was normal). On examination, pt was asthenic thin with muscular disorders such as hypotrophy of quadriceps and gastrocnemius muscles. The pt had a slow AF with mean HR 52 bpm. Cardiac ultrasound showed dominant dilated, hypokinetic right ventricle (RV EDV 122 ml, RV ESV 74 ml, mean GS RV -8.8%, RVOT diameter 36 mm), bi-atrial dilatations (LA volume 77ml, RA vol - 190ml), a severe tricuspid insufficiency, a moderately dilated left ventricle (LV EDV 146ml, LV ESV 89ml, LVE diameter 60 mm) with LVEF of 40%. Coronary angiography revealed no visible pathologies, however cardiopulmonary exercise testing evaluated VO2 peak 15 ml/kg/min. Blood serum creatinekinase (CK) concentration was 267 U/L and brain natriuretic peptide (BNP) level was 790 pg/ml. Neurological examination revealed hypotrophy of quadriceps and calf muscles but without reducing of the limb strength. The 24 hour ECG Holter monitoring detected a slow AF (mean HR 44 bpm, max HR 69 bpm), intermittent complete heart block with HR 25 bpm, episodes of non-sustained ventricular tachycardias (VTs), polymorphic ventricular extrasystoles (VEs>400/hour). DNA mutations were detected by performing SSCP method and direct sequencing. We detected missense mutation c.569G>C in 3rd exon LMNA. Polyphen analysis predicted the Arg190Pro mutation to be possibly damaging. Signs of the laminopathy as a conduction defect (complete heart block), cardiac arrhythmias (slow AF, VTs) and skeletal muscle abnormality with increased creatine kinase level which are typical findings in cardiolaminopathy were detected in pt. However, pt had diagnostic criteria ARVC: cut-off values of ≥36 mm for diastolic RVOT diameter in the short-axis view and fatty infiltration dilated RV by MRI, but she has not a clinical ECG manifestations of ARVC, including characteristic precordial T wave inversions and presence of epsilon wave. The clinical and genetic status of this pt illustrates evolution disease is presented in Figure 1 as the schematic diagram of the MOGE(S) system classification. Conclusion. The Arg190Pro LMNA mutation causes a phenotype different from traditional cardiolaminopathy. Our findings suggest that cardiomyopathy affecting primarily the right side of the heart is not always caused by desmosomal pathology. Our observation highlight the challenges in classifying cardiomyopathies, as there often is significant overlap between the traditional categories.



MOGE representation

Moderated Poster Session 2 – Comorbidities in heart failure

Saturday 23 May 2015 13:15–14:15

Location: Poster Area

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Sympathetic activity in CHF patients with HF-PEF: does it play a role in prognosis?

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Background: Prognosis is similar in patients with chronic heart failure (CHF) either with reduced ejection fraction(HFREF) or preserved ejection fraction (HFPEF). Sympathetic activity(SA) is increased in HFREF, and associated with poorer outcomes. However, little is known about SA and prognosis in HFPEF. We aimed to study SA in both groups and evaluate the impact on prognosis.

Methods:To evaluate the impact of SA, norepinephrine (NE,pg/ml) was determined in 742 consecutive CHF patients referred to our CHF unit. Patients were followed to detect events. Analysis was performed in two categories according ejection fraction:HFPEF(LVEF≥45%) and HFREF(LVEF <45%).

Results:Baseline characteristics were:mean age 72 ± 11, 324(44%) were female, 329(44%) had HFPEF and 139(45%) were in NYHA class III-IV. Median follow-up was 15 ± 8 months, and mortality was 17%. In adjusted multivariate analysis using General Linear Model HFPEF patients had lower levels of NE compared to HFREF (485[457-515] vs 538[509-567];p-value=0.016 respectively). Adjusted cox-analysis was performed showing that high NE levels (above 70th percentile) is an independent predictor of all-cause mortality in the global cohort (OR1.7;95%[1.2-2.4];p-value:0.004). As previously described, we also found association in HFREF and mortality (OR1.9; CI[1.2-3];p-value=0.007). Interestingly, when we analysed HFPEF, although they had lower NE levels, SA was also associated with mortality (OR2;95%CI[1.1-3.5];p-value=0.018,respectively). Figure 1 shows survival in HFPEF patients according NE.

Conclusions:HFPEF is associated with lower SA compared to HFREF. However, high NE levels play a role in terms of prognosis. According to this observation, further investigation on the potential role of beta-blocker use in HFPEF should be studied.

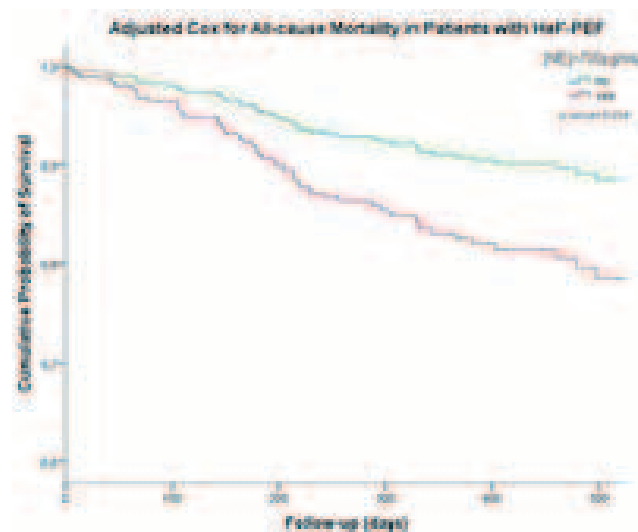


Figure 1

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Prediabetes and the outcome in chronic heart failure

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Chronic heart failure (HF) is an epidemic of the 21st century. The outcome in HF is poor, as 50% of patients do not live longer than 5 years. Prediabetes (preDM) can be described as impaired fasting glucose (IFG) or impaired glucose tolerance (IGT). The ESC/EASD guidelines states that "prediction of CV risk in people with pre-diabetes is poorly understood". The purpose of our study was to investigate the impact of preDM on mortality in HF patients.

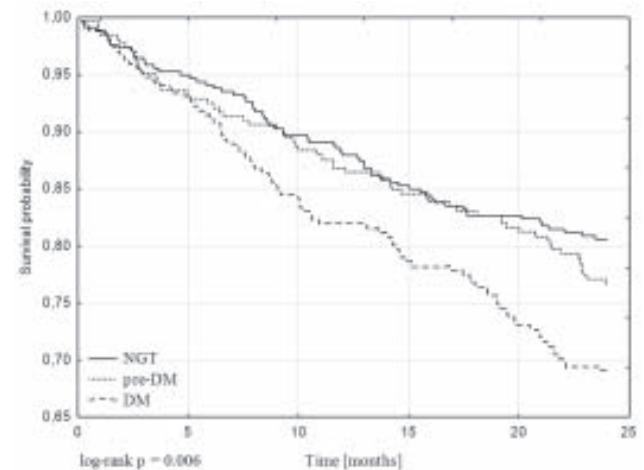
Methods: Stable HF patients were divided into 3 groups: normal glucose tolerance (NGT, the reference group), preDM and type 2 diabetes mellitus (DM). The mortality rates were compared between the groups (log-rank test). Moreover, hazard ratios (HRs) of 2-year mortality were assessed in Cox model adjusted for age, sex, BMI, etiology and duration of HF, eGFR as well as concentrations of CRP and NT-proBNP.

Results: Out of 877 patients included into the study, 271 (30.9%) had DM and 266 (20.3%) - preDM. Median age was 54 [IQR 11] years, 13.1% were female and 63.5% had ischaemic etiology of HF. Median LVEF was 23 [8]%, while NT-proBNP 1458 [2619] pg/ml. The mortality rate during 2-year follow-up was 27.3%.

2-year mortality rates for NGT, preDM and DM were 19.4%, 23.3% and 31.0%, respectively (log rank p=0.006). There were no significant difference in survival between NGT and preDM groups (p=0.27), while mortality in DM group was significantly higher in comparison to NGT or preDM (p=0.0013 and p=0.043, respectively) (Figure).

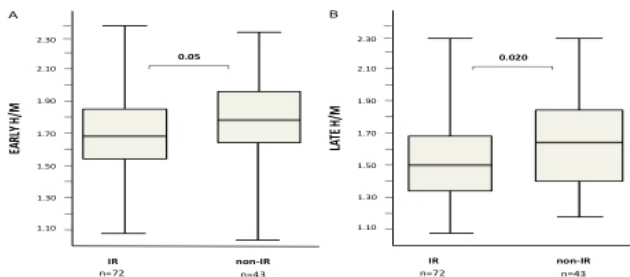
In adjusted model HRs (95% CI) for preDM and DM groups were [1.18 (0.83-1.68), p=0.37] and [1.58 (1.11-2.23), p=0.01], respectively.

Conclusions: Chronic heart failure patients with prediabetes (IFG or IGT) had similar 2-year mortality as those with normal glucose tolerance and significantly worse than diabetic patients.



Kapla-Meier curves

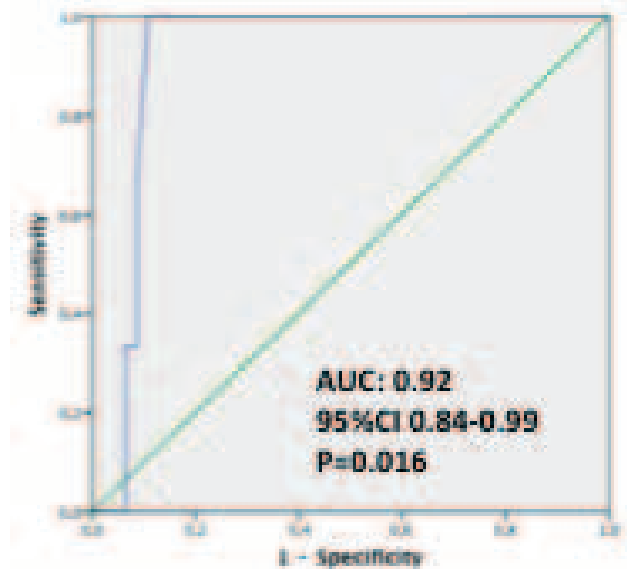
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Insulin resistance is associated with impaired cardiac sympathetic innervation in patients with heart failureS Paolillo¹; G Rengo²; T Pellegrino³; R Formisano⁴; R Carotenuto³; A Rapacciuolo¹; D Leosco⁴; B Trimarco¹; A Cuocolo³; P Perrone Filardi¹¹Department of Advanced Biomedical Sciences, Section of Cardiology, Federico II University of Naples, Naples, Italy; ²Division of Cardiology, "Salvatore Maugeri" Foundation, IRCCS, Institute of Telese Terme (BN), Italy, Naples, Italy; ³Federico II University of Naples, Department of Advanced Biomedical Sciences, Section of Imaging, Naples, Italy; ⁴Federico II University of Naples, Department of Translational Medical Sciences, Naples, Italy**Purpose:** Insulin resistance (IR) represents, at the same time, cause and consequence of heart failure (HF) and affects prognosis in HF patients, but pathophysiological mechanisms remain unclear. Hyperinsulinemia, that characterizes IR, enhances sympathetic drive and it can be hypothesized that IR is associated with impaired cardiac sympathetic innervation in HF. Yet, this hypothesis has never been investigated. Aim of the present study was to assess the relationship between IR and cardiac sympathetic innervation in non diabetic HF patients.**Methods:** One-hundred fifteen patients (87% males; 65 ± 11.3 years) with severe-to-moderate HF (left ventricular ejection fraction 32.5 ± 9.1%), underwent iodine-123 meta-iodobenzylguanidine (123I-MIBG) myocardial scintigraphy to assess sympathetic innervation and Homeostasis Model Assessment Insulin Resistance (HOMA-IR) evaluation to determine the presence of IR. From 123I-MIBG imaging early and late heart to mediastinum (H/M) ratios and washout rate were calculated.**Results:** Seventy-two (63%) patients showed IR and 43 (37%) were non-IR. Early (1.68 (IQR 1.53-1.85) vs 1.79 (IQR 1.66-1.95); p=0.05) and late H/M ratio (1.50 (IQR 1.35-1.69) vs 1.65 (IQR 1.40-1.85); p=0.020) were significantly reduced in IR compared to non-IR patients (Figure 1 A-B). Early and late H/M ratio showed significant inverse correlation with fasting insulinemia and HOMA-IR.**Conclusion:** Cardiac sympathetic innervation is more impaired in patients with IR and HF compared to matched non-IR patients. Since, reduced MIBG uptake reflects reduced pre-synaptic norepinephrine uptake due to cardiac nervous system overactivity, this observation lends mechanistic support to the independent adverse impact of IR on prognosis in patients with HF.

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Longitudinal global strain as a predictor of cardiotoxicity in breast cancer patientsA Andreia Magalhaes¹; M Menezes¹; N Cortez-Dias¹; M Saraiva²; D Silva³; AR Francisco¹; L Santos¹; P Costa¹; L Costa⁴; M Fluzza¹¹Santa Maria Hospital, Department of Cardiology, Lisbon, Portugal; ²University of Lisbon, Medical School, Lisbon, Portugal; ³Hospital Fernando Fonseca, Cardiology, Lisbon, Portugal; ⁴Santa Maria Hospital, Department of Oncology, Lisbon, Portugal**Propose:** To identify echocardiographic predictors of left ventricular dysfunction after chemotherapy (CT) in patients (pts) with breast cancer.**Methods:** Prospective study of pts diagnosed with breast cancer without structural heart disease or previous CT. Clinical and echocardiographic evaluations were performed before the start of CT and at 1, 3, 6, 9 and 12 months of follow-up. The echocardiographic assessment included the measurement of left ventricular ejection fraction (EF), tissue Doppler annular systolic velocity (S') and myocardial deformation analysis by speckle tracking. Cardiotoxicity was defined as a decline in initial EF of at least 5% to less than 55%.**Results:** 92 women, 53 ± 13 years, undergoing potentially cardiotoxic therapy (anthracycline: 77%, cyclophosphamide: 94%, trastuzumab: 31%) were studied. At baseline, mean EF was 68 ± 5%, septal and lateral S' were 7.9 ± 1.9 m/s and 9.3 ± 2.6 m/s, respectively, and longitudinal global strain was -20 ± 2%. During the median follow-up of 12 months, 16% of pts showed a decline in EF. Overall, the EF decline reach statistical significance 3 months after CT (68 ± 5% vs. 65 ± 5%;

P=0.02) and progressed to 12 months (68 ± 5% vs. 64 ± 5%; P=0.008). Cardiotoxicity was detected in 5 pts (6.8%). These pts had a lower initial EF (63 ± 4% vs. 68 ± 5%; P=0.029) and a lower initial S' velocity (7.0 ± 1.0 vs. 9.3 ± 2.6; P=0.013). The pts who developed cardiotoxicity showed a lower longitudinal global strain assessed at 3 months (-15.6 ± 0.9 vs. -19.4 ± 2.7; P=0.009). Longitudinal global strain at 3 months after CT showed high accuracy in predicting the development of cardiotoxicity (AUC 0.92 ± 0.04; P=0.016).

Conclusion: Longitudinal global strain measured 3 months after CT was a strong predictor of subsequent development of cardiotoxicity in pts with breast cancer.

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Three years of clinical experience of a cardio-oncology service in the United KingdomP Moliner-Borja¹; N Pareek²; E Mc Alindon³; R Khattar²; J Baksi²; R Sharma²; S Rosen²; AR Lyon²¹Hospital del Mar Medical Research Institute (IMIM), Heart Diseases Biomedical Research Group, Barcelona, Spain; ²NIHR Cardiovascular Biomedical Research Unit, Royal Brompton Hospital, Cardio-Oncology Service, London, United Kingdom; ³Wolverhampton Hospital NHS Trust, Wolverhampton, United Kingdom**Purpose:** Cardiac toxicity caused by cancer therapies (CTC) can result in early discontinuation of anti-cancer treatments. This is associated with a worse prognosis of these patients. CTC may be reversible with prompt diagnosis and institution of cardio-protective treatments. There has thus been an increasing demand for Cardio-Oncology services, however, there is little information about the clinical experience of these services in a real world setting.**Methods:** We evaluated baseline patient characteristics, type of cancer, anti-cancer treatment, diagnostic tests, rates and types of cardio-toxicity and medical treatments, in a cohort of 311 patients who were referred to our Cardio-Oncology Service from August 2011 to April 2014.**Results:** The mean age was 63 ± 15 years and 147 were male (47%). Pre-existing cardiovascular risk factors were common: hypertension n = 116 (37%), ischaemic heart disease n = 36 (12%) and chronic heart failure n = 25 (8%). The most common reasons for referral were risk assessment before cancer treatment (n = 130, 42%) and new LV dysfunction (n = 54 (17%). The most common cancers were breast (25%) and sarcomas (17%). The majority (214 (69%)) had potentially curative disease, whereas 97 patients (31%) had metastatic disease.

203 patients (65%) received medical therapy: anthracyclines n = 80 patients (39%), ErbB2 antagonists n = 45 (22%) or tyrosine kinase inhibitors n = 58 (29%). Echocardiographic evaluation showed LVEF 35-55% in 56 patients (31%) and LVEF < 35% in 15 patients (8%). Cardiac MRI detected late gadolinium enhancement in 30 patients (19%). BNP was raised in 149 patients (81%) whereas troponin was positive only in 10 (6%). 56 patients (28%) developed CTC, defined as a drop in LVEF because of chemotherapy. Of them, 45 patients had an established cardiomyopathy when they were referred. 34 patients developed CTC secondary to anthracyclines and 22 due to molecular targeted therapies. After the first visit in our unit, 97 patients of the chemotherapy group (48%) were treated with ACEI or ARB, the same number with

a beta-blocker, 11 patients were treated with aldosterone antagonists (5%), 43 with diuretics (21%), and 34 (18%) with statins.

Conclusions: This is the first descriptive analysis reporting the medical activity of a UK Cardio-Oncology service. We observed a higher CTC rate than reported in the literature, reflecting the referral bias of higher risk patients and high rates of established cardiomyopathy. More studies are needed to understand the clinical outcomes of these patients and the benefits in their prognosis attributed to Cardio-Oncology Units.

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Gaps in management among HFREF outpatients with diabetes mellitus

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Purpose: Heart failure (HF) is a complex syndrome with several dimensions. Turkish Research Team-HF (TREAT-HF) is a network which has been undertaking multicentric observational cohort studies in HF among HF centers. Diabetes mellitus (DM) is a frequent accompaniment of HF

Methods: Combined data from derivation and validation cohorts of TREAT-HF network were presented and patients with and without DM were compared with regard to attitudes and management.

Results: There were 585 males and 242 females in the combined cohort (n = 827). Patients with DM were older (63.6 ± 10.5 vs. 60.3 ± 14.4 years, p = 0.001) than patients without DM. Mean EF was similar in HFREF patients with and without DM (31 ± 9 vs 32 ± 9%, p = 0.353). Gender distribution was favoring female predominance among patients with DM compared to patients without DM (60/104 vs 182/480, female/male respectively, p = 0.022). Hypertension and coronary artery disease were more prevalent in patients with DM than in patients without DM (64.6% vs 21.5%, p < 0.001; 61% vs 39.4%, p < 0.001 respectively). Regular exercise is undertaken less frequently among patients with DM compared to patients without DM (11.1% vs 58.7%, p < 0.001). Furthermore, regular measurement of weight was less frequent in patients with DM compared to patients without DM (36.6% vs 52.7%, p < 0.001). Distribution of NYHA Class was also significantly different in patients with and without DM (NYHA Class I-II-III-IV, 20/62/66/9 vs 80/298/205/28, p = 0.05) along with more frequent NYHA Class III in patients with DM. With regard to management, it was noticed that, life saving therapies were less frequently utilized in patients with DM compared to patients without DM (Table 1)

Conclusion: In the TREAT-HF network, it was shown that presence of DM was associated with negatives attitudes despite more severe profile among HFREF outpatients.

Table 1: Comparison of treatment profile

	DM(+)	DM(-)	p
Beta blockers	85.5%	90.5%	0.09
ACE inhibitors (or ARB)	71.4%	77.9%	0.09
MRA	49.7%	57.9%	0.06

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Effects of minor whole body glycometabolic disturbances on myocardial glucose uptake and perfusion in patients with heart failure

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Purpose: In heart failure (HF) patients, whole body glucometabolic disturbances are associated with deranged myocardial metabolism, perfusion and a poor prognosis. Abnormalities in myocardial glucose uptake (MGU) have been described in patients with HF and overt type 2 diabetes (T2D) during a hyperinsulinemic euglycemic clamp. However, it is less clear whether minor whole body glucometabolic disturbances affect myocardial glucose uptake (MGU) and perfusion (MBF) and whether this is present during daily life. We therefore investigated MGU and MBF in patients without known T2D during an oral glucose tolerance test (OGTT).

Methods: We included 35 patients with HF (left ventricular ejection fraction (LVEF) of 34 ± 9%) and no overt T2D (IFCC < 48 mmol/mol). The patients underwent echocardiography, quantitative positron emission tomography (PET) with

measurements of baseline (rest) and adenosine stimulated myocardial perfusion (H2O-PET) and glucose uptake (FDG-PET) on two separate days. OGTT was performed during the FDG-PET to reflect daily life food intake in a standardized setup.

Results: The patients had a plasma glucose level of 5.7 ± 0.8 mM and an IFCC of 40 ± 4 mmol/mol. The average MGU was 0.18 ± 0.06 μmol/g/min and the MBF was 0.77 ± 0.16 ml/g/min at rest, 2.03 ± 0.94 ml/g/min at adenosine stress with an MBF reserve (MBFR) of 2.61 ± 1.08. Patients with a normal OGTT (N = 18) had higher MGU as compared to patients with an abnormal OGTT (N = 17) (0.20 ± 0.06 vs 0.16 ± 0.06 μmol/g/min, p = 0.05) whereas MBF (p = 0.79) and MBFR (p = 0.58) did not differ between groups. There was an inverse relation (r² = 0.24, p = 0.004) between whole body insulin resistance (measured by peak p-glucose levels during OGTT) and MGU. This association was still significant (p = 0.01) after correction for LVEF, MBF, rate pressure product and perfusable tissue index.

Conclusion: Our study shows that even minor whole body glucometabolic disturbances are associated with abnormalities in MGU but not MBF during simulated daily life conditions in HF patients. Whether these early abnormalities regarding MGU carry prognostic information and whether reversal has beneficial effects needs to be investigated in prospective studies.

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Risk factors for the occurrence and irreversibility of cardiotoxicity caused by trastuzumab therapy

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Purpose: Cardiotoxicity is the most important side effect of trastuzumab, humanized monoclonal antibody to the HER2 protein, in use for immunotherapy of breast cancer. It is mainly manifested as a reduction in left ventricular contractility without myocardial necrosis and the process is therefore mostly reversible. However, sometimes the disease can progress to irreversible dilated cardiomyopathy. So far, many risk factors explaining cardiotoxicity have been identified, but it is still unclear how to assess individual risk. Also, there are no defined factors that can predict irreversibility of the disease.

Methods: In this prospective study, we have analyzed 387 patients (pts) with non-metastatic breast cancer, treated with trastuzumab for one year with the standard adjuvant therapy protocol. Cardiotoxicity was defined with the reduction of left ventricular ejection fraction (LVEF) by 15% from the baseline or by 10% of normal values. Echocardiography was performed before the beginning and in three months period during therapy. If cardiotoxicity was established, pts were suspended from the trastuzumab therapy, with monthly echocardiography controls.

Results: Cardiotoxicity was established in 51 pts (13.17%). Multivariate analysis revealed an increased risk of cardiotoxicity in pts with the D/D genotype, a tumor of the left breast and with a positive family history of cardiovascular disease. A decreased risk of cardiotoxicity was found in patients previously treated with FEC protocol. Complete recovery of the cardiac function was found in 28 pts and they managed to finish trastuzumab protocol. Due to only partial recovery of the cardiac function or cardiotoxicity after readministration, trastuzumab therapy was not finished in 23 pts. Pts with irreversible cardiotoxicity had significantly greater reduction of LVEF (15:27 %, p < 0.0001), higher mean serum level of NT-proBNP (134.7:92.3 ng/L, p = 0.01) and in those pts trastuzumab was started earlier after prior chemotherapy (27:33.5 days, p = 0.037). Only 6 pts had symptomatic moderate or severe heart failure.

Conclusion: Pts with D/D ACE genotype, tumor of the left breast and positive family history of cardiovascular disease have a higher risk of developing cardiotoxicity with trastuzumab therapy and should be treated as high risk pts. Trastuzumab induced cardiotoxicity is more likely to be irreversible in pts with a more extensive decrease of the LVEF and a higher serum NT-proBNP level. The time between prior chemotherapy and administration of trastuzumab shorter than 30 days is more often associated with irreversible cardiac impairment.

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Body composition assessments by multi-frequency body impedance analysis (BIA) in heart failure patients

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Background: Heart Failure (HF) is a systemic disabling syndrome associated with changes in body composition, i.e. tissue wasting and development of cachexia.

While impaired body fluid distribution and congestion are well recognized by clinicians, early changes in metabolic balance and unintended weight loss are not well addressed.

Methods and Results: 29 patients (10 female) with an established diagnose of HF and on standard HF medical therapy were studied. Patients' history, physical and cardiac examination were performed at baseline (V1). Body composition was assessed at baseline (V1) and after 9 months (V2) by multi-frequency body impedance analysis (BIA). The BIA body composition assessment had been previously validated in an independent population. Functional capacity was assessed by 6-Minute walk-test (6MWT) walking distance at V1 and V2.

Body weight and BMI did not change during 9 months follow-up (V1 $83,3 \pm 12,0$ kg (Mean+SD) to V2 $83,9 \pm 12,6$ kg, $p > 0.05$ for weight and V1 $28,9 \pm 4,3$ kg/m² to V2 $29,1 \pm 4,3$ kg/m², $p > 0.05$ for BMI). By contrast adipose tissue mass increased (V1 $40,8 \pm 11,4$ to V $44,0 \pm 11,0$, $p < 0.05$, while lean tissue mass decreased (V1 $40,3 \pm 11,7$ to V2 $38,0 \pm 10,9$, $p < 0.05$). These significant changes in body composition were not observed in a control population.

Hydration status did not change (Intracellular water (ICW) V1 $20,2 \pm 4,6$ L to, $19,5 \pm 4,4$ L, extracellular water (ECW) V1 $20,2 \pm 4,6$ L to V2 $19,5 \pm 4,4$ L, and Overhydration (OH) V1 $2,0 \pm 2,8$ L to $19,1 \pm 3,9$ L, all $p > 0.05$). Interestingly, a correlation of 6MWT walking distance and Lean Tissue Mass was $R^2 = 0.41593$.

Conclusion: A significant change in body composition after 9 months was observed in patients with HF. A replacement of lean tissue by adipose tissue was observed. By contrast, global measures such as body weight and BMI did not reflect this dynamic. The observed correlation between functional capacity and body composition underscores the clinical relevance of these body composition changes. A significant increase in ATM and decrease in LTM was observed. Multi-frequency BIA may be an easy and useful tool for body composition assessment in HF patients with relevant additional clinical information.

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Careful patient selection for renal denervation warrants a positive effect on arterial stiffness and left ventricular mass

This research is funded by the European Social Fund under the Global Grant measureD Palionis¹; A Berukstis²; N Misonis²; L Ryliskyte²; J Celutkienė²; D Zakarkaitė²; K Cerlinskaite³; N Valeviciene¹; A Tamosiunas¹; A Laucevičius²

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After the sequence of Symplicity HTN trials, the impact of the procedure on lowering blood pressure (BP) and cardiovascular risk is still debatable. Our study is characterised by strict and extensive patient selection criteria for renal artery sympathetic denervation (RASD), which seem to warrant a positive effect of the procedure on BP, arterial stiffness and left ventricular mass 6 months after RASD, although it should be confirmed in larger controlled trials. We present initial results of the multimodal (applanation tonometry, echocardiography and cardiac magnetic resonance (CMR)) pilot study that aimed at carefully selecting proper patients and investigating the effects of RASD on cardiac morphology and central hemodynamic parameters in 15 patients with resistant arterial hypertension prior and 6 months after RASD. The study findings have shown significant BP decrease ($190/112 \pm 23/12$ to $153/91 \pm 18/11$ mm Hg, $p < 0.002$), decrease of the arterial markers (carotid-femoral pulse wave velocity decreased from 11.46 ± 2.92 m/s to 9.17 ± 2.28 m/s and augmentation index decreased from 25.47 ± 10.55 to 21 ± 12.19 , $p < 0.006$), significant left ventricular mass index decreased by 10% both by echocardiography (140.83 ± 38.46 to 115.26 ± 25.37 g/m², $n = 14$, $p < 0.001$) and CMR (108.32 ± 39.02 to 97.25 ± 30.06 g/m², $n = 15$, $p = 0.003$). Significant decrease of CMR retrograde flow volume in the ascending aorta non-dependent on BP was also found (8.21 ± 4.43 to 5.37 ± 3.51 ml/s, $p = 0.02$).

Rapid Fire 2 – Young rapid fire: the best of basic

Saturday 23 May 2015 14:15–15:45

Location: Agora

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MicroRNAs during inhibition of endocannabinoid signaling in cardiac remodeling

FP7-PEOPLE-2011-CIG-294278 A E Foinquinos Marin¹; J Fiedler¹; A Zimmer²; C Nozaqui²; R Geffers³; J Viereck¹; K Schimmel¹; S Batkai¹; T Thum¹

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Purpose: The endocannabinoid system is known to play a role in fibrosis, inflammation and cell death and its deregulation has been implicated in cardiovascular diseases like myocardial infarction and consequent heart failure. Although several studies suggest the cardioprotective effect of the cannabinoid receptor CB1 inhibition, the exact underlying molecular mechanism is still unknown. MicroRNAs (miRNAs) provide a complex layer of post-transcriptional regulation that modulates key biological processes such as tissue remodeling in heart failure. It can be assumed that many cardiac effects of chronic CB1 inhibition alter miRNA expression. The aim of this study is to identify the role of miRNAs in the chronic effect of CB1 receptor inhibition in cardiac fibrosis and left ventricular remodeling.

Methods and Results: Fibrosis was induced in mice by chronic administration of Angiotensin II (AngII 1,5 mg/kg/day) with osmotic minipumps for two weeks. During the AngII administration period, treatment with CB1 receptor antagonist Rimonabant, or vehicle was given every second day. Hemodynamic parameters were measured by non-invasive echocardiography and cardiac pressure volume catheter. Two weeks of AngII infusion increased systolic and diastolic pressure in all groups, and CB1 inhibition could significantly reduce pressure in end diastole. Echocardiographic parameters showed that left ventricular dysfunction induced by AngII administration was prevented by CB1 antagonist treatment. Histological assessment showed a significant reduction of fibrosis in the CB1 antagonist group, confirmed by the repression of pro-fibrotic genes like CTGF, TGF- β , α -SMA in the same group. CB1 KO mice also exhibited less fibrosis after AngII administration. To assess the role of miRNAs after CB1 inhibition, next generation deep RNA sequencing of fractionated cardiac fibroblasts was performed. Two major miRNA candidates were downregulated during AngII delivery and upregulated after CB1 antagonist treatment. Additionally, in vitro studies showed that the CB1 inhibition impairs human cardiac fibroblast proliferation and increases cardiomyocyte viability.

Conclusions: In AngII-induced cardiac remodeling, LV function is preserved by chronic CB1 antagonist treatment and cardiac fibrosis is reduced with concomitant downregulation of fibrogenic genes. Also, miRNAs are sensitive to CB1 antagonist treatment, thereby affecting cardiac fibrosis. The current study employs a novel concept regarding chronic CB1 treatment and leads to a better understanding of its anti-fibrotic mechanism of action.

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Human cardiomyocyte progenitor cells do not improve cardiac function in a porcine model of chronic ischemic heart failure

and the Netherlands CardioVascular Research Initiative (CVON) S J Sanne Johanna Jansen Of Lorkeers¹; JMIH Gho¹; S Koudstaal¹; GPJ Van Hout¹; PPM Zwetsloot¹; IE Hoefler¹; MJ Goumans²; PA Doevendans¹; JPG Sluijter¹; SAJ Chamuleau¹

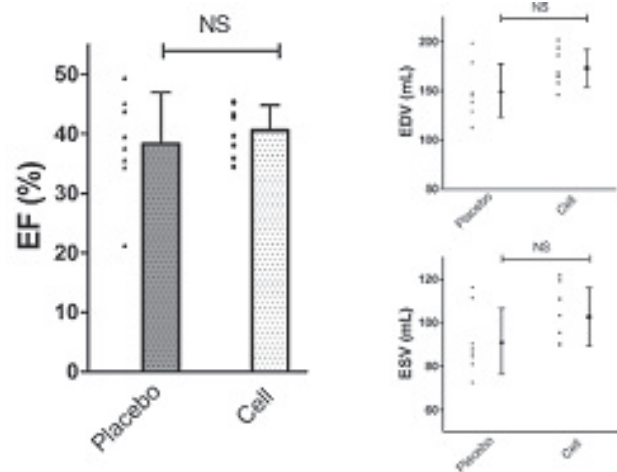
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Background: Recently cardiomyocyte progenitor cells (CMPCs) were successfully isolated from fetal and adult human hearts. Direct intramyocardial injection of human CMPCs (hCMPCs) in experimental mouse models of acute myocardial infarction significantly improved cardiac function compared to controls.

Aim: Our aim was to investigate whether intracoronary infusion of fetal hCMPCs in a pig model of chronic myocardial infarction is safe and efficacious, in view of translation purposes.

Methods & Results: We performed a randomized, blinded, placebo controlled trial. Four weeks after ischemia/reperfusion injury by 90 minutes of percutaneous left anterior descending artery occlusion, pigs (n=16, 68.5±5.4 kg) received intracoronary infusion of 10 million fetal hCMPCs or placebo. All animals were immunosuppressed by cyclosporin (CsA). Four weeks after infusion, endpoint analysis by MRI displayed no difference in left ventricular ejection fraction, left ventricular end diastolic and left ventricular end systolic volumes between both groups. (Figure) Serial pressure volume (PV)-loop and echocardiography showed no differences in functional parameters between groups at any timepoint. Infarct size at follow-up, measured by late gadolinium enhancement MRI showed no difference between groups. Intracoronary pressure and flow measurements showed no signs of coronary obstruction 30 minutes after cell infusion. No premature death occurred in cell treated animals.

Conclusion: Xenotransplantation of hCMPCs via intracoronary infusion is feasible and safe, which is important in view of translational purposes. However, no significant effect on left ventricular performance and infarct size compared to placebo was noted in this porcine model of chronic myocardial infarction.



MRI: EF, ESV and EDV at follow up

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Microarray analysis of differential mRNA expression in hearts of rats with diabetic cardiomyopathy

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Objective: Diabetic cardiomyopathy is considered one of the most common cardiovascular complications of diabetes. However, the exact molecular mechanisms are still obscure. This study was designed to investigate differential expression of mRNA extracted from myocytes of diabetic rats. Results from this study would provide more and novel clues for further studies on diabetic cardiomyopathy.

Methods: Rats were divided into control group (Ctrl), diabetic cardiomyopathy group (DbCM) and insulin treated group (ISN). Diabetes in rats was induced by streptozotocin intraperitoneal injection. In ISN, rats with diabetic cardiomyopathy received subcutaneous injection of insulin (4-8U/day) for continuous 6 weeks. Cardiac function was confirmed by ventricular intubation hemodynamic examination. In Ctrl and DbCM, rats received saline sc injection. Agilent Whole Genome Oligo Array

was utilized to analyze mRNA differential expressions in heart samples. Results of microarray were validated by real-time PCR.

Results: 1510 mRNAs were found up-regulated while 1657 mRNAs were found down-regulated in DbCM compared with Ctrl; 775 mRNAs were found up-regulated while 614 mRNAs were found down-regulated in ISN compared with DbCM. Notably, genes including WDNM1 homolog, Sln (sarcolipin), Nppa (natriuretic peptide precursor A), Mybphl (myosin binding protein H-like), Hamp (hepcidin antimicrobial peptide), Myl7 (myosin light chain 7), Upk1b (uroplakin 1B), Msln (mesothelin) were found up-regulated in DbCM but correspondingly down-regulated after insulin treatment in ISN. Pathway analysis showed that pathways including PPAR, histidine metabolism, calcium and PI3K-Akt signaling pathways were possibly involved in DbCM. These changes were validated by RT-PCR.

Conclusion: The mRNA differential expression profiling could provide basis for further investigation of mechanisms of DbCM.

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Diastolic adaptation as a central mechanism in the myocardial response to acute haemodynamic overload

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Introduction: Myocardial stretch causes an immediate (Frank-Starling response) and a delayed (slow force response) increase in contractility in order to adapt cardiac output to acute haemodynamic overload. On the other hand, diastolic adaptation and optimization of cardiac filling under these conditions has not been described yet.

Aims: To assess the diastolic response to myocardial stretch in the rodent heart and isolated cardiomyocytes, and in the in vivo human heart.

Methods: Isolated rat hearts (n=9, 300 bpm, 37°C) were perfused at constant pressure according to the Langendorff technique and acutely stretched from 3 to 10mmHg by a balloon inserted into the left ventricle (LV). Pressures were recorded over 15 minutes. Force measurements in single skinned cardiomyocytes from control (n=4) and stretched (n=4) LV were performed and passive tension was measured at sarcomere lengths (SL) ranging between 1.8µm to 2.3µm. A catheter was inserted through the aortotomy of patients submitted to cardiac surgery (n=7). After the surgery and during a period of hemodynamic stability, LV pressure and volume were recorded immediately before and 15 minutes after volume overload and Trendelenburg positioning. Statistical significance was set at p < 0.05.

Results: In isolated hearts, diastolic pressure decreased 43.3 ± 2.4% after 15 minutes of stretch. Passive tension of permeabilized cardiomyocytes was significantly lower in the previously stretched group for all SL (N.m-2): 1.8 ± 0.2 vs 6.2 ± 0.6; 2.1 ± 0.1 vs 6.6 ± 1.0; 2.8 ± 0.4 vs 6.7 ± 1.2; 3.4 ± 0.4 vs 8.6 ± 1.5; 4.1 ± 0.4 vs 10.0 ± 1.8; 6.5 ± 1.3 vs 15.0 ± 1.5. In the in vivo human hearts, there was an increase of the end-diastolic pressure (EDP) from 12 ± 3 to 18 ± 3 mmHg after the increase of the end-diastolic volume (EDV) from 182 ± 32 to 205 ± 32 mL, and a subsequent drop of the EDP, after 15 minutes of adaptation, to 12 ± 4 mmHg, whereas the EDV did not decrease significantly (187 ± 30 mL).

Conclusion: Our results showcase a new mechanism of diastolic adaptation, which consists of an acute decrease in LV stiffness after stretch. This mechanism was also observed in the in vivo human heart and is preserved at the myofibrillar level. This original description identifies a new element central to the cardiac response to haemodynamic overload.

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Primary skeletal myoblasts from chronic heart failure patients exhibit a reduced proliferation capacity and a disturbed adiponectin pathway

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Purpose: Alterations of skeletal muscle, including impaired muscle energy metabolism are common in chronic heart failure (CHF). Recently, we demonstrated that CHF patients have a functional adiponectin resistance at the level of the skeletal muscle. Increased levels of circulating adiponectin have been documented in CHF patients and are linked to poor prognosis. Consequently, primary skeletal muscle myoblasts cultures from CHF patients are an attractive tool for investigating the underlying mechanisms of adiponectin resistance in vitro.

Methods: Myoblasts cultures were initiated from satellite cells isolated from a biopsy of the skeletal muscle (m. vastus lateralis) of 8 CHF patients and 8 healthy subjects. Dynamic high-resolution assessments of CHF myoblast proliferation were performed using the xCELLigence live cell analysis system. mRNA expression levels of adiponectin, the adiponectin receptor AdipoR1 and downstream adiponectin-related genes were quantified by RT-PCR.

Results: Myoblasts from CHF patients demonstrate a reduced proliferation capacity compared to myoblasts from age- and gender-matched healthy donors (p=0.032). Adiponectin expression was increased in CHF cultures (38.51 ± 1.14 versus 40.12 ± 1.24), whereas AdipoR1 was downregulated (p=0.051). In addition, downstream-located genes involved in lipid (PPAR) and glucose metabolism (AMPK) and their target genes ACADM and Hexokinase 2, respectively, were reduced in CHF muscle cells compared to healthy cultures. Immunohistochemical staining confirmed the presence of adiponectin in skeletal muscle myoblasts from CHF patients.

Conclusion: Primary CHF myoblast cultures demonstrated a decreased proliferative capacity in comparison to healthy cultures. The features of adiponectin resistance were preserved in vitro. Therefore, CHF myoblast cultures might allow further in vitro exploration of adiponectin resistance and underlying mechanisms of muscle wasting in CHF.

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Decreased mitochondrial respiration and increased fractional ROS production in Stat3-deficient mice with peripartum cardiomyopathy

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Purpose: In peripartum cardiomyopathy (PPCM), expression of signal transducer and activator of transcription 3 (STAT3) is reduced, and cardiomyocyte-restricted deletion of STAT3 (STAT3-CKO) predisposes to PPCM. As a key upstream event, expression of the mitochondrial superoxide dismutase (Mn-SOD) was reduced and formation of reactive oxygen species (ROS) increased in STAT3-CKO mice. This leads to cathepsin D-mediated cleavage of the protective 21kDa prolactin to a maladaptive 16kDa cleavage product. Reducing the production of (21kDa and thus, 16kDa) prolactin with bromocriptin prevents PPCM in STAT3-CKO mice. Due to its causative role in disease development, we analyzed mitochondrial function and ROS production in PPCM.

Methods: Mitochondrial respiration (Clark-electrode), O₂-EPR spin-trap and H₂O₂ formation (Amplex Red) were determined in the absence and presence of ADP (30 µM - 1 mM) from hearts of STAT3-CKO and wild-type mice (WT) without (nullipara; WT: n=6; STAT3-CKO, n=6) or after 2 pregnancies (peripartum; PP; WT: n=9; STAT3-CKO: n=7), respectively.

Results: In mitochondria from nullipara mice, no differences in respiration, O₂-formation or H₂O₂ emission occurred. In PP mice, however, ADP-induced respiration was reduced in STAT3-CKO compared to WT mice (p < 0.05) at 30 and 100 µM ADP, respectively. Under state 4 conditions, mitochondrial O₂-formation was higher in STAT3-CKO than in WT (p < 0.05) and tended to be higher during state 3 (100 µM ADP). In contrast, H₂O₂ emission was reduced during state 4 and 3 in STAT3-CKO mitochondria, respectively. Accordingly, the ratio of H₂O₂ per O₂- was decreased in PP STAT3-CKO compared to WT (p < 0.05), indicating decreased Mn-SOD activity. As a consequence, the ratio of O₂- formation per O₂ consumption was increased in mitochondria from PP STAT3-CKO versus WT (p < 0.05), indicating increased fractional O₂- formation. Despite reduced net H₂O₂ emission in PP STAT3-CKO mice, the fractional emission of H₂O₂ per O₂ consumption was increased in PP STAT3-CKO vs. WT (p < 0.05). Preliminary data (n=1-2) indicate a restoring effect of bromocriptin on defective mitochondrial respiration and MnSOD activity.

Conclusions: We conclude that in STAT3-CKO mice with PPCM, decreased Mn-SOD activity increases the fractional O₂- formation in mitochondria, deteriorating ETC function and respiratory capacity. At the same time, increased fractional H₂O₂ emission from mitochondria may induce cellular oxidative stress. Consequently, drugs that reduce mitochondrial ROS formation may be useful for the treatment of PPCM in addition to the protective actions of bromocriptin.

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Ischaemic accumulation of succinate controls reperfusion injury through mitochondrial ROS

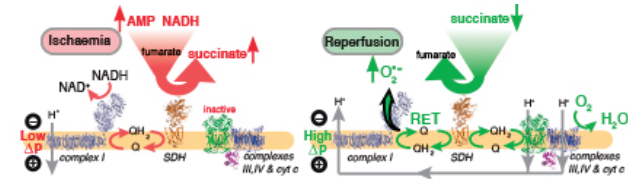
Medical Research Council (UK), Canadian Institutes of Health Research, Gates Cambridge Trust, and the British Heart Foundation E Edward Chouchani¹; V Pell¹; E Gaude¹; D Aksentijevic²; S Sundier³; M Duchon³; M Shattock²; C Frezza¹; T Krieg¹; M Murphy⁴

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Purpose: Ischaemia-reperfusion (IR) injury occurs when blood supply to an organ is disrupted and then restored, and underlies heart attack and stroke. While reperfusion of ischaemic tissue is essential for survival, it also initiates oxidative damage and cell death through generation of mitochondrial reactive oxygen species (mtROS). Although mtROS production in IR is established, it is considered a non-specific response to reperfusion. Here, we applied in vivo metabolomics to determine whether distinct metabolic pathways could instead control mitochondrial ROS during IR.

Methods & Results: We applied a comparative metabolomics method in five in vivo tissue models to identify metabolic signatures that were both distinct to ischaemia and common across many tissue types. We unexpectedly identified selective accumulation of the citric acid cycle intermediate succinate as a universal metabolic signature of ischaemia in a range of tissues which is responsible for mtROS production during reperfusion. We show ischaemic succinate accumulation arises from reversal of succinate dehydrogenase (SDH). Upon reperfusion, the accumulated succinate is rapidly re-oxidised by SDH, driving extensive ROS generation by reverse electron transport at mitochondrial complex I. Decreasing ischaemic succinate accumulation by pharmacological inhibition is sufficient to ameliorate in vivo IR injury in murine models of heart attack and stroke.

Conclusions: We have identified a conserved metabolic response of tissues to ischaemia and reperfusion that reveals a novel pathway for metabolic control of ROS production in vivo, while demonstrating that inhibition of ischaemic succinate accumulation and its oxidation upon subsequent reperfusion is a potential therapeutic target to decrease IR injury in a range of pathologies.



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The soluble guanylate cyclase activator cinaciguat inhibits pressure overload-induced cardiac hypertrophy

Hungarian Scientific Research Fund (OTKA 105555) to B.M.B.T. Nemeth¹; C. Matyas¹; A. Olah¹; L. Hidi¹; M. Ruppert¹; A. Lux¹; D. Kellermayer¹; G. Merkely¹; B. Merkely¹; T. Radovits¹

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Purpose: Pathological cardiac hypertrophy is observed in pressure overload of the left ventricle. Elevated intracellular cGMP-levels have been reported to prevent the development of pathological myocardial hypertrophy. We investigated the effects of chronic activation of the cGMP producing enzyme, soluble guanylate cyclase (sGC) by cinaciguat in a rat model of pressure overload-induced cardiac hypertrophy.

Methods: We performed aortic banding (AB) to evoke pressure overload-induced cardiac hypertrophy in our rats. Sham operated animals served as controls. Experimental and control groups were treated with 10 mg/kg/day cinaciguat (Cin) or placebo (Co) p.o., respectively. Development of cardiac hypertrophy was investigated by echocardiography. We performed left ventricular (LV) pressure-volume analysis with a pressure-conductance microcatheter to assess cardiac function. In addition to our functional experiments, histological and molecular biological measurements were carried out.

Results: Echocardiography showed marked myocardial hypertrophy in the AB-Co group following 6 weeks of pressure overload of the heart (left ventricular mass index [LVMI]: 3.15 ± 0.09 AB-Co vs. 2.09 ± 0.05g/bwkg Sham-Co) which was verified by post mortem investigation of the hearts (heart weight/tibial length ratio [HW/TL]: 38.4 ± 1.5 AB-Co vs. 29.3 ± 0.8mg/mm Sham-Co) and by histology (cardiomyocyte diameter [CD]: 17.37 ± 0.04 AB-Co vs. 14.55 ± 0.12µm Sham-Co). Increased left ventricular dimensions (left ventricular end-diastolic volume: 414 ± 19 AB-Co vs. 341 ± 19µl Sham-Co) were observed while ejection fraction and fractional shortening remained unchanged. Cinaciguat did not alter blood pressure (183 ± 7 AB-Co vs. 177 ± 5mmHg AB-Cin, p = n.s.) but effectively attenuated left ventricular hypertrophy (LVMI: 2.57 ± 0.06g/bwkg, HW/TL: 33.5 ± 0.9mg/mm, CD: 15.08 ± 0.10µm, p < 0.05 vs. AB-Co), and normalized the maladaptive increase in contractility (end-systolic pressure-volume relationship [ESPVR]: 1.000 ± 0.057 Sham-Co, 1.232 ± 0.049 AB-Co vs. 0.969 ± 0.073mmHg/ml AB-Cin, p < 0.05) following AB.

Conclusions: Our results demonstrate that chronic stimulation of the NO-cGMP signaling pathway by pharmacological activation of the soluble guanylate cyclase might be a novel therapeutic approach in the prevention of pathological myocardial hypertrophy.

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Development of therapeutic and preventative strategies for takotsubo syndrome

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Takotsubo syndrome (TTS) is an acute heart failure characterised by a hypokinetic apical myocardium coupled to a hyperkinetic basal myocardium. First reported in 1990, little is known about its pathophysiology, and even less about possible treatments. We investigated possible mitigating and exacerbating factors for TTS, either as pre-treatments or post-treatments. Those found to be useful as a pre-treatment could guide research into preventing recurrent TTS; therapies that reduce the heart failure once established can guide research into alternatives to the current treatment for TTS that causes cardiogenic shock (i.e. ECMO). Previously we have reported that levosimendan can reduce apical dysfunction, as can PTX pre-treatment.

We used two rat models of TTS: epinephrine (4.3x10⁻⁷mol/kg) IV bolus (isoflurane anaesthesia) to produce apical hypokinesia within 20 minutes that resolves within 60 minutes; and isoprenaline (50mg/kg) IP injection (ketamine/midazolam anaesthesia) that produces apical hypokinesia within 90 minutes and resolves over a matter of days. We have investigated the effects of sex, ovariectomy (along with hormone replacement) and anaesthesia on TTS.

Epinephrine model: compared to males, females had a significantly reduced mortality rate (6.25% vs. 46%, p < 0.01) and did not show apical dysfunction; ovariectomised rats had a very high mortality rate (75%), both through acute VF and cardiac failure. 2-week estradiol therapy (238ug/day) significantly reduced mortality (10%, p < 0.001). Isoprenaline model: we found that anaesthesia with isoflurane instead of ket/mid completely inhibited apical dysfunction, which was ordinarily very reproducible under ket/mid anaesthesia. Treatment with isoflurane after induction of TTS resulted in some mortality through acute cardiac decompensation. A subset of rats were injected with isoprenaline while conscious and imaged 3 hours later: these showed a reduced level of apical dysfunction.

Our data agrees with published data that isoflurane pretreatment can prevent apical dysfunction: this did not translate into isoflurane being a potential therapy as it worsened the heart failure. Further research is needed to establish why this occurs and we caution the use of isoflurane in acute TTS patients. Ketamine/midazolam anaesthesia appears to potentiate TTS induction, which may allude to the induction pathway: We hypothesise that ketamine could potentiate the effect of the exogenous catecholamine. Estrogen, lost in post-menopausal women (the primary TTS patient), and isoflurane may play a critical role in dampening the initial response to catecholamines.

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Modulation of survivin reverses cardiac and pulmonary remodeling in monocrotaline-induced pulmonary arterial hypertension

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Purpose: Cardiac and lung expression of the inhibitor of apoptosis survivin and its inhibitor smac was characterized in the progression of monocrotaline(MCT)-induced pulmonary arterial hypertension(PAH). The effects of survivin antagonist terameprocol(TMP) were assessed, both in vitro and in vivo.

Methods I: adult male Wistar rats received a subcutaneous injection of MCT(60mg/Kg) or equal volume of vehicle. On days 1,3,7,14 and 21 after injection (n=7-12), right ventricular(RV) pressures were measured, heart and lungs were weighted and collected for histological analysis, immunohistochemistry and western blot. II: adult male Wistar rats injected with MCT were treated with TMP (166 mg/Kg,ip;MCT-TMP, n=7) or vehicle (MCT-V,n=9) on days 7, 12 and 17 after injection and compared with a SHAM group (n=7). On day 21, RV pressure and cardiac output were measured and heart and lungs were weighted and collected for histology. III: Primary cultures of pulmonary artery smooth muscle cells(PASMC) were obtained from sham and MCT rats (day 21) in order to assess the effects of TMP in proliferation and apoptosis.

Results: Survivin upregulation and smac downregulation were present since day 7 after MCT injection and preceded the hemodynamic manifestations of PAH. Increases in RV systolic pressure, dP/dtmax and dP/dtmin were only present since day 14. In vivo, TMP treatment reduced RV hypertrophy and pulmonary arterial wall thickness, decreased RV systolic pressure, dP/dtmax and dP/dtmin and normalized cardiac output. TMP inhibited proliferation and induced apoptosis of PASMC in a dose-dependent manner (Fig 1).

Conclusions: Our findings suggest that survivin has a role in PAH. TMP could be an effective and selective therapeutic strategy for PAH by reversing cardiac and pulmonary remodeling and improving hemodynamic features.

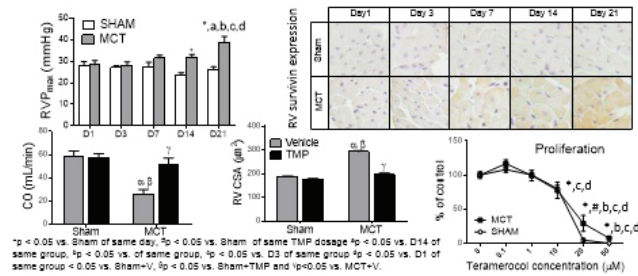


Fig 1 - Results

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Pharmacological inhibition of galectin-3 and aldosterone pathways prevents isoproterenol-induced left ventricular dysfunction and fibrosis in miceG Giuseppe Vergaro¹; M Prud'homme²; R Merval²; C Passino¹; M Emdin¹; JL Samuel²; A Cohen Solal²; C Delcayre²¹Gabriele Monasterio Foundation, Pisa, Italy; ²Inserm UMR-S 942, Paris, France

Background: Galectin-3 (Gal-3) is involved in cardiac inflammation, fibrogenesis and remodeling. Previous evidences show that Gal-3 interacts with aldosterone in promoting macrophage infiltration and vascular fibrosis, and that Gal-3 genetic and pharmacological inhibition prevents cardiac remodeling in a pressure overload heart failure (HF) model. We aimed to test the effect of selective inhibitors of either Gal-3 (modified citrus pectin, MCP) or aldosterone (canrenoate) on left ventricular (LV) function in a HF murine model.

Methods: Thirty-two 3-5 month old male mice with cardiac specific hyperaldosteronism (AS mice) underwent isoproterenol subcutaneous injections, and were then randomized to receive placebo, MCP, canrenoate or MCP+canrenoate for 14 days (n=8 for each group).

Results: Isoproterenol induced a rapid and persistent decrease in left ventricular fractional shortening in placebo-treated mice (-20% at day 14), that was markedly improved (p < 0.001 vs placebo) by treatment with MCP or canrenoate. MCP and canrenoate also reduced the extent of cardiac hypertrophy and fibrosis, as well as the expression of genes involved in fibrogenesis (Coll-I and Coll-III) and macrophage infiltration (CD-68 and MCP-1). Gal-3 gene expression (p < 0.05 vs placebo) and protein level (-34% and -52% vs placebo) were blunted by both MCP and canrenoate. Combined treatment with Gal-3 and aldosterone antagonists resulted in additive effects compared to MCP or canrenoate alone on cardiac hypertrophy, fibrosis, LV dysfunction and on Gal-3 protein level.

Conclusions: Gal-3 participates to the mechanisms of aldosterone-mediated myocardial damage in a HF murine model with cardiac hyperaldosteronism. Inhibition of Gal-3 and aldosterone can reverse isoproterenol-induced LV dysfunction, by reducing myocardial inflammation and fibrogenesis. Gal-3 inhibition may represent a new promising therapeutic option in heart failure.

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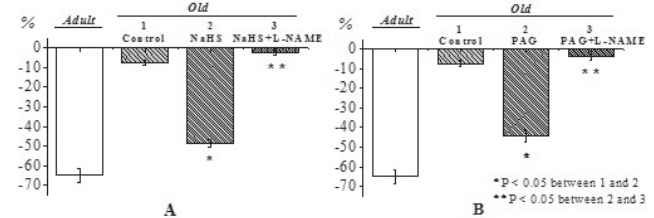
Modulators of hydrogen sulfide restore endothelium-dependent relaxation of aortic smooth muscles in old ratsK Konstantin Drachuk¹; A Kotsjura¹; V Sagach¹¹Bogomoletz Institute of Physiology, Kiev, Ukraine

Background and Purpose: The age-associated reduction of nitric oxide (NO) bioavailability results in impairment of the endothelium-dependent relaxation of smooth muscles, which leads to cardiovascular diseases such as arterial hypertension, atherosclerosis, diabetic angiopathy, etc.

Experimental approach: We studied the effects of hydrogen sulfide donor (NaHS) and an inhibitor of cystathionine-gamma-lyase-dependent pathway of H₂S synthesis (propargylglycine, PAG) on acetylcholine (ACh)-induced relaxation of aortic smooth muscles (SM) in old rats.

Results: The experiments on isolated aortic segments from the old rats have shown that the effect of ACh, endothelium-dependent vasodilator, results in less pronounced relaxation of aortic SM (7.5% ± 1.4%), comparing with adult ones (64.9% ± 3.5%). Joint action of the donor and inhibitor resulted in growing of aortic SM relaxation up to 48.8% ± 1.9% (Figure 1, A) and 44.5% ± 3.2% (Figure 1, B) after NaHS and PAG addition, respectively. Those effects of NaHS and PAG were removed by blocking NO synthesis in endothelium (by adding L-NAME) (Figure 1, A, B). In biochemical experiments, NaHS increased both H₂S and NO₂⁻ pools, and the activity of cNOS in the heart tissue and in the blood plasma of adult rats. PAG in the heart mitochondria evoked paradoxical changes in the biochemical indicators. In particular, H₂S and NO₂⁻ pools were shown to be increased, rather than decreased, by more than 112% and 162% (according to baseline) respectively. An addition of PAG resulted also in growing activity of cNOS (almost triples).

Conclusions: Thus, the data obtained indicate that NaHS and PAG may contribute to restoration of endothelium-dependent aortic SM relaxation of old animals via H₂S and NO synthesis stimulation.



Changes in ACh-induced SM vasorelaxation

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Titin A-band truncation in mice causes stress-induced dilated cardiomyopathyI G Lunde¹; H Wakimoto¹; MA Burke¹; V Soukoulis¹; WA Linke²; J Gorham¹; D Conner¹; G Christensen³; JG Seidman¹; CE Seidman¹¹Harvard Medical School, Department of Genetics, Boston, United States of America; ²Ruhr University Bochum (RUB), Bochum, Germany; ³Institute for Experimental Medical Research, Ullevaal University Hospital, Oslo, Norway

Purpose: Approximately 20% of dilated cardiomyopathy (DCM) patients carry heterozygous truncating mutations in the giant protein titin (TTNΔ). Titin spans the cardiomyocyte sarcomere from Z-disc to M-line and is important for assembly, contraction, relaxation and signaling. Truncating mutations are overrepresented in A-band. To study disease mechanisms, we developed a mouse with titin A-band truncation (TTNΔA) and assessed cardiac morphology, function, and transcriptional profile.

Results: To generate TTNΔA mice we introduced lox-P sites flanking exons 276-277 and crossed with Ella-Cre mice, causing a frameshift and premature stop codon in the proximal A-band. 28 heterozygous intercrosses produced 120 pups: none were homozygous TTNΔA (p = 6*10⁻¹⁰-10). Genotyping (n = 125) revealed homozygous embryos at E8.5-E10.5, with fetal demise at E10.5. Heterozygous male and female mice (age 6-60 weeks) were viable, fertile and not different from wildtype (WT) in appearance, activity, or echocardiographic phenotype. Digital PCR of RNA from TTNΔA hearts (n=3) showed mutant transcripts levels 0.4-fold that of WT allele, and gels and immunoblots detected no mutant titin protein. TTNΔA and WT mice (n = 5-6 per study) were stressed for ten weeks by voluntary cage-wheel running and two weeks of isoproterenol infusion, evoking no difference in echocardiographic phenotypes. Compound TTNΔA/LMNA mutation mice showed no exacerbation of DCM compared to LMNA mice (LVIDd 4.02mm vs. 3.97mm, both p < 0.05 vs. WT). By contrast, TTNΔA mice treated for two weeks of ANGII infusion showed hypertrophy with exacerbated diastolic dysfunction (longitudinal strain rate 12.3s⁻¹ vs. WT: 9.6s⁻¹, p < 0.05) and 3.8-fold higher BNP mRNA. Thoracic aortic constriction (TAC) exacerbated DCM in TTNΔA: LVIDd at 1 week 3.75mm vs. 3.38mm in WT (p < 0.05) and at 4 weeks 4.36mm vs. 3.77mm (p < 0.05). TAC increased left atrial diameter, lung weight and BNP in TTNΔA vs. WT. RNAseq (n=3) analyses of TAC and ANGII treated TTNΔA vs. WT confirmed reduced TTN transcripts and showed differential expression (fold change >1.5/<0.67, p < 0.001) of 1465 and 1434 transcripts. Pathway analyses implicated TGFβ as upstream regulator and identified the cardiotoxic categories hypertrophy, cell death, infarction, dilation and damage.

Conclusions: Transcripts encoding a titin A-band truncation are expressed but do not yield detectable mutant protein. Homozygous mice are embryonic lethal, while heterozygous mice have no overt cardiac phenotype, and tolerate chronotropic stress. Increased afterload induces DCM in titin A-band truncation mice and promotes expression of cardiotoxic pathways.

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Osteoglycin increases cardiac inflammation by enhancing toll-like receptor 4 activation.M Marieke Rienks¹; A Papageorgiou¹; D Westermann²; W Verhesen¹; R Leeuwen Van¹; G Summer¹; P Carai³; S Heymans¹¹Maastricht University, CARIM, Department of Cardiology, Maastricht, Netherlands;²Charite - Campus Benjamin Franklin, Cardiology & Pneumology, Centrum 11³Cardiovascular Medicine, Berlin, Germany; ³Catholic University of Louvain (UCL), Molecular and Vascular Biology, Department of Cardiovascular Sciences, Leuven, Belgium

Background: Because Toll-Like Receptors (TLRs) are considered as an important link between innate immunity, inflammation and cardiovascular disease, new therapeutic strategies modulating TLR activation are evolving. Full

understanding of their complexity and the many identified endogenous ligands however, remains key for the development of new effective drugs. While extracellular matrix components have been identified as potential endogenous TLR-ligands, the role of osteoglycin (OGN) in innate immunity and inflammation is currently unknown.

Methods and Results: Treatment of murine protein lysates with various enzymes allowed us to identify differential OGN glycosylation depending on the key underlying pathophysiological process. While OGN-dermatan sulfate was found in relation to murine and human cardiac fibrosis, OGN-chondroitin sulfate-dimer was found in relation to murine and human cardiac inflammation. Indeed, cell fractionation and co-immunoprecipitation revealed the interaction of the OGN-dimer with TLR4 in both murine and human leukocytes. Furthermore, liposaccharide stimulation of HEK-Blue™-mTLR4 cells (knock-down versus control) and bone-marrow-derived-macrophages (wild-type (WT) versus knock-out (KO)) demonstrated significantly more cytokine production and secretion in the presence of OGN as a consequence of increased MAPKs phosphorylation. This enhanced immune-activation was confirmed in a murine endotoxin-shock-model and resulted in significantly more cardiac inflammation upon CVB3-induced murine viral myocarditis in OGN WT mice ($7.56 \pm 1.78\%$ in WT versus $1.58 \pm 0.43\%$ in KO). Finally, magnetic Dynabead isolation allowed us to identify a clear OGN-positive leukocyte population in human buffy coats with a very distinct pro-inflammatory phenotype.

Conclusion: The newly discovered role for OGN in TLR4 activation could be of great interest for identifying or dampening exaggerated immune responses in heart disease, thereby prohibiting the development of heart failure.

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Alterations promoted by epicardial adipokines in cardiac structure

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¹Faculty of Medicine University of Porto, Department of Physiology and Cardiothoracic Surgery, Porto, Portugal

Introduction: Heart failure is a condition with increasing prevalence in developed countries and is associated with obesity. Adipose tissue is now considered an 'endocrine organ' that secretes numerous bioactive peptides, termed adipokines. In obesity, due to adipocyte hypertrophy and dysfunction, there is an increased secretion of proinflammatory adipokines. These adipokines produced by epicardial adipose tissue can act in a paracrine manner directly on the myocardium and influence their structure and function. In this work we aim to evaluate the changes in cardiac structure caused by adipokines secreted by the epicardial adipose tissue of obese rats.

Methods: Epicardial adipose tissue of 25-weeks-old lean and obese ZSF1 rats was collected for adipokines' expression and adipocytes cross-sectional area assessment as well as for a 24h DMEM incubation to acquire conditioned medium. Subsequently, organotypic cultures were prepared from 7 day-old Wistar Kyoto cardiac explants and incubated for 24h with the conditioned media previously obtained from both groups. After incubation, cross-section area of cardiomyocytes and fibrosis were evaluated.

Results: The histological and molecular studies of epicardial adipose tissue revealed hypertrophy of adipocytes in obese animals ($1505 \pm 80.01 \mu\text{m}^2$ vs $7595 \pm 265.5 \mu\text{m}^2$, $p < 0.0001$), as well as a significantly increase in expression of several adipokines. Among these overexpressed adipokines are visfatin (0.42 ± 0.18 AU vs 1.4 ± 0.33 AU, $p < 0.05$), leptin (0.12 ± 0.032 AU vs 0.93 ± 0.18 AU, $p < 0.0001$), apelin (0.08 ± 0.03 AU vs 0.24 ± 0.04 AU, $p < 0.05$) and chemerin (0.33 ± 0.096 AU vs 0.90 ± 0.16 AU, $p < 0.05$) that are involved in fibrosis and hypertrophic pathways. In organotypic cultures, conditioned media from obese ZSF1 epicardial adipose tissue triggered a significant increase in the cross-sectional area of cardiomyocytes ($100.7 \pm 18.98 \mu\text{m}^2$ vs $111.25 \pm 24.02 \mu\text{m}^2$, $p < 0.05$) and in fibrosis ($3.48\% \pm 1.51\%$ vs $4.79 \pm 1.53\%$, $p < 0.05$) compared to the conditioned medium from lean rats ZSF1.

Conclusions: Adipokines produced by epicardial adipose tissue of obese animals appear to impact myocardial structure by inducing collagen deposition and promoting cardiomyocyte hypertrophy.

Clinical Case 2 – Thousands of reasons of a very big heart

Saturday 23 May 2015 16:00–17:30

Location: Agora

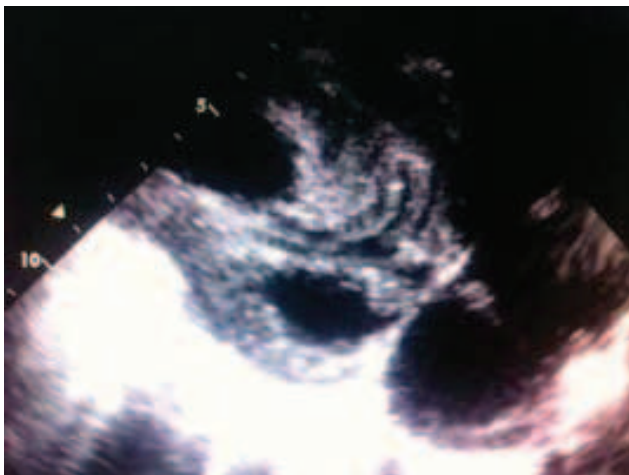
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An unusual aspect of hypertrophic cardiomyopathy

N Mouine¹; F Oussibla¹; R Amri¹; M Cherti¹

¹ mohamed V university souissi, cardiology B department, rabat, Morocco

Left ventricular hypertrophic cardiomyopathy is a rare congenital cardiomyopathy that affects both children and adults. We report a 13 year old girl, with Noonan syndrome, admitted for effort dyspnea, clinical examination showed ejectional systolic murmur in aortic area. Transthoracic echocardiography showed atypical aspect of hypertrophic cardiomyopathy with a large spiral recessus of infero septal and inferior wall of left ventricle, she was previewed for septal myectomy but she died few days after diagnosis



a spiral aspect of infero septal wall

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Heart failure caused by restrictive cardiomyopathy. Role of integrated diagnostics for the etiologic diagnosis

CL Lanzillo Chiara¹; CC Commisso Cosimo¹; FC Summaria Francesco¹; LFM Lauri Francesco Maria²; SE Salustri Elisa²; LC Calo' Leonardo¹

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Introduction: The restrictive syndrome is an echocardiographic diagnosis formulated on the basis of finding of normal diastolic volumes ventricles, systolic function under the normal limits and atria dilatation together with increased ventricular diastolic filling pressures (eg. E / A > 2, DT <130 msec, IVRT <70 msec, E / E ' > 15, dilated inferior vena cava). They differ from restrictive cardiomyopathy when, the increased ventricular diastolic filling pressures are associated with more specific morphological alterations. **CASE REPORT:** A 43 years old diabetic female, with a history of repeated episodes of acute heart failure, complicated by cardiac arrest. Some years before an electromyography (EMG) documented signs of myopathy with normal nerve conduction. The patient was referred to our Emergency Department for pulmonary edema and anasarca complicating an acute heart failure. Therefore, blood tests were performed with evidence of thrombocytopenia and hyperbilirubinemia (prior diagnosis of Gilbert's syndrome) and examination urine with detection of significant proteinuria. Electrocardiogram show a first degree atrioventricular block and diffuse QRS low voltage on ECG leads. We therefore

performed an urgent echocardiogram showing a slightly dilated left ventricle with global hypokinesia, moderately depressed global systolic function (FE 38%), grade III diastolic dysfunction, bilateral atriomegalia and circumferential mild pericardial effusion. These morpho-functional findings were confirmed by a nuclear magnetic resonance in the absence of signs of edema and/or myocardial fibrosis (negative late post-contrast-enhanced). During hospital stay a continuous ECG monitoring reported frequent episodes of sustained ventricular tachycardia. A serum creatine kinase and either serum either urinary immunofixation were performed excluding secondary forms. In view of the suspected restrictive cardiomyopathy by desmin accumulation (diagnosis of restrictive syndrome, conduction disturbance, EMG-graphic evidence of myopathy) the patient underwent endomyocardial biopsy with tally framework compatible with desminopathy. **Conclusions:** Restrictive cardiomyopathy by accumulation of desmin can be the first manifestation of a systemic disease that affects the heart muscle, skeletal muscle, and respiratory system. The pathogenesis of the disease seems to be linked to mutations of proteins such as desmin and alphaB-crystalline with autosomal dominant genetic transmission. The prognosis of the disease is conditioned by events brady- and/or tachy-arrhythmic causing palpitations, syncope and, in some cases, sudden cardiac death. In conclusion when echocardiogram findings meets the criteria of restrictive syndrome a desminopathy should be ruled out with an integrated imaging and bio-molecular assessment in order to stratify the individual arrhythmic risk and to screen first-degree relatives of the proband.

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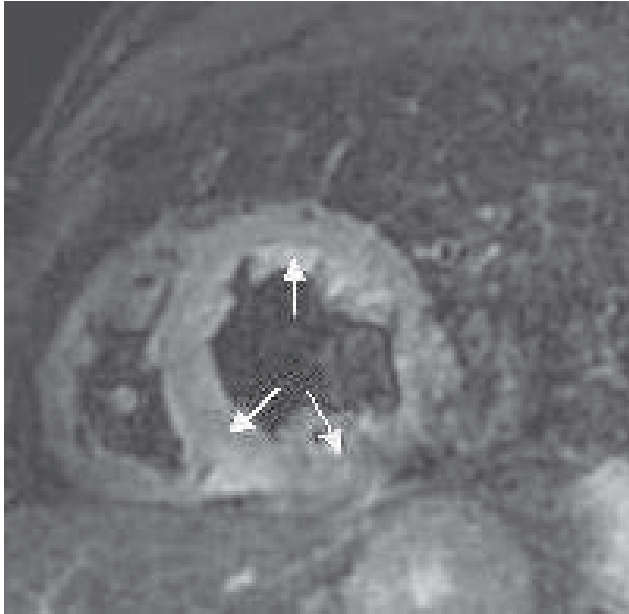
Beyond amyloidosis: a case of cardiac light chain deposition disease

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A48-year-old man was admitted to our Institution with a suspicion of subacute myocarditis, the complaint of fatigue and worsening dyspnoea (NYHA class III) in the previous month, and with the evidence at cardiac magnetic resonance imaging of severe left ventricular (LV) systolic dysfunction (LV ejection fraction 26%), hypertrophy and dilation, myocardial oedema at T2-STIR sequences, and diffuse late gadolinium enhancement. At admission, physical examination disclosed tachycardia (heart rate: 110 beats/min), slight hypotension (arterial pressure: 110/60 mmHg), bibasilar crackles at lung auscultation, with no signs of peripheral oedema. ECG showed sinus rhythm, negative T waves in lateral leads and diffuse QRS complex low voltages. At blood analysis C-reactive protein was slightly increased (0.41 mg/dL), eGFR was 71 mL/min/1.73m², HS-TnT was normal (9.42 ng/L, upper ref. limit: 14), while NT-proBNP was markedly increased (2348 ng/L). Further laboratory workup, including rheumatological and microbiological analyses, did not provide significant informations. Given the increase in the gamma zone at serum protein electrophoresis, immunofixation was performed and a monoclonal component (IgG lambda) was detected. Moreover, a mild increase in circulating lambda free light chain was observed (352 mg/dL, ref. values: 90-210). Echocardiography confirmed the severe impairment of LV systolic function, and revealed grade II diastolic dysfunction, mild-to-moderate mitral regurgitation and absence of pericardial effusion. Cardiac catheterization did not reveal coronary atherosclerosis and showed increased wedge pressure (20 mmHg) and reduced cardiac index (2.65 L/min/m²). Myocardial biopsy was also performed, showing diffuse interstitial fibrosis and no evidence of amyloid deposition at Congo Red staining. Irrespective of treatment with bisoprolol, ramipril, spironolactone, furosemide and levosimendan, the patient later presented with progressive haemodynamic worsening and frequent ventricular tachyarrhythmias and was treated with prophylactic implantation of cardioverter-defibrillator. Systemic amyloid deposition was excluded through histology also on periumbilical fat and bone marrow. Cardiac light chain deposition disease was thus suspected (a monoclonal gammopathy characterized by nonamyloid deposition of immunoglobulin light chains), as later confirmed by

immunohistochemistry on myocardial specimens revealing reactivity for lambda light chains within the fibrotic areas. After haematological evaluation, treatment with bortezomib was suggested, but the patients showed further deterioration of haemodynamics, hypotension, worsening renal function (eGFR 34 mL/min/1.73m²) and marked increase in natriuretic peptides (NT-proBNP 16,587 ng/L). He was therefore moved to an Intensive Care Unit for stabilization and pre-transplant evaluation, where the patient died while receiving support with extracorporeal membrane oxygenation, two months after admission.



Abstract Figure

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Asymmetric hypertrophic cardiomyopathy in generalized lipodystrophy characterized by cardiovascular magnetic resonance

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Introduction: Lipodystrophy is a rare syndrome characterized by loss of adipose tissue, insulin resistance, hypertriglyceridemia, steatohepatitis, splenomegaly, acanthosis nigricans and cardiomyopathy. It can be congenital or acquired with partial or generalized involvement. The most frequent cardiac finding is that of an hypertrophic symmetric cardiomyopathy which progresses with age.

Case presentation We describe here a case of a 30 years old male with generalized lipodystrophy who came to our cardiovascular magnetic resonance (CMR) laboratory to assess cardiac involvement. CMR showed a focal area of hypertrophy involving the basal anterior septum and basal anterior free wall with normal wall thickness of remaining left ventricle segments (Figure 1.A). There was also an intramyocardial area of late gadolinium enhancement with the same distribution (Figure 1.B), with no evidence for myocardial edema and/or fatty infiltration at that same level. No left ventricular outflow obstruction was found.

Discussion: Asymmetric hypertrophy has been rarely reported in young patients with lipodystrophy. Our finding is important even more, as asymmetric hypertrophy with late enhancement in the hypertrophied segment is a typical feature of sarcomeric hypertrophic cardiomyopathies and has been linked to adverse prognosis.

Conclusion In this case, CMR imaging was used to assess cardiac involvement in generalized lipodystrophy, and documented asymmetric non-obstructive left ventricular hypertrophy with a distinct area of late gadolinium enhancement. Our finding might help shedding new light on the yet mysterious pathophysiology of cardiac involvement in lipodystrophies. However, more studies are needed to better characterize the big range of cardiac abnormalities that can occur in these rare diseases.

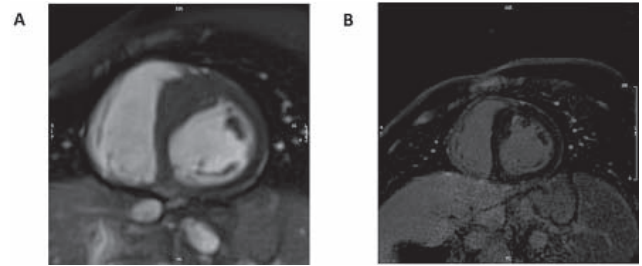


Figure 1

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A tale of two cardiomyopathies in one patient. Ten years after arrhythmogenic right ventricular cardiomyopathy, diagnosis of senile amyloidosis

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Background and case presentation: in 2005 a 65-year old with a family history of sudden death underwent a cardiac characterization because of recurrent palpitations, with the evidence of ventricular tachyarrhythmias with a left bundle-branch block morphology, confirmed at long-term ECG recording, with a final magnetic resonance imaging diagnosis of arrhythmogenic right ventricular cardiomyopathy (right ventricle features: end-diastolic volume 105 mL/m², end-systolic volume 109 mL or 53 mL/m², ejection fraction 50%, bulging in the free wall co-localized with with fibrofatty replacement). He received an implantable cardioverter-defibrillator with three subsequent appropriate shocks on ventricular tachycardias, despite of sotalol treatment. The patient remained symptomless till June 2013 (age of 73), when he complained of worsening dyspnoea (NYHA class III). Lower limbs oedema were evident, as well as respiratory crackles and a III heart sound. EKG showed previously unrecognized atrial fibrillation and reduced QRS complex voltages on peripheral leads, despite the echocardiographic evidence of apparent severe left ventricular hypertrophy (interventricular septum 19 mm, left ventricular mass index 145 g/m²), biventricular systolic dysfunction (left ventricular ejection fraction 40%, tricuspid annular plane systolic excursion 14 mm, tissue Doppler imaging of tricuspid annulus S wave 7 cm/s), severe diastolic dysfunction with restrictive filling (E/A 2.3). Biomarker assessment evidenced increased NT-proBNP (9773 ng/L) and elevation of high-sensitivity troponin T (86 ng/L, URL<14ng/L). These data arose the suspicion of amyloid cardiomyopathy, despite serum protein electrophoresis and plasma free-light chain were quite normal, periumbilical fat biopsy was negative, and cardiac magnetic resonance was not performed due to the presence of the device. Therefore the patient underwent total body Tc99m-HDP scintigraphy, showing marked and diffuse myocardial radiotracer deposition. Senile amyloid cardiomyopathy was then diagnosed and the patient was treated accordingly, with diuretics for fluid removal, beta-blockers, angiotensin converting enzyme inhibitors, spironolactone for cardiomyopathy, as well as with diflunisal for amyloid disease. Patient has done therefore rather well up to now (NYHA class II, stable plasma NT-proBNP 9349 ng/L), with a progressive loss in systolic function (LVEF 35%, December 2014), hospital admissions due to pneumonia fever, successfully treated with antibiotic therapy, precipitating heart failure symptoms.

Conclusions: arrhythmogenic right ventricular cardiomyopathy and concomitant senile amyloid cardiomyopathy.

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Atypical presentation of Danon disease - diagnostic options

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¹Medical University of Warsaw, Warsaw, Poland

Case report description: 16-year-old man was admitted from home to the cardiology department for the evaluation of rest dyspnea. He suffered from progressive increase in breathlessness over the previous 2 months. The patient had no previous history of cardiovascular disease, but his mother suddenly died at the age of 44 with a dilated cardiomyopathy of unknown origin. On admission tachypnea, tachycardia and hepatomegaly were observed, late inspiratory crackles throughout both lung fields and a systolic murmur with a maximum at the apex were audible.

Procedures and techniques used: Blood analysis revealed mildly elevated troponin I (1,50 ng/l) and C-reactive protein levels and noticeable elevation of alanine aminotransferase (800 U/l), aspartate aminotransferase (340 U/l), and creatine kinase (470 U/l). ECG showed sinus tachycardia and LBBB, QRS duration >210 ms. Chest X-ray confirmed pulmonary oedema and cardiomegaly. Transthoracic echocardiography showed LV dilation (LVIDd = 70 mm), severe concentric hypertrophy (RWT = 0.70) without LVOT obstruction and all of the 4 chambers enlarged. Moreover global

hypokinesis with EF=30%, impairment of RV function (TAPSE=10) and pulmonary hypertension (TRPG=52 mmHg) was noted. Cardiac magnetic resonance (CMR) revealed subendocardial perfusion defects in most of the segments on first pass images acquired at rest. LGE was present in the subendocardium and transmurally in the anterior and lateral walls (fig. 1).

Possible differential diagnosis: Based on the LGE pattern sarcomeric hypertrophic cardiomyopathy, amyloidosis, Anderson-Fabry disease and ischemic cardiomyopathy were excluded. Endomyocardial biopsy and muscle biopsy were performed. Electron microscopy confirmed the presence of autophagic vacuoles containing myeloid bodies, electron-dense granular material, and variable cytoplasmic debris (figure 2). LAMP 2 protein deficiency was confirmed on immunofluorescence study of skeletal muscle, confirming the diagnosis of Danon disease (figure 3 & 4).

Diagnosed disease: Danon disease is inherited as an X chromosome-linked dominant trait and characterized by the triad of hypertrophic cardiomyopathy, myopathy, and intellectual disability. Strikingly only the 1st of this triad was present in our patient. Danon disease is caused by loss-of-function mutations in the LAMP2 gene, which encodes lysosome-associated membrane protein 2 (LAMP-2), a transmembrane protein localized in the limiting membranes of lysosomes and late endosomes. LAMP-2 deficiency leads to a failure in macroautophagy. The only effective treatment option is heart transplantation.

Conclusions and implications for clinical practice: 1. This case demonstrates CMR potential to distinguish between ischaemic and non-ischaemic cardiomyopathies as well as to differentiate non-ischaemic aetiologies.

2. Instead of endomyocardial biopsy, muscle biopsy may be considered as reliable even in patients without myopathy.

Poster Session 1

Saturday 23 May 2015 08:30–17:30

Location: Poster Area

ACUTE HEART FAILURE

P191

Young people hemodynamics in conditions of endothelial dysfunction

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NO-synthase failure may be causes a reduction in the endothelium production, L-arginine deficit, impaired diffusion to smooth muscle cells and others. The endothelium dysfunction development promote smoking, hyperhomocysteinemia, physical inactivity, salt load, intoxication (alcohol), metabolic disorders, infection, hormonal changes (menopause). Purpose. To study the hemodynamic students with endothelial dysfunction.

Methods: The study was carried out in 39 male students aged 20-21 years. Assessment of the vascular endothelium functional state was performed rheographically by the test with reactive hyperemia.

The integral central hemodynamic parameters were investigated: systolic blood pressure (BP_{syst.}), diastolic (BP_{diast.}), mean blood pressure (MAP), heart rate (HR), minute volume of blood (MV), stroke volume (SV), stroke index (SI), total peripheral resistance (TPS) and the work of the heart (HW).

On the basis of indicators rheogram evaluations were central and peripheral hemodynamics (the rapid rise rheogram - a1, the pulse wave propagation in large vessels and the slow ascent rheogram - a2, the time of the peripheral vessels hyperemia, the a1/a2 - the ratio of blood flow in large and small vessels.

Results: Students with DE (n=22), compared to students without DE, n=17 along with lower values ΔPF_{max.}, had higher values AD_{syst.}, AD_{diast.}, MAP, TPR, HW, SV, SI, as a consequence of failure of vasoactive properties of vascular endothelium its effect on depressive function automatism.

The causes of changes in the parameters of fast and slow filling of the vessels, as well as their sum a1+a2 revealed a decrease in the index a1, reflecting the increase in the tone of large vessels, as well as an increase in a2, reflecting the slowing of peripheral blood flow, decrease in a1+a2, as a consequence of the total disorder of the central and peripheral hemodynamics.

Conclusion: The of central hemodynamics in students with DE characterised the activation of the cardiovascular system and lower its effectiveness indicates. Reducing of the ΔPK_{max} is a manifestation of endothelial dysfunction, causes hemodynamic changes and risk factors of hypertension. The tendency to raise blood pressure, heart rate, heart beat in a DE is obvious that it is an important its correction for arterial hypertension prophylaxis.

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Measurement of parathyroid hormone in acute heart failure

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¹Hospital Clinica San Carlos, Internal Medicine, Madrid, Spain; ²Hospital Infanta Leonor, Madrid, Spain; ³Hospital del Sureste, Arganda Del Rey, Spain; ⁴Gregorio Marañon Hospital, Madrid, Spain

Objectives: to compare the values of PTH and vitamin D in patients hospitalized for heart failure (HF) and impaired renal function.

Methods: Data from patients admitted with the diagnosis of HF were analyzed (ICD 9: 428), in which he had made determining the values of PTH. A descriptive analysis of clinical variables collected. With the results, we carried out a bivariate analysis to detect significant differences between patients with GFR ≥ 30 ml / min (GFR > 30) and <30 ml / min (GFR <30). Finally, a ROC curve varying to parathormone (PTH) and the diagnosis of advanced renal failure (defined by FG <30 mg / min / m³) was performed. The area under the curve with confidence interval 95% and established the cutoff of maximum sensitivity (S) and specificity (E) and negative predictive value (NPV).

Results: A total of 55 admissions were evaluated in the study period. The mean age of subjects hospitalized with HF was 82.63 years (SD 6.96), with a frequency of 61.1% women (n=33). The mean hemoglobin levels objectified in the patients in our study group were 11.51 g / dL (SD 1.49), creatinine 1.49 mg / dL (SD 0.90), FG 54.15 mL / min (29.08), calcium 8.99 mg / dL (0.81), vitamin D 14.75 ng / mL (12.55), 123.86 PTH pg / mL (DE 70, 51) and proBNP 10,525 pg / mL (SD 29.235). Following a bivariate analysis, the variables significantly associated (p < 0.05) to the group of patients with GFR <30 creatinine were 2.67 mg / dL (SD 1.25) and PTH 180.88 pg / mL (SD 72.04), compared to 1.17 mg / dL (SD 0.45) and 102.73 pg / dL (SD 52.52) respectively, in patients with GFR > 30 ml / min. On the other hand, under the ROC curve area of 0.83 (CI 0.72 to 0.96 with p < 0.05) was obtained, obtaining a high S and E together to PTH in 130, 5 pg / mL, with 80% and 75%, respectively.

Discussion: increased PTH levels in patients with renal failure admitted for acute HF is observed in Internal Medicine. Vitamin D deficiency has also been frequent. For a cutoff of PTH 130.5 pg / dL in the ROC curve we obtained a sensitivity of 80% with a specificity of 75% for diagnosis of renal failure with filtered below 30 ml / min. The determination of PTH and vitamin D on admission for decompensated HF can identify which patients with chronic renal insufficiency established. Further studies are required to assess the prognostic potential role of PTH elevation in morbidity and mortality in patients with heart failure at admission.

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Hyponatremia in acute decompensated heart failure: impact on prognosis

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Inchronic heart failure, hyponatremia (hypoNa) identifies patients (P) with worse prognosis. In acute decompensated heart failure (ADHF), this association has not been clearly established.

Aims: To assess the prevalence of hypoNa and its impact on prognosis in P admitted for NYHA class III/IV ADHF.

Methods: 396 consecutive P were included in the analysis. HypoNa was defined as serum sodium <136 mEq/L. Demographic and clinical comparisons were done according to natremia on admission. In-hospital and 90-day mortality were reported.

Results: HypoNa was detected in 49.9% of P. No differences were found in terms of age, gender, cardiac rhythm and previous treatment. P with hypoNa were more likely to have worse left ventricular ejection fraction (38 ± 17 vs 42 ± 13%; p < 0.05) and pre-existing renal dysfunction (38.4 vs 26.2%; p < 0.01). On admission, this group was characterized by lower systolic blood pressure (128 ± 32 vs 137 ± 34 mmHg; p < 0.05), clinical evidence of hypoperfusion (15.8 vs 9.1%; p = 0.01), low T3 serum level (78.2 vs 62.1%; p < 0.01), higher uraemia (65 ± 35 vs 54 ± 27 mg/dL; p < 0.001), liver dysfunction (48.3 vs 38.2%; p = 0.01) and higher intra-abdominal pressure (11 ± 7 vs 5 ± 6 mmHg; p < 0.01).

More in-hospital complications were seen in P with hypoNa such as worsening heart failure (WHF) (20.7 vs 14.2%; p < 0.05) and diuretic resistance (11.5 vs 5.7%; p = 0.01).

In-hospital mortality was 8.1% and 13.5% at 90-day follow-up.

Independent predictors of death were low T3 serum levels (OR 2.7; 95%CI 1.03-7.4; p < 0.05), diuretic resistance (OR 2.5; 95%CI 1.06-6.1; p < 0.05) and liver dysfunction (OR 2.2; 95%CI 1.1-4.6; p < 0.05).

Although hypoNa was related to increased mortality during hospitalization (OR 2.4; 95%CI 1.3-4.5; p < 0.01), only low T3 (OR 4.9; 95%CI 1.1-21.5; p < 0.05) and WHF (OR 3.2; 95%CI 1.3-8.5; p < 0.05) were independent predictors of in-hospital mortality.

After discharge, liver dysfunction was the only independent predictor of mortality at 90-day follow-up (OR 2.6; 95%CI 1.06-6.5; p < 0.05).

Conclusions: Hyponatremia was highly prevalent in our population admitted for ADHF. Although hyponatremia was associated with more complications during hospitalization, no effect on prognosis could be confirmed.

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Global longitudinal strain as a marker of cardiac function in patients with acute heart failure and preserved ejection fraction

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Purpose: Acute heart failure with preserved left ventricular ejection fraction (HFpEF) is a frequent challenge for the health care systems. Clinical outcomes among these patients remain poor, which need an improved understanding of LV dysfunction in this population. Global longitudinal peak systolic strain (GLPSS) reveals subclinical myocardial dysfunction. The purpose of this study was to evaluate the relationship between GLPSS and acute decompensated HFpEF.

Methods: We enrolled patients admitted with acute heart failure between 2009-2013 who took echocardiography and had left ventricular ejection fraction more than 50% and did not have valvular heart disease. Myocardial strain was assessed in the three apical projections by automated function imaging. Association between GLPSS and clinical variables was analyzed.

Results: A total of 221 patients with acute decompensated HFpEF were included (mean age: 66 years old). Median GLPSS was -13.7%. There was a wide distribution of GLPSS with 28% of patients having values better than -16%, the institutional lower limit of normal. A total of 35% had GLPSS worse than -12% indicating significantly impaired left ventricular long axis function despite preserved ejection fraction. There was a significant association between GLPSS and left ventricular mass index ($p < 0.05$). However, there was no significant correlation between GLPSS and diastolic parameters. GLPSS was not associated with age.

Conclusions: Among patients with acute decompensated HFpEF, GLPSS showed wide distribution ranging from normal to severely impaired myocardial long axis function. The relationship between GLPSS and left ventricular mass index indicates that GLPSS could be a marker of cardiac function in patients with acute decompensated HFpEF associated with left ventricular hypertrophy.

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Cardiogenic shock mechanism complicating STEMI and its impact on the prognosis: about 126 cases

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Introduction: Cardiogenic shock is the expression of an acute and severe dysfunction of cardiac pump causing a profound alteration of peripheral perfusion and progressive tissue anoxia. This is the most dangerous complication of myocardial infarction (MI) in the acute phase.

Objects: Studying the mechanisms of cardiogenic shock complicating STEMI, hospitalized in our department and their impact on prognosis.

Methods: This is a single-center, retrospective and descriptive study, conducted from medical observations of patients hospitalized with myocardial infarction complicated by cardiogenic shock between January 2009 and December 2014

Results: In our study, 126 patients were collected, with an incidence of 6.7%. The average age of our patients was 62.67 ± 12.09 years. A male predominance was observed with a sex ratio of 5/1. 38.1% of the population were diabetics, 12 patients (9.5 % of the population) had a history of myocardial infarction. 5 patients had previous left ventricular dysfunction on echocardiography. The admission average delay was 9 hours and 24 minutes. The average time for installation of shock compared with myocardial infarction was 12.5 ± 13.53 hours. The shock was early in 97 patients or 77% of the population. Over half of the patients were already under vasoactive drugs to their admission. A quarter of patients (31 patients or 24.6 %) was stable at admission and secondarily had presented a delayed shock. The mean ejection fraction of the left ventricle was $37.26 \pm 17.10\%$. The extent myocardial ischemia was the most frequent shock mechanism (69 % of cases). Mechanical complications accounted for 21.4 % of cases. The extension of the infarction to the right ventricle was observed in 12 patients. Myocardial revascularization treatment was performed in 112 patients (88.9 %). The angioplasty was realized in 77% of cases, thrombolysis in 11.1 % of cases and a surgical treatment in 11.9 % of cases. Surgical treatment was urgently indicated in 9 patients. Overall mortality was 72.6 %. The mortality rate of patients with mechanical complication was 88.9 % versus 69.9% in the extensive myocardial ischemia group and 80 % in the group extension to the right ventricle. No significant difference was observed between the different mechanisms of shock ($p = 0.250$).

Conclusion: Cardiogenic shock complicating STEMI is a poor prognosis with a high mortality rate, independently of the pathophysiological mechanism.

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Prognostic contribution of the electrocardiogram in patients admitted for acute heart failure

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Introduction: The prognosis of patients with heart failure has improved considerably over the last decade. However, heart failure still carries a high risk of mortality up to 10% per year according to recent clinical tests.

Object: To determine the clinical characteristics and predictors of 6-month mortality of patients admitted for acute heart failure.

Methodes: Our study concerned 234 inpatient on acute heart failure. The demographic, clinical, echocardiographic and laboratory were collected. All our patients benefited from the completion of at least two electrocardiograms (ECGs) that have been thoroughly analyzed.

Results: The mean age was 65 ± 13.8 years, 65% were male. Hypertension was noted in 60.3 % and 51.7% diabetes. Most of our patients (60.3 %) had a clinical congestive heart failure. We were able to determine the causal heart disease in almost all cases (97.4 %). The main causes of IC were ischemic heart disease (48.7%), Hypertension (21.4 %) and dilated cardiomyopathy (14.5%). The precipitating factor most frequently noted was ischemic attack (35%) followed by pulmonary disease (20.5%). On admission, the atrial fibrillation was noted in 36.8 % of cases and a ventricular excitability disorder was observed in 6.4% of our patients. There average width of the QRS complex was 102 ± 20 ms with a minimum 70 ms and a maximum of 170 ms, 16.2 % of patients had a QRS > 130ms. During hospitalization, the occurrence of ventricular excitability disorder was noted in 4.3 % of cases, that of the atrial fibrillation was observed in 3.4% of patients.

At 6 months, 25 cases (11.2%) deaths were reported. The occurrence of ventricular excitability disorder ($p < 0.0001$), atrial fibrillation ($p = 0.001$) and a QRS > 130 ms ($p = 0.003$) were predictive of mortality at 6 months. In multivariate study including all data, a width of QRS greater than 130 ms (OR, 6.15 ; 95% CI, 1.25-30.15 ; $p = 0.025$) was independently predictive of medium-term mortality of patients admitted for acute heart failure.

Conclusion: The ECG can be a great prognostic contribution. if they are used simultaneously; clinical, electrocardiographic and biological data, can predict a poor prognosis in patients admitted for acute heart failure and helps to adapt therapeutic strategies.

P197

Acute decompensated heart failure in women: just a difference of gender?

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Introduction: Women are half of worldwide population. However, they are under-represented in international heart failure randomized trials. Limited prospective information is available about this significant group.

Purpose: to compare characteristics and outcomes of women and men admitted for acute decompensated heart failure (ADHF) in NYHA III/IV functional class.

Methods: 618 consecutive patients (P) admitted for ADHF between March 2011 and December 2014, were included in the analysis. Demographic and clinical variables were compared according to gender. Treatment, in-hospital and 180-day outcomes were reported.

Results: a total of 269 P (43.5%) were female. Women were older (74 ± 15 vs. 70 ± 14 years old; $p < 0.01$) with a greater proportion of hypothyroidism (23% vs 9%, $p < 0.01$). In this group, history of chronic obstructive pulmonary disease (12% vs 24%, $p < 0.01$), chronic kidney disease (21.4% vs 43.6%, $p < 0.01$), cardiac surgery (13% vs 32%, $p < 0.01$), coronary angioplasty (11.2% vs 21%, $p = 0.02$) and previous admission for ADHF (36.5% vs 46%, $p = 0.02$) were less frequent. Fewer women were under angiotensin-converting-enzyme inhibitors or angiotensin receptor blockers (52.6% vs 62.7%, $p = 0.02$) than men, but no differences were detected in beta-blockers or mineralocorticoid receptor antagonists use.

Preserved ejection fraction was more common among women (55% vs 29%, $p < 0.01$) as well as normal coronary arteriograms (50% vs 34.2%, $p < 0.01$). Less liver dysfunction was observed (49% vs 64.8%, $p < 0.01$) at admission.

During hospitalization females did not present higher event rate, such as worsening heart failure, cardiorenal syndrome, diuretic resistance or ultrafiltration requirement. In-hospital mortality was 11.2% vs 8.2% ($p = NS$) and at 180-day follow-up 15.6% vs 18% ($p = NS$) between women and men, respectively. In a multivariate analysis, worsening heart failure predicted in-hospital mortality in women (OR 3.2; IC95% 1.1-8.9; $p = 0.02$), as long as diuretic resistance (OR 4.3; IC95% 1.5-12; $p < 0.01$) and inotropes use (OR 4.1; IC95% 1.3-13; $p < 0.01$) did in men. Readmission rate was similar in both populations at 180-day follow-up.

Conclusions: Women and men admitted for ADHF have different clinical characteristics, with a similar prognosis during hospitalization and 180-day follow-up. Although mortality predictors are different between these groups, they seem to have similar impact on prognosis.

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Five years monitoring of pulmonary congestion in chronic heart failure patients in outpatient clinic

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Assessment dynamic of pulmonary congestion in patients with congestive heart failure (CHF) for long period of time by noninvasive technique may help understand mechanisms of Acute Heart Failure (AHF) development and AHF hospitalizations. In this study we used a new type of impedance technique based on calculated lung impedance (LI) rather than on the traditionally measured transthoracic impedance for monitoring CHF patients.

Aim: To determine the dynamics of pulmonary congestion development in CHF patients.

Method and Results: LI change is adequately reflects dynamics of pulmonary congestion and decreasing LI reflects increasing lung fluid.

Signs, LI and ratio of the instantaneous LI to the calculated baseline LI (Δ LI/R) were monitored monthly in the outpatient clinic in 250 CHF patients (68 ± 11 years-old, male- 80%, LVEF- 28 ± 9%) at NYHA II/III/IV (107/100/43). Initial NT-proBNP level was 3594 ± 5114 pg/ml. Duration of follow up was 36 ± 22 months (6940 visits).

For assessment dynamics of pulmonary congestion in long standing follow up we introduced an additional parameter, the mean annual DLI Ratio (DLIR/year). DLIR/year was calculated as the arithmetic average of all available monthly measurements within the same year. Of 250 study patients, 179 were admitted for AHF, 31 for non-AHF causes only and 40 were not hospitalized at all during the follow up period. The average number of AHF hospitalizations in 179 CHF patients was 1.05/year. 92 of 179 patients had follow up period > 5 years. 32 of 40 patients had also follow up period > 5 years. Results calculation DLIR/year were for patients without AHF hospitalizations (-11%; -8%; -8%; -7%; -8%), (group1), for patients with AHF hospitalizations < 1.05/year (-17%; -15%; -16%; -15%; -16%), (group 2) and for patients with AHF hospitalizations > 1.05/year (-24%; -23%; -30%; -33%; -37%), (group 3), (p < 0.01 between groups). In group 1 and 2 there were not changes in pulmonary congestion between years (p = NS), but in group 3 was a significant increasing in pulmonary congestion since third year follow up, p < 0.01).

Conclusion: From our findings follows that a degree of pulmonary congestion (reflected by degree of DLIR/year decrease) is a main predictor of AHF hospitalizations.

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The urgency and performance of prehospital emergency services in acute heart failure

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Purpose: the role of early management of acute heart failure (AHF) patients is stressed in recent consensus papers. However, real-life data on pre-hospital emergency medical services (EMS) is scarce.

Methods: We included patients with AHF from three academic emergency departments from July 2012 to 2013 and divided them to those transferred by EMS and non-EMS group. Data was collected from electronic EMS and hospital patient records and databases. Complaints were assessed by dispatching centre and urgency was divided into four categories: immediate (target response time from call to site < 8min, A-B), urgent (<30min, C), low-urgency (<120 min, D). Group A had emergency physician on board, and the others paramedic. Time from the start of emergency call to admission to hospital was recorded. The time included treatment of the patient and transportation to the hospital.

Results: EMS group contributed to 100 (11.5%) of total 873 AHF admissions. Mean age in EMS group was 76.2 (10.8) years and non-EMS 75.6 (11.9) years. Male patients comprised 52.4% of EMS and 45.0% of non-EMS. The primary causes for EMS were dyspnoea (38%), general weakness (27%), chest pain (9%), other complaints (14%), and for 12% transportation from a nursing home or primary care. The proportions of urgency categories were A 3%, B 30%, C 46% and D 20%. The mean time from call to hospital was 1h 6 min (SD 22 min).

Time from call to hospital in EMS		
Urgency category	Time from call to site	Time from call to hospital admission
Group A	0:11 (0:05)	1:10 (0:00)
Group B	0:09 (0:03)	1:08 (0:08)
Group C	0:16 (0:05)	1:01 (0:18)
Group D	0:44 (0:26)	1:45 (0:29)

Time is in hours:minutes. Mean (SD)

P200

Ivabradine in acute decompensated systolic heart failure is safe and effective to achieve target values of heart rate at hospital discharge

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Purpose: Acute decompensated heart failure (ADHF) is a growing problem associated with major morbidity and mortality. Heart Rate (HR) has been recognized as a therapeutic target in chronic HF. Higher HR at hospital discharge in patients with ADHF has been associated with greater 1-year mortality and 30-day readmissions. The aim of this study was to evaluate the safety and effectiveness of ivabradine to achieve target values of HR at hospital discharge.

Methods: Fifteen consecutive patients with ADHF in sinus rhythm, left ventricular ejection fraction <35%, hemodynamically stable without inotropic support and HR>70bpm in spite of treatment with beta-blockers or when this was contraindicated or not tolerated, began treatment with oral ivabradine. Clinical data at admission (T0), immediately before initiation of ivabradine (T1), 24h (T2); 48h (T3), 72h (T4) after, and at discharge (T5) was obtained.

Results: Admission HR was 103 ± 24 bpm. Ivabradine was initiated in 47% of the patients in the first two days. HR decreased 11.9 ± 10.1bpm at T2 (p 0.000); 14.3 ± 11.8 at T3 (p=0.000); 17.2 ± 14.7 (p=0.001) at T4 and 21.7 ± 13.9 at T5 (p=0.000). There was no significant change in systolic and diastolic blood pressure at any of the five periods. T5: PAS -1.3 ± 19.6 (p=0.796); PAD 4.2 ± 13.5 (p=0.247). Admission HR and the magnitude of HR reduction correlated significantly. Rho = 0.796 (p = 0.000). 33% of the patients had a PAS < 100 mmHg prior to the initiation of ivabradine. In this group neither was detected a significant change in systolic and diastolic blood pressure.

The discharge HR was 70 ± 9 bpm. 87% of the patients were discharge with beta-blockers. Ivabradine did not have to be withdrawn for adverse effects in any patient. The dose at discharge was 5 ± 1.3 mg twice daily.

Conclusion: Ivabradine was safe and effective to achieve HR target at discharge. Many patients with ADHF maintain a heart rate above 70bpm despite treatment with beta-blocker or this are contraindicated or not tolerated. In this setting the ivabradine is an option to consider requiring appropriately designed studies.

Baseline clinical variables.					
Age, yrs	60 ± 16.5	IC de novo n (%)	9 (60)	Hospital stay, days	9 ± 4
Males n (%)	10 (67)	Dilated cardiomyopathy n (%)	10 (67)	Inotropos n (%)	4 (27)
HTA n (%)	11 (73)	Left ventricular EF, %	26 ± 7	Beta-blockers initiated n (%)	11(73)
Diabetes n (%)	6 (40)	Nt-ProBNP, pg/ml	4034 ± 3409	Day Beta-blockers initiated	4 ± 3

Table 1.

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Low T3 serum concentration and mortality in acute decompensated heart failure: too little evidence for a strong predictor

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Small, retrospective reports showed an association between low T3 serum concentration and prognosis in cardiac disorders. This association has not been clearly established for patients (P) with acute decompensated heart failure (ADHF).

Aims: To assess prevalence and impact of low T3 (LT3) concentration in P hospitalized for NYHA functional class III/IV ADHF.

Methods: 396 consecutive P were included in the analysis. Demographic and clinical variables were compared according to T3 serum levels on admission. LT3 was defined as T3 level <0.79 ng/ml. In-hospital and 90-day prognosis were reported.

Results: LT3 was observed in 278 P (70.2%) on admission. TSH levels did not differ between groups. P with LT3 were older (71 ± 15 vs 65 ± 16 years old; p < 0.01), had worse renal function (creatinine 1.56 ± 0.3 vs 1.13 ± 0.6 mg/dL, p = 0.01), more hyponatremia (Na+ < 136 meq/L) (65 vs 36%; p < 0.01) and liver dysfunction (54 vs 39%; p < 0.01). Cardiac rhythm, heart rate and left ventricular function were similar between groups.

Independent predictors of LT3 level were anemia (OR2; 95%CI 1.1-3.6; $p < 0.05$), hyponatremia (OR2.1; 95%CI 1.3-3.6; $p < 0.01$) and liver dysfunction (OR2.1; 95%CI 1.2-3.6; $p < 0.01$).

During hospitalization, more complications were observed in P with LT3, such as: worsening heart failure (WHF) (22.3 vs 11.9; $p < 0.05$), diuretic resistance (12.6 vs 4.3%; $p = 0.01$) and persistent hyponatremia at discharge (35 vs 22.7%; $p < 0.05$). In-hospital mortality was 8.1% and 13.5% at 90-day follow-up.

Independent predictors of death were LT3 (OR 2.7; 95%CI 1.03-7.4; $p < 0.05$), diuretic resistance (OR 2.5; 95%CI 1.06-6.1; $p < 0.05$) and liver dysfunction (OR 2.2; 95%CI 1.1-4.6; $p < 0.05$).

Only LT3 (OR4.9; 95%CI 1.1-21.5; $p < 0.05$) and WHF (OR3.2; 95%CI 1.3-8.5; $p < 0.05$) were independent predictors of hospital mortality. After discharge, only liver dysfunction was independently associated to 90-day mortality (OR2.6; 95%CI 1.06-6.5; $p < 0.05$).

Conclusion: Low T3 concentration is highly prevalent in ADHF and it predicts complications and death during hospitalization. However, T3 serum level is not frequently evaluated during hospitalizations for ADHF, probably because the question remains whether this is just a marker of prognosis or a target of treatment.

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Characteristics, management, and relationship between guideline-recommended therapy and mortality rates of patients with acute heart failure in EDs: a report of the Beijing AHF registry

This work was supported by The Beijing Municipal Commission of Health and Family Planning [2009-SHF04]. G Guogan Wang¹; S Wang¹

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Abstract Aims: Acute heart failure (AHF) causes high mortality and morbidity. The Beijing Acute Heart Failure Registry Study (Beijing AHF Registry) aimed to assess the characteristics, management, and relationship between guideline-recommended therapy (GRT) for AHF and mortality in the Chinese population.

Methods and Results: This prospective registry enrolled 3335 patients (median age 71 years, 53.2% male) presenting with AHF in 14 emergency departments (EDs) in Beijing between 1 January 2011 and 23 September 2012. Coronary heart disease (43.3%) and was the commonest aetiology, while infection (71.0%) was the main precipitant, of AHF. Overall mortality rates in EDs, and at 30 days and 1 year post-discharge were 3.81%, 15.3%, and 32.2%, respectively. Beta-blockers, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, and mineralocorticoid receptor antagonists (MRAs) were given after discharge to 39.9%, 28.7%, and 23.6% of patients, respectively. Following propensity score matching, patients with intravenous vasodilators in the ED showed decreased mortality at 30 days, compared to untreated patients (9.5% vs. 19.7%, respectively). Patients given beta-blockers or MRAs showed higher survival rates at 1 year, compared to untreated patients (beta-blockers, 81.7% vs. 70.3%; MRAs, 82.9% vs. 72.2%). The hazard ratios of 30-day mortality for patients with intravenous vasodilators in the ED, and of 1-year mortality for those given beta-blockers or MRAs after discharge were 0.457, 0.564, and 0.563, respectively, when compared with untreated patients.

Conclusion: AHF accounted for high mortality, and GRT, which is protective against AHF, was underused in the Chinese population. Therefore, it is essential to establish a national clinical programme to promote the standard implementation of GRT in the management of AHF.

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Impact of digoxin use in patients with atrial fibrillation and heart failure: data from the Korean heart failure (KorHF) registry

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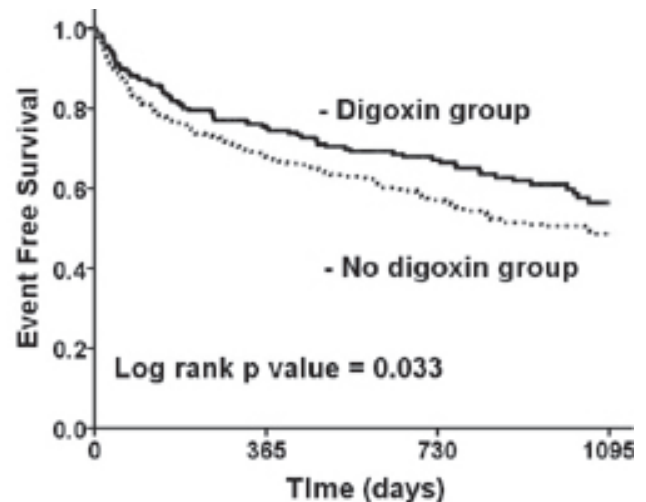
Purpose: Recent meta-analysis showed that beta blocker therapy did not lead to a significant reduction in all-cause mortality in patients with atrial fibrillation and heart failure (HF). We aimed to evaluate the clinical impact of digoxin use in Korean patients with atrial fibrillation and HF, using large HF database.

Method: From June 2004 to April 2009, 3,200 patients with acute decompensated HF were enrolled in Korea HF registry. Among them, 708 patients with atrial fibrillation and HF were analyzed. The primary endpoint was a composite of all-cause mortality and rehospitalization up to 3 years.

Results: Among study patients, 263 patients (37%) took digoxin during hospitalization. In multivariate Cox-proportional hazard model, body mass index (hazard ratio [HR] 0.92, 95% confidence interval [CI] 0.86 to 0.98), heart rate (HR 1.01, 95% CI 1.01 to 1.02), hemoglobin (HR 0.85, 95% CI 0.75 to 0.96), BUN (HR 1.02,

95% CI 1.02 to 1.03), sodium (HR 0.95, 95% CI 0.91 to 0.99), beta blocker use (HR 0.25, 95% CI 0.12 to 0.52), and digoxin use (HR 0.35, 95% CI 0.19 to 0.63) were independently associated with the primary endpoint. When analyzed according to left ventricular ejection fraction, beneficial effect of digoxin was shown only in patients with HF with reduced ejection fraction.

Conclusions: In Korean patients with atrial fibrillation and HF, use of digoxin during hospitalization was related to decreased mortality up to 3-year follow up. This finding could have an impact on the management of patients with atrial fibrillation and heart failure.



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Blood pressure at admission determines medical prescription and clinical outcomes of patients with decompensated heart failure

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Purpose: Blood pressure (BP) at admission and discharge has been reported to affect clinical outcomes in patients with heart failure despite some controversies. However there has been no study evaluating whether admission blood pressure influences medical treatment and clinical outcomes in acute decompensated heart failure patients.

Methods: We analyzed the data from Korean Acute Heart Failure (KorHF) Registry which was conducted nationwide from June 2004 to April 2009 at 24 hospitals in Korea. A total of 3,200 acute decompensated heart failure patients were included in the registry. We investigated the association of initial blood pressure at admission and clinical outcomes and prescription of angiotensin-converting enzyme inhibitor/angiotensin receptor blocker/ beta-blocker (ACEI/ARB/BB). The primary outcome was composite of mortality and readmission during 1-year after hospital discharge.

Results: Admission systolic (SBP) and diastolic BP (DBP) increase was associated with decrease in primary outcomes (by 1mmHg increase of SBP, crude hazard ratio [HR] 0.9963, 95% confidence interval [CI]: 0.9943-0.9982, $p < 0.0001$ and by 1mmHg increase of DBP, crude HR 0.99, 95% CI: 0.9867-0.9932, $p < 0.0001$). By multiple regression analysis DBP was an independent risk factors of mortality and re-hospitalization (HR 0.9927, 95% CI 0.9867-0.9988, $p < 0.0196$), but SBP was not. The cut-off value of SBP and DBP for increasing clinical outcomes were 118.5 mmHg (sensitivity 0.3965, specificity 0.6727) and 78.5mmHg (sensitivity 0.5682, specificity 0.5228), respectively by ROC curve. The SBP < 118.5 mmHg and DBP < 78.5mmHg were independent predictor for primary outcomes (adjusted HR 1.33, 95% CI 1.15-1.54, $p < 0.0001$ and adjusted HR 1.23, 95% CI 1.12-1.48, $p = 0.0004$, respectively).

The cut off SBP/ DBP value of not using in-hospital ACE/ARB/BB were 129.5/80.5mmHg. DBP of 80.5mmHg was an independent determinants of not prescribing the drugs (adjusted OR 0.755, 95% CI: 0.582-0.977, $p = 0.0329$). Both lower SBP (<129.5) and DBP (<80.5mmHg) combined with no use of the drugs (ACE/ARB/BB) were independent predictor of poor clinical outcomes at 1-year. (adjusted HR 1.677, 95% CI: 1.380-2.037, $p < 0.0001$ and adjusted HR 1.653, 95% CI: 1.355-2.017, $P < 0.0001$, respectively)

Conclusions: Lower blood pressure at admission increase mortality, re-hospitalization at 1-year and decrease in-hospital prescription of ACE/ARB and BB in patients with acute decompensated heart failure. The cut-off value of SBP/DBP for primary outcome was 118.5/78.5 mmHg and that for use of ACE/ARB/BB was 129.5/80.5mmHg.

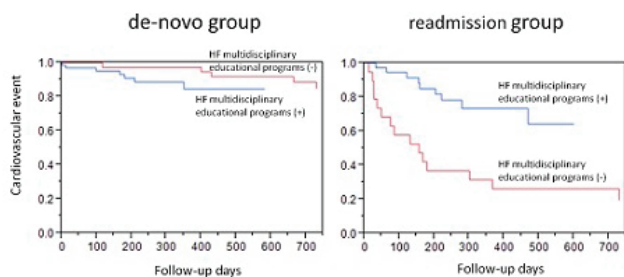
P205

Heart failure multidisciplinary educational programs are effective in patients with re-admission than de-novo acute heart failureK Keisuke Kida¹; N Suzuki¹; C Itoh¹; K Ashikaga¹; K Suzuki¹; T Harada¹; YJ Akashi¹¹St.Marianna University School of Medicine, Department of Internal Medicine, Division of Cardiology, Kawasaki, Japan

Background: Multidisciplinary educational programs can reduce mortality and rehospitalization of patients with acute decompensated heart failure (ADHF). Since little has been known about its impact on prognosis in ADHF patients, this study aimed to investigate the usefulness of our program in these patients.

Methods and Results: This retrospective study included 162 patients with ADHF who were admitted to our hospital between February 2010 and March 2014. The multidisciplinary group educational program established in our hospital in August 2012 was employed. Patients with a previous history of heart failure were classified as acute decompensated chronic heart failure (readmission group; n=58) and the remaining patients were regarded as de novo ADHF (de-novo group; n=104). The incidence of cardiovascular events significantly decreased after the employment of HF multidisciplinary group educational program in not the de-novo group (p=0.1835) but the readmission group (p=0.0156).

Conclusions: This study demonstrated that our heart failure multidisciplinary group educational program contributed to significant cardiovascular event reduction in ADHF patients with prior hospitalization but not in de-novo ADHF patients.



P206

The effect of thrombolytic therapy on right ventricle dysfunction in patients with intermediary risk pulmonary embolismA Alexandru Ion¹; C Andrei¹; C Sinescu¹¹University of Bucharest Carol Davila, Bagdasar Arseni Emergency Hospital, Cardiology Department, Bucharest, Romania

Purpose: The intermediary risk pulmonary embolism (PE) is a heterogeneous disease. The in-hospital mortality varies from 2% to 20%. There are very few studies regarding the effect of thrombolysis on RV dysfunction, assessed by echocardiography. The purpose of this study is to prove an improvement of the RV dysfunction by thrombolytic therapy compared to anticoagulant therapy in intermediary-high risk PE patients.

Method: We selected 40 patients with acute intermediary-high risk PE (both echocardiographic and biochemical markers of RV dysfunction positive, and PESI >85), the first documented episode. The study group included 19 patients which received thrombolytic treatment (t-PA, 10 mg bolus, 90 mg in 2h), followed by unfractionated heparin (UFH). The patients had no contraindications for thrombolysis, were younger than 75 y.o and did not have a severe renal failure (Cr Cl > 30ml/min). The control group included 21 patients which did not fulfil the criteria for study group and were treated only with UFH therapy. The patients were assessed by echocardiography on admission and on discharge, regarding the signs of RV dysfunction (myocardial contraction velocity, TAPSE, RV diameter). The treatment related bleedings were studied. The two groups were similar regarding sex distribution (47% males in the study group, 52% males in the control group).

Results: The echocardiographical markers of RV dysfunction were improved in both groups post treatment, but more in the study group. The myocardial contraction velocity had a more important post treatment increase in the study group (71.55% vs 28.98%), this being correlated with a more significant increase of TAPSE in this group (58.7% vs 25.4%). Meanwhile the RV diameter had a significant post treatment decrease in both groups, but more important in the thrombolysed patients (22.03% vs 17.50%). Only one patient from the study group had a significant nonfatal bleeding, meanwhile none of the patients from the control group had a significant bleeding.

Conclusion: The thrombolytic treatment has a benefit effect on the echocardiography markers of RV dysfunction in patients with intermediary-high risk PE, especially on myocardial contraction velocity.

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Are we prescribing too little heart failure medication to acute heart failure patients discharged with a NT-proBNP reduction of less than 30%?Netherlands Heart Foundation Susan Stienen¹; K Salah¹; LWM Eurlings²; M Metra³; V Lazzarini³; L Bettari⁴; YM Pinto¹; WEM Kok¹¹Academic Medical Center, University of Amsterdam, Department of Cardiology, Amsterdam, Netherlands; ²Maastricht University Medical Centre (MUMC), Maastricht, Netherlands; ³Civil Hospital of Brescia, Brescia, Italy; ⁴Hospital of Cremona, Cremona, Italy

Purpose: A NT-proBNP reduction of less than 30% from admission to discharge in patients admitted for acute decompensated heart failure (ADHF) is a strong predictor for readmissions and mortality within 6 months. Our aim was to study whether ADHF patients discharged with a NT-proBNP reduction of $\leq 30\%$ receive less HF medication at discharge than patients with a NT-proBNP reduction of $>30\%$.

Methods: The study population was assembled from 3 ADHF cohorts of patients with LVEF <45%. NT-proBNP was measured at admission and discharge. Between patients attaining $\leq 30\%$ or $>30\%$ reduction in NT-proBNP at discharge, we compared combinations of HF medication at discharge (diuretics, ACE-inhibitors or Angiotensin Receptor Blockers (ARB), beta blockers (BB) and aldosterone antagonists (MRA)) and how often HF medication was discontinued or initiated between admission and discharge. Prescription of HF medication was documented at admission and discharge.

Results: A total of 493 patients (median age 71, 71% male) was studied. A NT-proBNP reduction of $\leq 30\%$ in NT-proBNP was demonstrated in 37% of patients. No significant differences were found in combinations of HF medication at discharge or in the frequency of discontinuation of HF medication (Table). Prescription of the most complete HF medication was low in both groups. Of the patients who did not receive a BB or MRA before admission, significantly less patients in the $\leq 30\%$ group were discharged with these medications (31 vs. 43%, p=0.04 for MRA; 35 vs. 57%, p<0.01 for BB).

Conclusions: ADHF patients discharged with a NT-proBNP reduction of $\leq 30\%$ demonstrate similar prescription patterns of HF medication at discharge and similar discontinuation rates compared to patients discharged with a NT-proBNP reduction of $>30\%$. BB and MRAs were significantly less initiated during admission in patients discharged with a NT-proBNP reduction of $\leq 30\%$. Further studies need to identify the potential benefit from intensified medical therapy in this population at risk.

Combinations of discharge HF medication

	>30% reduction in NT-proBNP (n=312)	<30% reduction in NT-proBNP (n=181)	p-value
Diuretics only	12 (4)	8 (5)	NS
ACEi/ARB or MRA or BB *	141 (46)	81 (47)	
ACEi/ARB + MRA or ACEi/ARB+BB or MRA+BB *	65 (21)	40 (23)	
ACEi/ARB + MRA + BB*	90 (29)	43 (25)	

* combinations also possible with diuretics

P208

An east-west comparison of self-care barriers in heart failure (hf)S L Lim¹; SP Chan²; KY Lee¹; A Ching¹; RJ Holden³; SP Collins⁴; CSP Lam¹¹National University Heart Centre, Department of Cardiology, Singapore, Singapore; ²National University of Singapore, Department of Medicine, Singapore, Singapore; ³Indiana University School of Informatics and Computing, Department of BioHealth, Indianapolis, United States of America; ⁴Vanderbilt University, Department of Emergency Medicine, Nashville, United States of America

Purpose: Barriers in HF self-care contribute to HF hospitalisations, but geographic differences have not been well-studied. We aimed to compare self-care barriers in HF patients managed at tertiary centres in an Eastern (Singapore) vs Western (US) nation.

Methods: Acute HF patients were prospectively assessed within 24h of admission with a standardised instrument (47 distinct self-care barriers), contemporaneously in both nations. We used factor analysis to determine patterns for sources of barriers, and structural equation model to assess differences between East and West.

Results: Patient factors constituted the top 5 barriers in both groups (Table). Despite similar age and comorbidities, Western patients perceived a higher level of barriers compared to Eastern patients, even after adjusting for sex, age and comorbidities (p<0.01). Perceived physical, mental and functional limitations were greater in

Western patients, whereas lack of knowledge about disease and self-care were greater in Eastern patients.

Conclusion: Self-care barriers are highly prevalent among HF patients, and differ substantially between East and West. The implications of these findings for public health education and planning, as well as the impact on patients' outcomes, deserve further study.

	Eastern (Singapore) (N = 34)	Western (US) (N = 31)
Age (mean±SD)	64.6±10.1	66.2±13.9
Sex (% males)	61.8	38.7
Charlson Comorbidity Index	5.9±1.8	5.7±2.1
Number of self-care barriers (median)	10	16
Type of self-care barrier (% prevalence)		
Degree of sickness	61.8	67.8
Comorbidities	50.1	74.2
Lack of motivation	17.6	43.3
Feeling frustrated	58.8	64.5
Physical disabilities	55.9	71.0
Memory and attention deficits	8.8	54.9
Functional limitations	45.3	58.0
Low literacy	29.4	35.5
Knowledge about disease	35.3	64.5
Knowledge about self-care	32.4	45.2

P209

PCT-guided antibiotic treatment in patients with dyspnea in the emergency department

The Biomarkers in Cardiology research team received research grants for this study (BIC-2) from Abbott Diagnostics and BRAHMS Thermofisher. M Moeckel¹; A Anna Slagman²; J O Vollert³; F Holert⁴; M Stockburger⁵; C Mueller⁴; R Muller⁶; J Searle¹

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Introduction: Patients with dyspnea in the Emergency Department (ED) represent a high-risk group with the highest in-hospital mortality as compared to other leading symptoms. The most frequent diagnoses in these patients include acute heart failure (AHF) and pneumonia. It has recently been shown that PCT combined with natriuretic peptides might be a helpful marker for the guidance and timely initiation of antibiotic treatment in these patients. This study evaluates the 90-day mortality in ED-patients with acute dyspnea stratified by the biomarkers procalcitonin (PCT) and atrial natriuretic peptide (ANP) and by antibiotic treatment.

Material and Methods: Patients with a leading symptom of dyspnea were recruited in the ED. Blood was drawn within 2 hours after admission. PCT (PCT sensitive) and ANP (MR-proANP) were measured from heparin plasma on the Kryptor-Device (BRAHMS Thermofisher). Antibiotic treatment was assessed during the ED-stay. Diagnoses were gold-standard diagnoses adjudicated by an independent cardiologist. Mortality was assessed after 90 days via telephonic interrogation.

Results: Of 305 patients with acute dyspnea, 18.7% (n = 57) had a final diagnosis of AHF and 7.5% (n = 23) had pneumonia. The ANP-value was above a previously defined cut-off value of above 300 pmol/L in 85 patients (27.9%). Subgroups based on PCT-value and antibiotic treatment and the corresponding mortality in these subgroups is shown in figure 1.

Conclusion: A significant number of patients with high PCT did not get early antibiotics on the basis of clinical judgement and this subgroup had the highest mortality (18.5%). Thus there is potential for early PCT-guided AB-use in ANP-positive patients with dyspnea.

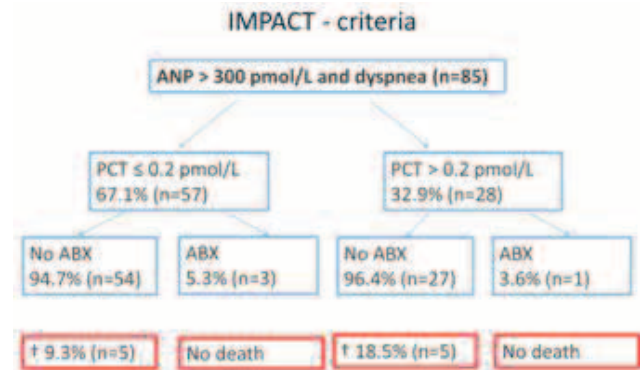


Figure 1: Patient flow and mortality

P210

Evaluating the efficacy, safety and tolerability of serelaxin when added to standard therapy in asian patients with acute heart failure: The RELAX-AHF-ASIA trial

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Purpose: In Asia, Acute heart failure (AHF) is typically observed in younger patients who present with severe signs and symptoms of congestion. Whilst evidence exists indicating the therapeutic benefits of serelaxin (recombinant human relaxin-2) in Caucasian populations, data remain scarce in Asian patients with AHF. The RELAX-AHF-ASIA trial (ClinicalTrials.gov identifier: NCT02007720) is aimed at evaluating the efficacy, safety and tolerability of serelaxin when added to standard therapy in patients with AHF in Asia.

Methods and Results: This multicentre, randomised, double-blind, placebo-controlled phase III trial will enrol approximately 1520 patients with AHF across Asia (China, Hong Kong, Japan, Korea, Malaysia, Philippines, Singapore, Taiwan and Thailand). Patients with dyspnoea due to AHF, systolic blood pressure ≥125 mmHg, and with mild-to-moderate renal dysfunction will be randomised within 16 hours of presentation to a 48-hour intravenous infusion of 30 µg/kg/day serelaxin or placebo on top of standard therapy. The trial's primary objective is to demonstrate the superiority of serelaxin to placebo on top of standard therapy, as assessed by a clinical composite endpoint consisting of early improvement in signs and symptoms of congestion at Day 2 and prevention of in-hospital worsening of HF (WHF) or rehospitalisation due to HF, renal failure or death through Day 5. The key secondary objectives are to assess the effect of serelaxin compared with placebo on top of standard therapy on reducing the time to in-hospital WHF through Day 5 and decreasing the cardiovascular and all-cause mortality through Day 180. Safety and tolerability of serelaxin are also evaluated. The study is ongoing, with 71 patients enrolled as of 09-Jan-2014, and updates on progress will be presented.

Conclusions: RELAX-AHF-ASIA is currently one of the largest randomised clinical trial in Asian patients with AHF. It is designed with a novel composite primary endpoint aimed at demonstrating the clinical benefits of serelaxin when added to standard therapy in patients with AHF in Asia. In addition this landmark trial will provide valuable insights into the Asian phenotype of AHF.

P211

Clinical and paraclinical determinants of in-hospital mortality in patients with acute heart failure

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Purpose: To identify several clinical and paraclinical parameters with short term prognosis (in-hospital mortality - IHM) for patients admitted with severe AHF: Acute

Pulmonary Edema(APE) or Chronic Decompensated Heart Failure(CDHF) NYHA class IV.

Methods: The study was a retrospective one, in which we included 114 patients diagnosed with AHF with its clinical presentations APE or CDHF NYHA class IV. Following parameters were analyzed: systolic blood pressure(SBP), heart rate, BUN, creatinine, sodium, hemoglobin, possible on-set of arrhythmic disorders.

We correlated these parameters with IHM and clinical profiles and tried to find if there is any statistical evidence. We identified the parameters with independent prognosis using a multivariable logistic regression model.

Results: 114 patients, mean age 73 years, 51.75% males; APE 37.72% vs CDHF 59.65%. Following clinical and paraclinical parameters were identified as prognostic factors, with or without statistical value for IHM: SBP before therapy <140mmHg has a sensibility of 50% and a specificity of 67% in mortality prediction; a heart rate at admission>135bpm associates a 3.17 times higher risk of mortality($p=0.03$). The occurrence of supraventricular arrhythmias was associated with higher risk of mortality, yet without statistical value; supraventricular arrhythmias are closely related to clinical profiles at presentation: patients with CDHF vs APE have a 4.8 higher risk of developing one of them. IHM was 3.8 higher in patients with a cutoff value of creatinine at admission of 1.65mg/dL($p=0.01$). An elevation of 0.3mg/dL associated a 1.61 higher risk of mortality($p=0.00$). The admission BUN value of 31.26mmol/l grants a 2.61 higher risk of mortality($p=0.02$). In addition, any elevation of BUN despite its initial value, determines a major impact on IHM($p=0.0004$). A sodium level lower than 136.2 mEq/L was highly predictive for mortality-2.78 times a higher risk($p=0.01$). Decreasing sodium levels during admission was related to higher mortality($p=0.00006$). The hemoglobin cut-off value for negative prognosis was ≤ 13.4 g/dL and brought a 3.22 higher risk of mortality($p=0.029$). Any decrease of hemoglobin levels during admission, was related clinically and statistically with increase rate of decrease($p=0.025$).

Conclusions: Some easy to obtain and analyse parameters correlate themselves with higher rate of IHM for AHF patients. Among them, SBP before therapy <140mmHg, sodium level <136.2mEq and an increase in creatinine levels with >0.3 have outlined themselves as factors with independent prognostic value.

P212

Peculiarities of the course of heart failure in patients with myocarditis on the background of left his bundle branch block

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The value of left His bundle branch block (LBBB) was not under consideration with regards to heart failure (HF) and its relationship with the etiology and severity, as well as, contractility and diastolic functions of myocardium.

Purpose of the study: to study the peculiarities of heart failure in patients with myocarditis in the background of full LBBB.

Materials and Methods: 19 patients were examined with heart failure who had LBBB (Group 1) at the age of $36,7 \pm 1,1$ years and 31 patients with heart failure (Group 2) without LBBB ($32,5 \pm 1,0$ years). Clinically, the severity of heart failure was determined by the assessment scale of clinical condition

Results: Total score on the assessment scale for the clinical conditions in Group 1 patients with different classes of heart failure was higher and did not differ significantly compared with Group 2 patients ($p > 0,05$). By exercise tolerance, it was found that there were no differences in the load applied for patients of 1st and 2nd groups ($p > 0,05$). Quality of life assessed by the Minnesota questionnaire showed that poorer indicators were in Group 1 patients and those with more severe heart failure ($p < 0,05$).

As the progression of heart failure in patients with LBBB, increase was observed in the thickness of the posterior wall and interventricular septum of the left ventricle (LV), LV myocardial mass index and the size of the left atrium ($p < 0,05$). In patients of Group 1, ejection fraction (EF) was lower compared with Group 2 ($p < 0,05$).

With the progression of heart failure, in Group 1 right ventricular ejection fraction ($57,4 \pm 1,7\%$) begins to prevail over the function of the left ventricle ($47,1 \pm 1,0\%$) and diastolic dysfunction is in restrictive nature.

Outcome: Thus, in patients with myocarditis with heart failure full LBBB promotes early remodeling of the myocardium with impaired systolic function of both ventricles, but also with severe diastolic dysfunction of myocardium.

P213

Effect of body mass index in the outcome after acute decompensated heart failure according to the presence of diabetes mellitus

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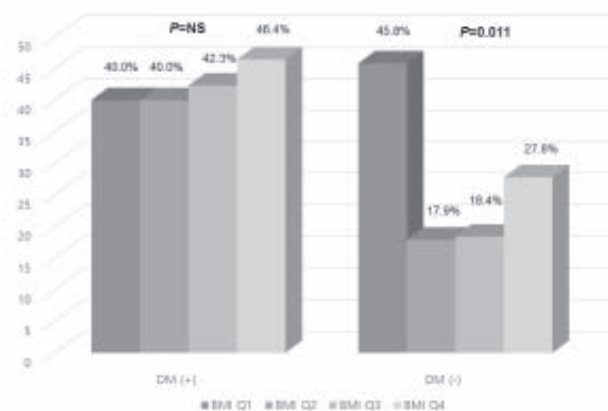
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Background: Obesity and diabetes mellitus (DM) is a risk factor for acute decompensated heart failure (ADHF). However, patients with very low body mass index (BMI) shows worse outcome after heart failure. The objective of this study was to investigate the effect of BMI in the outcome after ADHF

Method: From January 2009 to December 2011, 255 consecutive patients who were presented with acute decompensated heart failure at an emergency department of a regional tertiary university hospital were retrospectively enrolled in the present study. Patients were divided into four groups according to the BMI quartile. Q1 (<19.9 kg/m²), Q2 (≥ 19.9 kg/m², <22.15 kg/m²), Q3 (≥ 22.15 kg/m², <24.46 kg/m²), Q4 (≥ 24.46 kg/m²). A composite of death, heart failure readmission was evaluated according to the BMI quartile and they were further compared in the subgroups of DM and non-DM.

Result: Patients showed similar composite outcome in the patients with DM. However, In the patients without DM, lowest quartile of BMI showed worst outcome (45.8%), the next place was highest quartile (27.8%). Patients with normal or overweight according to the Asian criteria showed similar incidences of composite outcome (17.9%, 18.4% respectively).

Conclusion: In the patients with DM, composite event was similarly high according to the quartiles of BMI. However, in non-DM patients, lowest quartile of BMI showed worst outcome.



P214

Prognostic implications of visit-to-visit blood pressure variability in the patients with heart failure

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Background: Recently, many literatures have been showed that visit-to-visit blood pressure variability (BPV) is associated with cardiovascular events and mortality independently of high blood pressure (BP) values. But the prognostic value of BPV has not yet been validated in heart failure patients.

Methods: We evaluated the patients hospitalized for acute decompensated heart failure (ADHF) in ten regionally-representative tertiary university hospitals who registered in the Korean Acute Heart Failure (KorAHF) Registry from March 2011 to December 2013. Of the 5,627 patients, 900 patients with atrial fibrillation were excluded. The average BP and BPV, as determined by the standard deviation (SD) and coefficient of variation (CV) of systolic and diastolic BP, were recorded at the time of discharge and in outpatient clinic at 3 months, 6 months and 12 months after discharge. The cardiovascular outcome was defined as a composite of death and rehospitalization with aggravated heart failure.

Results: A total of 3,727 patients (1703 females) were analyzed. Mean age was 67.4 ± 15.3 . Average BP was $132.1 \pm 31.5/78.1 \pm 18.8$ mmHg at the time of admission and $115.2 \pm 18.2/67.1 \pm 11.5$ mmHg at the time of discharge. Average BP was $117.0 \pm 16.0/68.0 \pm 9.3$ mmHg and visit-to-visit BPV was $12.6 \pm 7.8/8.5 \pm 5.2$ mmHg by SD and $10.7 \pm 6.4/12.6 \pm 7.8$ % by CV during the follow up. After a mean follow up duration of 138.3 ± 77.0 days, 250 patients (6.7%) died and 625 patients (16.8%) were rehospitalization with aggravated heart failure. The patients with clinical event showed significantly lower SBP (114.4 ± 16.8 vs. 117.7 ± 15.7 , $P < 0.001$) and DBP (66.1 ± 9.0 vs. 68.5 ± 9.3 , $P < 0.001$), but systolic BPV (12.4 ± 8.1 vs. 12.6 ± 7.8 by SD, 10.9 ± 6.8 vs. 10.7 ± 6.3 by CV) and diastolic BPV (9.0 ± 5.6 vs. 8.4 ± 5.2 by SD, 13.7 ± 9.2 vs. 12.3 ± 7.3 by CV) were comparable between two groups. In multiple regression analysis, average SBP and DBP was independent predictor of clinical

outcomes, but systolic BPV and diastolic BPV did not predict clinical event. In survival analysis, there was also no association between systolic/diastolic BPV and the composite clinical outcomes.

Conclusions: In contrast with other clinical entity, these findings suggest that visit-to-visit BPV is not associated with clinical outcomes in heart failure patients.

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Prognosis in acute heart failure according to the cause of decompensation

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Purpose: Heart failure (HF) is responsible for the majority of hospitalizations due to cardiovascular disease, and different clinical triggers are related to the cardiac decompensation. Objective: To evaluate the prognosis of patients hospitalized due to acute heart failure, according to the cause of decompensation.

Methods: We retrospectively evaluated data from 731 patients consecutively admitted in a private cardiovascular center due to acute heart failure during the year of 2013. We analyzed the frequency of each factor assigned as the trigger of the decompensation of HF among these patients, and also the length of stay and the number of deaths in each group. The infection group was compared with the other 2 groups separately, using Fisher's exact test for categorical variables and Student's t-test for continuous variables.

Results: The main cause of HF decompensation in hospitalized was infection (34.6% of cases), followed by progression of the disease (26.1%), poor compliance (17.2%), arrhythmia (9%) and hypertension (6%). The factor "infection" was associated with more days of hospitalization (Table), above the average of other triggers (10 x 6.95 days; p < 0.01). The number of days in ICU in the cases of decompensation due to infection was also higher than the average from other causes (5.8 x 3.35 days; p < 0.01). In addition, of the 48 deaths in 2013, 58% (n = 28) were in patients with decompensated HF due to infection, and among these 28 deaths 15 were secondary to evolution of sepsis, in 6 there were predominance of the cardiac condition while the remaining 7 deaths showed mixed shock (cardiac and septic) or other complications related to both conditions leading to death.

Conclusion: Infection was the main factor of decompensation, requiring a longer hospital stays, more days in the ICU and being responsible for most of the deaths occurred in patients hospitalized for acute HF. Studies of specific approaches in acute HF triggered by infection are warranted.

	Infection (n= 253)	Noncompliance (n = 126)	Progress of disease (n = 191)	P value
ICU stay (days)	5.8 (+- 9)	3.7 (+- 3.9)	3.2 (+- 3.1)	0.013 and < 0.001
Length of stay (days)	10 (+-9.2)	7 (+- 5.7)	8.1 (+- 7.3)	0.019 and < 0.001
In-Hospital mortality	11.1%	3.2%	5.2%	0.009 and 0.039
Readmission in 30 days	21.3%	19.8%	12%	0.78 and 0.011

P216

Old and young: does heart failure care about age?

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Purpose: Elderly patients represent an increasing proportion of the hospitalized acute decompensated heart failure (ADHF) patients. Furthermore, HF is a leading cause of morbidity and mortality in this age group. Therefore, we aimed at comparing the clinical and biological characteristics between the very elderly, a less studied age group, and young patients, the usual clinical trial candidates, with ADHF, which may help in better understanding the proper management of elderly HF patients.

Method: We retrospectively analyzed 181 consecutive pts admitted for ADHF between January - June 2013 in an Internal Medicine Department. We retrieved demographic, clinical and paraclinical characteristics from the patients admission charts. We compared different characteristics between patients under 80 years of age (young HF group (YNG)) and the very elderly (ELD) (patients above 80 years of age). LV ejection fraction > 45% was considered preserved LV systolic function, glomerular filtration rate (eGFR) was estimated using CKD-EPI study equation and chronic kidney disease (CKD) was considered at eGFR <60ml/min/1.73m².

Results: We studied 181 pts, mean age 73.3 ± 11.11 years. The ELD included 59

pts (32.5%) and the comparison with the YNG is displayed in the table.

Conclusions: The very elderly ADHF pts are more frequently women with a high burden of CKD. However, the number of HF drugs is lower than in the YNG and they are less likely to receive a beta blocker or spironolactone. With the increasing life expectancy, this population is becoming an important patient prototype.

Characteristic	ELD (59 pts)	YNG (122 pts)	P
Age (years)	84.9±3.5	67.6±8.9	-
Female, ÷	61.0	40.9	0.01
Overweight, ÷	13.5	30.3	0.01
Hypertension, ÷	79.6	82.7	0.9
Diabetes mellitus, ÷	21.1	29.5	0.7
CKD, ÷	68.8	39.0	0.00
HF with preserved EF, ÷	59.3	47.5	0.1
≥3 HF drugs, ÷	61.0	75.4	0.04
Beta blockers, ÷	61.0	80.3	0.00
Spironolactone, ÷	13.5	44.2	0.00

P217

Cardiogenic shock complicating acute coronary syndromes

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Introduction: Despite advances in the treatment of patients with acute coronary syndromes (ACS), cardiogenic shock (CS) remains the leading cause of death in these patients.

Purpose: Determine characteristics and management of patients with an ACS complicated by CS. Determine predictors of development of CS during hospitalization and predictors of in-hospital mortality.

Methods: Retrospective study of 2064 patients consecutively admitted for ACS in a Coronary Unit over a period of 4 years.

Results: During the years under study, 111 patients (5.4%) developed CS. Patients with CS were more likely to be older (69.8 ± 13.2 vs 63.5 ± 13.1 years, p < 0.001); there were no significant differences in other clinical characteristics. Myocardial Infarction with ST segment elevation (STEMI) was more frequent in patients with CS (p < 0.001). Patients with CS underwent less often coronary angiography (p < 0.001), revascularization (p = 0.004) and were less treated with β-blocker (p < 0.001) and ACE inhibitors therapy (p < 0.001).

In multivariate analysis, predictors of occurrence of CS during hospitalization were: tachycardia (OR 3.2, 95% CI 1.6-6.3), systolic blood pressure <100 mmHg (OR 4.1, 95% CI 2.1-8.0), GFR <60ml/min (OR 2.5, 95% CI 1.2-5.2), STEMI (OR 4.1, 95% CI 2.0-8.0) and Killip class > 1 (OR 3.5, 95% CI 1.8-6.8) at admission.

The in-hospital mortality of patients with CS was 45%, compared with 1.7% in those who did not develop CS. Factors associated with an increased mortality in patients with CS included absence of coronary revascularization (OR 4.9, 95% CI 1.5-16.0), GFR <60ml/min (OR 4.4, 95% CI 1.3-15.6), advanced age (OR 6.4, 95% CI 1.6-26.2) and LVEF ≤ 35 % (OR 3.9, 95% CI 1.3-12.4).

Conclusion: According to the literature, our review showed that CS in the context of ACS is associated with a high mortality. We identified clinical markers that are associated with the development of CS and may spot patients at risk earlier. Absence of coronary revascularization remains an independent predictor of mortality in CS.

P218

Acute heart failure on admission predicts early mortality of STEMI: an analysis of the real-world 3000 STEMI patients

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Purpose: Routine evaluation of STEMI patient is needed to improve the outcome of the patient. We sought to evaluate the STEMI care based on a real world registry.

Methods: Data was derived from an ongoing prospective, observational registry that aims to enroll all patients with acute coronary syndrome admitted to the emergency department of a national cardiac referral hospital. Between 2008-2013, 3000 STEMI patients were retrospectively analyzed. Logistic regression analysis was performed to identify the predictors of in-hospital mortality of STEMI patients.

Results: The mean age of STEMI patient was 55.5 ± 10.2 years and most of them were male (67%). Most of the STEMI patients (62%) were referred from other hospital, had smoker (64%), anterior wall MI (60%) and killip class 1 on admission

(69%). The in-hospital mortality of STEMI patients who had an onset of infarction between 6 to 12 h was significantly higher than patients who presented within the first two hours after symptom onset (8.8% vs. 7.3%, $p=0.017$, respectively). The over all in-hospital mortality was 6.8%. After a multivariable analysis, Killip class 2 to 4 on admission was the strongest predictor of in-hospital mortality (OR = 3.60; 95% CI 2.67 to 4.86, $p < 0.001$) (Table 1).

Conclusion: Late STEMI presenters (6 to 12 h after symptom onset) was associated with a higher in-hospital mortality than very early presenters (≤ 2 h). Moreover, Killip class 2 to 4 on admission was the strongest predictor of in-hospital mortality. A systematic chain of network activation including pre and in-hospital protocols is needed to improve the outcome of STEMI patients.

Table 1

Variables	Odds Ratio (95% Confidence Interval)	P Value
Age ≥ 65 years	1.88 (1.34 - 2.64)	0.001
Male gender	0.75 (0.49 - 1.15)	0.192
Diabetes Mellitus	1.86 (1.39 - 2.51)	0.001
Smoker	1.05 (0.73 - 1.49)	0.791
Symptom onset ≤ 2 hours	1.42 (0.77 - 2.61)	0.256
Symptom onset 6-12 hours	1.50 (1.08 - 2.09)	0.015
Killip class 2 to 4	3.60 (2.67-4.86)	<0.001

Multivariable predictors of in-hospital mortality

P219

High sensitive troponin is associated with high risk clinical profile and outcome in acute heart failure

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Background: Accurate risk stratification is important in patients with acute heart failure. The value of high sensitive cardiac T troponin (hsTnT) in this setting has not been evaluated yet and, so far, is unknown.

Methods: 187 patients admitted with acute heart failure between 2013 and 2014 were selected, excluding those with acute coronary syndromes or sustained cardiac arrest; hsTnT was measured at admission using commercial kits and normal value was below 14 ng/L. The total amount of patients with upper normal hsTnT was evaluated in the population and its relationship with outcomes during hospitalization and at 90 days as well.

Results: 93% (n = 174) had a high hsTnT value; the median hsTnT value at admission was 42 ng/L (IQR 24-81). Patients with ischemic etiology, ejection fraction < 45% and those with cardiogenic shock at admission had higher hsTnT values (51 ng/L IQR 27-89 vs 35 ng/L IQR 23-68, $p=0.039$; 43ng/L IQR 25-67 vs 25 ng/L IQR 16-30, $p=0.0004$ and 73 ng/L IQR 53-113 vs 39 ng/L IQR 24-58, $p=0.004$, respectively). During the hospitalization, patients that received inotropic therapy or vital support (ventricle or respiratory assistance and dialysis) had higher hsTnT values (76 ng/L IQR 50-107 vs 39 ng/L IQR 23-58, $p=0.002$ y (86 ng/L IQR 57-131 versus 40 ng/L IQR 23-58, $p=0.002$, respectively). At 90 days of follow up, 28 deaths (15.5%) and 27 acute heart failure re-admissions were recorded. A hsTnT value > 43 ng/L ($p=0.021$), hypotension at admission ($p=0.002$), cardiogenic shock presentation ($p < 0.0001$) and left ventricle ejection fraction < 45% were associated with death and/or acute heart failure re-admissions. At multivariate analysis, inotropic therapy was and independent factor associated with death and re-admissions ($p=0.007$).

Conclusions: hsTnT elevation was an almost constant feature in this population and was related with ischemic etiology, left ventricle dysfunction and cardiogenic shock presentation; hsTnT helped to identify patients with worse outcomes during hospitalizations and higher risk of death and acute heart failure re-admissions.

P220

Prognostic significance of worsening heart failure in patients hospitalized for acute decompensated heart failure

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Purpose: The aim of the study was to evaluate prognostic significance of worsening heart failure (WHF) in patient hospitalized for acute decompensated heart failure (ADHF).

Methods: In retrospective analysis we enrolled 51 consecutive patients (mean age:

61.8 years, female: 26.9%) admitted to hospital with ADHF diagnosis. Patients were divided into 2 groups: WHF (n = 32, 62.7%) and non-WHF (n = 19, 37.3%). WHF was defined as worsening of signs and/or symptoms during the acute phase of a heart failure episode requiring an intensification of intravenous therapy for heart failure or mechanical ventilation, renal or circulatory support within 5 days from baseline. Prognostic measures including all-cause mortality, rehospitalization for cardiovascular causes and combined endpoint consisted of death and rehospitalization were collected 1 year and 3 years after the date of discharge.

Results: In whole study population we observed 32 rehospitalizations (62.7%) and 8 deaths (15.7%) within 1 year, whereas within 3 years the number of rehospitalizations has grown up to 46 (90.2%) and deaths up to 16 (31.1%). Within 1 year number of rehospitalization was significantly higher in patients without WHF (non-WHF: 78.0% vs. WHF: 50.0%, $p=0.04$), whereas in patients, who experienced WHF number of death was higher, but not statistically significant (WHF: 21.9% vs. non-WHF: 5.3%, $p=0.1$). Within 3 years there were no differences between the groups in terms of rehospitalization (WHF: 78.1% vs. non-WHF: 94.7%, $p=0.1$) and death (WHF: 31.25% vs. non-WHF: 31.58%, $p=0.9$). Cox proportional hazards analysis has revealed that experience of WHF during hospitalization was not associated with greater risk of mortality and rehospitalization within 1- and 3- years after discharge. Furthermore, in Kaplan-Meier analysis survival probability free from death, rehospitalization or combined endpoint calculated at 1- and 3- years after discharge was similar in both groups.

Conclusion: WHF was a very frequent finding in patients with ADHF and affected even 62.7% of the study population. Occurrence of WHF during hospitalization for ADHF was not associated with unfavorable prognosis.

P221

Pattern of arrhythmias and its correlates in acutely decompensated heart failure patients at a west african cardiology practice

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Purpose: Heart failure (HF) is a complex clinical syndrome and cardiac arrhythmias are important feature that contribute to symptoms, periodic decompensations in about 24% - 29%, and mortality in the form of sudden death.

We evaluated acute HF patients in a cardiovascular practice in West Africa for the frequency, types and relationship of arrhythmias to underlying heart disease and function.

Methods: Two hundred (200) adults with acute HF and 50 controls were recruited. Demographic and clinical parameters were obtained, blood samples for biochemical parameters drawn and ECG and echo were performed. Data was analysed using SPSS version 17.0.

Results: The 200 HF cases comprised of 104 males (52%) and 96 females (48%), whilst the controls were 25 (50%) males and 25 (50%) females. The mean age of cases and controls were similar, 52.9 \pm 15.8 Vs 51.0 \pm 15.9 years, $P=0.43$.

Majority of the subjects, 62% had hypertension, 9.5% diabetes mellitus while 28.5% other preexisting CVD.

Subjects had higher LV mass and lower EF than the controls 286.91 \pm 101.80gms vs 149.6 \pm 34.94gms, $p < 0.0001$ and 45.27 \pm 14.10% vs 66.23 \pm 10.30%, $p < 0.0001$ respectively.

Frequency of systolic dysfunction was 53% in the cases and 0% in the controls, $p < 0.0001$ and diastolic dysfunction was higher in the cases 56.5% Vs 28% ($P < 0.0001$).

Of the HF cases, 25.5% had atrial and junctional rhythm, 3% ventricular rhythm while all the controls were in sinus rhythm. The frequency of arrhythmias was higher in the HF 78% Vs 26%, $p < 0.0001$.

Sinus tachycardia was the commonest arrhythmia in 26.5% of HF cases.

Atrial fibrillation was the commonest sustained rhythm occurring in 22% of the cases followed by premature ventricular complexes 20% and 2% had sustained VT.

Of the 156 HF cases with arrhythmia, 67.9% had systolic dysfunction (EF < 50%); The mean EF was significantly lower in the heart failure patients with arrhythmia compared to those without arrhythmia (44.12 \pm 14.32% Vs 49.37 \pm 12.63%, $p=0.03$).

Dilated cardiomyopathy (DCM) was the most common echocardiographic heart disease and was found in 56.5% of the HF subjects and 82.3% had arrhythmias. There was no relationship between the underlying heart disease and arrhythmia frequency.

Conclusion: Atrial fibrillation remains the most important rhythm abnormality and the frequency and severity arrhythmia seen is related to the degree of cardiac dysfunction. The underlying heart disease did not have much effect on the frequency or type of arrhythmia in these HF patients.

P222

Predictors of re-admission rates at 6 months after hospitalization for acute heart failure

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Purpose: Increased rates of re-hospitalization have been reported in the short-term after an admission for acute heart failure (AHF). The role of vascular function on prognosis has been little studied in patients hospitalized with AHF. The aim of the current study was to identify predictors of re-admission at 6 months after a hospitalization for AHF and investigate the potential prognostic role of vascular function in these patients.

Methods: Our study included 91 patients (mean age 71 years, 79% males) who were admitted for AHF syndrome (new onset or decompensation of chronic heart failure) and were followed-up for 6 months after discharge. A comprehensive medical history was taken and the functional status at admission (NYHA class) was recorded. Standard demographic, clinical and laboratory parameters were included in analyses. A complete echocardiographic (conventional and tissue Doppler parameters) study, a 6-minute walking test and peripheral vascular studies (assessment of brachial artery flow mediated dilation using ultrasound, carotid-femoral pulse wave velocity, central augmentation index, estimated central aortic pressures, large and small vessel compliance using tonometry) were performed in all subjects 24-48 hours prior to discharge.

Results: There were 28 (31%) patients with preserved left ventricular ejection fraction (LVEF>40%, i.e. HF-PEF), 50 (55%) had ischemic etiology of heart failure, while 22 (24%) appeared with NYHA IV on admission. LVEF was $37 \pm 15\%$ (mean \pm SD). During the 6-month follow-up, 23 (25%) patients were admitted to the hospital for a new AHF syndrome. In univariate Cox regression analysis, the presence of non-ischemic heart failure (HR 2.51, $p=0.036$), BMI (HR 1.09, $p=0.072$), serum HDL (HR 0.96, $p=0.058$), diastolic blood pressure (HR 1.04, $p=0.033$), central diastolic blood pressure (HR 1.04, $p=0.041$), LVEF (HR 1.04, $p=0.013$) and $E/E' > 15$ (HR 2.22, $p=0.077$) were associated with readmission at 6 months. In multivariate analysis, $E/E' > 15$ ($p=0.004$) and higher LVEF ($p=0.006$) were independent predictors of readmission at 6 months in our population.

Conclusion: In our population of AHF patients, increasing left ventricular filling pressures and higher LVEF were associated with increased readmission rates indicating probably the high morbidity associated with pulmonary congestion and HF-PEF. Interestingly, vascular function did not appear to play an important role in the prognosis of re-hospitalization rates at 6-months after an episode of AHF.

P223

Heart failure on admission is the main mortality predictor in patients suffering from post-infarction rupture of interventricular septum

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Purpose: Patients with the post-infarction rupture of interventricular septum very often present with serious extent of acute heart failure. Purpose of this study was to determine main clinical features of patients with post-infarction rupture of interventricular septum and main predictors of post-operative survival.

Methods: From January 1989 to June 2009 in our Institute for Cardiovascular Diseases we treated 85 patients with this complication of acute myocardial infarction. Full clinical and operative data were obtained for 74 patients (43 males, mean age 65.57 ± 10.4).

Results: Complication's median time was 7 days from acute myocardial infarction. Inferior infarction was present in 36 (48.6%), anterior infarction in 26 (35.1%), and combined anterior and inferior infarction in 12 (16.2%) patients. Selective cardiac catheterization revealed the coronary artery occlusion in two thirds of patients, and most of them had multivessel coronary disease. Pulmonary edema at admission was present in 19 patients (25.67%) and 39 of them (52.7%) were in cardiogenic shock. 32 patients received surgical treatment with closure of the post-infarction septum defect (14 also received the aortocoronary bypass graft), while 42 patients were treated medically. Early mortality in surgically treated patients was significantly lower (43.6%) compared to medically treated ones (85.7%) ($p < 0.0001$). Survival was not related to age, extent of coronary artery disease and concomitant procedures performed (bypass vs. no bypass) in surgically treated patients. Infarction extent and heart failure stage (Killip III and IV) were independent mortality predictors.

Conclusions: Surgical treatment of the post-infarction rupture of interventricular septum is a treatment of choice decreasing mortality. Heart failure stage (Killip III and IV) on admission was the main independent predictor of intrahospital survival.

P224

Trends changing overtime of heart failure patients in Indonesia

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Purpose: In this present study, we determined the trends changing overtime according to the characteristics of heart failure patients in Indonesia.

Methods: We retrieved all the heart failure (HF) patients' data in heart failure registry National Cardiovascular Center Harapan Kita, Jakarta, Indonesia. From which, we examined retrospectively and compared the characteristics of HF patients in 2012 ($n=1264$) and 2013 ($n=539$). The data were analyzed using bivariate methods such as chi square test and independent t-test.

Result: There was an increase in patients with rehospitalization of HF in 2012 (68%) than 2013 (89.3%); [$p < 0.001$]. The length of stay was also increase from 6.32 days of hospitalization to 8.43 days of hospitalization ($p < 0.001$). From patients' history, we found that history of percutaneous coronary intervention (16.4% vs 10%; $p < 0.001$), history of chronic kidney disease (27.4% vs 18.8%; $p < 0.001$), and history of myocardial infarction (61.8% vs 47.6%; $p < 0.001$), hypertension (41.7% vs 34.1%; $p=0.003$), and diabetes mellitus (42.8% vs 34.9%; $p=0.002$) were found higher in 2012 than 2013. However, smoking habit (46.1% vs 53.4%; $p=0.005$) and decompensated HF (70.6% vs 78.5%; $p < 0.001$) were higher in 2013. In addition, HF with new york heart association (NYHA) IV classification was found significantly increased from 2012 to 2013 (11.1% vs 79.1%; $p < 0.001$). Meanwhile, no different of patients' mean age ($58.30 + 14.48$ vs $58.56 + 13.87$ years; $p=0.736$) and left ventricular ejection fraction (LVEF) [$38.20 + 18.92\%$ vs $38.56 + 18.98\%$; $p=0.763$] between those years.

Conclusion: Our study showed that there were some changing trends of heart failure patients' characteristics in Indonesia between 2012 and 2013.

P225

Predictors of heart failure occurrence in a population of acute myocardial infarction patients

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Purpose: the aim of the study was to evaluate the level of heart failure in acute myocardial infarction patients in a tertiary cardiology center; their demographic and clinical background on hospital admission; and the main predictors in occurrence of heart failure during acute myocardial infarction hospitalization.

Methods: we prospectively analyzed demographic and clinical data on 587 consecutive AMI patients from January 2013 to September 2014; Framingham criteria were used to determine HF patients on admission and Killip class ≥ 2 at any time of hospitalization with follow-up extended to three weeks; valvular and nonischemic cardiomyopathies were excluded; a logistic regression model was used to define predictors of heart failure occurrence.

Results: heart failure was identified in 156 (26.5%) pts of our AMI population; heart failure group differed significantly from the rest regarding: age (69.4 ± 11.2 vs 61.7 ± 11.6 , $p < .0001$); sex (male) (62.3% vs 82.4%, $p < .0001$); heart rate on admission (80.16 ± 19.35 vs 70.64 ± 11.13 , $p < 0.001$); systolic BP on admission (119.6 ± 30.5 vs 132.9 ± 24.2 , $p = .001$); prior MI (21.8% vs 6.8%, $p < .0001$); glycemia on admission (168.5 ± 83.2 vs 143 ± 77.4 , $p = .007$); prior HTN treatment (35.5% vs 64.5%, $p = .031$); prior coronary revascularization (10.4% vs 3.5%, $p = 0.012$); peripheral vascular disease (11.4% vs 3.5%, $p = .005$); chronic renal disease (12.3 vs 4%, $p = .005$); EF (36.9 ± 9.1 vs $57.2 \pm 5.7\%$, $p < .0001$); anemia (18.9% vs 7.9%, $p = .003$); AF occurrence (8.5% vs 1.8%, $p = .003$); no significant differences in HTN ($p = 0.923$), diabetes ($p = 0.114$), dyslipidemia ($p = .987$); presence of STEMI (.141); smoking ($p = 0.054$). Independent predictors of HF occurrence in logistic regression were: EF OR 4.78 (95%CI: 1.73-13.03); prior revascularization OR 3.84 (95%CI: 1.34-11.6); peripheral vascular disease OR 2.14 (95%CI: 1.57-4.36); age OR 1.83 (95%CI: 1.25-3.16); sex OR 0.42 (95%CI: 0.23-0.76); prior MI OR 1.89 (95%CI: 1.12-4.03); systolic BP on admission OR 0.87 (95%CI: 0.63-0.91); anemia OR 1.69 (95%CI: 1.37-2.85).

Conclusions: regardless lowering trends in mortality following AMI, heart failure remains an important complication in our daily clinical practice; special attention should be paid to the most vulnerable population especially elderly pts, women, those with known coronary disease and comorbidities.

P226

Clinical characteristics and prognosis of the elderly patients with acute decompensated heart failure

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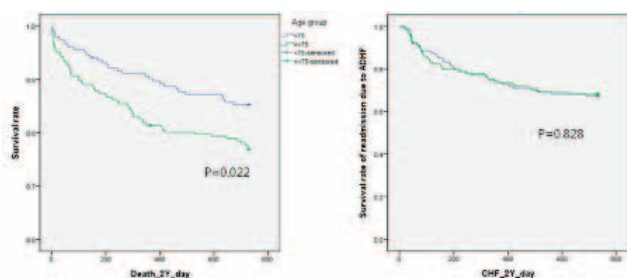
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Purpose: In our island, the proportion of elderly population is increasing continuously. Elderly patients have become a main group of acute decompensated heart failure (ADHF). We sought to their clinical characteristics and prognosis.

Method: We enrolled 451 patients with ADHF who were residents of our Island from 2005 to 2013. They were divided into two aged groups: ≥ 75 (group 1; $N = 247$, 82.5 ± 5.5 years) and < 75 years old (group 2; $n = 204$, 61.9 ± 11.2 years)

Results: More patients in group 1 were female and non-smokers, and had co-morbid conditions such as hypertension and COPD. The 3 common cause of ADHF were Ischemic heart disease(34.4%), hypertension(18.6%) and valvular heart disease(14.6%). On the other hand, those in group 2 were ischemic heart disease(27%), D-CMP(20.1%) and valvular heart disease(18.6%). In group 1, NYHA functional class and cardiac biomarker (serum CKMB and serum NT-pro BNP) was higher. Echocardiographic finding were also similar in both group except E/E' (23.32 ± 12.27 vs. 20.02 ± 8.27 , $p = 0.006$). Less patients in group 1 were taking beta-blockers (37% vs. 48%, $p < 0.021$) and calcium channel blocker (26.3% vs. 17.6%, $p < 0.028$). The proportion of ACE inhibitor/ARB and diuretics use were similar. 2-year mortality was higher in group 1 (24% vs. 15%, $p < 0.022$), but 2-year readmission rate due to ADHF of group 1 was not different (30% vs. 31%, $p = 0.828$)

Conclusions: More than half of ADHF patients in Jeju Island were over 75 years old. Current treatment of ADHF was similar in both aged group except beta-blocker usage. Elderly group showed high mid-term mortality but morbidity due to ADHF were not different with younger group. More tailored therapeutic strategy may be required to improve long-term prognosis in elderly ADHF patients.



Survival curve of Death and readmission

CHRONIC HEART FAILURE

P227

Severe systolic dysfunction prognosis in a specialised unit

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Purpose: Frequent hospitalizations represent a deterioration in the quality of life of patients in advanced heart failure stages. The objective of this study is to analyze the characteristics and pattern of hospital admissions of patients with heart failure and severe dysfunction of left ventricle followed in a unit of heart failure (UIC) in the 12 months prior to death.

Methods: Were analyzed retrospectively qualitative and quantitative variables of the patients followed in our unit from 2008 to 2013 as well as the pattern of hospitalization in the last 12 months prior to his death, comparing them with no dead patients

Results: We followed to 599 patients in our unit there were 47 dead (7.9%). The average age was 70 ± 9.7 years, being 66% men and 34% women. They had an average of $30 \pm 11\%$ left ventricular ejection fraction of which 45.5% were diabetic, 18.2% EPOC, 31.8% had renal failure, analytically with NTproBNP 283 ± 547 and uric acid 6 ± 4 mg/dl

Sinus rhythm were 27.3% of patients and a heart rate 70 ± 24 bpm. Advanced functional grade (II-IV NYHA) was 70% of them, being treated with an angiotensin-converting-enzyme inhibitor 65% of patients, 10% with angiotensin II receptor blockers, 65% with b blockers, 70% with aldosterone antagonist, 95% with oral diuretic, 45.5% with antiplatelet therapy

72% of patients died from cardiac cause: 40.3% directly related to heart failure cause (multiorgan failure/cardiogenic shock) and 13.8% sudden death; and the rest of cause not heart.

Patients who died in this period had a greater number of hospital readmissions (1.62 versus 0.2 $p < 0.000$) in relation to patients who were still alive and presented an average hospitable stay 2.24 times longer (28.55 days versus 12.77 days, $p < 0.039$)

Conclusions: Patients with heart failure in advanced stages have a greater number of readmissions and hospital stays which represents an important consumption of healthcare resources, specially their last year of life. It is important to implement and promote palliative measures for the final phases of life in these patients.

P228

Preference for erectile dysfunction treatments in patients with chronic heart failure

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Objective: to evaluate variations in sexual and erectile function in subjects with chronic heart failure (CHF) after optimization of CHF treatment.

Methods: 160 patients men (age range 40-76 years; mean age 60 years), with CHF and erectile dysfunction (ED), were divided two groups, one under symptomatic treatment of ED; were asked all of them to complete the International Index of Erectile Function IIEF-5 before (at baseline) and 3 months after optimization of treatment of CHF.

Results: Among 160 patients studied, 47,3% have an optimal treatment of CHF versus 52,7% have not, more than 60% of patients with optimal treatment of CHF (and without symptomatic treatment of ED) showed significant improvements on the 5 domains of the IIEF-5, compared to 25% of patients without optimal treatment and under symptomatic treatment of ED (the difference was statistically significant).

Conclusion: the results of this study support that optimal treatment of CHF improves erectile function in patient with erectile dysfunction secondary to CHF better than symptomatic treatment alone.

P229

Validation of peripheral arterial tonometry as diagnostic procedure for detection of sleep disordered breathing in patients with chronic heart failure

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Background: This study examines the validation of a portable device using peripheral arterial tonometry (PAT) as a measurement of SDB in patients with heart failure especially in patients with chronic heart failure (CHF). A high prevalence (about 70%) of SDB in patients with heart failure is known. While 36% of CHF-patients are suffering from obstructive sleep apnea (OSA), 40% are diagnosed with central sleep apnea (CSA).

Patients and Methods: For validation of the PAT device 20 patients with CHF are investigated. PAT measurements are additionally performed within a scheduled polysomnographic examination (PSG). PAT recording is used in diagnostic night and therapeutic night. Data of both measurements (PSG and PAT) will be analyzed and compared in reference to specific types of SDB. Thus, it shall be shown that PAT can detect therapy evoked changes in apnea-hypopnea-index (AHI), oxygen-desaturation-index (ODI) and oxygen saturations.

Results: At this point 11 patients with CHF are examined. All of them are diagnosed with SDB, detected by both PSG and PAT. In particular, seven patients had primarily OSA, while four patients had primarily shown CSA. This was only detected by PSG.

Discussion: So far it seems likely that PAT examination can detect SDB in patients with CHF, but it is not able to distinguish between OSA and CSA. Furthermore it shall be investigated if accurate detection of SDB by PAT depends on type of CHF (heart failure with reduced ejection fraction = HFREF versus heart failure with preserved ejection fraction = HFPEF). Additionally, it shall be analyzed if haemodynamic changes under therapy can be seen in PAT's raw data.

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Smoking habit and other risk factors in heart failure patients-results from CRO-HF Registry

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Therisk factors are important in development of heart failure (HF). The aim of the study was to analyse the smoking habit and other risk factors in patients with HF.

Results: A total of 2203 in-hospital HF patients from CRO-HF Registry were analyzed: 46.7% females-f, 53.3% males-m, median age 76 y, 37.8% preserved LVEF. History of hypertension was recorded in 67.5%, diabetes in 34.4%, ACS in 22.7%, renal failure in 19.2%, COPD in 17.3% and atrial arrhythmia in 53.7% patients.

Active smokers were 11.1% (14.8% m, 6.4% f) and 15.6% former smokers (24.9% m, 3.9% f). Smoking was related with COPD. Among HF-COPD patients (19.7% m, 14.7% f, $P = 0.009$), active smokers was 30.6%, former 24.8% and 13.9% non smokers ($P < 0.001$).

Overweight was 46.3%, obese 25% patients, 51.9% had anaemia, 46.8% azotemia, 32% hyperlipidemia, 79.3% hyperuricemia and 99.8% hyperglycemia.

The frequent "triggers" of HF were hypertension-55.5%, arrhythmia-51.3%, valvular heart disease-32.8%, ACS-19.7% and infections-19.6%. In-hospital mortality rate was 13.8%.

Conclusion: Smoking habit had one third, higher body weight two thirds, and anaemia more than half of patients. The frequent concomitant diseases were hypertension, diabetes, ACS, arrhythmia, renal failure and infections. The risk factor correction should be important target in prevention of HF.

P231

Nor polypharmacy nor length-of-stay are correlated with survival in old old patients (> 85 years) with chronic heart failure

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Background: For the old old patients (pts) with congestive heart failure the use of combinations of drugs can easily lead to a sort of "evidence-based" polypragmasie and a longer length-of-stay (LOS).

Methods: We analyzed a lot of 125 pts older than 85 years (mean 87.43 +/- 2.54 years, range 85-99 years), 53.6% male, enrolled consecutively between January 2011 - December 2012, diagnosed with congestive heart failure. We have compared some features of two subgroups: survivors (S=112 pts) vs deceased (D=13 pts).

Results: The old old patients group included patients diagnosed mainly with ischemic dilated cardiomyopathy (57/45.6%), alcoholic cardiomyopathy (4/3.2%), mixed (26/20.8%), hypertensive cardiopathy (31/30.4%), in NYHA class II (61/48.8%), class III (55/44%) and class IV (9/7.2%), with length of hospitalization of 8.10+/-3.98 days and the rate of re-hospitalization 6.4% and the death rate 10.4%. Number of drugs taken was 5.53+/-1.86 in S group vs 5.85+/-1.86 in D group (p=0.421) and the length-of-stay was 8.18+/-3.79 in S group vs 7.38+/-5.53 in D group (p=0.06). There were significant differences between group S vs D in: NYHA class, non-smoker status, hemoglobin level (12.57+/-1.92 vs 11.20+/-1.87 g/dl, p=0.017), blood urea nitrogen (58.38+/-28.92 vs 77.30+/-47.99 mg/dl, p=0.04), serum uric acid (6.32+/-1.99 vs 8.91+/-4.27 mg/dl, p=0.001), serum sodium (139.97+/-4.55 vs 136.69+/-7.12 mg/dl, p=0.024) and BNP (524.49+/-116.87 vs 2480.75+/-951.99 pg/ml, p=0.001).

Conclusions: The number of drugs given to old old patients has not proven to reduce the length of stay, the rate of death and re-hospitalization. Hyponatremia, anemia and increased urea and serum uric acid are associated with increased mortality of old old patients.

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Comparative study of changes in venous pH during exercise in untrained healthy volunteers and patients with chronic heart failure

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Purpose. pH- blood level is critical for life. Alterations in acid base status which may lead to incorrect clinical decisions will be discussed. There is a narrow range of pH values that the human body and its enzyme-supported system operates within. Changes in venous pH during maximal exercise in heart failure (HF) patients is not well studied. The purpose of the present study was to measure the time-related changes in venous pH during maximal exercise in untrained healthy volunteers and heart failure patients with III NYHA class. **Methods.** 17 untrained healthy volunteers, mean age 26+/-7 years, 15 men, BMI 24+/-4; and 38 heart failure (HF) patients with III NYHA class, mean age 48+/-11 years, 32 men, BMI 27+/-2 were evaluated during progressive treadmill exercise. The ventilatory variables were recorded breath-to-breath (Oxycon Pro, Jaeger, Germany). The cubital venous catheter was installed in all subjects before exercise test. Blood samples were taken at baseline and at 1-minute intervals during test. PH, lactate and HCO₃-concentration were estimated using analyzer i-STAT, cartridge CG4 (Abbot, USA). **Results.** Oxygen consumption at peak exercise in HF patients was lower than that in healthy volunteers: 13.4+/-23.7 and 38+/-5.3 ml/min/kg, respectively, p < 0.05. Venous pH mean values at baseline were 7.39+/-0.03 and 7.38+/-0.04 in untrained healthy volunteers and HF patients, respectively, p > 0.05. Venous pH mean values at peak exercise were 7.17+/-0.05 and 7.36+/-0.05 in untrained healthy volunteers and HF patients, respectively, p < 0.05. **Conclusions.** The pH-range during maximal exercise in heart failure patients with III class is narrower than that in untrained healthy volunteers.

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Chronic heart failure and diabetes: two frequent companions in clinical practice

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Purpose: Diabetes, a frequent comorbidity in patients with heart failure, influences the clinical characteristics in patients hospitalized for chronic heart failure. The objective of the study was to analyze the clinical characteristics of patients with chronic heart failure and diabetes, hospitalized in the internal medicine clinic of a university emergency hospital over a period of 6 months, as compared with those without diabetes.

Methods: A total of 412 patients with chronic heart failure were included. Clinical and laboratory variables, along with the treatment, were retrospectively reviewed from the hospital database.

Results: From the 412 patients hospitalized with chronic heart failure, 67 were diabetics (16.26%). The main comorbidities in the group of patients with heart failure and diabetes were: 48 patients had arterial hypertension (71.64%), 43 dyslipidemia (64.17%), 38 ischemic heart disease (56.71%), 33 valvular diseases (49.25%), 21 chronic kidney disease (31.34%), 20 atrial fibrillation (29.85%), 18 dilatative cardiomyopathy (26.86%), 13 pulmonary hypertension (19.40%). Heart failure patients with diabetes were younger (mean age 65 ± 2 y vs 71 ± 3 y) and had a higher prevalence of ischemic etiology and atrial fibrillation comparing with heart failure patients without diabetes. Also, in-hospital mortality and length of stay (8.2 vs 6.7 days) were higher in diabetics. Sex distribution of patients with heart failure and diabetes was: 31 women (46.26%) and 36 men (53.73%). 86.56% of heart failure patients with diabetes were obese; only 32.75% of those without diabetes were obese. All diabetic patients were treated with oral antidiabetics; 14 were treated with insulin.

Conclusions: Heart failure patients with diabetes had higher short-term mortality and duration of hospitalization compared with patients without diabetes; also, they were younger than non-diabetic patients. Diabetic patients with heart failure had greater body mass index than heart failure patients without diabetes and were more likely to have more advanced renal disease.

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Religious beliefs towards the end of life among patients with chronic heart failure

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Background: Religious beliefs may influence decision-making about end-of-life care among patients with Chronic Heart Failure (CHF) and may change towards the end-of-life. Data in CHF are scarce. Aims of this longitudinal observational study were: to explore whether preferences for life-sustaining treatments and end-of-life care are influenced by religious beliefs among patients with CHF; and to explore whether religious beliefs change towards the end-of-life.

Methods: This study included 427 patients with CHF of the TIME-CHF study (69% of the original sample; 62% male; mean age 76.6 (7.5) years; 62% NYHA class III). Confession, strength of religious beliefs (Religion Questionnaire), preferences for CPR, and willingness to trade survival time for excellent health were assessed (Time Trade-Off tool). The relationship between religious beliefs and preferences for CPR and willingness to trade survival time at baseline was explored. In addition, changes in religious beliefs between baseline and 12 months were explored among patients who died between 12 and 18 months.

Results: 47% were Catholic, 42% Protestant, 5% other and 6% atheist. Atheist patients more often preferred 'Do Not Resuscitate' (DNR) than Catholic patients (56% vs 32%, respectively, p=0.03). Patients with strong religious beliefs as assessed with the Religion Questionnaire were less likely to prefer DNR than patients without religious beliefs (p < 0.05). There was no relationship with willingness to trade survival time (p > 0.05). The belief in afterlife increased among patients who died between 12 and 18 months (p=0.04), while feeling supported by religion tended to decrease at the end of life (p=0.07).

Conclusions: CHF Patients with strong religious beliefs are less likely to prefer DNR. Religious beliefs may change towards the end-of-life. Therefore, exploring religious beliefs and the influence on preferences for life-sustaining treatments as part of advance care planning seems to be important.

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Effectiveness of using low dose MRA's in heart failure patients unable to tolerate recommended doses: A single-centre observational study in an Irish population

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Purpose: Mineralocorticoid Receptor Antagonists (MRA) have been proven to lower hospitalization rates for worsening heart failure, have a significant improvement in heart failure symptoms and are recommended in selected patients by current ESC guidelines.

Managing a mostly older cohort of patients with advanced heart failure and multiple co morbidities including chronic kidney disease can be challenging. One such challenge is the difficulty in up-titrating MRA's to the recommended daily dose. There is limited data on the effectiveness of lower dose MRA's in reducing hospitalisations or NYHA class.

We examined the effectiveness of lower doses of Eplerenone (<225mgs OD- mean dose = 22.5mg) and Spironolactone (<25 mgs OD mean dose = 12.5mg) in 37 patients attending an outpatient heart failure service.

Method: A retrospective study examined 37 patients currently attending the heart failure service in the last quarter of 2014 (average age 77 years, 13 female, 24male) in NYHA class 2 to 4, 24 with reduced EF (<40%) and 13 patients with HFPEF (EF 50%).

All patients attending the service observed to be on lower dose MRA's were included in the study. All available patient records were examined pre and post introduction of lower dose MRA's to determine EF, EGFR, Creatinine level, Systolic BP, NYHA class and admission rates. Admission rates also included episodes of decompensating heart failure managed in an ambulatory setting with IV diuretics from 2011 to 2014.

Results: The mean number of admissions per patient prior to introduction of MRA's was 1.16 compared to 0.37 post introduction. The results indicate a significant reduction in admission rates post introduction of lower dose MRA's ($p = 0.001$).

NYHA class was shown to be reduced significantly ($p = 0.0001$). Prior to introducing lower dose MRA's the mean NYHA class was 3.2 compared to 2.5 post introduction of MRA.

There were no significant changes in EF, Creatinine level, EGFR or Systolic BP.

Potassium levels were not significantly different post introduction. However the mean Potassium level prior to introduction of low dose MRA was 3.8mmols compared to 4mmols post introduction.

Conclusion: This study suggests the use of lower dose MRA's in patients unable to tolerate recommended daily doses will still benefit from a reduction in admission rates and an improvement in NYHA class.

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Clinical features of chronic heart failure in patients with rheumatoid arthritis

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Purpose: Rheumatoid arthritis (RA) refers to diseases that increase the risk of cardiovascular disease, including chronic heart failure (CHF). CHF in patients with RA develops due to systemic damage, presence of concomitant cardiovascular disease and influence of anti-rheumatic therapy, mainly glucocorticoids (GC). The purpose of this study was to analyze the clinical features of CHF in patients with RA and to assess the association of this phenomenon with severity of RA (activity, progressive course, systemic manifestations), presence of concomitant arterial hypertension (AH), coronary heart disease (CHD), GC treatment duration.

Methods: We observed 96 patients (82 female and 14 male) with a significant clinical signs of RA and CHF functional class (FC) 2-3 (NYHA) in age from 42 to 74 years, mean age 58.34 ± 4.56 years. All participants underwent a standard examination for verification of CHF, as recommended by the ESC 2012. Along with this we analyzed the association of CHF with RA activity and duration, presence of erosive arthritis, extra-articular manifestations, levels of laboratory markers of inflammation, duration of GC therapy, as well as the degree of blood pressure elevation and clinical manifestation of coronary artery disease.

Results: Systolic dysfunction was found in 11 patients, the remaining 85 patients had myocardial structural damage and / or signs of diastolic dysfunction. Related hypertension was diagnosed in 71 patients, clinical signs of coronary artery disease were determined in 43 patients, with no significant differences in the severity of CHF in patients depending on the presence of CHD. We revealed a direct relationship between the activity, duration and the presence of systemic manifestations of RA on the one hand and the FC of heart failure - on the other. In the group of RA patients without clinical signs of CHD BNP levels correlated with the levels of CRP and pro-inflammatory cytokines. Systolic dysfunction was observed predominantly in patients with long standing (>10 years) progressive RA who had been treated by systemic GC.

Conclusions: Thus, high disease activity in long standing erosive RA and GC treatment were the most significant factors associated with CHF and contribute to the development of systolic dysfunction.

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Effects of spironolactone on the left ventricular hypertrophy in chronic heart failure with preserved ejection fraction

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Background: The activation of renin-angiotensin-aldosterone systems plays a key role in the development of myocardial hypertrophy and fibrosis. However, ACE inhibitors can't inhibit the left ventricular (LV) remodeling sufficiently, which may be related with 'aldosterone escape' phenomenon. The use of aldosterone antagonists may have additional benefits in LV structural parameters improving.

Aim: To evaluate the effects of spironolactone (SPRL) on LV hypertrophy in patients with chronic heart failure (CHF) with preserved ejection fraction (EF).

Methods: We observed 79 patients (48 men and 31 women, mean age 54.5 ± 10.5 years) with stable coronary arterial disease (CAD) and mild CHF (no higher II functional class (NYHA)) with preserved systolic function of the LV (EF > 45%). The patients were randomly divided into 2 groups: SPRL group was treated with the standard therapy (ACE inhibitors or angiotensin receptor blockers II, β -blockers, statins, antiplatelet agents) plus SPRL (25 mg/day, titrated to 50 mg/day if tolerated) and control group was treated with standard therapy only for the next 6 months. Transthoracic echocardiography (TTE) for all patients at baseline and after 6 months was performed. The LV posterior wall thickness (LVPWT), intraventricular septal thickness (IVST), relative wall thickness (RWT) and LV mass index (LVMI) were determined. Patients were classified into 4 subgroups of LV geometric pattern according to the LVMI and RWT.

Results: At baseline there were no significant differences between two groups ($p > 0.05$). After 6 month both groups significantly reduced the IVST compared with the initial data, but it was strongly expressed in the SPRL group ($p = 0.012$). There were no significant changes in parameters of LVPWT and RWT in both groups ($p > 0.05$). The addition of SPRL treatment significantly reduced the number of patients with concentric LV hypertrophy - from 22 (55%) to 7 (17.5%) ($\chi^2 = 10.6$, $p = 0.001$) and increased the number of patient with normal geometry - from 2 (5%) to 11 (27.5%) ($\chi^2 = 5.88$, $p = 0.015$); however, it didn't significantly improve the eccentric LV hypertrophy ($p = 0.653$). The patients with concentric remodeling have appeared in SPRL group - 7.5%. There were no significant improvement in the LV geometric pattern in control group ($p > 0.05$).

Conclusions: These results indicated that the addition of SPRL to the standard treatment is clinically useful to improve the LV geometric pattern and reduce the LV hypertrophy in patients with stable CAD and mild CHF with preserved EF.

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Changes in novel biomarkers of hypertrophy and fibrosis are better predictors of cardiovascular admission than those of cardiac myocyte stretch in patients with chronic heart failure

British Heart Foundation Pump Priming Grant (RE/08/003) S Susan Piper¹; D Hipperson²; J Decourcy²; R Sherwood²; G Amin-Youssef²; A Shah¹; TA McDonagh¹

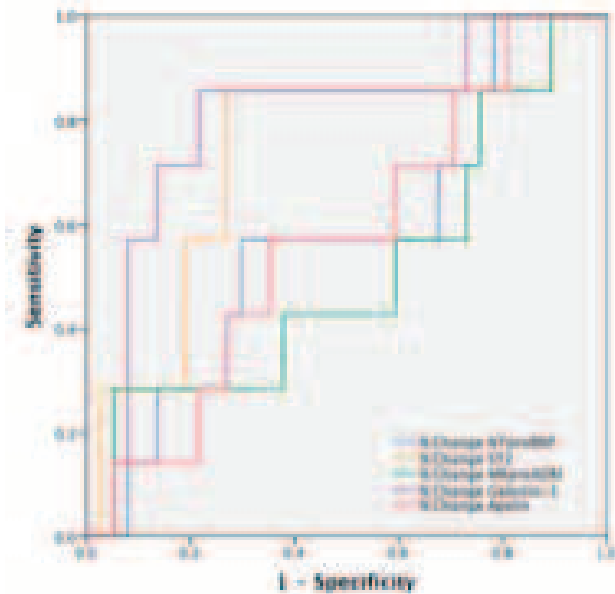
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Background: The B-type natriuretic peptides, BNP and NTproBNP, are established markers of cardiac myocyte stretch advocated for diagnostic and prognostic use in heart failure patients. The evidence for serial monitoring to predict decompensation in heart failure has, however, been mixed. We examined serial concentrations of four novel biomarkers to ascertain superiority over NTproBNP in predicting cardiovascular admission; sST2 and Galectin-3, both markers of hypertrophy/fibrosis, and Apelin and Mid-regional pro-adrenomedullin (MRproADM) both markers of cardiac myocyte stretch.

Methods: We prospectively studied 50 patients with stable CHF due to LV systolic dysfunction. All patients were on optimum doses of prognostically indicated medications and in NYHA Class I-III. Mean age was 67.3 years (SD 11.568), 82% were male and 48% had IHD. Mean LVEF was 30.7%. Patients were followed for a period of 6 months with samples drawn at baseline, 1 month, 3 months and 6 months.

Results: On ROC analysis, AUC for % change in the respective biomarkers and CV admission was 0.803 ($p = 0.012$) for Galectin-3, 0.734 ($p = 0.052$) for sST2, 0.571 ($p = 0.553$) for Apelin, 0.506 ($p = 0.962$) for MRproADM and 0.571 ($p = 0.553$) for NTproBNP. Comparable results were found for absolute changes in biomarker concentrations with AUC of 0.807 ($p = 0.011$), 0.734 ($p = 0.052$), 0.417 ($p = 0.490$), 0.546 ($p = 0.700$) and 0.579 ($p = 0.511$) respectively.

Conclusion: Markers of hypertrophy/fibrosis, sST2 and Galectin-3, are better predictors of CV admission than either NTproBNP or other novel markers of cardiac myocyte stretch. This may reflect longer-term adverse pathophysiological changes associated with hypertrophy and fibrosis compared with those of stretch. Further studies are required to corroborate these findings.



ROC analysis for % change

P239**Central sleep apnea and arrhythmic disorders in stable patients with systolic ventricular dysfunction**

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Introduction: From 30 to 50% of patients with chronic and stable heart failure with systolic ventricular dysfunction may suffer sleep related respiratory disorders, mostly central apnea and Cheyne Stokes respiratory pattern. These disorders have been related with cyclic sympathetic hyperactivity and greater occurrence of ventricular arrhythmias. Our objective was to document the prevalence of central apnea among patients with systolic dysfunction and study its association with the presence of arrhythmias during sleep, mid-term clinical follow up was performed in such a matter.

Methods and Materials: We selected 81 consecutive patients in a prospective manner that were clinically stable during the last month (57,1 +/- 1,5 years, Left Ventricular Ejection Fraction 29,4 +/- 1,3%, Male 87%). Nocturnal polysomnography with simultaneous holter cardiac monitoring was performed. We analyzed the heart rate, the presence of cardiac pauses and the occurrence of premature beats or tachycardia in patients diagnosed with central sleep apnea (group I) and in patients without respiratory disorders (group II) observed in the polysomnography test and compared the results. The need for hospitalization because of cardiac deterioration was registered.

Results: In our cohort of patients, 31,6% were diagnosed with central sleep apnea. There were no significant differences between group I and group II taking into account sex, age, etiology of heart failure (52 vs 36,2% ischaemic, 36 vs 44,8% idiopathic), NYHA class function or pharmacologic treatment. There were no differences in the median, maximal or minimal heart rate between groups, neither in the presence of supraventricular premature beats or supraventricular tachycardia. There was a greater incidence of ventricular premature beats both isolated ($p=0,001$) and paired ($p=0,004$) in group I as well as ventricular tachycardia ($p=0,043$) and cardiac pauses >2 seconds ($p=0,027$). Group I 96% vs Group II 42,4% ($p<0,001$) required hospitalization on follow up.

Conclusions: More than one third of patients with stable and chronic systolic heart failure suffer sleep apnea. In those patients nocturnal ventricular arrhythmias and hospitalization are more frequent.

P240**The plasma levels of fibronectin in patients with ischemic heart failure: links with endogenous intoxication and hemodynamic parameters**

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The purpose of study was to evaluate of plasma fibronectin (FN) levels in patients with chronic heart failure (HF) and its relations with other heart failure signs.

Materials and methods: 389 patients with HF of ischemic genesis and 30 apparently healthy persons (control) were observed. The FN plasma level was detected by ELISA method. Endogenous intoxication was detected by erythrocyte absorption test. Analyses were performed with Statistica system software, version 12.0.

Results: The average age of observed patients was (68,2 ± 11,9) years. Due New York Heart Association criteria the following functional classes of HF were diagnosed: II FC - in 64 patients (16,5%), III FC - in 258 patients (66,3%), IV FC - in 67 patients (17,2%). The average period of HF was 10,0 [5,0; 15,0] years. 277 (71,2%) patients had history of myocardial infarction (MI), and 27 (6,9%) of them had recurrent MI. In 195 (50,1%) patients the second class of stable angina was verified. 107 (27,5%) patients had third functional class of angina. The more often comorbidities in observed patients with HF were: arterial hypertension (AH) - in 308 (78,9%) persons; 2 type Diabetes Mellitus - in 79 (20,3%) persons; chronic kidney disease - in 76 (19,5%) cases; atrial fibrillation - in 32 (8,2%) patients; peripheral artery disease - in 19 (4,9%) patients; history of stroke - in 34 (8,7%) persons.

The average FN level in HF patients was higher for 1,24 times compare control group: (257,68 ± 7,24) µg/mL vs (207,56 ± 13,62) µg/mL ($p<0,05$). We also verified of more higher concentration of FN in patients with atrial fibrillation: (354,60 ± 27,19) µg/mL compare (259,55 ± 7,88) µg/mL in patients with sinus rhythm ($p<0,01$). During HF progression the FN plasma levels was increased at II-III FC (NYHA), but decreased at FC IV.

The lineal multiply regression analysis showed the more important links between FN and endogenous intoxication, left atrium size and end-systolic volume of left ventricle. Conclusions. The ischemic heart failure is characterized by high fibronectin plasma levels. The highest fibronectin concentration was detected in patients with atrial fibrillation. The most important risk-factors for fibronectin level are endogenous intoxication, left atrium size and end-systolic volume of left ventricle.

P241**Improvement in diastolic function and functional class of heart failure with preserved ejection fraction in hypertensive patients: ramipril vs eprosartan**

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Purpose: To compare the effect of long-lasting therapy with Ramipril and Eprosartan on diastolic dysfunction (DD) and functional class of heart failure (HF) in hypertensive phenotype of HF with preserved ejection fraction (HFpEF)

Methods: The study enrolled 101 patients with essential hypertension (49,5% men; mean age 50,11 ± 0,79 years) with left ventricular hypertrophy (LVH), DD and preserved ejection fraction (EF>50%). Functional class of HF was evaluated on the basis of a six minute walk test (6MWT). All patients were randomly assigned to treatment with Ramipril (R-gr; n = 56, mean dose=15,3mg±1,2 mg/daily) or Eprosartan (E-gr; n=45, mean dose=850 ± 12,4 mg/daily), associated to diuretic (Indapamid 1.5 mg/daily). Ambulatory blood pressure monitoring (ABPM), transthoracic echocardiography (TE), and 6MWT were performed at baseline and after 6- and 12-months of treatment.

Results: Compared to the baseline, there was a statistical improvement in diastolic function after 6 months of treatment in both groups, and this tendency was even more evident at the end of the study: only 20 patients (35,71%) in R-gr and 2 patients (4,44%) in E-gr presented delayed relaxation (DR), ($p<0,001$) vs 53 patients (94,64%) in R-gr and 43 patients (95,56%) in E-gr, ($p>0,05$) at the beginning of study. At baseline, pseudonormal filling (PsnF) was registered in 3 patients (5,36%) in R-gr and 2 patients (4,44%) in E-gr ($p>0,05$), but no patients showed this pattern after 12 months of follow-up period. At this time, normal diastolic filling (NDF) has been noticed in 36 patients (64,29%) in R-gr vs 43 patients (95,56%) in E-gr, ($p<0,001$). According to baseline functional disturbances during 6MWT, patients were categorized in functional class of HF (NYHA) as follows: II NYHA-60,7% patients (pts), III NYHA-39,3% pts in R-gr vs 60,00% and 40,00%, respectively, in E-gr ($p>0,05$). At 12- month of follow-up examination, 31,5% pts showed I NYHA, 54%-II NYHA, and 14,4%- III NYHA in R-gr vs 42,3%, 49% and 8,6% respectively, in E-gr ($p<0,001$).

Conclusion: Both drug-regiment with Ramipril and Eprosartan have shown beneficial effect on diastolic dysfunction and have improved the functional class of heart failure in hypertensive patients, but these improvements were significantly greater in the Eprosartan group.

P242**Dementia-related adverse effects in the prospective comparison of ARNI with ACEI to determine impact on global mortality and morbidity in heart failure trial (PARADIGM-HF)**

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America; ⁶University of Gothenburg, Department of Molecular and Clinical Medicine, Gothenburg, Sweden; ⁷Medical University of South Carolina, Charleston, United States of America; ⁸Novartis Pharmaceutical Corporation, Hanover, United States of America; ⁹University of Texas Southwestern Medical School, Dallas, United States of America

Background: Inhibition of neprilysin, an enzyme degrading natriuretic and other vasoactive peptides, is beneficial in heart failure with reduced ejection fraction, as shown in PARADIGM-HF which compared the angiotensin receptor neprilysin inhibitor (ARNI) LCZ696 (sacubitril-valsartan) to enalapril. As neprilysin is also one of many enzymes clearing amyloid- β peptides from the brain, there is theoretical concern about the long-term effects of LCZ696 on cognition. Therefore, we examined dementia-related adverse effects in PARADIGM-HF.

Methods: Patients with NYHA class II-IV heart failure (HF), a LVEF \leq 40% and a mildly elevated BNP/NT proBNP were randomized to LCZ696 200mg bid or enalapril 10mg bid in a 1:1 ratio. We searched adverse event reports (AERs) coded using the Medical Dictionary for Regulatory Activities (MedRA) using Standardized MedRA Queries (SMQs) with "broad" and "narrow" preferred terms (PTs) related to cognition, memory, dementia-like and related events.

Results: 8399 patients aged 18-96 yrs were randomized and followed for a median of 2.25 yrs (up to 4.3 yrs). The narrow SMQ search identified 27 relevant AERs: 15 (0.35%) on enalapril and 12 (0.29%) on LCZ696 (HR 0.79, 0.37-1.70). The numbers using the broad search were: 83 (1.96%) and 86 (2.05%), respectively, HR 1.03 (0.76, 1.39). The most common PTs in each treatment group are shown in the Table.

Conclusion: We found no evidence that LCZ696, compared with enalapril, increased dementia-related adverse events in PARADIGM-HF.

Broad SMQ Dementia	LCZ696 n (%)	Enalapril n (%)
Confusional state	12 (0.29)	18 (0.43)
Somnolence	11 (0.26)	9 (0.21)
Amnesia	10 (0.24)	7 (0.17)
Delirium	10 (0.24)	8 (0.19)
Agitation	7 (0.17)	3 (0.07)
Memory impairment	6 (0.14)	6 (0.14)
Dementia	6 (0.14)	10 (0.24)
Narrow SMQ Dementia		
Dementia	6 (0.14)	10 (0.24)
Dementia Alzheimer's type	2 (0.05)	2 (0.05)
Vascular dementia	2 (0.05)	1 (0.02)

P243

Biomodal and echocardiographic profile of patients with HFpEF

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Purpose: Heart failure with preserved ejection fraction (HFpEF) is a common stage in the course of various cardiovascular disorders. It comprises abnormalities in cardiac structure and function, as well as complex biomodal activation, which are responsible for major clinical outcomes. Our study aimed at characterizing the biomodal and echocardiographic profile in such patients.

Methods: We studied plasma levels of NT-proBNP, uric acid, total and conjugated bilirubin, hemoglobin, kidney function (eGFR - MDRD equation) and echocardiographic parameters of left ventricular remodeling and diastolic dysfunction in a cohort of 99 patients with HFpEF of different etiologies.

Results: Almost all patients (97 out of 99) had left ventricular (LV) concentric remodeling, quantified by a relative wall thickness (rwt) \geq 0.42, irrespective of the presence or absence of arterial hypertension, diabetes mellitus, ischemic heart disease, valvular heart disease or atrial fibrillation. The only comorbidity which correlated significantly with LV concentric remodeling was chronic kidney disease (rwt = 0.61 \pm 0.19 as compared to 0.54 \pm 0.08 in patients without chronic kidney disease, p = 0.042). rwt significantly correlated with E/E' ratio (r = 0.480, p = 0.001) and plasma NTproBNP values (r = 0.337, p = 0.002). Plasma uric acid correlated with plasma NT-proBNP (r = 0.259, p = 0.017) and functional NYHA class (r = 0.234, p = 0.031). One third of patients had levels of hemoglobin below 12 g/dl. Hemoglobin levels inversely correlated with plasma NT-proBNP values (r = -0.318, p = 0.002). Conjugated bilirubin correlated with mitral E/A ratio (r = 0.401, p = 0.031), plasma NTproBNP values (r = 0.283, p = 0.026) and functional NYHA class (r = 0.267, p = 0.036).

Conclusions: Patients with HFpEF have prominent left ventricular concentric remodeling, irrespective of the etiology of heart failure. This concentric remodeling is more pronounced in patients with associated chronic kidney disease and correlates with left ventricular diastolic dysfunction and biomodal activation. Anemia is a prevalent comorbidity in heart failure and it is associated with higher NT-proBNP levels. Plasma uric acid and conjugated bilirubin correlate with functional NYHA class and biomodal activation, thus being potential markers of disease severity.

P244

Can the conundrum of cardiac regeneration be solved by a catheter intervention?

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Purpose: We conceptualized that hemodynamic changes induced by a simple trans-coronary sinus catheter intervention induce regenerative molecular pathways. During normal embryonic development hemodynamic pressure in the primitive beating heart tube is sensed by endocardial layers transducing this "mechanical" epigenetic information as normal developmental impulse enhancing structural maturation. Mechanotransduction induced by temporal elevation of blood pressure in cardiac veins by PICSO is believed to be the central signal in this process reopening the morphogenetic gate to reenter cardiac development thus inducing structural regeneration.

Methods: Patients were treated with PICSO after electrode testing during CRT placement for 20 minutes. Serum of PICSO and control patients was collected before and after the intervention or the equivalent time in controls. Septal cardiomyocytes of a heart transplant recipient with dilated cardiomyopathy were excised during heart transplantation and cultured. Serum of study patients was then co-cultivated and pre and post-interventional values were compared to controls. Furthermore HCM57 cardiomyocytes were incubated with patient's serum with or w/o PICSO treatment, pre- and post PM implantation and the time course of KLF-4 protein levels after PICSO-treated serum incubation compared to control serum.

Results: A significant enhancement of cardiomyocyte proliferation was observed when cocultivated with patient serum treated with PICSO as compared to pre-intervention and both control values. There was also a significant upregulation of the pluripotency marker KLF-4 protein in probes co-cultivated with PICSO sera coinciding with a 72% reduction in mortality in treated patients followed over 5 years.

Conclusion: Here we show that molecular and clinical evidence emphasizes the proposed hypothesis. The revival of an imbedded albeit dormant developmental process in the human adult and failing heart via activation of coronary venous endothelium can be restored. Proliferation of cardiomyopathic cardiomyocytes and the expression of pluripotent signaling molecules are surrogates indicating structural recovery. Reduction in mortality shown here close the gap between molecular findings and clinical significance. Although these data have to be corroborated in a large multicenter Trial, the ease of the intervention with a simple catheterization of the coronary sinus and with manageable treatment times ensure the great potential that a solution for the conundrum of cardiac regeneration might be within clinical reach.

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Optimised management of over-80-year-old heart failure patient improves outcomes: HF80 Pilot randomised study

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Introduction: The prevalence and incidence of heart failure (HF) in elderly patients are increasing worldwide. The management of HF with reduced left ventricular ejection fraction (HFREF) in over-80-year-old patients follows international guidelines despite the lack of a dedicated study. The question therefore remains: is there a benefit in optimising the management of HF with reduced LVEF in over-80-year-old?

Materials and methods: The HF80 pilot study is a prospective study. Over-80-year-old patients hospitalised for HFREF were randomised in an optimised group (optimised management) or a control group (usual care). Primary endpoint was quality of life (QoL) at 6 months (Minnesota Questionnaire).

Results: The trial was stopped prematurely, according to prespecified rules, after thirty-four patients were included (n = 17 in each group). There was no difference in QoL at baseline and at 6 months between the 2 groups (p = 0.14 and p = 0.64, respectively), although a significant improvement was observed between baseline and 6 months in the optimised group as opposed to the control group (-20.2 \pm 25.2, p = 0.01 vs. -9.9 \pm 19.0, p = 0.19). Mortality at 12 months was lower in the optimised

group (17.7% vs. 47.1%, $p=0.047$). There was no increase in acute renal failure, hyperkalaemia or falls in the optimised group ($p=0.49$, $p=1$, $p=1$, respectively). Moreover, ACE inhibitors were significantly less reduced or halted ($p=0.04$) while beta-blockers were further increased ($p=0.003$) in this group.

Conclusions: Optimising the management of HFREF in over-80-year-old patients, according to the modalities of the HF80 Pilot Study, is both effective (improved QoL at 6 months and decreased mortality at 12 months) and safe (no observable increase in side-effects).

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Chronic Heart Failure Patient short term prognostic analysis using a simple clinical biological score

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CHF is a severe disease associated with a high risk of re-hospitalization and death. Most of prognostic scores focusing on long term follow up and are complex. On the opposite of acute heart failure scores, there is no real score that could be used by clinicians in order to analyze the instability of HF and the risk of short term (6 months) re-hospitalization or death.

We have analyzed the prognostic performance of several clinical biological and echocardiographic data in a prospective cohort of 1310 consecutive patients followed in our heart failure out patient hospital with systolic heart failure. Mean follow up was 52 months (6- 84 months). 3287 medical examinations pairs were finally analyzed. The events taken in account should be before the next planned out patient hospitalization (6 months). Our patients were mostly male (70%) and young (mean age 63 years old (15-96), 70% were in sinus rhythm, 10% demonstrate clinical congestion (lower limb oedema). Mean LVEF was 36 % (+- 10%). Mean BNP was 424 (+-200) pg/ml. HF aetiology was dilated in 50% and ischaemic in 40% of patients. During follow up 387 events (death or HF hospitalizations) followed out patient hospitalizations.

In our cohort, heart rate (cut off 60 and 80 bpm), weight variation (decrease 2kg/ increase more than 4 kg between two consecutive out patient hospitalization), NYHA class variation (increase of more than 1 class), BNP absolute value (<200, 200-500 and > 500 pg/ml) and BNP variation (decrease more than 30%) were statistically associated with a risk of events.

We have created a simple score (from 5 to 11 points) associating these different parameters classifying easily the patients.

Conclusion: A simple score could help clinicians to analyse the short term risk of death and hospitalization in a chronic setting in CHF patients. This could be useful in order to target high risk sub groups of patients that could benefit from an enhanced follow up or more aggressive management.

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Heart failure patients who stop taking medications are at risk for hospitalization

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Purpose: Medication nonadherence predicts hospitalization in HF patients, but the phase of nonadherence most responsible is unclear (initiation, implementation, or discontinuation). Our purpose was to determine which phase is most responsible and to identify characteristics of patients in that phase.

Methods: Adults with chronic HF were enrolled from 3 clinic sites in the US. Medication adherence over 6-months was measured using medication-event monitoring system (MEMS). Medication initiation was defined as percent of time to first dose taken, discontinuation as percent of time after the last dose was taken, and implementation as the period between. Clinical data were abstracted from medical records by nurses. Trail Making Test B was used to measure complex attention; higher scores indicate worse attention. Higher scores on the American National Adult Reading Test (ANART) indicate higher premorbid intellect. Higher scores on the PHQ-9 indicate more depression. Higher scores on the Charlson Comorbidity Index indicate more chronic conditions. All analyses used adaptive modeling methods.

Results: Of the 218 patients with MEMS data, 6 (2.8%) did not initiate their medicines immediately (median 13% of time in study). All 218 patients had some implementation phase data with most (53.7%) completing the full study. 83 (38.1%) patients met criteria for early discontinuation ($\geq 3.1\%$ of the full study period). Early discontinuation was the best predictor of hospitalization (risk factors shown in table). Area under the curve was very good for this model (0.75).

Conclusion: Discontinuing the medication regimen risks hospitalization in adults with chronic HF. Complex patients with multiple chronic conditions, numerous medications, depression, problems with attention and analytic skills may consider stopping medicines if not assisted to integrate the regimen into their lives.

Risk factors for early discontinuation

interaction term 1	interaction term 2	variable	risk factor	variable	risk factor	group n (%)	OR	95% CI
Charlson	≥ 4 vs. < 4	TMTB score	≥ 94 vs. < 94			33 (15.1)	6.31	2.58-15.4
ANART	≤ 37 vs. > 37	months of dx	≤ 21 vs. > 21			36 (15.1)	4.77	2.04-11.2
Meds #	≥ 7 vs. < 7	PHQ-9 total	≥ 9 vs. < 9			25 (11.50)	5.96	2.18-16.3
ANART	≤ 37 vs. > 37	pulse	≤ 58 vs. > 58			24 (11.0)	3.86	1.45-10.3

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Impact of Arg16Gly and Gln27Glu polymorphism ADRB2 gene on cardiovascular events in patients with heart failure

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Introduction: There is a wide evidence of the gene polymorphism influence on Arg16Gly and Gln27Glu polymorphism of ADRB2 gene has been demonstrated to be contribute to cardiovascular events. The results are different and depend on social, demographic and other factors.

Aim: To study if ADRB2 gene polymorphism Arg16Gly and Gln27Glu are correlated with heart failure.

Methods: We enrolled 151 HF patients (age 64.6 ± 10.4 and left ventricular ejection fraction $53.8 \pm 11.4\%$) and analyzed 1 year fatal and non-fatal cardiovascular events in association with Arg16Gly and Gln27Glu polymorphism ADRB2.

Results: Our results are statistically significant ($p < 0,05$) after comparing heart failure and non-cardiovascular diseases group with the frequency of occurrence genotypes Arg16Gly and Gln27Glu ADRB2. They show that subjects carrying the Glu27 of ADRB2 are more represented in HF patients ($p=0,04$). Mortality was 9,5% and was highest in the Arg16Arg (42%, $p=0,03$) and Glu27Gln (56%, $p=0,03$) genotypes. Fatal myocardial infarction was associated with Glu27Gln (60%, $p=0,035$) and non-fatal cardiovascular events (myocardial infarction, stroke, HF decompensation) - with the Arg16Arg polymorphism.

Conclusion: The Glu27Gln genotype ADRB2 more characterized HF patients than subjects without cardiovascular diseases ($p=0,04$). Myocardial infarction and stroke are frequent in HF patients with Arg16Arg and Glu27Gln polymorphism ADRB2, however, non-fatal- Arg16Arg ($p=0,04$).

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Construction of rating scale for men with heart failure (EAFSH_IC) sexual function

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Introduction: Sexual dysfunction is common in patients with heart failure (HF) 1. Studies showed its relationship to decreased quality of life and adherence to treatment 2. However, there are no specific rating scales of sexual function for men with HF.

Objective: To develop the Sexual Function Assessment Scale men with IC (EAFSH_IC).

Methods: a methodological study consists of five stages. At first, an integrative literature review, the second was the validation of the defining characteristics of the nursing diagnosis of sexual dysfunction NANDA-I taxonomy, then the committee of judges and the completion of the pre-test.

Results: integrative review analyzed 10 articles which explained as causes of sexual dysfunction in patients with heart failure, alteration of the endothelium, atherosclerosis, exercise intolerance, use of drugs, psicogênicos and hormonal factors. The defining characteristics of higher prevalence were related to physical effort (0.95), early diagnosis dysfunction together with (0.92), treatment (0.90), excitement (0.75) tiredness (0.63), pain (0.63) and fear (0:54). After evaluation of the judges the scale comprised 20 statements that verify the man's sexual function with IC. The alpha Conbrach for the 20 items of the scale was 0.860, which indicates a high level of reliability.

Discussion: The construction of EAFSH_IC brings to clinical practice greater accuracy to verify the sexual function of men with HF. Subsidize health professionals in screening and treatment of changes in sexual function.

Conclusion: It is expected to EAFSH_IC the identification of the causal factors of sexual dysfunction in men with HF for targeting interventions and achieve results

that improve the quality of life for them. The elaborate scale requires psychometric assessment for future application.

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Severity of sepsis and congestive heart failure in Type 2 diabetic patients undergoing surgery for gangrene, abscess, or cellulitis

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The aim of the study was to evaluate the interconnection between the severity of sepsis and congestive heart failure in Type 2 diabetic patients undergoing surgery for purulent-necrotic complications.

Methods: We analyzed 320 symptomatic consecutive Type 2 Diabetic patients (142 women and 178 men) aged 57.8±8.2 years undergoing surgery for gangrene, cellulitis, or abscess. Patients were divided into 4 groups: without sepsis 91(28.4%), with sepsis 112(35.0%), severe sepsis 79(27.7%), and septic shock in 38(11.9%). All the patients underwent laboratory tests, ECG, echocardiography.

Results: Among purulent complications prevailed gangrene of lower extremities 171 (53.4%). Partial foot amputation was in 74 (43.3%) cases, ankle disarticulation in 44 (25.7%), below-knee amputation was in 29 (17%), above-knee amputation (transfemoral) in 24 (14%). Abscess or cellulitis of lower limb was in 81 (25.3%) and 68 (21.3%), respectively. We diagnosed coronary heart disease functional class III in all selected patients, congestive heart failure functional class II (NYHA) was in 52 (16.3%), III in 190 (59.4%) and IV in 78 (24.4%) patients, left ventricle ejection fraction (LVEF) >55% in 121(45.5%), 55-30% in 145(54.5%). In severe sepsis and septic shock, we found a significant decrease in blood pressure and LVEF (p < 0.001) (Table). Blood coagulation and renal function worsen significantly with increasing severity of sepsis. BUN was significantly higher in septic patients than without it (p < 0.001).

Conclusion: With an increase in the severity of septic complications in Type 2 diabetic patients undergoing surgery for purulent-necrotic complications, increased functional class of congestive heart failure (NYHA), decreased LVEF, and increased BNP.

Laboratory and instrumental tests

Data	No sepsis	Sepsis	Severe sepsis	Septic shock	P-value
Systolic blood pressure	158.7±14.4	154.1±22.8	88.7±9.4*	64.1±7.8*	≤0.001
Diastolic blood pressure	93.4±5.3	91.9±8.6	63.4±5.3*	31.9±7.6*	≤0.001
LVEF, %	54.3±3.3	48.7±4.1	43.3±4.4	38.3±3.1*	≤0.001
HbA1C, %	9.1±1.1	13.9±0.5*	14.4±2.5*	13.9±0.9*	≤0.001
Fibrinogen, mg%	511±152	722±132	754±127	995±165*	≤0.001
Blood urea, mmol/l	7.1±1.9	12.4±1.6	12.1±2.2	16.8±2.7*	≤0.001
Blood creatinine, mmol/l	88±18	123±27*	167±17*	163±47	≤0.001
Brain natriuretic peptide, ng/ml	232±28	395±35*	412±32*	445±41	≤0.001

* - comparison with group without sepsis

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Evaluation of gender features of risk factors of chronic heart failure

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Objective: Assessment of chronic heart failure (CHF) prevalence and differential treatment in Azerbaijan based on retrospective evaluation.

Materials and methods: Retrospective analysis of 1824 case histories of CHF patients hospitalized in cardiology departments of SRI of Azerbaijan in 2013.

Results: Among hospitalized patients Azerbaijan Institute of Cardiology, the prevalence of heart failure is 51.4% of the total number of patients hospitalized in the Cardiology Institute of Azerbaijan.

The main etiologic factors of chronic heart failure in 79.9% of cases are ischemic heart disease and hypertension. Revealed significant differences in the etiology of heart failure in men and women, as well as in patients of all ages. The prevalence of heart failure in men was 56.8% in men with CHF recorded 1.3 times more likely than women; 41% of patients with CHF were older than 60 years. CHF with left

ventricular ejection fraction <45% was diagnosed in 84% of patients. It should be noted that, among patients with CHF with preserved left ventricular ejection fraction, the number of women with CHF increases to 22%, and it is higher than in men in 2 times.

Conclusion: There are gender differences in the structure of chronic heart failure patients: men more common have CHD (myocardial infarction), women - AH. In women with CHF occurs predominantly with preserved LV ejection fraction, the percentage of patients with this variant CHF increases to 22%, and it is higher than in men in 2 times.

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Effect of ivabradin in patients with ischemic heart disease and chronic heart failure

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Purpose: Ischemic heart disease (IHD) is still the main reason for death also in Slovenia. In disease development the heart rate (HR) has an important role. The HR and blood pressure are an indicator of heart burden. It has been proved by trials (ASSOCIATE, BEAUTIFUL, SHIFT) that ivabradin reduces the HR and improves aerobic capacity. We were interested for antiischemic and antianginal effect of ivabradin, its influence on physical performance, well-being and possible side-effects special in patients (pts) with chronic heart failure (CHF).

Methods: We studied 312 pts (162 women and 150 men) with IHD. There were 84 pts with CHF. All pts were on beta blockers, ASA and ACE inhibitors. Clinical evaluation, ECG recording, blood pressure measurement, ergospirometry, as well as survey about well-being were performed at the beginning, after 1 month and 3 months. The pts started to take ivabradine 5 mg twice per day. After one month followed an control examination. In pts with HR over 60 we started with ivabradine 7.5 mg twice per day.

Results: The results showed significant reduction of HR from 78 to 59 B/min. The systolic blood pressure reduced from 144 to 132 mm Hg and diastolic from 86 to 78 mm Hg. The angina pectoris attacks decreased from 1.88 to 0.59 attacks per week. Consumption of short acting nitrates was reducing from 1.32 to 0.14 pills per week. Physical performance increased from 4.4 to 5.6 METs. 296 pts at the end of study described better well-being. In subgroup with HF we had 49 women and 35 men. We found out the same reducing of blood pressure, HR, angina pectoris attacks and consumption of short acting nitrates. Physical performance increased from 4.8 to 5.3 METs. There were no side effects in both groups.

Conclusions: In this small study we confirm that ivabradin is good antiischemic and antianginal drug and it significantly improves physical performance and quality of life. It is reasonable to combine it with other drugs which we use them for treating IHD and CHF. In pts with IHD, stable angina pectoris, CHF and asthma ivabradine is a decision therapy.

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The presence of pulmonary hypertension and previous hospitalizations for heart failure are independent predictors of mortality or rehospitalisation in patients with advanced heart failure

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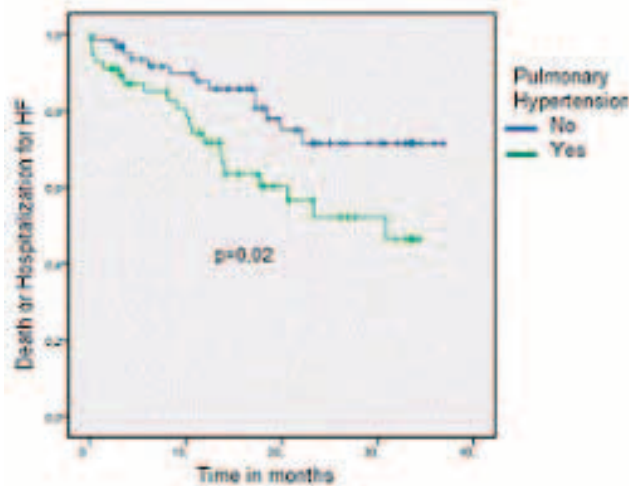
Objectives: The waiting time for heart transplantation (HTx) has steadily increased in Spain. This increases the risk for worsening heart failure (HF) and death in patients with advanced HF. Our aims were to assess characteristics of patients referred for evaluation to a HTx unit and identify predictors of mortality or hospitalization for HF.

Methods: Retrospective analysis of consecutive patients referred for evaluation to an outpatient clinic between 2011 and 2014. Endpoints evaluated were a) A combined end point of all cause mortality or hospitalization for HF and b) All cause mortality free of urgent HTx. Cox regression analysis and survival Kaplan-Meier curves were performed to identify predictors of risk.

Results: 125 patients were included, age 56.4±9.8 y, 78% males, 41% ischemic CMP. Mean LVEF was 23.8±6%, 56 (45%) had pulmonary hypertension (PH) and 63 (50%) reduced right ventricular (RV) function. After a median follow-up of 14±10 m, 26 pts underwent HTx and 34 died or had hospitalization for HF. Total survival free of hospitalization or HTx was 72.8%. Cox regression analysis identified the presence of hospitalizations for HF in the previous 12 months (HR 1.8; 95% IC: 1.3-2.5; p<0.001) and PH with and without RV dysfunction (HR 6.6, 95% IC: 1.2-37.5; p=0.032 and HR 4.1, 95% IC: 1.4-12.5; p=0.01) as independent predictors for death or rehospitalisation and the presence of hospitalization for HF as the only predictor for all cause mortality free of urgent HTx (HR 7.7, 95% IC: 1.7-35.2; p=0.008).

Conclusions: In patients with advanced HF, the presence of PH determined by echocardiography with or without RV dysfunction is predictor of death or rehospitalisation. Hospitalization for HF in the previous 12 months was an independent

predictor of all cause mortality and HF.



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Correlation between clinical and echocardiographic parameters and the 6 minutes walk test in ambulatory outpatients with systolic heart failure

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Background: The use of 6-minute walk test (6MWT) for assessing the functional status capacity of patients with chronic heart failure is commonly applied as prognostic gauges for systolic HF patients.

The aim of study was to verify the impact of 6 minutes walk distance (6MWD) in patients with chronic heart failure (CHF) and to analyze the relation between clinical and echocardiographic data and the 6MWT in patients with chronic systolic heart failure.

Methodes and Results: 814 patients (age 63years, 68% males) with CHF underwent a six-minute walk test in a therapeutic unit of heart failure. Clinical data, biological and echocardiographic parametres were compared.

We divided patients for 3 groups: group 1: 6MWD <300 m (n=740), group 2: 300<6MWD<450 m (n=54) and group 3: 6MWD > 450m (n=20). 154 patients (19%) were in NYHA fonctionnal class III: 96% (n= 148) patients in group 1, 3%(n=5) in group2 and 1% (n=1) in group 3 (p=0.04). Age, hypertension, diabetes, dyslipidemia, Ischemic heart disease, strock attack did not differ among the groups.

However male sex, diastolic dysfunction (p=0.01), right ventricular systolic dysfunction (p<0.0001), hospitalization rate for cardiac decompensation (p<0.0001), high heart rate were higher in the group with 6MWF <300 m.

Conclusion: In systolic heart failure outpatients, lower functional capacity during six minute walk is associated with more hospitalizations for cardiac decompensation, more diastolic dysfunction and right ventricular systolic dysfunction with goog correlation with NYHA fonctionnal class.

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The relationship of renal dysfunction with predictors of chronic heart failure

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Purpose: Renal dysfunction is widespread and associated with the poor prognosis in chronic heart failure (CHF). We aimed to estimate the relationship between predictors of CHF and renal function in Russians.

Methods: 175 CHF I-IV NYHA class patients with left ventricular ejection fraction (LVEF, Simpson) <45% without primary renal and oncological diseases were studied. Median (interquartile range) of age was 64.0(56.0-71.0) years; LVEF - 30.8(25.7-37.1) %, 86% males. We analyzed CHF predictors and estimated glomerular filtration rate (eGFR, MDRD and CKD-EPI formulas), 24-hour urinary albumin excretion (UAE). All patients were stable on optimal medical therapy.

Results: CHF was due to coronary artery disease in 81% (1 myocardial infarction (MI) in anamnesis was in 50%, 2 - in 23%, 3 - in 5%), dilated cardiomyopathy - in 9%, arterial hypertension (AH) - in 10% of patients. eGFR was lower in ischemical in comparison with non-ischemical CHF [68.2 (55.0-82.5) vs. 88.2 (65.4-98.6) ml/min/1.73m², p=0.006]. Number of MI correlated with eGFR (r= -0.33, p=0.005).

76% of patients had AH in anamnesis with duration 10 (0-20) years, maximal systolic 180 (115-200) and diastolic 100 (90-110) mm Hg. eGFR was lower [66.8 (50.7-85.3) vs. 82.1 (74.4-97.3) ml/min/1.73m², p=0.009] and UAE was higher [50.0 (37.0-78.0) vs. 35.5 (23.6-48.1) mg/24h, p=0.015] in patients with AH history in comparison with others. Total cholesterol >5.2 mmol/l was in 45%, triglyceride > 1.7 mmol/l - in 17% of patients. Decreased high-density lipoprotein was in 41% of patients and was associated with lower eGFR [50.6 (47.1-59.6) vs. 60.9 (52.8-68.7) ml/min/1.73m², p=0.044]. Diabetes mellitus (DM) was in 13.5% of patients. eGFR was lower in these patients vs. with others [54.8 (43.0-60.9) vs. 66.6 (50.5-81.6) ml/min/1.73m², p=0.009]. LV hypertrophy (LVH) was in 97%, abdominal obesity - in 68% of patients; 22% had 1st, 6% - 2nd and 1% - 3rd degree of obesity. 37% of patients were current smokers, 57% - smokers in the past. Duration of smoking was 30 (20-38) years, smoker index was 15 (0-30) package/years. 24% were alcohol abusers; frequency of alcohol intake was 4 (1-15) days per month. LVH, obesity, smoking and alcohol abusing weren't associated with renal dysfunction.

Conclusions: Such predictors of chronic heart failure as ischemical etiology, arterial hypertension, dyslipidemia and diabetes mellitus are associated with severity of decreasing of glomerular filtration rate and elevation of urinary albumin excretion and may contribute to progression of cardiorenal syndrome.

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Are there differences in the effect of Tolvaptan depending on the renal function? results of clinical experience

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Purpose: Tolvaptan, a vasopressin receptor antagonist has been accepted as a therapeutic alternative for refractory hyponatremia treatment in heart failure (HF) patients. We aimed to assess differences in Tolvaptan response according to renal function.

Methods: We reviewed data from all patients admitted for HF and refractory hyponatremia (Na <135 mEq/L despite fluid restriction and/or hypertonic saline) treated with Tolvaptan. Patients were divided in two groups according to their glomerular filtration rate [MDRD (mL/min/1,73m²)] at the moment of receiving Tolvaptan (group A <60 and B >60). Na, potassium [K (mEq/L)], creatinine [Cr (mg/dL)] and MDRD, diuresis (mL/h), blood pressure (mmHg) and weight (kg) were evaluated at administration, 24 and 48 hours after.

Results: 35 patients were included (25 in A and 10 in B). Baseline characteristics are shown in table 1. Plasma Na was lower in B (128 ± 4 vs 130 ± 3 in A) with a significant increase in both groups at 24 (134 ± 2 in A vs 134 ± 5 in B) and 48 hours (135 ± 3 in A vs 136 ± 3 in B). Diuresis increased significantly in both groups at 24 hours (273 (95% CI 40-505) in A and 227 (95% CI 120-334) in B) which correlated with a corresponding significant weight loss in group B. We found no changes in K, Cr, MDRD or blood pressure.

Conclusions: In our experience, Tolvaptan was safe and effective in increasing sodium plasma level and diuresis regardless the renal renal function.

	Group A n=25	Group B n=10
Age × ± st	72 ± 13	72 ± 15
Sex female/male n (%)	14 (56) / 11 (44)	4 (40) / 6 (60)
Cardiomyopathy n (%)		
Ischemic	7 (28)	4 (40)
Valvular	9 (36)	1 (10)
Ischemic + Valvular	3 (12)	0 (0)
Others	6 (24)	5 (50)
Ejection fraction < 50 n (%)	14 (56)	4 (40)
Treatment n (%)		
Furosemide	21 (84)	8 (80)
Aldosterone antagonist	16 (64)	4 (40)
Administered dose 15/30mg n (%)	23 (92) / 2 (8)	9 (90) / 1 (10)

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Significance of exertional oscillatory ventilation in patients with chronic heart failure and comorbid chronic obstructive pulmonary disease

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Introduction: Exertional oscillatory ventilation (EOV) occurs in many patients with chronic heart failure (CHF) and is a predictor of adverse outcomes in this population. Many CHF patients (20-40%) have also chronic obstructive pulmonary disease (COPD) which frequently delays diagnosis of CHF and complicates assessment of prognosis. The pathogenetic mechanism of EOV is still not clear; however, the breathing pattern of EOV is similar to central sleep apnoea. It is hypothesized that EOV is primarily related to impaired ability to augment cardiac index during exercise with secondary circulatory delay causing instability in the feedback loop of ventilatory control.

Aim: We aimed to estimate prevalence of EOV and its clinical significance in patients with CHF and comorbid COPD.

Material and Methods: It is a prospective analysis of 69 CHF patients (47 with CHF alone and 22 with both CHF and COPD). These patients underwent a symptom-limited treadmill exercise test with metabolic gas exchange measurements using RAMP protocol. EOV was defined by Corrá criteria as cyclic fluctuations in ventilation during over 60% of exercise, and with amplitude over 15% of the average amplitude at rest.

Results: Twenty-two patients with both CHF and COPD presented with similar age and NYHA class, and higher ejection fraction (EF) in comparison with those with CHF only. Cardiopulmonary exercise tests showed significantly lower breathing reserve (BR) and higher PETCO₂ in the group with COPD. EOV occurred in 23.2% of all the patients. Prevalence of EOV in both groups did not differ significantly ($p=0.807$). A 3-month follow-up showed no significant differences in mortality and hospitalization rates between the patients with CHF only and those with comorbid COPD.

Conclusion: COPD does not influence occurrence of EOV in patients with CHF. Further studies are required to evaluate if EOV has the same prognostic value in patients with CHF regardless of pulmonary diseases.

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Community home visits nurse-directed intervention in Oman to reduce hospital readmission among patients who are suffering from chronic heart failure

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Introduction: The growing number of patients with chronic heart failure has increased both the pressure on hospital resources and the need for community management of the condition. Because of the prevalence and expense of chronic heart failure, significant efforts have been made to develop home visit service that will improve clinical and financial outcomes.

Aims: This study attempts to identify the effectiveness of community home visit nurse-directed intervention in Oman in reducing hospital readmission rates among patients who are suffering from heart failure.

Methods: We conducted a prospective, clinical trial of the effect of community home visit intervention by a nurse on rates of readmission within 3 months and 6 months of hospital discharge.

Patients with specific criteria were identified by the discharge planner and referred to the community nurses. After one week from the discharge date, patients were visited by the community nurses. The intervention consisted of comprehensive education of the patient and family, a prescribed diet, social-service consultation, a review of medications and patients' adherence to it, and vigilant follow-up with early recognition of problems, as well as identification and management of patients' comorbidities.

Results: The primary outcome measure was achieved in the all patients (total of 54) who received the intervention in the first 3 months. Whereas, after 6 months it had been noted that 10 patients out of 54 was readmitted in the hospital. The reasons of readmission were different causes. There was a significant reduction in the readmission rate before and after the introduction of the intervention. For instance; 30 day readmission rate in single center before receiving the intervention was 27%, and after the intervention 15% (27 vs. 15, $P < 0.01$). On the other hand quality-of-life scores at 6 months improved more from base line for patients who received the intervention ($P=0.001$). Because of the reduction in the hospital admissions, there was an improvement in the beds availability in Sohar Hospital medical wards.

Conclusion: A community home visit nurse-directed intervention can reduce the readmission rate among heart failure patients and improve patient's quality of life.

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Predictors of one-year outcome of heart failure patients with atrial fibrillation compared to heart failure patients with sinus rhythm

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Purpose: The aim of the study was to identify clinical predictors of one-year outcome of patients (pts) hospitalized for heart failure (HF), depending on whether they were in sinus rhythm (SR) or had atrial fibrillation (AF).

Methods: The study included Polish pts hospitalized for HF participating in the Heart Failure Pilot Survey of the European Society of Cardiology, who were followed for 12 months after discharge. Pts with paced heart rhythm were excluded from the study. The primary endpoint was all-cause death at 12 months.

Results: The final analysis included 587 pts. AF occurred in 215 pts (36.6%). Compared to pts with SR, pts with AF were older; more often had a history of previous HF hospitalization; were less likely to smoke; were more frequently treated with aldosterone antagonists, loop diuretics, anticoagulants and digoxin but less frequently with antiplatelets before index hospitalization; were characterized by a higher NYHA class; higher heart rate and lower diastolic blood pressure at hospital admission; had higher serum creatinine and lower hemoglobin concentration at admission; less frequently had coronary angioplasty or coronary artery bypass grafting performed during index hospitalization; had higher heart rate at discharge; were more often prescribed anticoagulants and digoxin but less often statins, angiotensin-converting enzyme inhibitors and antiplatelets at discharge. There was no significant difference between pts with AF and pts with SR in terms of in-hospital mortality (5.1% vs 2.4%, respectively; $p=0.1$). The primary endpoint occurred in 41 of 215 of AF pts (19.1%) and in 40 of 372 SR pts (10.8%; $p=0.006$). In a multivariate analysis, independent predictors of the primary endpoint in AF pts were: higher NYHA class (HR 1.95; 95%CI 1.11-3.42; $p=0.02$) and heart rate (HR 1.02; 95%CI 1.00-1.03; $p=0.04$) and lower serum sodium concentration at admission (HR 0.89; 95%CI 0.85-0.94; $p=0.0001$) and higher heart rate at discharge (HR 1.02; 95%CI 1.01-1.04; $p=0.01$). In pts with SR, independent predictors of the primary endpoint included: older age (HR 1.04; 95%CI 1.01-1.07; $p=0.007$), lower serum sodium concentration at admission (HR 0.86; 0.80-0.94; $p=0.0006$) and higher heart rate at discharge (HR 1.03; 1.01-1.05; $p=0.01$).

Conclusions: In the studied group of real-world HF pts, serum sodium concentration at hospital admission and heart rate at hospital discharge were independent prognostic factors in both, pts with AF and pts with SR. In contrast to pts with SR, in AF pts, heart rate at hospital admission was also predictive of long-term mortality.

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Predictors of readmission for heart failure patients in Bahrain

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Background: Readmission rate for patients with heart failure is reported to be high. Identifying factors that predict readmission of these patients are highly valuable. It can stratify these patients' readmissions and enhance their management strategy. We aim to study readmission predictors for heart failure patients in our Medical Complex in Bahrain.

Methods: Adult patients admitted and discharged with principle diagnosis of heart failure were enrolled. The enrollment period was from January 1st till March 31st, 2012. Follow up was extended to March 31st, 2013. The study was prospective were demographic, clinical, laboratory, length of stay and medications at admission and discharge were collected. Number of readmissions and mortalities was recorded during the follow up period. During each readmission, compliance was verified by direct questioning and follow-up visits attendance monitoring. The above listed clinical parameters were also collected. Basic and advance statistics were conducted using statistical package. Univariate and multivariate regression was done to identify the predictive power of various variables included.

Results: 245 patients were included during the enrollment period. Their mean age was 64 ± 13.5 years. 69% (169 out of 245) were male. Systemic hypertension and diabetes mellitus were found in 73% and 64% respectively (179 and 157 out of 245). During the follow up period 48% (117 out of 245) were readmitted. Mortality was recorded in 9% (23 out of 245). Of the 42 clinical factors studied; 3 were found to be significantly associated with readmission in logistic regression model. A heart rate of 78 beats per minute at discharge with adjusted odd ratio (aOR) 2.36 (95% CI 1.37 - 4.07, $p=0.05$), Coronary artery disease aOR 1.81 (95% CI 1.04 - 3.40, $p=0.05$) and diabetes mellitus aOR 1.88 (95% CI 1.01 - 3.24, $p=0.05$) were the most predictors for mortality and readmissions.

Conclusion: Few clinical variables can predict readmission for heart failure patients. The above identified might represent country or institution specific predictors for heart failure readmission that have to be verified by future studies. It can guide

the clinicians to adopt a synchronized approach where cardiac abnormalities, non-cardiac co-morbidities and nation specific factors to be well integrated.

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Enhanced external counterpulsation therapy improves clinical outcomes, quality of life and functional effort capacity in patients with symptomatic heart failure

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Objectives: Chronic heart failure is an important health problem that limits the daily life, quality of life, effort capacity and physiological condition of the patients. In subset of these patients symptoms persist despite optimal medical management. Enhanced External Counterpulsation (EECP) is a non-invasive Food and Drug Administration approved therapy which improves symptoms and clinical outcomes in patients with heart failure. However, there is limited data in Turkish cohort. In this study, we investigated the clinical effects of EECP on multiple parameters associated with quality of life, functional effort capacity and physiological status in Turkish patients with symptomatic chronic heart failure.

Methods: 21 individuals who were diagnosed with symptomatic chronic heart failure (left ventricular ejection fraction $\leq 40\%$) with NYHA II-III were enrolled in the study. Eligible patients were assigned to 35-session EECP treatment. NYHA classification, SF 36 quality of life questionnaire, Minnesota living heart failure questionnaire, quality of life index cardiac version IV and Beck depression scale were assessed and 6 minute walk test was performed before and after EECP treatment.

Results: The mean age of the patients was 57.4 ± 12.5 years. Patients underwent an EECP treatment course of 35 hours with an excellent compliance rate. EECP therapy resulted in significant improvement in NYHA functional class, quality of life index, effort capacity and physiological condition in all patients without any adverse event ($p=0.001$) (Table 1).

Conclusion: EECP treatment significantly improved clinical parameters and effort capacity in patients with symptomatic heart failure. These results suggest that EECP is an effective and a safe therapy in Class II-III heart failure patients whose symptoms persist despite optimal medical management.

Table 1

	Before EECP	After EECP	N	P
NYHA class	1.6 \pm 1.5	0.6 \pm 0.7	21	0.001
SF36 score	75.5 \pm 5.2	119.9 \pm 13.6	21	0.001
Minnesota living heart failure score	66.7 \pm 29.5	22.8 \pm 26.2	21	0.001
BECK score	8.2 \pm 7.9	2.4 \pm 4.6	21	0.001
Quality of life index cardiac version-IV	288.8 \pm 34.1	346.3 \pm 49.5	21	0.001
6 minute walk test	237 \pm 46.8	364 \pm 50.9	21	0.001

The effects of EECP on multiple parameters

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The prevalence of sleep-disordered breathing and the predictors of the increased apnea-hypopnea index in patients with chronic heart failure

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Background: Sleep-disordered breathing (SDB) is a widely spread co-morbidity in patients with chronic heart failure (HF) that not only leads to a poor quality of life, but also a shorter life expectancy.

Methods: A total of 132 patients with chronic HF (mean age: 67 ± 11 y, 23% female, left ventricular ejection fraction [LVEF] $37 \pm 13\%$, body mass index [BMI] 28.9 ± 5.2 kg/m², New York Heart Association [NYHA] class 2.2 ± 0.7) underwent polygraphy screening between 2011 and 2014. Patients were screened for SDB using the Embletta portable diagnostic system. SDB was defined as an apnea-hypopnea index $\geq 5/h$. Patients with LVEF $\leq 40\%$ were categorized as HF with reduced ejection fraction [HFrEF], LVEF $> 40\%$ as HF with preserved ejection fraction [HFpEF].

Results: A total of 58 (44%) patients were diagnosed to have SDB and showed an increased apnea-hypopnea index. Patients with SDB (mean age: 68 ± 10 y, 17% female, LVEF $33 \pm 12\%$, BMI 28.9 ± 5.9 kg/m², NYHA class 2.3 ± 0.7) showed lower LVEF compared to patients without SDB ($33 \pm 12\%$ vs. $40 \pm 13\%$, $p < 0.05$). In patients with HFrEF ($n = 47$, 81%) SDB was more common than in patients with HFpEF ($n = 11$, 19%). Logistic regression analysis showed that reduced LVEF and

higher creatinine level were predictive (both $p < 0.05$) for increased apnea-hypopnea index.

Conclusion: In patients with chronic HF, predictors of SDB include reduced LVEF and high level of creatinine. This fact buttresses the view that patients with more advanced HF are more likely to develop SDB. Screening for SDB provides an easy tool to identify patients with this co-morbidity.

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Correlation between the respiratory muscle strength, and self reported fatigue in heart failure

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Purpose: Respiratory muscle function can be affected in heart failure (HF) and this can reduce the blood flow to the peripheral muscles, causing widespread muscle atrophy may lead to fatigue, and decreases in activities of daily living. Hence the need to identify the correlation that respiratory muscle strength has with the self-reported fatigue in patients with HF for interventions to be proposed in a targeted, systematic and reasoned.

Methods: We conducted a retrospective observational descriptive study with 12 files of patients that were analyzed in a University Heart Failure Clinic. The Dutch Fatigue Scale (DUFs) and the Dutch Exertion Fatigue Scale (DEFS) questionnaires were applied. The respiratory muscle strength was tested by a analogical type manometer (Ger-Air, Famabras). This study was approved by the Research Ethics Committee of the University.

Results: The respiratory muscle strength Pimáx was -56 ± 20 cm H₂O (Predicted -81 ± 4 cm H₂O), and the Pemáx 41 ± 19 cm H₂O (Predicted 80 ± 7 cm H₂O). In relation to self reported fatigue got the following average DUFs 25 ± 8 and DEFS 21 ± 12 . There was an inverse between Pemáx with DUFs ($r = -0.70$; $p = 0.830$) and an inverse, strong and significant correlation between intensity MIP with DUFs ($r = -0.70$; $p = 0.016$) and an inverse correlation, significant and moderate Pimáx with DEFS ($r = -0.628$; $p = 0.029$).

Conclusion: The results of this study showed that the lower respiratory muscle strength, both Pimáx as Pemáx, the greater the degree of self-reported fatigue in the questionnaire Dutch fatigue Scale.

HEART FAILURE DIAGNOSIS

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ST2: a new cardiovascular biomarker for the diagnosis and prognosis of heart failure

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Biomarkers play an important role in the diagnosis and management of HF. There is interest in understanding their potential as a part of a strategy to reduce readmission. A single biomarker might not reflect all the faces of HF syndrome and a multimarker strategy may better characterize the complexity of HF. Natriuretic peptides are the most commonly used markers in this regard.

Blood samples were analyzed from 110 patients from Intensive care and Cardiology Department, admitted for acutely decompensated HF for ST2, NT-pro BNP, TnI, CK, CK-MB, Homocystein, IL-6, hsCRP, and routine clinical chemistry parameters at the admission and discharge from the hospital.

The present study investigated the value of combining NT-pro BNP (a marker of myocardial stretch), TnI (a marker of myocyte injury) and ST2 (reflective of myocardial fibrosis and remodeling). ST2 - a member of the interleukin /IL-1 receptor family, has been linked to the development of cardiac fibrosis, hypertrophy, ventricular dysfunction and has emerged as a new cardiovascular biomarker. It was proved its potential role alone or as a part of multimarker strategy to predict readmission and prognosis of the patient.

Conclusion: The preliminary results of the study confirm the statement for the role of this new biomarker ST2 for predicting the recent re-hospitalization corresponding to the stage of the HF. Our further efforts will be directed to investigate which combination of markers will give best integrated approach to predict and reduce readmission of such patients.

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Comparative assessment of utility of audiocardiographic indices in the diagnosis of systolic heart failure

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Introduction: Impaired exercise tolerance caused by dyspnea is a symptoms of heart failure that is characterized by low specificity and therefore its quick interpretation may be difficult. Audiocardiography is a modality that is easy to use and is characterized by high diagnostic utility in systolic heart failure.

Aim: The aim of the study was to assess utility of audiocardiographic indices in the diagnosis of systolic heart failure and to compare them with other, commonly used diagnostic modalities.

Methods: Patients with exercise-induced dyspnea underwent echocardiography, audiocardiography, 6-minute walk test and assessment of NT-proBNP level.

Results: 79 patients at an average age of 62.5 years (55 males) were divided into the following groups: (A) with left ventricular ejection fraction (EF) $\geq 50\%$ (41 subjects) and (B) with EF $< 50\%$ (38 subjects). Patients from group B had higher NT-proBNP values (2184.6 ± 2076.9 pg/ml vs. 96.3 ± 74.0 pg/ml, $p < 0.0005$) and shorter distance in 6-minute walk test (6MWT) (421.26 ± 78.97 m vs. 535.21 ± 123.56 m, $p < 0.003$). In this group EF was lower ($34.39 \pm 1.06\%$ vs. $59.03 \pm 4.52\%$, $p < 0.0005$), left ventricular end-diastolic diameter (LVEDD) was higher (57.30 ± 8.55 mm vs. 47.27 ± 5.14 mm, $p < 0.0005$) and E/e' was higher (15.58 ± 5.61 vs. 9.91 ± 2.53 , $p < 0.0005$). In group B audiocardiography demonstrated: higher acoustic strength of S3 (4.31 ± 1.80 vs. 3.24 ± 0.65 , $p < 0.003$), longer electromechanical activation time (EMAT) (111.75 ± 25.04 ms vs. 85.89 ± 11.35 ms, $p < 0.0005$), higher EMAT/RR ($12.42 \pm 3.92\%$ vs. $9.12 \pm 1.64\%$, $p < 0.0005$) and longer QRS duration (119.41 ± 28.63 ms vs. 99.87 ± 15.77 ms, $p < 0.001$) and shorter left ventricular systolic time (LVST) (325.89 ± 37.71 ms vs. 345.61 ± 26.05 ms, $p < 0.007$).

High sensitivity and specificity of EMAT in identification of hemodynamic abnormalities and high specificity with low sensitivity for S3 and QRS were demonstrated.

Conclusions: Audiocardiography can be a valuable diagnostic tool in suspected left ventricular systolic dysfunction. EMAT is characterized by the highest diagnostic value. EMAT < 100 ms indicates low risk of hemodynamic abnormalities.

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Heart failure in cirrhotic patients??

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Introduction: While the occurrence of liver cirrhosis in cases of advanced heart failure was well recognized long ago, the development of heart failure as a complication of liver cirrhosis was only brought to light few decades ago.

We conducted this study to assess the cardiac function in patients with liver cirrhosis.

Methods: We compared echocardiographic findings in 2 groups: group I including 27 patients with liver cirrhosis, and group II with 28 healthy subjects. In group I, we excluded patients with conditions modifying myocardial function (hypertension, diabetes, ischemia, moderate to severe valve disease...).

Results: The left ventricle ejection fraction ($p = 0.17$), the Peak systolic longitudinal strain (PLS) ($p = 0.5$), the s wave on lateral left ventricle wall ($p = 0.5$) and left ventricle Tei index were similar in both groups ($p = 0.38$). However the right ventricle shortness fraction (37% vs 50% , $p = 0.006$), the s wave on lateral right ventricle wall (8.2 vs 12 cm/s, $p = 0.008$) and the right ventricle Tei index (32% vs 52% , $p = 0.03$) were significantly lower in group I.

Based on mitral-flow pattern and tissue-Doppler, diastolic dysfunction was present in 14 patients (51%) versus 5 healthy subjects (17%), $p = 0.008$. Echocardiographic abnormalities were not different according to cirrhosis etiologies

Conclusion: Many cardiovascular abnormalities occur in patients with liver cirrhosis that mandate echocardiographic evaluation, the impairment of right ventricle and left ventricle diastolic function happen precociously. These dysfunctions are secondary to hemodynamics modifications in such patients, mainly the hepato-pulmonary syndrome.

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Use of natriuretic peptides to screen for cardiac dysfunction in patients with type-2 diabetes mellitus. an echocardiographic report from sica-diabetes study

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Background: Patients with type-2 diabetes mellitus (T2DM) and raised plasma concentration of amino-terminal pro-brain natriuretic peptide (NT-proBNP) have a worse prognosis. This is presumed to reflect the severity of cardiac dysfunction but of varied pathophysiology.

Method: Patients receiving treatment for T2DM for at least 12 months, aged > 40 years and not already known to have heart or renal failure, had NT-proBNP measured by their family doctor and were invited to attend for further investigations, including echocardiography.

Results: Of 95 patients, plasma NT-proBNP was < 125 ng/L in 43 (45%) and > 400 ng/L in 21 (22%). Compared to patients with lower NT-proBNP, those with higher NT-proBNP were older, had more often ischemic heart disease and atrial fibrillation. They also had larger left atrial volumes, lower left atrial emptying function, higher left ventricular (LV) filling pressures (E/E'), pulmonary artery systolic pressure and greater inferior vena cava diameter. Left ventricular dimensions and ejection fraction (LVEF) were similar across NT-proBNP subgroups, but $> 40\%$ of patients with NT-proBNP ≥ 125 ng/l had impaired global longitudinal strain (vs 8% in those with NT-proBNP < 125 ng/l, $p = 0.002$).

Conclusions: Higher plasma concentrations of NT-proBNP in patients with diabetes are associated with more severe cardiac dysfunction; predominantly LV diastolic or long-axis systolic dysfunction. The high prevalence of LA dysfunction might merely reflect LV dysfunction but might also be a primary pathology. A substantial minority of patients had a reduced LVEF.

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Usefulness of a new proposed TNM-like classification for heart failure staging: comparison with the classic NYHA

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Purpose: NYHA is the most used HF classifications. However, it is not comprehending clinical features and other organs involvement. We proposed a new staging system for HF, named HLM, analogous to the TNM evaluation used in Oncology. HLM refers to heart damage (H), lung involvement (L), and malfunction of peripheral organs, such as kidney, liver, brain and hemopoiesis. The aim was a preliminary comparison between HLM and NYHA to achieve most accurate prognosis of HF patients in terms of rehospitalization and mortality.

Methods: We performed a prospective and observational registry of 400 consecutive patients. As TNM, any alterations in heart (H instead of T), lung (L instead of N), organs as kidney, liver, brain and blood (M as Multiorgan, instead of Metastasis), was evaluated, based on HLM nosology. By the sum of H, L and M values (i.e. score), four stages were determined: stage 1, with a score of 1 or 2; stage 2, score 3-4; stage 3, score 5-6; stage 4, score > 6 . Each patient was also classified using NYHA.

Results: Among 400 patients, regarding to the cardiac evaluation, left ventricular (LV) systolic dysfunction rate was 8.47%, right ventricle systolic dysfunction rate was 12.35%, LV diastolic dysfunction was 19.25%. Regarding to the lung, 70% of patients showed a pulmonary involvement. As regard to the malfunction of other organs, kidney was involved in 8.47% of patients, liver in 37.5%, brain in 9.8%, blood in 21.35%. According to HLM, patients were classified as follows: 13.5% in stage 1; 36.75% in stage 2; 44% in stage 3 and 5.75% in stage 4. Considering the NYHA classification, 7% was in class I, 46% in class II, 41.25% in class III and 5.75% in class IV. Comparing HLM with NYHA, the mortality rate was as follows: 0% in HLM 1 vs 0% in NYHA I ($p = 1.000$); 2.7% in HLM 2 vs 4.3% in NYHA II ($p = 0.559$); 10.8% in HLM 3 vs 13.3% in NYHA III ($p = 0.508$); 52.1% in HLM 4 vs 21.7% in NYHA IV ($p = 0.065$). The rehospitalization rate was as follows: 0% in HLM stage 1 vs 0% in NYHA I ($p = 1.000$); 4.7% in HLM stage 2 vs 6.5% in NYHA II ($p = 0.635$); 14.2% in HLM 3 vs 16.1% in NYHA III ($p = 0.554$); 60.8% in HLM 4 vs 26.1% in NYHA IV ($p = 0.036$).

Conclusions: Comparing HLM with NYHA, our proposed nosology seems to be more accurate to stratify risk in term of rehospitalization and mortality, mostly in advanced stages. As emerging by our preliminary data, HLM could be useful for the physician in the patient management and in the decision making for addressing the best patient-centered therapy. Differently from NYHA, HLM adds objective parameters of cardiac, pulmonary and multi-organ involvement.

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A complete audit cycle evaluating the compliance of primary and secondary services with UK guidelines for heart failure

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Purpose: In 2010, the National Institute for Health and Care Excellence (NICE) published new recommendations to encourage appropriate referral of patients with suspected heart failure. These guidelines suggest that primary care physicians should refer symptomatic patients urgently (seen within 2 weeks) if they either have evidence of a previous myocardial infarction (MI) or an N-terminal pro-brain natriuretic peptide (NTproBNP) result above 2000, and routinely (seen within 6 weeks) if their NTproBNP result lies between 400-2000. In December 2012, Wolverhampton care providers incorporated these recommendations into clinical practice. With the objective of assessing whether these services are following the national guidelines, a retrospective audit cycle was undertaken, the primary aim being to evaluate if local general practitioners (GPs) are correctly referring those with suspected heart failure, and the secondary aim being to analyse whether patients are seen within the recommended time frame.

Methods: The audit cycle was carried out between October 2013 and August 2014. The first phase of the audit included 34 patients referred to the new heart failure clinic over a three-month period. Eight months later, following the distribution of the audit results to practicing cardiologists and GPs in the area, the second phase of the audit was commenced, and included 66 patients referred over the same time frame.

Results: In the first phase of the audit, seven (21%) of the 34 patients were referred incorrectly (due to an absent NTproBNP result in the presence of no previous MI) but all were accepted and seen in the heart failure clinic. Two (6%) of the 34 patients were not seen by the secondary care team within the recommended time frame. In the second arm of the audit, 13 (20%) of the 66 patients were incorrectly referred for the same reason as the first phase, three of whom were seen in clinic. In contrast to the first phase, 17 (26%) of the patients referred were not seen within the suggested time period.

Conclusions: Following our primary audit, changes to the protocol for refusal of incorrect referrals were made and improvements to NTproBNP testing were subsequently seen. However, despite circulation of our findings, the percentage of incorrect referrals did not improve and the number of patients seen within the correct time frame decreased. Further recommendations therefore include conducting informative face-to-face sessions with GPs and investigating the reasons why fewer patients were seen within the recommended time frame set out by NICE.

ARRHYTHMIAS AND TREATMENT

P271

Evolution of left ventricular ejection fraction after radiofrequency catheter ablation of the cavotricuspid isthmus

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Background: Reversible left ventricular dysfunction has been related to the presence of arrhythmias, including auricular flutter (AFL). Radiofrequency catheter ablation of the cavotricuspid isthmus (ICT) for typical auricular flutter is a successful technique and complications are extremely rare. For these reasons, this is a first-line and established treatment to prevent flutter recurrence.

Methods: A total of 53 patients who consecutively underwent a successful typical AFL ablation were analyzed (mean age 65 years, 78% men). Left ventricular ejection fraction (LVEF) on the first day and one month after procedure, was measured by transthoracic echocardiography during sinus rhythm. In this study we analyze changes in left ventricular ejection fraction (LVEF) in these patients and factors associated with its improvement.

Results: A total of 20 patients showed an improvement in LVEF. Evolution of LVEF is shown in table 1.

Univariate analysis showed a reduced basal LVEF ($p < 0.01$), dilated cardiomyopathy ($p = 0.032$), and history of heart failure ($p = 0.027$) as factors associated with improvement of LVEF. Patients presenting with a persistent form of AFL showed a non-significant trend toward ($p = 0.08$) a better LVEF, compared with those presenting paroxysmal or permanent forms.

On multivariate analysis, a reduced basal LVEF was the only predictor of improvement of LVEF a month after the procedure ($p = 0.029$).

Conclusions: Successful radiofrequency catheter ablation of the cavotricuspid isthmus (ICT) for typical auricular flutter procedure in patients with reduced ejection fraction, provides a significant improvement of LVEF one month after the procedure. Hence, it can be assumed that a tachycardiomyopathy component exists and ejection fraction becomes an important factor to take into account when deciding the ICT ablation.

Evolution of ejection fraction.

	BASAL LVEF	mean(%)+/-SD	ONE MONTH FOLLOW-UP mean (%)+/-SD	p-value
All patients	59 +/- 12		61 +/- 11	0.15
Normal LVEF	64.2 +/- 6		64.4 +/- 4	0.86
Reduced LVEF (<55%)	41.6 +/- 8		50.6 +/- 7	0.047

SD=Standard Deviation LVEF=Left Ventricular Ejection Fraction

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Obstructive sleep apnea syndrome and significant bradyarrhythmias in stable patients with left ventricular dysfunction

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Background: The obstructive sleep apnea syndrome (OSA) has important cardiovascular effect and has been established your association with cardiovascular disease in patients with preserved fraction ejection. Bradyarrhythmias associated with OSA would be due to increased parasympathetic tone and not structural anomalies.

Objectives: The aim of this study is to assess the association between OSA and occurrence of sinus pauses or bradycardia in patients diagnosed with left ventricular dysfunction in ambulatory follow-up.

Methods: A total of 90 consecutive patients diagnosed with left ventricular dysfunction in stable condition were prospectively selected. Echocardiography, polysomnography and Holter monitoring (24 hours) was performed in all patients.

Results: The mean age of patients was 56.2 ± 11.2 years. 87.8% of patients were men and 24.4% had diabetes mellitus. The ejection fraction was $28.4 \pm 9.5\%$. 44% of patients had ischemic heart disease and 33.3% were diagnosed OSA (group 1). In the bivariate analysis, group 1 average heart rate and minimum measured by Holter was lower ($p < 0.007$ and $p < 0.002$), regardless of age, the diagnosis of atrial fibrillation and therapy with beta-blockers and digoxin. In group 1, there was a greater presence of electrocardiographic pauses of two seconds or more ($p < 0.026$). Although we found association between the presence of pauses and lower heart rates with OSA, the presence of atrial fibrillation (AF), age and NYHA class; in multivariate analysis only the presence of AF demonstrated significant association with bradyarrhythmias. This was associated ($p < 0.008$) with worse NYHA functional capacity.

Conclusion: In patients with ventricular dysfunction, OSA doesn't explain the presence of significant bradycardia and sinus pauses. In our study, this ECG findings was associated with the presence of AF during Holter, which is associated with worse NYHA functional capacity.

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Influence of second- and third-degree heart block on 30-day outcome in patients with heart failure after acute myocardial infarction

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Purpose: This study was conducted to investigate the prognostic value of heart block among patients with heart failure after acute myocardial infarction (AMI) treated with drug-eluting stent (DES).

Methods: A total of 13,862 patients with AMI, registered in the nation-wide AMI database between January 2005 and June 2013, were analyzed. Second- (Mobitz type I or II) and third-degree atrioventricular block (AVB) were considered as heart block in this study. Thirty-day major adverse cardiac events (MACE) including all causes of death, recurrent myocardial infarction, and revascularization were evaluated.

Results: Percutaneous coronary intervention with implantation of DES was performed in 89.8% of the patients. heart block occurred in 378 patients (2.7%). Thirty-day MACE occurred in 1,144 patients (8.2%). Patients with heart block showed worse clinical parameters at initial admission, and the presence of heart block was associated with 30-day MACE in univariate analyses. However, the prognostic impact of heart block was not significant after adjustment of potential confounders ($p = 0.489$). Among patients with heart block, patients with a culprit in the left anterior descending (LAD) coronary artery had worse clinical outcomes than those of patients with a culprit in the left circumflex or right coronary artery. LAD culprit was a significant risk factor for 30-day MACE even after controlling for confounders (odds ratio, 5.28; 95% confidence interval, 1.22-22.81; $p = 0.026$).

Conclusion: In conclusion, despite differences in clinical parameters at the initial admission, heart block was not an independent risk factor for 30-day MACE in patients with heart failure after AMI treated with DES in adjusted analyses. However, a LAD culprit was an independent risk factor for 30-day MACE among patients with heart block.

P274

Influence of PVCs on all-cause mortality in patients with CHF and different LVEF

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Aim: investigate correlation between PVCs and all-cause mortality in patients with CHF.

Methods: We followed 226 consecutive patients with CHF (NYHA II-IV) during 7 years. Patients were on optimal medical therapy. There were not any ICD implantation before treatment or during follow up. 139 patients had LVEF \leq 35% (median 26 [22;30]) and 87 patients have LVEF $>$ 35%. (median 45[40;52]). We made 24 hours ECG to count PVCs burden.

Results: Patients with LVEF \leq 35% and number of PVC $>$ 1000 beats/day have higher risk of death. (relative risk (RR) 0.79 95% CI 0.54 - 0.95). PVC didn't increase risk of death in patients with LVEF $>$ 35% (RR 0.75 95% CI 0.39 - 1.44).

Conclusion: PVC influence mortality in patients with LVEF \leq 35% but not in patients with LVEF $>$ 35%.

P275

Ventricular arrhythmias and other predictors of sudden cardiac death in patients after myocardial infarction

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Objective: To study the detection of ventricular arrhythmia (VA) in the 10-14 day Q-mycardial infarction (MI) and their relationship with the development of sudden coronary death (SCD).

Materials and Methods: We examined 131 patients with primary Q-wave MI, aged 30 to 69 years (51.9 ± 9.13 years). By all patients for 10-14 days of disease it was performed daily ECG monitoring of an electrocardiogram (ECG) and echocardiogram (EchoCG). To characterize ventricular premature beats were used gradation and classification B.Lown M.Wolf (1971) and prognostic classification J.Bigger (1982). The period of observation was 24 months.

Results: During the follow-up of 131 patients died suddenly 17 (12%) patients. Of these 8 (47.1%) died in the first 6 months, 5 (29%) per year, and 4 (23%) after 1 year from the onset. During follow-up there were 17 cases of SCD. The analysis revealed a predominance of baseline in the group of patients who died anterior localization of MI aneurysm, heart failure. In the group of the deceased with accurate frequency prevailed polymorphic and monomorphic frequent VA. Identified positive correlation: direct between age and heart rate, and VA and negative correlation between ejection fraction and VA, and age.

Conclusion: The identification of a high heart rate at rest, frequent ventricular arrhythmias, mainly polymorphic, and severe systolic dysfunction in the early follow-up (12-14 days) associated with a high risk of sudden cardiac death, having a positive correlations also with age of the patients. In this case, ventricular arrhythmias of the heart can not be regarded as independent predictor of sudden cardiac death, given the negative correlation their relationship with the myocardial contractility.

P276

Early decrease of NTproBNP after electrical cardioversion of atrial fibrillation

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Purpose: Sinus rhythm restoration improves haemodynamic function of the heart. Symptoms resolve during first hours, but there is poor data about biochemical markers of heart failure measured early after cardioversion.

Method: Thirty patients with a new onset of atrial fibrillation, starting 48 hours to 2 weeks before hospitalization, were enrolled into the study. Blood samples were taken before, 6 hours and 24 hours after the successful electrical cardioversion. N-terminal pro-B-type natriuretic peptide (NT-proBNP) plasma concentration, as a sensitive marker of heart failure, was examined, by using quantitative enzyme immunoassay.

Results: Almost all patients (29 of 30) was found to have the concentration of NT-proBNP above heart failure cut-off level of 125 pg/ml at baseline. The median NT-proBNP level, as compared with precardioversional state (1559 pg/ml, min 115 - max 5796), was significantly lower 6 hours (1288 pg/ml, min 115 - max 3797; $p < 0.001$) and 24 hours (470 pg/ml, min 66 - max 3797; $p < 0.001$) after restoration of the sinus rhythm.

Conclusions: The study demonstrates, that the NT-proBNP plasma concentration, which is derived from the myocardium, decreases as early as 6 hours and 24 hours after the cardioversion. Early down regulation of NT-proBNP, indicates quick resolution of the excessive diastolic wall stretch, which occurs during atrial fibrillation.

P277

Prevention of arrhythmias in patients with acute myocardial infarction during treatment with bioflavonoids

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The aim of the study was to evaluate the impact of bioflavonoids (Quercetin) on the frequency of reperfusion arrhythmias in patients with acute myocardial infarction.

Materials and methods: The study was conducted in 43 patients (mean age 52 ± 2 , 1roky) with newly diagnosed acute Q-mycardial infarction who were divided into two groups - control group (25 people) who received standard therapy (anticoagulants, antiplatelet agents, nitrates, β -blockers, ACE inhibitors, diuretics, thrombolytic therapy (streptokinase, i/v, 250.000-500.000 IU) and the main group (18 people), which on a background of standard therapy received Quercetin. Research of arrhythmias was performed using Holter monitoring.

It was found that ventricular extrasystoles IVa and IVb gradation according to the classification after B.Lown (1971) occurred in all patients of control group and in 25% of patients of main group. Number of episodes of ventricular extrasystoles of these classes in the control group was higher: $8,0 \pm 1,0$ vs $0,7 \pm 0,2$ ($p < 0,01$) in patients treated by Quercetin. Ventricular extrasystoles of these classes in both groups were occurred after coronary artery recanalization. The duration of ventricular extrasystoles of high grade in the control group was 12 hours after restoration of coronary blood flow, and in the main group - only 6 hours. Paroxysms of supraventricular and ventricular tachycardia rarely occurred in patients treated by Quercetin - 5.5% vs. 24% in controls; ($p < 0.01$).

Thus, the use of Quercetin in patients with acute myocardial infarction before coronary artery recanalization not only reduced the incidence of ventricular extrasystoles and quantity, but also significantly shortened the period of their existence in the reperfusion period.

P278

Implementation of a screening protocol for WCD-Utilisation as a SCD-risk assessment

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Introduction: Doubtlessly the ICD-therapy has become standard therapy to minimize the SCD-risk for defined patient-groups. According to the results of randomized trials and current guidelines an ICD for secondary prevention should not be implanted within the first 40 days after myocardial infarction and 90 days after revascularization respectively. After diagnosis of heart failure optimal medical treatment for up to three months has to be administered before the final indication for primary prevention ICD-implantation can be made. Sticking to the current guidelines these patients have a well-documented high risk of SCD and usually leave the hospital unprotected. The challenge in clinical everyday life is to determine these high risk patients and try to protect them before discharge from hospital.

Therefore we implemented a screeningprotocol based on the HRS recommendation by categorizing the patients in three simplified groups. With a structured workflow we tried to standardize the management of these patients during the time to reevaluation.

Methodology: In addition to the implementation of our own screening-protocoll we developed a workflow to structure follow up and reevaluation of the patients with lifevest. This workflow was integrated in our established pacemaker data base. After 10-12 weeks we reevaluated the patients LVEF, arrhythmic events and determined the final therapeutic pathway

Results: 89 pts. fulfilled the criteria for a WCD. These could be grouped into the following groups:

ICM 27 (30,3%)

NICM 52 (63,8%)

Others 10 (11,2%)

At the end of the wearing time 40,4% received an ICD, 32,6% showed an improvement of ejection fraction no longer belonging to the high risk group. The other 27% were still in follow up. Most ICD were implanted in the group of the ischemic cardiomyopathies (56%) whereas 38% of the patients with non ischemic cardiomyopathy received an ICD.

Summary: The implementation of a screening protocol and workflow led to a standardized registration and protection of heart-failure patients with high risk for PHT up to reevaluation of the definitive therapy. The average weartime was about 22h. Due to the connection during waiting time 96% of the patients were reevaluated in our hospital.

As a consequence of the guideline-related time of optimal medical treatment at the end one third of our patients had no more indication for an ICD. Among the patients receiving an ICD at the end of the WCD-wearing time were significant more patients with ischemic cardiomyopathy than non-ischemic.

P279

Clinical predictors of serious arrhythmic events in patients with non-ischemic heart failure

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Purpose: Risk stratification of serious arrhythmic events in patients with non-ischemic heart failure (HF), beyond the assessment of left ventricular ejection fraction (LVEF), remains an important clinical challenge. This study aims to determine the clinical value of different noninvasive and invasive tests for predicting serious arrhythmic events in patients with non-ischemic HF.

Methods: 106 non-ischemic HF patients underwent a comprehensive clinical and laboratory evaluation, including two-dimensional echocardiography, 24-hour Holter monitoring, cardiopulmonary exercise testing (CPX), and an invasive electrophysiological study. All patients were followed prospectively at the HF clinic at our institution.

Results: During a mean follow-up of 493 ± 300 days, the primary end-point (syncope, appropriate therapy by an implantable cardioverter-defibrillator (ICD), or sudden cardiac death) occurred in 10 patients (9.4%). In multivariable analysis, alcoholic etiology (HR 9.96; 95% CI 1.8 to 55; $p=0.008$), presence of exercise periodic breathing (EPB) during CPX (HR 8.4; 95% CI 1.8 to 40; $p=0.007$) and presence of non-sustained ventricular tachycardia (NSVT) > 10 beats on Holter monitoring (HR 25.4, 95% CI 4.4 to 146; $p < 0.001$) were independent predictors of the primary end-point. The absence of all of these factors ($n=78$, 73.6%) identified a subset of patients with very low-risk of future arrhythmic events, with a negative predictive value of 97.4%. Independent predictors of risk in the multivariable analysis were included in a risk prediction score based on their HRs: NSVT ≥ 10 beats on Holter monitoring (25 points), alcoholic etiology (10 points), and EPB during CPX (8 points). Patients were then classified according to the proposed score: low-risk group ($n=78$, score of zero points), intermediate-risk group ($n=18$, score between 1-10 points) and high-risk group ($n=10$, score > 10 points). The incidence of the primary end-point was 2.6%, 11% and 60% in each category of risk, respectively ($p < 0.001$).

Conclusions: In this cohort study of non-ischemic HF patients, alcoholic etiology, presence of EPB during CPX and NSVT > 10 beats were independent predictors of serious arrhythmic events. A prediction score based on these characteristics identified subgroups of low- and high-risk of future events, and might help to better stratify HF patients that will get the best clinical benefit with ICD implantation.

P280

Outcome and complications after implantable cardioverter defibrillator therapy in hypertrophic cardiomyopathy: experience of a tunisian center

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Background: Patients with a high risk hypertrophic cardiomyopathy (HCM) may benefit from implantable cardioverter defibrillator (ICD) therapy.

Objective: The aim of this study was to evaluate the outcome and complications after ICD therapy in patients with HCM.

Methods: We report a retrospective study about 18 tunisian patients with HCM followed between 2006 and 2013 and who received ICDs for the primary prevention of sudden cardiac death.

Results: The 18 patients were predominately young at implantation with a mean age of 43 years. The mean follow up period was 3.3 years. Defibrillators were activated appropriately in 7 patients (39%), by providing defibrillation shocks or antitachycardia pacing, with the restoration of sinus rhythm. The rate of appropriate defibrillator discharge was 11.7% per year. A total of 3 patients had episodes of inappropriate discharges (16.6%) due to atrial fibrillation with a rapid ventricular rate (5.5%), lead displacement (5.5%) and oversensing (5.5%). The rate of inappropriate defibrillator discharge was 5% per year. Inappropriate shocks occurred in 1 patient without and 2 with appropriate ICD interventions ($p=0.5$). Major complications occurred in 28% of the cases (8.5% per year) included infection requiring removal of the defibrillator (5.5%), lead displacement (5.5%) and inappropriate shocks (16.6%).

Conclusion: In a high risk HCM cohort, ICD interventions for life-threatening ventricular tachyarrhythmias were frequent and highly effective in restoring normal rhythm. However, inappropriate ICD intervention and complications are not uncommon. That's why, the selection of high risk patients is mandatory and represents a relevant challenge in this pathology.

P281

The new risk prediction model for sudden death in patients with hypertrophic cardiomyopathy and defibrillator

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Purpose: Hypertrophic cardiomyopathy is one of the main causes of sudden death in young people. Recent clinical practice guidelines include a risk prediction model for sudden death (HCM Risk-SCD), which facilitates the decision of whether to implant a defibrillator.

The aim of our study was to ascertain the percentage of events in our series of primary prevention ICD recipients with hypertrophic cardiomyopathy and whether HCM Risk-SCD predicts the onset of arrhythmic events.

Methods: This was an observational, retrospective cohort study, which included 48 primary prevention defibrillator recipient patients with HCM. We compiled their demographic and clinical characteristics, estimated 5-year risk using HCM Risk-SCD, and collected the documentation on arrhythmias during follow-up.

Results: The majority were male (66.7%) and mean age at implantation was 44.44 ± 14.46 years. NSVT was the most prevalent risk factor (66.67%), followed by a family history of sudden death (47.92%). Mean HCM Risk-SCD was $6.15 \pm 5.01\%$. HCM Risk-SCD was the only factor independently associated with the onset of ventricular tachyarrhythmia, above any other classic risk factor or association (OR = 1.46 [CI 95% 1.051-2.013]; $p=0.02$). None of the 11 patients estimated as low risk using HCM-Risk-SCD suffered any appropriate events ($p < 0.05$).

Conclusions: During an average follow-up of 4 years, 16.67% presented appropriate events (4.16%/year).

The use of the new risk prediction model, HCM Risk-SCD, seems to facilitate better prediction of appropriate events than classic risk factors, and allows a quantitative estimation of the risk of sudden death at five years.

P282

Not enough genetic analysis in hypertrophic cardiomyopathy patients in real clinical practice

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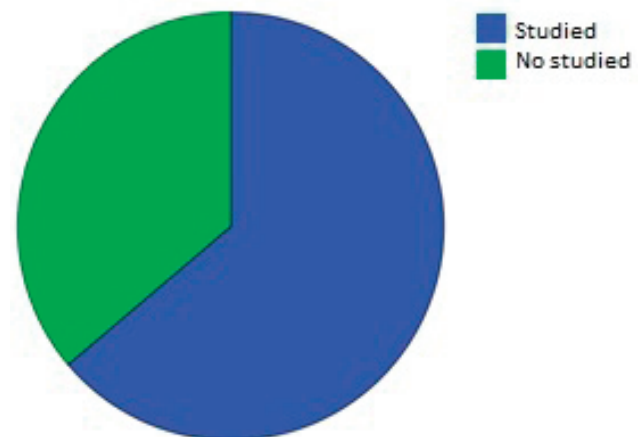
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Purpose: Recent 2014 European Society of Cardiology (ESC) Guidelines recommend genetic counselling in all patients when hypertrophic cardiomyopathy (HCM) cannot be explained solely by a non-genetic cause (class of recommendation IB). Our study aimed to review requests for genetic tests in real clinical practice. We reviewed genetic analysis ordered in HCM patients with cardioverter-defibrillators implanted (ICDs), due to the fact that the high risk clinical profile of this population could raise the interest of cardiologists in order genetic analysis.

Methods: we retrospectively studied 47 consecutive patients with HCM from our hospital or referred to our center in order to receive an ICD, from 2008 to the end of 2014.

Results: The mean age of our study population was 55.8 ± 16 years. 77% of ICDs were implanted for primary ($n=36$) prevention of sudden cardiac death (SCD) and the remaining 23%, for secondary prevention ($n=11$). Positive familiar antecedents for HCM and/or SCD in the same patient were found in 72.7%. Only 63.8% of this population was genetically studied while in 36.2%, genetic analysis was not even considered.

Conclusions: Despite genetic testing is recommended in all patients fulfilling diagnostic criteria for HCM in the recent 2014 ESC Guidelines (IB), not enough genetic analysis are being performed. Not even in a selected group where a higher percentage of tests was expected due to its high risk clinical profile. However, genetic testing clinical value is known to be becoming more and more important each day. Moreover it facilitates the gathering of information from other family members and it has been proved to be a cost-effective strategy. Therefore we encourage clinicians to incorporate genetic analysis in HCM in their daily practice.



P283

The role of endothelin system in the formation of chronic heart failure in patients with hypertrophic cardiomyopathy

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Purpose: To analyze the genetic polymorphisms and active biological markers encoding endothelin system in patients with hypertrophic cardiomyopathy (HCM) and chronic heart failure (CHF).

Materials and Methods: 40 patients (22 men, 18 women) with HCM and CHF NYHA I-IV were enrolled, mean age was 51,5 ± 2,16 years. 40 healthy controls were studied (22 men, 18 women), mean age was 50,4 ± 2,84 years. 50% of patients had a progressive course (PC) of the disease, stable course (SC) was observed in 35%, 15% had atrial fibrillation (AF). All patients were investigated according standard cardiac algorithm, genotyping of gene polymorphisms (EDN1 - Lys198Asn, EDNRA-H323H, NOS3 - Glu298Asp) and biological markers in serum (nitric oxide, endothelin-1, TGF- α , IGF-1, TNF- α , IL-1 β , IL-10, von Willebrand factor and NT-proBNP).

Results: Analysis of the parameters of intracardiac hemodynamics confirmed the presence of diastolic heart failure in the study group. The largest value of E/A was observed in patients with PC (E/A=1.044, p=0.048). There were significant differences in the mean value of atrioventricular relations (AVR) in exploring causes of HCM (p=0.0010). Maximum of atrioventricular relation was found in patients with chronic heart failure at a variant of AF (AVR=1.205). The size of the left atrium in AF variant was significantly higher than in SC (p<0.004).

In analyzing the polymorphisms modifier genes of endothelin system were identified association of genotype G/T polymorphism EDN1-Lys198Asn with more severe diastolic disorders (type 1) than with genotype G/G (p=0.001). In PC with CHF II-IV NYHA was dominated unfavorable allelic variants of genes that modify the functioning of the endothelin system (NOS3-T / T, p=0.03, EDN1-G / T, p=0.06, EDNRA-T / T, p=0.046, C / C, p=0.044), when SC - only favorable variants of polymorphisms (EDN1-G / G, p=0.001, EDNRA-C / T, p=0.033).

The comparison of activity of endothelial dysfunction markers has revealed correlation with intracardiac hemodynamics: von Willebrand factor with E/A (r=-0.345, p=0,046), TGF- α with E/A (r=0,4216, p=0,013), NTproBNP with the size of the left atrial (r=0,3629, p=0,045).

Conclusion: 1. The most severe degree of diastolic dysfunction revealed in unfavorable courses of HCM. 2. It were determined that the unfavorable allelic variants of genes modify the functioning of endothelin system (NOS3-T / T, EDN1-G / T, EDNRA-T / T, C / C), characteristic of the PC with CHF II-IV NYHA. 3. It was confirmed that the NTproBNP is a prognostic marker of CHF.

P284

Left ventricular asynchrony in patients with hypertrophic cardiomyopathy evaluated by 2D speckle tracking imaging

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Introduction and Aim: Hypertrophic cardiomyopathy (HCM) is a primary heart disease characterized by disorganized myocardial architecture. It's well known that the distribution and magnitude of left ventricle (LV) hypertrophy (LVH) are not uniform in patient with HCM with result's in regional heterogeneity and dys-synchrony of both LV and right ventricular (RV) systolic function.

Aim: To evaluate longitudinal and radial left ventricular (LV) dys-synchrony in patients with LVH, and to compare abnormalities associated with HCM and LVH second to hypertensive heart disease(HLVH) using 2D speckle tracking imaging

Methods: 2D for chamber long-axis and basal, middle, and apical short-axis of LV images were acquired in 97 patients with LVH including 67 HCM and 30 HLHV, and in 30 age-matched controls. Radial strain, longitudinal strain, time interval from the R-wave to peak radial strain (Trs), and time to peak longitudinal strain (Tls) were measured in 06 equidistant segments at each level of the 03 LV short-axis and 4C long-axis views using 2D speckle tracking analysis. To assess LV dys-synchrony, Trs(rs)-18SD, the standard deviation (SD) of Tls(s) was calculated.

Results: LV Ejection fraction was comparable between patients with HCM and HLHV's group. LV mass index was higher in HCM group (270 ± 65g Vs 160 ± 23g, p=0,003). Global longitudinal strain(GLS), radial (RS)and circumferential (CS) strain were significantly lower in HCM compared to HLHV group (-15,3 ± 6,4% Vs -17,9 ± 4,3%, p=0,001 for GLS) (23,2 ± 9,8% Vs 28,7 ± 7,8%, p=0,003 for RS) and (-12,6 ± 8,6 % Vs -18,1 ± 8,4%, p=0,001 for CS)

For the contraction delay, longitudinal delay as well as radial delay were longer in HCM than in HLHV (53,5 ± 23 ms Vs 28 ± 4 ms for the longitudinal delay, p=0,01) and (96 ± 38ms Vs 72 ± 30ms for radial delay, p=0,01)

In the follow up, the radial delay is correlated with no sustained ventricular arrhythmia in HCM patients (143 ± 16 vs 98 ± 23 ms p=0,002)

Conclusion: Our findings indicate that impairment of intraventricular systolic asynchrony in patients with HCM is strongly associated on the one hand with degree of LV hypertrophy, and on the other hand with increased risk of non-sustained ventricular tachycardia on ambulatory Holter ECG recording. Myocardial heterogeneity results in HCM against an anatomical and electrical background that may determine a non-uniform dispersion of cardiac impulse and a regional delay in systolic activation of LV ventricular wall and multiple microscopic re-entry circuits, generating polymorphic life threatening ventricular tachyarrhythmias and sudden cardiac death.

P285

Long anterior mitral valve leaflets determine the development of dynamic left ventricular outflow tract obstruction in hypertrophic cardiomyopathy

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Background: Development of left ventricular outflow tract obstruction (LVOTO) in patients with hypertrophic cardiomyopathy (HCM) is of importance in explaining symptoms and designing management strategies. It is caused mostly by septal hypertrophy, which through the Venturi effect causes systolic anterior movement of the mitral valve (SAM) and consequently LVOTO. The aim of this study was to evaluate the prevalence and predictors of LVOTO.

Methods: We performed exercise echocardiography, including measurements of LV morphology and function and anterior mitral leaflet (AML) length, in 51 HCM and compared them with 50 healthy controls. A starting workload of 30 watt with an increase of 10 watt/ 2 minutes was used. Measurements were made at rest; Valsalva maneuver; peak exercise and post exercise. A LVOT gradient of >30 mmHg was taken as a sign of LVOTO.

Results: Patients stopped exercise because of exhaustion (leg tiredness and/or mild breathlessness and rarely due to chest pain (n = 7)). 20% of the patients had resting LVOTO, 48% during Valsalva, 28% at peak exercise and 64% at post exercise. Patients who developed LVOTO at peak exercise were more prone to have post exercise LVOTO (p = 0.02), less systolic blood pressure rise (p = 0.013) and longer AML (p = 0.002). Stepwise multiple regression analysis including variables that were different between non-LVOTO and LVOTO during exercise showed the AML length as the only independent predictor (β value 0.84, p = 0.004) of LVOTO.

Conclusion: In a sample of HCM patients, peak exercise LVOT obstruction is relatively uncommon but when present, is related to long AML. The resulting attenuated rise of systolic blood pressure may contribute to their symptoms and potentially prognosis.

	Controls (50)	HCM (51)	P-value	HCM LVOTO exercise (13)	HCM non-LVOTO exercise (38)	P-value
Delta SBP, mm Hg	54±16	45±26	0.056	29±26	51±24	0.013*
IVSD+PWT, mm	16±3	28±5	0.001	29±5	28±5	ns
LVEF, %	71±8	53±12	0.001	55±10	52±13	ns*
Resting gradient (obstruction), mm Hg (%)	-	20±10 (20)	-	23±11 (50)	19±10 (17)	ns*
Valsalva gradient (n=27) (obstruction), mm Hg (%)	-	29±13 (48)	-	31±12 (23)	29±13 (50)	ns*
After exercise gradient (n=44) (obstruction), mm Hg (%)	-	35±15 (64)	-	43±11 (39)	32±15 (94)	0.02*
Delta lateral e', cm/s	8.6±4.3	5.2±4.5	0.001	7.5±4.8	4.4±4.2	0.063*
Ant mitral leaflet length, mm	23±2	24±6	0.001	29±6	24±5	0.002*

CARDIOMYOPATHY

P286

Meta-Analysis on the PCR proof of parvovirus B19 genomes in endomyocardial biopsies of patients presenting with myocarditis or dilated cardiomyopathy

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Introduction: Diverse viral infections have been associated with myocarditis (MC) and its sequelae, dilated cardiomyopathy (DCM). Whereas the disease specificity of enterovirus has been confirmed in this setting by meta-analysis, this relationship is not established for parvovirus B19 (B19V) genomes, yet. We aimed to summarize the published results on the association of B19V genomes with MC/DCM in a meta-analysis.

Methods: Using multiple PubMed search modes, n = 197 publications referring to B19 and MC or DCM were retrieved. Out of these, n = 29 publications with met the inclusion criteria with data from prospective analyses on >10 unselected patients presenting with MC or DCM (dataset: MA01). Data retrieved simultaneously both from controls and MC/DCM patients were available from n = 8 from these publications (dataset: MA02).

Results: The demographic data of the n = 3,599 patients of the dataset MA01 were as follows: mean age: 47.1±3.1 years; men: n = 1,920 (53.3%). Echocardiographic data showed a mean LVEF: 38.4±12.8% and a mean LVEDD: 55.5±16.7 mm, respectively. B19V genomes were detected in 42.6±17.9% of the EMB in this cohort by PCR. The dataset MA02 comprised n = 634 subjects (mean age: 46.7±6.7 years; men: n = 291 / 45.9%). The MC/DCM-patients (n = 500) had not significantly different demographic data compared to controls (n = 134; donor hearts, hypertensive and ischemic heart disease). LVEF was significantly higher in controls (mean: 62.8±8.8%) versus MC/DCM-patients: 35.4±9.5%; p = 0.0056). However, the rate of B19V positivity in myocardial tissues was not statistically different in controls (mean: 38.8±24.1%) versus the MC/DCM-patients: 45.5±24.3%; p = 0.5881).

Conclusions: This systematic review summarizes the prevalence of B19V genomes as detected by PCR being present in ca. 43% of EMB from MC/DCM-patients. However, this detection rate in MC/DCM-patients does not differ significantly from the findings in control myocardial tissues. Therefore, the "Bioportfolio" phenomenon known for B19V in other human tissues equally applies to myocardial tissues, and implies biologically irrelevant latency of B19V genome in a high proportion of myocardial tissues, both in MC/DCM-patients and in controls. This also explains that the mere PCR detectability of B19V genomes was not a valid criterion for successful immunomodulatory treatment strategies in MC/DCM (i.e. antiviral interferon treatment). Further characteristics such as B19V replication, the proof of active anti-B19V humoral and cellular responses, may be pertinent to achieve a meaningful differentiation of biologically relevant myocardial B19V infections.

P287

The influence of antianemic therapy on the clinical status and C-reactive protein level at patients with nonischemic dilated cardiomyopathy and anemia

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Aim: To evaluate the effectiveness of treatment with iron supplementation (Fe3+-polimaltose complex) and its combination with low doses of erythropoietin alfa on clinical status and levels of C-reactive protein (CRP) at patients with dilated cardiomyopathy and anemia at the end of 3-month observation.

Methods: 26 patients with DC with anemia (HYNA class was 3,2±0,3), mean age 32,2±13,3 years (men / women, 14/12) were divided into two: group (I) of standard CHF therapy with iron and erythropoietin-alpha supplementation at a dose of 2000ME/weekly, and group (II) with only the standard therapy, which included ACE inhibitors, beta blockers, digoxin, diuretics. The average level of hemoglobin amounted to 106,63±17,0g/l. The average level of CRP - 4,5±2,0 mg / l. Therapy was initiated in patients with symptomatic heart failure and continued for 1 month under the control of Ht. These were estimated value of hemoglobin, the clinical condition by the six-minute walk test (6MWT) and CRP level in the serum.

Results: Baseline 6MWT in groups I and II, respectively amounted to 189,6±8,1±30,4m and 198±48,2m, the average SBP and DBP in both groups was equal to 107 1±2,4 and 70,29±7,6mmHg. After 3 months of observation it was showed a significant increase of hemoglobin level in group I up to 11% (118,3±9,3g / l; p=0.03) with reaching of hematocrit up to 39.4% compared to group II where reduction of hemoglobin on 5% (101,63±11g / l; p>0.05) was noted. Despite this, in both groups was determined a significant improvement of clinical status in the form of an increase in exercise capacity according 6MWT up to 57% and 62% (up to ±330 and 319±36,4m 28,4m respectively; p<0,05) with no significant intergroup differences. Thus, an increased systolic and diastolic blood pressure was

more pronounced in group I comparing with group II, representing an increase on 8 and 11% (116±11,6 78,09±3,6mmHg) vs 4 and 8%, respectively (111±12,6 and 76,09±8,6mmHg.; p=0.12). Analysis of the dynamics of CRP showed a significant decrease in its concentration in both groups up to 2,6±0,4mg / l (p<0.05) (43%), with no significant differences between them.

Thus, the results of our research there is a positive dynamics of indicators, hemodynamics and exercise capacity CRP levelson the basic therapy. In this case, the correction of anemia of iron and EPO has additional advantages in the form of increased levels of hemoglobin, a more pronounced effect on SBP and DBP.

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Controversial issues of treatment of patients with dilated cardiomyopathy in everyday clinical practice according to the first national register of dilated cardiomyopathy in the russian federation

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Purpose: To assess the use of modern treatment methods for patients with dilated cardiomyopathy in usual clinical practice.

Methods: The study included 23 hospitals from 20 regions of Russia. In these hospitals 63761 patients observed with chronic heart failure among them 1271 patients diagnosed with dilated cardiomyopathy. Special questionnaires were sent to the hospitals of 20 regions of Russia. Questionnaires investigated the number of patients with chronic heart failure and dilated cardiomyopathy, diagnostic and treatment methods which had been used.

Results: 574 patients with dilated cardiomyopathy were included in the study. The average age was 47.61 (11.265) years (83% male, 17% female), II-III Class NYHA, mean LVEF 32,9±7,5%, with symptomatic heart failure for median 2,3 [1,0;4,0] years. Angiotensin converting enzyme inhibitors were prescribed in 88,6%, beta-blockers in 84,5%. Daily dosage of angiotensin converting enzyme inhibitors and of beta-blockers was on average below the recommended target dose. According to the ECG in 42.4% of patients were identified atrial fibrillation, among them anticoagulant therapy remains limited - only 54.55% (n = 132). Most of the patients in this group were used aspirin - 61.75 % (n = 155). AV blockade II and III was identified in 4.9% (n = 28) patients among which pacemakers were implanted only 28.6% (n = 8). According to the register pacemakers have been implanted at 9.23% (n = 53) patients. A lower percentage of patients accounted for implantable cardioverter-defibrillators - 5.23% (n = 30), including 12 patients with ventricular tachycardia and 2 patients with ventricular fibrillation.

Conclusion: Patients with dilated cardiomyopathy were revealed weaknesses of treatment in daily clinical practice. Insufficient use of modern methods of treatment, such as the implantation of cardioverter-defibrillator.

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Left bundle branch block in nonischemic dilated cardiomyopathy: assessment and prognostic role of left ventricular dyssynchrony evaluated by volume/time curves at cardiac magnetic resonance

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Background: Left bundle branch block (LBBB) is frequently linked to left ventricular (LV) dyssynchrony and adverse prognosis in Heart Failure (HF). Analysis of LBBB patients with cardiac magnetic resonance (CMR) has been shown to be useful to assess left ventricular dyssynchrony and to predict clinical response to cardiac resynchronization therapy (CRT). We sought to evaluate association between different patterns of LV Volume/Time (V/T) curves at CMR, LBBB, clinical correlates and prognostic role in patients with nonischemic systolic HF.

Methods and Results: One-hundred-fifteen consecutive patients with LBBB were submitted between 2004 and 2014 to a complete cardiologic evaluation, including CMR with analysis of V/T curves of LV contraction, and follow-up for cardiac events. We distinguished two different patterns of global and segmental LV systole: a "narrow" pattern (NP) generated by synchronous contraction of wall segments; a "wide" pattern (WP), when delay in contraction between wall segments resulted in a prolongation of systolic peak with a flat or notched morphology. Fourteen patients presenting with normal LV dimensions and function all had NP. Out of 101 patients with HF, those with WP had higher levels of NT-proBNP, lower EF and higher LV volumes than those with NP, whereas no significant difference was found in QRS duration. At multivariate analysis only EF (p = 0.024) and NE (p = 0.028) were independent predictors of WP. At Kaplan-Meier analysis, the presence of WP was associated with a worse prognosis considering a composite end-point of cardiac death, hospitalization for HF and ICD shock (p < 0.005). At Cox analysis only presence of WP (p = 0.029) and level of NT-proBNP (p = 0.004) were independent predictors.

Conclusions: In nonischemic systolic HF patients with LBBB, presence of a WP at CMR V/T curves identifies greater LV dyssynchrony with possible major benefits from resynchronization therapy and is an independent prognosticator.

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Clinical and histological characteristics of dilated cardiomyopathy due to BAG3 mutations

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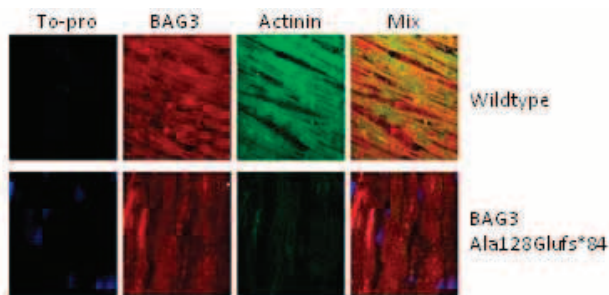
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Introduction: Mutations in BAG3 (BLC2-associated athanogene 3) gene have been recently described as a cause of Dilated Cardiomyopathy (DCM). Only a small number of cases have been reported, and the clinical and histological characteristics are mostly unknown. We sought to describe the clinical and histological findings in patients with BAG3 mutations from 5 families affected by DCM.

Methods: Characteristics and clinical course of 19 individuals with pathogenic mutations in BAG3 were analysed. BAG3 protein localization was studied in 3 explanted hearts.

Results: 19 subjects (46 ± 17 years, 63% male) with mutations in BAG3 gene were studied. Patients exhibited one of the following novel truncation mutations: Arg121*, Ala128Glufs*84, Arg301Serfs*6, Val439Glyfs*4 and Trp36*. 12 patients (63%) exhibited overt DCM (49 ± 15 years, 67% male) and 92% of them showed a severe phenotype: 10 patients had LVEF < 35%, 4 had been transplanted and 1 died suddenly aged < 35. Mean age at diagnosis was 39 ± 15 years and ages at HTx were 16, 18, 45 and 64. 4 patients (33%) had history of sustained ventricular arrhythmias. 5 (26%) patients (30 ± 7 years, 60% male) did not show DCM, but presented borderline systolic function (mean LVEF 53 ± 1%) with enlarged LV end-diastolic diameter (111 ± 7% of predicted by Henry formula). 2 asymptomatic obligate carriers (aged 70 and 72) could not be clinically evaluated. An age-dependent expression of the disease was found (p = 0.02). Immunohistological study by confocal microscopy showed severe myofibrillar disarray and delocalization of BAG3 from the Z discs (Fig.).

Conclusions: DCM caused by BAG3 mutations is characterized by high penetrance and an age-dependent expression. Truncation mutations in BAG3 gene cause protein disruption with protein delocalization.



Confocal microscopy

P291

Influence of the presence of combined and non-classical mutations in clinical presentation of familial dilated cardiomyopathy

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Purpose: The new techniques developed for genetic testing identify mutations not previously described and even combinations of them in patients with familial dilated cardiomyopathy. We conducted this study in order to know the clinical characteristics of patients with these mutations.

Methods: We studied all the index cases diagnosed of familial dilated cardiomyopathy at follow-up in our familial cardiomyopathy consultation, recording the results of the genetic studies conducted and clinical features of the patients.

Results: Of the 39 patients (57 years, 30.8% women), 28.1% had high blood pressure, 28.1% had diabetes mellitus and 37.5% had dyslipidemia. 6.3% presented sudden death, 38.7% had family history of sudden death, 84.4% had heart failure (36.7% with severe left ventricular dysfunction) and 3.1% presented syncope. An 84.4% had an ICD and a 23.3% had a CRT, presenting 33.3% left bundle branch block and 35.5% long QT. A 61.5% had at least one genetic mutation, presenting combined mutations the 41.7% and non-classical genes mutations the 58.3%.

There were no significant clinical differences between non-classical mutations carriers and classical mutations carriers. Patients with combined mutations had higher prevalence of heart failure (100% vs 50%, p = 0.023), and those with two mutations or more had higher prevalence of left bundle branch block (100% vs 25%, p = 0.019).

Conclusions: 1. A high percentage of patients with familial dilated cardiomyopathy were carriers of combined mutations and / or non-classical genes.

2. In our study, there were no significant clinical differences between patients with non-classical and with classical mutations.

3. Patients with combined mutations had higher prevalence of heart failure and higher prevalence of left bundle branch block.

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Prognostic value of left atrial volume in patients with non-ischemic dilated cardiomyopathy

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Background: Increased left atrial (LA) size is a prognostic marker of mortality in the general population. LA size varies considerably in patients with non ischemic dilated cardiomyopathy (DCM), but its clinical significance has not been widely studied. Our objective is to evaluate the long-term prognostic value of LA volume (LAV) in patients with non ischemic DCM.

Methods: We prospectively studied forty patients admitted with non ischemic dilated cardiomyopathy, in sinus rhythm. Complete echocardiographic study at rest was performed in all patients. The composite endpoint of acute heart failure or death during follow-up was assessed.

Results: The average age of patients was 60 years ± 10. The sex ratio was 4/1. Sixty percent of patients were smokers. Half of the population had hypertension. Only thirty percent of them had diabetes mellitus which was insulin-dependent in the majority of cases. The average of ejection fraction of left ventricle (SIMPSON BP) was 35,7% ± 9.

During six months of follow-up, two patients died and thirteen patients were hospitalized for acute heart failure. Univariate Cox analysis showed various potential echocardiographic markers of prognosis in our population, including LA size in M-mode (42,9 VS 40,5mm, p = 0.36), LA area (23,3 VS 22 cm², p = 0,58), LAV (121,7 VS 79,3ml/mm², p = 0.007), E/A ratio (1,95 vs 1,27; p = 0.019); E/A > 2 (, p = 0.0001) and mitral E/E' ratio (16 vs 14,8, p = 2.74). The only variable that remained in the multivariate model was LAV (p = 0.005).

Conclusion: LAV was shown to be an echocardiographic determinant of acute heart failure and death in our population with non ischemic DCM. The results of this study suggest that LAV assessment, which can be performed using echocardiography, a non-invasive, readily available and inexpensive imaging modality, contributes to risk stratification and should be a routine part of echocardiographic study in patients with non ischemic DCM.

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Acute myocarditis rather than post-infarction myocardial inflammation triggers the formation of beta1-adrenoceptor autoantibodies in the human: first data from the prospective ETICS-study

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In heart failure (HF) evidence for a pathogenetic relevance of autoimmunity steadily increases. Autoantibodies stimulating the cardiac beta1-adrenoceptor (beta1-aabs) are cardio-pathogenic and increase cardiovascular mortality-risk by 3-fold. Still, the events inducing such aabs and their effects on cardiac remodelling are unknown.

Methods: To address these issues, 13 European study-centers currently enrol 200 patients with a 1st acute myocardial infarction (FAMI) and 170 patients with acute (EMB-proven) myocarditis (AMITis) into the ETICS-study. At baseline (BL) and after 3, 6, and 12 months (M) patients are clinically assessed (comprising echo's & cMRI's at BL & 12M); blood is sampled to follow cardiac autoantibody-titers. Occurrence of functional beta1-aabs is assessed by a life-cell assay measuring cellular cAMP-production by fluorescence resonance energy transfer (FRET).

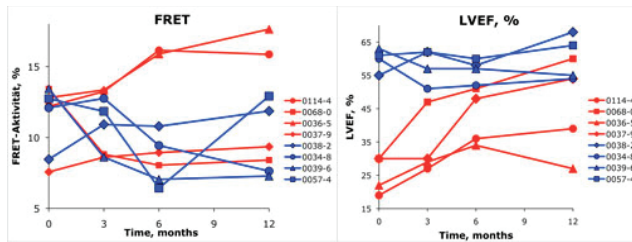
Results: The first 8 patients with complete follow-up (4 AMITis/4 FAMI) were assessed for beta1-aabs and cardiac function (LVEF). Whereas none of the FAMI-patients developed beta1-aabs, 2/4 of the AMITis-patients (50%) within 6M developed stimulating beta1-aabs (cut-off: 17% FRET-activity). In these patients cardiac function did not recover, whereas LVEF recovered in all beta1-aab negative patients (Figure).

Conclusion: Acute myocarditis rather than post-infarction cardiac inflammation triggers the formation of beta1-aabs. Antibody-positive patients might profit from early initiation/intensification of HF-therapy (incl. early beta-blockade) and/or novel anti-body-directed therapeutic approaches.

Figure:

Left: FRET-activity of IgG prepared from FAMI-(blue) or AMitis-patients (red lines) (t = 0, 3, 6 & 12M, pseudonyms).

Right: Time-course of the corresponding LVEF-measurements (% , determined by echo)



P294

Takotsubo cardiomyopathy: treatment & outcomes in a retrospective case series from the west of Ireland

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Purpose: To establish the demographics, treatment and outcomes of Takotsubo Cardiomyopathy in an Irish population

Methods: Patients were identified using keyword searches of electronic records of patient correspondence including coronary angiogram reports and outpatient clinic letters. Medical charts, coronary angiograms and echocardiograms were reviewed to identify those with a diagnosis of Takotsubo Cardiomyopathy.

Results: 23 patients were identified who were diagnosed with the condition during a 6-year period from 12/11/2007 to 02/01/2014. 22 (96%) were female.

Age at presentation ranged from 41 to 83. The mean age at diagnosis was 68, median age of 70. All patients had ECG changes: 5 had ST segment elevation, 1 ST depression and 13 had T wave inversion. 22 patients had elevated Troponin levels, 11 had elevated CK levels. All underwent coronary angiography and a left ventriculogram was performed in 19 cases (83%). Apical ballooning was evident in 18 of these cases and reverse or inverted ballooning pattern was seen in 1. No patient had obstructive coronary artery disease. 12 patients were diagnosed with severe LV dysfunction (LVEF \leq 35%), and 8 patients with moderate LV dysfunction (LVEF 36-44%) on echocardiogram. A stressor/precipitant was identified in 14 cases, which included situations such as the death of a family member, a heated argument, a house fire and an intravitreal eye injection.

19 patients were prescribed an ACE inhibitor, 17 a beta-blocker, 17 an antiplatelet agent, 10 a statin, and 7 a diuretic. 2 patients were prescribed Warfarin in addition to Aspirin. 4 patients were lost to follow-up. All 19 patients who had follow-up imaging were ultimately shown to recover normal LV function. Time to documented recovery ranged from 4 - 306 days. Mean time to documented recovery was 101 days, with a median time of 83 days. 2 patients had normal LV function within 9 days of diagnostic angiogram, and a further 8 patients had a normal LVEF within 97 days.

Conclusion: Consistent with the international experience, there was a preponderance of post-menopausal women diagnosed with the condition. A precipitating stressor was identified in over half of cases. ACE inhibitors, antiplatelet agents, and beta-blockers formed the mainstay of treatment. All patients with follow-up imaging were shown to recover normal LV function within one year, and approximately 50% of patients had a normal LVEF within 14 weeks of diagnosis.

P295

Left ventricular dysfunction in takotsubo miocardiopathy prognosis

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Introduction: The Tako-tsubo cardiomyopathy (TSC) is considered a transient and benign pathology, complications especially after the acute phase, but very long-term prognosis data are scarce. Our objective is to determine the long term prognosis of TSC associated to left ventricular systolic function.

Materials and methods: 67 cases of TSC (modified Mayo Clinic criteria) were prospectively collected between 2004-2013, (clinical variables characteristics and hospital complications were recorded. Follow up was obtained in 57 patients by analyzing A combined end-point of death, readmission and TSC recurrence was analyzed in 57 patients (mean follow up 24 months, range 6-108). A stratified analysis was performed according to the presence of left ventricular dysfunction (LVEF <45%)

Results: Of the overall, 85% of patients were women, mean age 68 \pm 11. Arterial hypertension was the most prevalent cardiovascular risk factors. (73%). Chest pain

was the most common form of presentation (78%); suddendeath/cardiac arrest occurred in 8%. There was an identifiable stressful event as a possible cause in 65% of cases; being an emotional event in 62% and a physical event in 33%

The Mean LVEF at baseline was 39 \pm 9%. Three Patterns of LV dysfunction were observed: apical (90%), mid-ventricular (9%) and basal form (1%) dyskinesia. During hospital stay, patients with left ventricular dysfunction showed longer QT intervals, greater enzymatic peak, and higher rate of stress triggers and also a higher in-hospital mortality. During follow-up, LVEF <45% (HR 8.9, 95% CI [1.012-79.7]; p=0.05) and CPK peak (HR 1.003, 95% CI [1- 1.005]; p=0.019), where both independent predictors of the combined end-point.

Conclusions: In patients with TSC, left ventricular dysfunction during the index admission behaved as a predictor of events during long term follow-up.

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Efficacy of reduce form of NAD-containing drug in normalization of markers of heart failure, inflammation, endothelial activation and Lipoproteins profiles in non-ischemic cardiomyopathy

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Purpose: Study sought to determine the effect of aggressive reduce form of nicotinamide adenine dinucleotide (NAD)-containing drug (Nadcin) therapy on surrogate markers in non-ischemic cardiomyopathy (NICM) patients and average low-density lipoprotein (LDL) concentrations. Nadcin is an attractive option for decreasing residual risk in statin-treated or statin intolerant patients.

Methods: 21 patients with NICM on standard maximized heart failure medication were enrolled in a randomized, controlled study. Inclusion criteria included a history of congestive heart failure (CHF) II functional class (FC) a New York Heart Association (NYHA) min 3 months secondary to NICM; ejection fraction \leq 45% but more than 35%; patients receiving maximized individual CHF therapy; or LDL >160 mg/dl. Exclusion criteria included a NYHA FC III- IV; diabetes; or cholesterol-lowering, antioxidant, estrogen replacement, or non-steroidal anti-inflammatory therapy. Treatment periods for atorvastatin before including in the study were 8 weeks. After randomization in the control group receive ATV in the same dose during 2 weeks and in the main group receive 1,0 mg of reduce form of NAD intramuscularly in dose 180 mg equivalent of 1,0 mg of NAD) once daily during 2 weeks. Plasma samples were obtained from patients at the start and end of each phase for analysis of N-terminal-pro brain natriuretic peptide (BNP), inflammation (high-sensitivity C-reactive protein (hsCRP), oxidized LDL-antibody (ox-LDL), soluble tumor necrosis factor (sTNF), and endothelial activation (circulating levels of endothelin-1). Analysis of samples was performed using an enzyme-linked immunosorbent assay. The data are expressed as mean \pm standard deviation. A value of p < 0.05 was considered statistically significant.

Results: After Nadcin therapy the intensity of CHF symptoms are reduced, biological markers of CHF, levels of BNP decreased from 265 \pm 34 to 121 \pm 34 fmol/ml, p < 0,005; markers of inflammation: hsCRP from 5,65 \pm 0,89 to 3,1 \pm 0,3 ng/ml, p < 0,001 and sTNF from 3,22 \pm 0,78 to 121 \pm 34 pg/ml, p < 0,005; there was a significant decrease in LDL concentration from 167 \pm 31 to 51 \pm 18 mg/dl (p < 0.01). In contrast, treatment only with ATV did not significantly changed in levels of proBNP and LDL-C also.

Conclusion: Based on these findings, it seems that the administration of NAD-containing drug, Nadcin, to a systolic heart failure population II FC NYHA occurs beneficial effect on the efficacy of treatment with statin.

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Speed of recovery of left ventricular function is not related to the prognosis of takotsubo cardiomyopathy: a portuguese multicenter study

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Introduction: Takotsubo cardiomyopathy (TC) is characterized by a transient left ventricular (LV) dysfunction. The speed of recovery of LV function is variable. The impact of the rate of LV function recovery on prognosis of TC is currently unknown.

Aim: To determine whether patients diagnosed with TC who have a faster recovery of LV function have better medium term prognosis.

Methods: A multicenter study involving 11 hospital centers and including all patients diagnosed with TC in the last 10 years. Echocardiography was analyzed

at admission, discharge and follow-up of patients. Complete recovery was defined as the normalization of the segmental motility abnormalities present in the initial echocardiogram. The timing of discharge and 15 days after hospital admission were defined as cut-off points for the determination of recovery of LV function. We evaluated whether patients with a faster recovery of LV function had better medium term prognosis.

Results: We included 142 patients with TC. Full recovery of LV function was observed in 45% of patients at discharge and in 63% of patients at 15 days after hospital admission. A mean follow up of 39.7 ± 30.7 months was performed.

Complete recovery of LV function during hospitalization was not associated with a lower incidence of death (1.6% vs 1.3%, $p=0.888$) or stroke / transient ischemic attack (TIA) (2.0% vs 4.6%, $p=0.437$) or lower recurrence of TC (2.0% vs 6.2%, $p=0.270$) in the follow-up.

Similarly, complete recovery of LV function at 15 days after hospital admission was not associated with a lower incidence of death (0% vs 2.8%, $p=0.270$) or stroke / TIA (2.4% vs 4.2%, $p=0.624$) or lower recurrence of TC (2.4% vs 5.6%, $p=0.430$) in the follow-up.

In multivariate analysis, a faster recovery of LV function was not an independent predictor of cardiovascular events in the medium term follow-up.

Conclusion: In this Portuguese multicenter study, patients with TC that presented a faster recovery of LV function didn't have a better medium term prognosis. However, the low rate of complications in the follow-up may have limited the study results.

P298 Nocturnal desaturation predicts major adverse cardiac event in cardiac amyloidosis

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Background: Sleep disordered breathing (SDB) is a known prognosis factor in heart failure (HF). There is neither epidemiological data nor known prognosis value of SDB in cardiac amyloidosis (CA): systemic (AL), transthyretin-related amyloidosis, familial (fTTR) or senile (sTTR).

Methods: Patients prospectively referred in our center between 2010 and 2013 for CA underwent cardiac and an overnight polygraphy assessment. Sleep apnoea syndrome (SAS) was defined as an apnoea-hypopnoea index $\geq 5/h$. Multivariate analysis was used to identify predictors of major adverse cardiac events (MACE) defined as death, heart transplantation and acute HF.

Results: 70 were included (31 had AL, 22 fTTR and 17 sTTR). Mean (SD) age, LVEF, and BMI of the overall cohort were respectively 71 ± 12 years, $49 \pm 13\%$ and 25 ± 4 kg/m². 63 (90%) patients presented SAS: 17 central and 46 obstructive apneas (OSA), without difference according CA type ($p=0.73$). At 12 months, 26 patients experienced MACE. Compared to 22 MACE-free patients with ≥ 12 months of follow-up, MACE-patients experienced longer time with arterial oxygen saturation $<90\%$ (SaO₂ <90) ($p=0.022$). SaO₂ <90 was the only independent predictor of MACE after multivariate analysis. Conclusion. The prevalence of sleep-disordered breathing is high (90%) in CAs population. In SDB and CA patients, prognosis is driven by oxygen desaturation.

P299 Prediction of peripartum cardiomyopathy: a validation of associated clinical characteristics among 3,474,622 delivering mothers

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Purpose: Characteristics associated with peripartum cardiomyopathy (PPCM) at the time of delivery include maternal age ≥ 30 years, African ancestry, hypertension, anemia, substance abuse, asthma, autoimmune disease, multiple gestations, and preeclampsia/eclampsia; however, these associations have not been independently validated.

Methods: Administrative hospital records were obtained from state agencies in California, New Jersey, New York, Vermont, and Colorado between the years 2007-2013. Records including the ICD-9 CM code for PPCM (674.5x) were analysed. Patient characteristics in the validation set were compared with the previously published derivation set. Performance of a previously published regression model and score calculated by counting the number of risk factors present was assessed using receiver operating characteristic area-under-the-curve (AUC) analysis. Novel characteristics associated with PPCM that added to the previous model were identified using multivariate logistic regression and the likelihood ratio test.

Results: In total, 486 of 3,474,622 (0.013%) of delivering mothers in the validation set had a diagnosis of PPCM compared with 535 of 4,003,912 (0.013%) in the original derivation set. There were no significant differences in clinical characteristics of PPCM patients between the derivation and validation sets with the exception of obesity (5.4% in the derivation vs. 14.2% in the validation set, $p < 0.001$), whereas there were significant differences between non-PPCM delivering mothers in the two sets in every clinical feature. The previously published multivariate logistic regression model performed well in both the derivation (AUC 0.82) and the validation datasets (AUC 0.8). The risk score also performed well in both the derivation (AUC 0.81) and validation sets (AUC 0.76). Novel PPCM-associated characteristics in the combined cohort included mood disorders defined as anxiety, depression, or bipolar disorder (OR of PPCM 1.98, 95% CI 1.49-2.63, $p < 0.001$) and obesity (OR of PPCM 1.72, 95% CI 1.33-2.24, $p < 0.001$).

Conclusions: The previously described clinical characteristics and risk score performed well in predicting PPCM in a large independent dataset. The presence of mood disorders and/or obesity may also be associated with PPCM at the time of delivery.

P300 Gender related differences in cardiac function in patients with hereditary transthyretin amyloidosis

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Purpose: Transthyretin (TTR) amyloid (ATTR) cardiomyopathy is a disorder mainly affecting elderly males, including those carrying the TTR V30M mutation. Previously, two types of ATTR fibrils have been detected, one consisting of a mix of full length and fragmented TTR (type A) and the other of only of full length TTR (type B). We aimed to investigate the dispersion of cardiomyopathy between genders, in relationship to fibril type in Swedish V30M patients.

Methods: We analysed echocardiographic data in 94 patients with ATTR V30M amyloidosis, with their fibril type determined as either type A or B. Analysis of left ventricular (LV) septal (IVS) and posterior wall (PWT) thickness, LV mass indexed to height and speckle tracking derived global and septal longitudinal strain was performed.

Results: Among patients with type A fibrils, the proportion of males presenting with an interventricular septal thickness (IVS) >12 mm was slightly higher compared to females ($p=0.052$). Males had significantly higher median IVS ($p=0.007$), posterior wall thickness ($p=0.010$) and LV mass corrected for height ($p=0.008$) and also lower septal strain ($p=0.028$), as compared to women.

Conclusions: Similar to male patients, the majority of women with type A fibrils showed signs of amyloid infiltration of the myocardium (IVS >12 mm). Nevertheless,

Echocardiographic descriptors

	Type A males n=30	Type A females n=11	p value	Type B males n=33	Type B females n=20	p value
Age, years	68 (62-73)	74 (65-81)	0.141	54 (39-65)	59 (45-67)	0.123
IVS > mm, %	97	73	0.052	42	25	0.247
IVS, mm	18 (15-20)	14 (12-16)	0.007	12 (10-15)	11 (10-13)	0.243
PWT, mm	12 (11-13)	10 (9-10)	0.010	10 (8-11)	9 (8-10)	0.054
LV mass indexed to height	1.66 (1.35-2.09)	1.14 (1.08-1.52)	0.008	1.18 (0.90-1.30)	0.97 (0.81-1.21)	0.248
Septal strain, %	-7.8 (-4.5- -11.8)	-11.9 (-8.8- -16.1)	0.028	-15.3 (-17.4- -20.1)	-16.4 (-15.8- -21.0)	0.270

IVS; Interventricular septal thickness, PWT; Posterior wall thickness, LV; left ventricular, Data expressed as median (interquartile range), significant differences between groups calculated with Mann Whitney U test and Fisher's exact test, $p < 0.05$ is considered statistically significant.

women tended to have less severe involvement, shown by lower LV myocardial thickness and tendencies towards a more preserved myocardial function. Whether this is a result of physiological differences where women generally have lower myocardial dimensions or if women have a slower disease progression remains to be elucidated.

P301

Prevalence of left ventricular systolic dysfunction in a portuguese population of left ventricular non-compaction cardiomyopathy - a multicenter study

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Introduction: Left ventricular non-compaction cardiomyopathy (LVNC) may be complicated with left ventricular (LV) systolic dysfunction and heart failure. The prevalence of LV systolic dysfunction in patients with LVNC ranges from 58 and 82% of cases in previous studies. However, natural history of LVNC is not clearly established and recent studies show that prognosis of LVNC seems to be better than previously described.

Aim: To characterize a Portuguese population of patients with LVNC and to determine the prevalence of LV systolic dysfunction in patients with LVNC.

Methods: Portuguese multicenter study involving 11 hospital centers and including all patients diagnosed with LVNC. We evaluated the clinical, electrocardiographic, echocardiographic and cardiac MRI data. We determined the prevalence of LV systolic dysfunction, considering it to be present when a LV ejection fraction was below 50%.

Results: We included 72 patients with LVNC, 57% males, with mean age 45 ± 19 years. Symptoms were present in 46% of patients, and dyspnea (38%) and palpitations (28%) were the most common symptoms. Most patients were in sinus rhythm (89%). A history of atrial fibrillation was present in 10% of the patients and non-sustained ventricular tachycardia in 10% of the cases. Family history of LVNC was identified in 8% of cases.

Diagnosis of LVNC was established by echocardiogram in 85% of patients. In this Portuguese population of patients with LVNC, the prevalence of LV systolic dysfunction is 47%. The average LV ejection fraction was $49 \pm 16\%$. Mitral regurgitation was detected in 15% of cases. Delayed gadolinium enhancement on cardiac MRI was found in 20% of patients. Cardiac death occurred in 2.8% of cases (mean follow-up of 48 months).

Conclusions: In this Portuguese population of patients with LVNC, the prevalence of LV systolic dysfunction is 47%, lower than previously reported in the literature, which supports the current idea that prognosis of LVNC may be better than previously described. Larger studies are needed to better understand the natural history of LVNC.

P302

The impact of renal insufficiency on cardiac events in cardiac sarcoidosis patients

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Objectives: The aim of this study is to demonstrate that renal insufficiency is a predictor of cardiac events in patients with cardiac sarcoidosis (CS).

Background: Cardiac events in sarcoidosis are known as one of the important prognostic factors. But the relation between renal sufficiency and cardiac events is still unclear.

Methods and Results: Among consecutive 68 patients who were suspected CS, 38 patients who were diagnosed as CS were investigated. Mean follow up period was 87.7 ± 71.7 months. Primary endpoints were defined as cardiac events including congestive heart failure hospitalization, sustained ventricular tachycardia, and cardiac death. Renal insufficiency which was defined as estimated glomerular filtration rate (eGFR) ≤ 60 ml/min/m² was present in 13 patients (34%). The mean ejection fraction (EF) of the 13 patients were significantly lower than other 55 patients. (39.0% vs 54.6%, $p < 0.001$) In univariate analysis, low ejection fraction and low eGFR were significantly associated with cardiac events ($p < 0.01$). Prognosis by Kaplan-Meier curve in CS with renal insufficiency was inferior to that of CS without renal insufficiency ($p < 0.001$). Among presence of renal insufficiency, basal ventricular septum thinning, left ventricular dysfunction (EF > 50%), and advanced atrio-ventricular block, presence of renal insufficiency was an independent risk factor by multivariate analysis. ($p < 0.01$, HR 6.6).

Conclusion: In our population of CS patients, the presence of renal insufficiency was a significant predictor of cardiac adverse events after initial diagnosis of sarcoidosis.

P303

Comorbidities and prognostic factors in alcoholic cardiomyopathy

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Purpose: Alcoholic cardiomyopathy is a common cause of dilated cardiomyopathy, but little is known about the effect of reducing alcohol intake and the impact of comorbidities on disease progression. The aims of our study were to define the long-term outcome of alcoholic cardiomyopathy and to determine prognostic markers.

Methods: We studied all the alcoholic cardiomyopathy patients in our heart failure consultation, recording their comorbidities, clinical characteristics, mortality and readmissions during follow-up.

Results: Of the 51 patients (61 years, 98% men), 43.1% had high blood pressure, 25.5% had diabetes mellitus, 33.3% had atrial fibrillation, 29.4% had COPD, 33.3% chronic kidney disease (CKD), and 8.2% had anemia, presenting a mean of comorbidities of 2.33 ± 1.55 . The 49% of the patients presented left bundle branch block. After a median follow-up of 73 months, 31 (60.8%) experienced recovery in left ventricular function, 14 (27%) remained clinically stable without improvement in systolic function, 10 (21.7%) had died from cardiovascular causes (9 from heart failure and 1 from arrhythmic storm), and 16 (31.4%) were readmitted for heart failure. CKD and the presence of left bundle branch block were independent predictors of left ventricular function recovery (OR 0.207, 95%CI:0.053-0.762, $p = 0.018$; OR 0.242, 95%CI:0.067-0.882, $p = 0.031$, respectively). Independent predictors of death at follow-up in alcoholic cardiomyopathy were CKD (HR 4.927, 95%CI:1.638-14.825, $p = 0.005$) and left ventricular function recovery (HR 0.264, 95%CI:0.082-0.852, $p = 0.026$), and independent predictors of readmissions at follow-up were CKD (HR 3.719, 95%CI:1.037-13.341, $p = 0.044$) and severe pulmonary hypertension (HR 11.147, 95%CI:1.138-109.198, $p = 0.038$).

Conclusions: 1. Alcoholic cardiomyopathy patients have high prevalence of comorbidities.

2. CKD and the presence of left bundle branch block were independent predictors of left ventricular function recovery.

3. Independent predictors of death at follow-up in alcoholic cardiomyopathy were CKD and left ventricular function recovery, and of readmissions at follow-up were CKD and severe pulmonary hypertension.

P304

Prevalence of overt left ventricular dysfunction ('burn-out phase') in a portuguese population of hypertrophic cardiomyopathy, a multicentre study

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Introduction: In hypertrophic cardiomyopathy (HCM), the left ventricular (LV) hypertrophy is usually associated to normal or supranormal LV ejection fraction. A minority of patients with HCM, however, progress to a stage of LV dilation and overt systolic dysfunction with reduced LV ejection fraction, also known as "burn-out phase". The prevalence of patients with HCM in the "burn-out phase" ranges from 2.4 and 4.9% in recent studies.

Aim: To characterize a Portuguese population of patients with HCM and to determine the prevalence of patients with HCM in the "burn-out phase".

Methods: Portuguese multicenter study involving 9 hospital centers and including all patients diagnosed with HCM. We evaluated the clinical, genetic, electrocardiographic, echocardiographic and cardiac MRI data. We determined the prevalence of the "burn-out phase", considering that "burn-out phase" was present when there was a LV ejection fraction below 50%.

Results: We included 356 patients with HCM, 58% males, mean age 61 ± 14 years. About 60% of patients were symptomatic, and dyspnea (58%), angina (15%) and syncope (11%) were the most common symptoms. The HCM was asymmetric in 75%, symmetrical in 11% and apical in 14% of patients. The average IVS thickness was 19 ± 5 mm and the posterior wall 11 ± 2 mm. The average LV ejection fraction was $64 \pm 10\%$. Obstruction at rest was found in 27% of cases and latent obstruction in 12% of cases. Mitral regurgitation was detected in 53% of cases. Delayed gadolinium enhancement on cardiac MRI was found in nearly half of the patients. Most patients were in sinus rhythm (84%). A history of atrial fibrillation was present on 20% of the patients and non-sustained ventricular tachycardia in 15%

of the cases. About 6% of patients had pacemaker and 8% had ICD. Family history of HCM was identified in 22% and family history of sudden death in 15% of cases. Genetic testing was performed in 168 patients (47%) and revealed genetic mutations in 46% of those cases. Cardiac death occurred in 1.7% of cases (mean follow-up of 5 years).

In this Portuguese population of patients with HCM, the prevalence of patients on the "burn-out phase" is 3.6%.

Conclusions: In this Portuguese population of patients with HCM, the prevalence of the "burn-out phase" is 3.6%, which is consistent with the findings of recent studies.

P305

Prevalence and clinical significance of left ventricular outflow tract obstruction in patients with takotsubo cardiomyopathy

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Purpose: Takotsubo cardiomyopathy (TTC) is regarded a benign disease since left ventricular function normalizes within a short time. However, a number of complications have been observed in patients (pts) with this syndrome.

This study evaluated the frequency and clinical significance of left ventricular outflow tract obstruction (LVOTO) in a large TTC registry.

Methods: From 37 heart centres, 324 pts (296 f, 28 m, age 68 ± 12) were included in a registry according to established TTC criteria. Complete data on complications were available in the last 209 registry pts, and those with and without LVOTO were compared.

Results: Complications developed in 108/209 pts (52%) within 2.6 ± 2.9 days after symptom onset; 51 of these pts (24%) experienced >1 complication. Most complications (77%) occurred within 3 days after symptom onset, however, 23% developed later (day 4 to 56).

During the acute phase, LVOTO (ranging from 20-100 mm Hg) was seen in 10/209 pts (5%). LVOTO occurred within the first 2 days after hospital admission in 7 pts (70%) and developed between day 3 and day 10 in 3 pts. Inotropic agents had been administered in 1 pt. Age, sex and symptoms were comparable in pts with or without LVOTO. The admission ECG showed a higher heart rate in association with LVOTO ($101 \pm 15/\text{min}$ vs $87 \pm 23/\text{min}$, $p=0.05$); other ECG parameters were not different. Cardiac markers were lower with LVOTO (CK 1.67 ± 1.2 vs 1.97 ± 4.1 , and troponin 11.7 ± 9.4 vs $21.4 \pm 56.3 \times$ upper limit of normal, $p=0.05$). Angiographic ejection fraction was comparable in both groups ($50 \pm 14\%$ vs $51 \pm 15\%$). LVOTO occurred with similar frequency in mid-ventricular and in apical ballooning (2/76 vs 8/133, $p=ns$). Transient mitral regurgitation (\geq grade II) was only seen in pts with LVOTO (2/10 vs 0/199, $p < 0.002$). Other complications (LV thrombus or stroke, pulmonary edema, arrhythmias, shock, death) were observed with similar frequency in both groups. Under betablocker therapy LVOTO resolved within 2-3 days in every patient.

Conclusion: LVOTO occurs in 5% of pts with TTC and may be associated with high grade mitral regurgitation. Since catecholamines can provoke or aggravate LVOTO, inotropic agents should be used only under echocardiographic guidance. With betablocker therapy LVOTO resolves within 3 days.

P306

Plasma renin activity and left ventricular remodelling in subjects with arterial hypertension

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Aim: Plasma renin activity (PRA) measurement is an approach to guide antihypertensive treatment. RAAS blockers are effective in renin-mediated hypertension, whereas anti-volume drugs (e.g. diuretics or calcium channel blockers) - in low-renin hypertension. RAAS-blockers have proven their ability to regress left ventricular hypertrophy (LVH). The aim of study was to compare LV characteristics in subjects with low-renin and renin-mediated hypertension to confirm potential benefits of this treatment approach.

Methods: PRA (radioimmune assay) was measured in 72 hypertensive subjects (age $61,1 \pm 7,6$ years, 30 male). PRA $< 0,65$ ng/ml/h was classified as volume (V)-type hypertension, PRA $> 0,65$ ng/ml/h - as renin (R)-type. Echocardiographic parameters of LV remodelling and its function were compared in subjects with two types of hypertension. LVH criteria were: LV mass index (LVMI) > 125 g/m² in males and > 110 g/m² in females. $p < 0,05$ was considered significant.

Results: 42 (58%) subjects had V-type hypertension, 30 (42%) - R-type. Despite patients with V-type hypertension were older (respectively, $63,1 \pm 9,1$ vs $60,3 \pm 6,4$

years, $p < 0,05$) and had higher systolic and diastolic BP ($162,6 \pm 14,1/103,7 \pm 11,5$ vs $157,9 \pm 17,1/95,0 \pm 7,8$ mmHg), respectively, $p < 0,05$). Patients with R-type hypertension vs those with V-type had significantly ($p < 0,05$) larger left atrium diameter ($3,9 \pm 0,4$ vs $3,7 \pm 0,5$ cm) and its volume index ($39,1 \pm 7,3$ vs $36,2 \pm 7,4$ ml/m²), relative wall thickness ($0,63 \pm 0,12$ vs $0,57 \pm 0,11$), LVMI ($145,9 \pm 35,6$ vs $134,3 \pm 38,4$ g/m²), deceleration time ($256,3 \pm 55,8$ vs $179,4 \pm 40,3$ ms), E/E' ($12,4 \pm 5,8$ vs $10,9 \pm 4,0$) and LVH prevalence (93% vs 62%).

Multivariate logistic analysis revealed independent association between PRA and LVMI ($\beta = 0,78$, $p < 0,001$) and diastolic function characteristics E/A ($\beta = -0,49$, $p < 0,001$), IVRT ($\beta = 0,34$, $p < 0,001$), DT ($\beta = 0,74$, $p < 0,001$), E/E' ($\beta = 0,68$, $p < 0,001$).

Conclusion: R-type hypertension is associated with adverse LV remodelling and diastolic dysfunction in hypertensive subjects. The finding confirms RAAS-blockers as a beneficial therapeutic approach in those subjects to decrease BP and LVH regression

P307

Amelioration of hypertensive induced HFpEF by inhibition of late sodium-influx with ranolazine

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Background: The heart failure with preserved ejection fraction -HFpEF- (or diastolic relaxation disorder) is a sign of leftventricular dysfunction induced by a long-term hypertension. It is observed as well despite effective treatment with antihypertensive drugs. The analysis and quantification of the diastolic relaxation disorder is feasible using tissue-Doppler-echocardiography by registration of the E'A'-ratio. Typical clinical symptoms are dyspnea and angina equivalents.

An influence on the heart failure with preserved ejection fraction may be induced by the drug ranolazine. Ranolazine inhibits the ischemic generated late sodium influx (I Na-late) and reduces consequently the ischemic induced intracellular sodium - and calcium-overload. Upon this mechanism the calcium dependent diastolic leftventricular wall tension will be decreased.

We hypothesized that ranolazine will improve hypertensive induced diastolic dysfunction through this mechanism.

Methods and Results: We report about 14 hypertension-patients ($72,8 \pm 10,2$ years) with exclusion of a macrocoronary induced ischemia, which complained of dyspnoea and/or angina equivalents under exercise. A coincidental exercise induced hypertension was excluded. Despite efficient continuation of the antihypertensive drugs all these patients showed a diastolic relaxation disorder with normal LV systolic function. After educational advertising Ranolazin (375 mg, 2x d.) was administered additionally. During the observation the blood-pressure and the heart rate showed no alteration. The patients by themselves reported a subjective amelioration. After $9,7 \pm 2,4$ days a significant ($p = 0,001$) decrease of the diastolic relaxation disorder was found in the control of tissue-Doppler-measurement (initial E'A'-ratio = $0,601 \pm 0,135$; E'A'-ratio under ranolazine = $0,771 \pm 0,184$). This normalization of the E'A'-index (as parameter of diastolic relaxation disorder) was observed in all 14 patients

Conclusion: The addition of ranolazine to efficient antihypertensive drug therapy in hypertensive patients resulted in an amelioration of symptoms like dyspnea and angina equivalents. In this context a significant ($p = 0,001$) decrease of the diastolic relaxation disorder was found in the tissue-doppler-measurement with normalization of the E'A'-index (as parameter of diastolic relaxation disorder). There was no change of blood pressure or heart rate. Our observation warrants controlled randomized studies on the effects of ranolazine induced late sodium influx inhibition in patients with hypertensive induced heart failure with preserved ejection fraction.

P308

Longitudinal global systolic dysfunction is associated with renin-type arterial hypertension

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Aim: Arterial hypertension phenotyping by plasma renin activity (PRA) may be a useful approach to improve BP control. Thus target organ damage evaluation is important in different types of arterial hypertension determined by PRA measurement. The aim of study was to compare left ventricular systolic function with speckle tracking technique in subjects with low-renin and renin-mediated hypertension.

Methods: PRA (radioimmune assay) was measured in 72 hypertensive subjects (age $61,1 \pm 7,6$ years, 30 male). PRA $< 0,65$ ng/ml/h was classified as volume (V)-type hypertension, PRA $> 0,65$ ng/ml/h - as renin (R)-type. Longitudinal global systolic deformation (LGSD) was evaluated by 2-D echocardiography (normal $< -18,6\%$) and compared in subjects with two types of hypertension. Multivariate regression analysis was applied to define determinants of LGSD. $p < 0,05$ was considered significant.

Results: 42 (58%) subjects had V-type hypertension, 30 (42%) - R-type. Despite patients with V-type hypertension were older (respectively, 63,1±9,1 vs 60,3±6,4 years, p<0,05) and had higher systolic and diastolic BP (162,6±14,1/103,7±11,5 vs 157,9±17,1/95,0±7,8 mmHg), respectively, p<0,05). Left ventricular ejection fraction was similar in the two subgroups: 64,8±5,9% in V-type, and 68,5±7,0% in R-type. Despite of normal EF impairment of LGSD was found in 75% among all patients and was significantly higher in subjects with R-type hypertension than in V-type, respectively, 97% vs 40% ($\chi^2=75,3$; p<0,001). Absolute LGSD values were, respectively, -16,6±3,3 [poTNB -17,9±3,4% (p<0,05). Multivariate regression analysis revealed independent association of PRA and LGSD ($\beta=1,94$, p<0,001).

Conclusion: Evaluation of longitudinal global systolic deformation reveals systolic dysfunction in 75% hypertensive patients. Systolic function impairment is associated with renin-mediated arterial hypertension.

P309

Blood pressure pattern in hypertensive patients with heart failure and preserved left ventricular ejection fraction

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Purpose: Patients with HF have increased sympathetic nervous activity, which may influence the blood pressure pattern. The aim of our study was to analyze the blood pressure (BP) profile in patients with HF symptoms.

Methods: We enrolled 100 patients attending the Service of Cardiology, University Hospital between 01.06.2013 - 01.09.2014. The patients were divided in 2 groups- the first group included patients with HF symptoms and systolic blood pressure (SBP) > 180 mmHg, and the second group included patients without HF symptoms, but also with SBP >180 mmHg. We excluded patients with important mitral or aortic valvular disease (regurgitation> II, stenosis> large), patients with systolic dysfunction or acute coronary syndrome and those with bradycardia <50/min or tachycardia > 120/min.

Each patient received antihypertensive treatment according to the current guidelines and was subjected to the following procedure: ambulatory BP monitoring (ABPM) after stabilization of BP <140/90 mmHg, 2 days subsequently in the morning. Systemic blood pressure was measured automatically on non-dominant arm by a non-invasive blood pressure monitoring system every 15 min in the day and every 30 min in the night. The parameters that we followed were: age, sex, dipper/nondipper profile, maximum systolic blood pressure (SBP) and maximum diastolic blood pressure (DBP), the pulse pressure (PP), the difference between maximum SBP and minimum SBP, the difference between maximum DBP and minimum DBP, the difference between BP at 0-5-15 min.

Results: The mean age was 64,96 years (max 85, min 45). Hypertensive patients with HF symptoms were older than patients without HF symptoms (the mean age was 70,68 years in patients with HF symptoms and 59,24 years in patients without HF symptoms) and most of the patients with HF symptoms were women (66%). The BP profile in patients with HF symptoms was more frequently nondipper and the BP was poorly controlled (the percent of values above >160/100 mmHg was greater in patients with HF symptoms). Patients with HF symptoms had a larger variation of SBP and DBP in 24 hours and a higher variation of BP between 1-15 min (p=0.0017). The PP was higher in patients with HF symptoms (with statistic significance p=0.008). No differences were registered related to BP variation between 0-3 min (p 0.42) and 0-5 min (p 0.42).

Conclusions: hypertensive patients with HF symptoms predominantly had nondipper profile, they were more frequently women, and the blood pressure was poorly controlled and had higher variation of SBP and DBP in 24 hours.

CO-MORBIDITIES

P310

Management and diagnosis of patients with syncope admitted to a general hospital

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Background: Syncope accounts for approximately 6% of all hospital admissions. It is a common and challenging complaint and, despite substantial researcher efforts for accurate diagnosis, there are still many cases of unexplained syncope. Although, the management of patients with syncope is not standardized, we aim to evaluate the strategy of management and diagnosis of syncope of patients admitted to a tertiary hospital. All cause mortality at 1 year was also analyzed.

Methods: We conducted a retrospective observational study including consecutive patients admitted with syncope as a primary diagnosis to a general hospital, from

January 1st 2013 to December 31st 2013. Institutional records regarding demographic and clinical characteristics, imaging and treatment modalities of patients diagnosed with syncope were analyzed.

Results: A total of 168 patients were admitted for syncope. Age was 71± 16 years (70% aged ≥ 65) and 68 % were male. Hospitalization was mostly in the department of Internal Medicine (55.4%), followed by Cardiology (29%). In-hospital stay was 10±8 days. A mean of 5 tests was performed per patient. All patients had, at least, one ECG which highlighted a significant proportion (21%) of abnormal features suggestive of primary electrical disorders or potential cardiomyopathy, 63% had transthoracic echocardiogram and 52% had a cranial computed tomography scan. A definite diagnosis was made in 84% of cases, neurally-mediated syncope being the most frequent, followed by cardiac syncope. The presence of prodromal symptoms did not contribute to determine the of cause of syncope (p=0.251). Discontinuation of anti-hypertensive agents was the most frequent measure, followed by pacemaker/defibrillator implantation. Overall-mortality at 1 year was 3%.

Conclusions: In the absence of a uniform strategy for management of syncope in everyday practice, many patients mostly elderly, are commonly hospitalized following a syncopal event. In this group of patients the only single test that could best determine the etiology of syncope is the ECG.

P311

Validating diagnostic accuracy of a portable sleep testing diagnostic device in an outpatient population of heart failure patients with sleep disordered breathing

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Sleep disordered breathing (SDB) is a frequent comorbidity in heart failure (HF) that increases morbimortality. It is an underdiagnosed entity, not only because SDB symptoms are similar to those of HF but also due to the cumbersome task of having to rely on the polysomnography (PSG), the ruling gold standard, only available on specialized laboratories. A type 3 home sleep testing diagnostic device was conceived to shorten these drawbacks. Its automated report, in the general population, revealed an excellent correlation with PSG. However, so far, no studies have included patients with HF.

Objectives: To obtain the diagnostic accuracy of the portable diagnostic device for SDB in a population of stabilized HF patients after recent hospital discharge.

Methods: Prospective, observational study of 40 patients discharged from an HF Unit of a central university hospital, who were submitted to simultaneous PSG and to the portable diagnostic test.

Results: Included 40 patients, 57% women, age 71 ± 11years, BMI 28 ± 5Kg/m². Left ventricular ejection fraction <50% in 47.5%. All patients in NYHA classes II-III at discharge.

Comparison of variables revealed statistical correlation between Apnea-Hypopnea Index (AHI), central apneas, hypopnea index and desaturation index of both tests. AHI≥15 was the cut-off with best diagnostic accuracy (Table 1)

Conclusion: compared with PSG, the portable diagnostic device showed a high diagnostic accuracy for SD when considering AHI>15 as cut-off point. This easily available method allows an early diagnosis and therefore timely treatment of SD of HF patients, aiming towards improving outcomes of the syndrome.

Diagnostic accuracy of the new test					
AHI (per hour)	S	Sp	PPV	NPV	AUC (ROC)
≥5	0,521	0,600	0,760	0,692	0,864
≥10	0,823	0,857	0,823	0,857	0,895
≥15	0,846	0,920	0,846	0,920	0,938
≥20	0,333	0,965	0,750	0,823	0,860

sensibility(S), specificity (Sp), Positive predictive value (PPV), Negative predictive value (NPV) and area under curve (AUC) for various hypothetical cut-off points of AHI

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Respiratory disorders during sleep in patients with chronic heart failure

Seventh Framework Programme (FP7/2007-2013) #241558, FTP "R&D in priority fields of the S&T complex of Russia 2007-2012" # 02.527.11.0007V Viktoriya Nepran¹; L Korostovtseva¹; S Kravchenko¹; Y Sazonova¹; K Malikov¹; A Kozlenok¹; Y Sviryayev¹; A Konradi¹; E Shlyakhto¹

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Introduction: According to the data from population and clinical studies there is a link between sleep breathing disorders (SBD) and heart failure (HF).

Objective: To study sleep architecture, SBD frequency and their relationship to HF severity. Design and methods. Sixty-six patients (56 men and 10 women), aged 27 to 77 years old, with systolic HF III-IV functional class (cardiomyopathy of various origin as the cause was diagnosed in 15 subjects and coronary heart disease - in 51 patients) were examined. All patients underwent physical examination; blood tests analysis [including the N-terminal brain natriuretic pro-peptide (NT-proBNP)], echocardiography, and polysomnography (Embla N7000, Natus, USA). Results. Polysomnography showed a decline in sleep quality, in particular, decreased sleep efficiency - 76.6 (32.3; 95.3)%; increased time awake after sleep onset - 112.5 (17.0; 408.9) min., and increased number of arousals - 12.8 (0.0, 44.0) per hour of sleep. SBD were detected in 58 (87.9%) patients (50 males and 8 females) with median apnea-hypopnea index (AHI) 21.5 (5.1; 59.6) episodes per hour of sleep, desaturation index 18.2 (0.8, 59.9) episodes per hour of sleep. Eight (12.1%) patients (6 men and 2 women) did not demonstrate respiratory disorders [median AHI 3.1 (0.0;-4.8) episodes per hour of sleep, desaturation index 5.6 (0.1 ; 22.6) episodes per hour of sleep]. Correlation analysis showed an inverse relationship between ejection fraction (Simpson) and central AHI ($\rho = -0.25$; $p = 0.04$). Obstructive and mixed AHI were not associated with the severity of systolic dysfunction ($\rho = 0.08$; $p > 0.05$ and $\rho = -0.15$; $p = 0.22$). Obstructive AHI, unlike other types of SBD, correlates with left ventricular end-diastolic volume ($\rho = 0.25$; $p = 0.04$). There was no association between SBD severity and NT-proBNP ($p > 0.05$). Conclusions. Patients with HF show low quality of sleep, which may be an additional prognostic factor in this group. The rate of SBD is extremely high in systolic HF (>80%) with the predominant obstructive sleep apnea (39%). The severity of central sleep apnea is associated with the severity of systolic dysfunction. We can assume that central SBD may be a marker of the severity of systolic dysfunction that requires further investigation in a prospective study.

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The role of bariatric surgery for improvement of hypertension in obese patients

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Purpose: The aim of this study was to evaluate if bariatric surgery can improve hypertension control leading to both anti-hypertensive therapy withdrawal and reduction of blood pressure values.

Methods: Eight-hundred sixty-four consecutive patients referred to our hospital, from March 2001 to February 2011, due to morbid obesity were initially enrolled in this retrospective study. In order to obtain two comparable groups, propensity-matching was applied. Finally, the study included 444 (51% out of initial 864 patients), 222 on diet (group D1) and 222 undergoing surgery (group S1), which were perfectly comparable.

Results: In group D1, 73 (33%) and 56 (25%) patients took AH therapy at baseline and follow up, respectively. In Group S1, 62 (28%) and only 9 (4%) patients took AH therapy at baseline and follow up, respectively. Hence, the rate reduction was significantly lower in group D1 than S1 (8% vs 24%, $p < 0.001$). If only patients on AH therapy at baseline were considered, the rate of therapy withdrawal was significantly higher in group S1 than in group D1 (87% vs 23%, $p < 0.001$). In patients taking AH therapy at baseline, the weight loss was significantly correlated to change of SBP ($r = 0.671$, $p < 0.001$) and DBP ($r = 0.470$, $p < 0.001$) over time

Conclusions: Bariatric surgery is effective to improve systolic and diastolic artery pressure and lead to a higher percentage of therapy withdrawing in obese patients, with a better control of blood pressure in those ones who keep on taking AH therapy.

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Clinical efficacy and safety of formoterol and tiotropium administration in patient with chronic heart failure due to coronary artery disease combined with chronic obstructive pulmonary disease

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Study of clinical efficacy and safety of formoterol and tiotropium administration in patient with chronic heart failure due to coronary artery disease combined with chronic obstructive pulmonary disease.

Purpose: to compare clinical efficacy and safety of formoterol and tiotropium administration in patient with chronic heart failure (CHF) due to coronary artery disease (CAD) combined with chronic obstructive pulmonary disease (COPD).

Methods: after enrollment in this trial 73 patients (47 men and 26 women), aged 63.2 ± 6.0 years, with CHF classes II to III (New York Heart Association) combined with moderate COPD (GOLD-2013) and with initial ejection fraction of the left ventricle (LVEF) less than 45%, were randomized to three groups - formoterol (n=26), tiotropium (n=25) and tiotropium+formoterol group (n=22). Patients of all groups received complex CHF treatment comprising diuretics, nebivolol, losartan, cardiac glycosides (subject to indications). Echocardiography, exercise tolerance

(6-min walk distance), 24-hour electrocardiography monitoring were assessed at baseline and after 6 months of treatment, respiratory function test was assessed at baseline, after 1 month and after 6 months. The quality of life was evaluated by MYHFQ, SGRQ and mMRC.

Results: 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 pulmonary hypertension decreased by 6.9%, 8.0% and 10.7%, episodes of silent myocardial ischemia decreased by 14.0%, 13.1% and 15.5%, respectively. Towards the end of the observation period, in all groups there was a confident and authentic increase of forced expiratory volume during 1st second (FEV1) which made 6.4%, 5.3%, and 8.5% accordingly. 6-min walk distance increased by 15.1%, 12.9% and 19.4% accordingly. Patients showed statistically significant and clinically meaningful reduction of SGRQ score (16.4%, 12.6%, 18.4%) and MYHFQ score (18.9%, 18.5%, 22.6%), significant improvements in MMRC dyspnea grade (15.1%, 14.2%, 20.0% respectively). All treatments were well tolerated.

Conclusions: the formoterol and tiotropium 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 pulmonary function. Efficacy of long-acting β -agonist (formoterol) and long-acting inhaled anticholinergic agent (tiotropium) in patient with CHF due to CAD combined with COPD are similar. Combination of these drugs significantly enhances the positive effects of the therapy.

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Renal status in patients with worsening heart failure hospitalized for acute decompensated heart failure

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Purpose: The aim of the study was to evaluate renal status in patients with worsening heart failure (WHF) hospitalized for acute decompensated heart failure (ADHF).

Methods: In retrospective analysis we enrolled 93 consecutive patients (mean age: 65.03 years, female=33%) hospitalized for ADHF. Patients were divided into 2 groups: WHF (n=61) and non-WHF (n=32). WHF was defined as worsening of signs and/or symptoms during the acute phase of a heart failure episode requiring an intensification of intravenous therapy for HF or mechanical ventilation, renal or circulatory support within 5 days from baseline. Renal function was assessed by serum creatinine (sCr), estimated glomerular filtration rate (eGFR) using MDRD equation and blood urea nitrogen (BUN).

Results: Admission renal function including sCr, eGFR and BUN was worse, but not statistically significant in patients with WHF (sCr: 1.51 ± 1.72 vs. 1.31 ± 0.47, $p = 0.53$; eGFR: 60.45 ± 25.88 vs. 63.29 ± 22.42, $p = 0.19$; BUN: 16.26 ± 17.83 vs. 14.24 ± 12.06, $p = 0.30$). There were no differences between the groups in mean values of sCr, eGFR and BUN obtained during first three days of hospitalization. Interestingly, individuals who experienced WHF had significantly lower value of eGFR on discharge (60.4 vs. 74.1 ml/min/1.73m², $p = 0.02$). Moreover, subtraction of admission and discharge values of eGFR was significantly higher in patients with WHF, that indicates deterioration of renal function during hospitalization course in these patients (Δ admission-discharge: 0.086 vs. -10.77 ml/min/1.73m², $p = 0.006$). Values of sCr and BUN on discharge did not differ between the groups.

Conclusion: Baseline renal status was similar between the groups with and without WHF, however subjects with WHF had worse renal function on discharge.

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Noncardiac pathology in patients with negative ventricular remodeling over 1 year after coronary revascularization

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The aim of this study was to analyze the structure of non-cardiac pathology in patients with negative cardiac remodeling over 1 year after coronary revascularization.

Material and Methods: The study included 87 patients (55 men and 32 women) after coronary revascularization who received treatment according to international guidelines for secondary prevention. Echocardiographic examination was performed initially and over 12 months after coronary revascularization. We evaluated: left atrium dimensions (LA), left ventricular parameters: left ventricular end-systolic (LVES, mm), end-diastolic diameter (LVED, mm), end-systolic volume (ESV, ml), end-diastolic volume (EDV, ml); longitudinal diameter in systole and diastole, sphericity index at systole (SIS), at diastole (SID), relative wall thickness (RWT), ejection fraction (LVEF). Depending on the dynamic of cardiac remodeling all patients were divided in two groups: group 1- patients with negative dynamic parameters of cardiac remodeling

(n=35), group 2 -patients without negative dynamics (n=52). The presence of non-cardiac pathology was analyzed in each group in accordance to the method Charlson.

Results: Charlson index of comorbidity was higher in group 1- 4,9 vs 2,3 in group 2 (p < 0,001). Patients in group 1 had more than one non-cardiac pathology; were older (mean age 63,8 ± 1,2 vs 57,4 ± 1,1) and had an advanced degree of heart failure (functional class NYHA III vs II).

Conclusion: The negative dynamic of heart remodeling after coronary revascularization was adversely influenced by the presence of multiple non-cardiac comorbidities.

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Clinical impact of cognitive impairment on patient's post-discharge environment in patients with hospitalized heart failure

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Purpose: Hospitalized heart failure (HHF) is a major public health problem in super-aging society. Although hospitalized elderly patients with cognitive impairment (CI) have lower rate of discharge to home compared with those without CI, limited data exist on the impact of CI on the post-discharge site of care in patients with HHF.

Methods: Two hundred eight consecutive HHF patients were enrolled in this study. The primary endpoints were in-hospital death and discharge to non-home environment.

Results: In 208 patients (age 80 ± 12 [SD] years, 50% male, previous HHF 41%, left ventricular ejection fraction 53 ± 13%), CI was found in 56 patients. In each of 3 groups categorized by systolic blood pressure on admission (>140 mmHg, 100-140 mmHg and <100 mmHg), the in-hospital death rate were 5%, 10% and 23%, respectively. Patients with CI were significantly older and had a significantly lower rate of prescription of angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (ACEi/ARB) before admission and a significantly higher rate of in-hospital falling and primary endpoints compared with those without CI (87 ± 7 vs. 77 ± 13 years, 32% vs. 58%, 14% vs. 2% and 61% vs. 17%; P < .05). There was no significant difference in systolic blood pressure on admission, previous HHF, NYHA class, ejection fraction, renal function, in-hospital length of stay, and in-hospital death between the two groups. In 193 patients without in-hospital death, prescription rate of ACEi/ARB was significantly increased at hospital discharge regardless of the presence of CI (90% with CI, 97% without CI; P < .05 vs. before admission, respectively)

Conclusions: Irrespective of heart failure severity, in-hospital CI is associated with decreased discharge rate to home and may be resulting from insufficient ACEi/ARB use. Further studies are warranted to elucidate the relation between CI and ACEi/ARB.

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Eritrocitary indexes as predictors of the cause of anemia or nutritional deficit in heart failure patients

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Classically, anemia is divided in microcytic, normocytic and macrocytic according to mean cell volume (MCV). Nowadays older patients with multiple comorbidities and many dietary defaults may have more than one deficit, making it difficult to predict the cause of the anemia based on MCV alone. Anemia is a frequent comorbidity in Heart Failure (HF) patients, usually normocytic, much associated with inflammation and chronic disease. In the last few years, iron deficiency gained importance concerning the cause of anemia in these patients. Little is known about the importance of vitamin B12 and folate in these patients.

Purpose: To evaluate the accuracy of MCV in predicting nutritional deficits in a HF Unit.

Methods: Prospective study of patients admitted consecutively in a HF Unit over a period of one year. Anemia was diagnosed according to the World Health Organization criteria. Microcytosis, normocytosis and macrocytosis were defined respectively as MCV < 80, 80-100 and > 100 fl. Iron deficiency (ID) was considered when ferritin < 100 ng/ml (absolute ID) or 100-299 ng/ml and transferrin saturation < 20% (functional ID). Vitamin B12 and folate deficit when its levels were below 200 pmol/L and 6.25 nmol/L, respectively.

Results: 202 patients were included; mean age was 74,95 ± 11,84 years, 30,2% (61) were male, with an ejection fraction of 57,9%. Hematinic deficiencies with respect to MCV are presented in the attached table.

Conclusion: MCV is not a good indicator to predict hematinic factors deficits. That is why B12 vitamin and folate levels should be evaluated in all HF patients, regardless of hemoglobin and MCV value.

MCV and hematinic deficiencies in HF

	Absolute ID	Relative ID	Vitamin B12 deficiency	Folate deficiency	Mean Hemoglobin
MCV < 80 fl	17 (9,5%)	1 (0,6%)	3 (16%)	0 (0%)	10,77 ± 1,86
MCV 80-100 fl	69 (38,5%)	31 (17,4%)	21 (11,3%)	3 (1,6%)	11,43 ± 1,8
MCV > 100 fl	2 (1,1%)	2 (1,12%)	3 (1,6%)	2 (1,1%)	10,61 ± 1,7

ID = Iron deficiency MCV = Mean cell volume

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Portable sleep monitor - an automatic screening method for sleep-disordered breathing in heart failure patients

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Background & Aims: Sleep-disordered breathing (SDB) worsen the prognosis of patients with Heart Failure (HF). Polysomnography is the gold standard for the diagnosis of SDB; however, it is time consuming and requires specialized labs and equipment, limiting its use in daily practice. Portable sleep monitors (PSM), practical tools that are able to generate automatic reports, have recently been demonstrated as useful for SDB screening. The purpose of this study was to evaluate the reliability of Type III PSM's automatic reports (AR) compared to manual validation (MV) by a cardiopulmonary technician.

Methods: We conducted a prospective observational study of patients consecutively discharged from a Heart Failure Unit of a central Hospital. A Type III PSM was used in all patients on the day prior to discharge. Patients with previous diagnosis of SDB and with PSM evaluation period shorter than 2 hours were excluded. For each patient we analysed: Apnea Hypopnea Index (AHI), number of central apneas (CA), number of obstructive apneas (OA) and episodes of Cheyne-Stokes breathing (CSB). The diagnosis of SDB was made when the AHI was > 15/hour. Results obtained from the AR were compared with those of MV performed by a cardiopulmonary technician.

Results: We examined 111 patients, 64,0% female, mean age of 75,5 ± 10,8 years old and body mass index of 26,8 ± 5,3 kg/m². The majority of patients (62,2%) had HF with preserved ejection fraction (mean of 54,5 ± 18,9%). Mean AHI was 19,7 ± 17,3/hour in AR and 18,9 ± 17,4/hour in MV. A strong positive correlation was found between parameters evaluated with both AR and MV: AHI, CSB, CA and OA (Spearman coefficients of 0,976; 0,991; 0,841 and 0,842, respectively; p < 0,01).

Conclusions: This study demonstrates that Type III PSM's automatic reports are accurate, supporting its application in clinical practice without requiring manual validation.

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Depression as an independent risk factor for all-cause mortality in heart failure patients

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Purpose: Depression is reported to be associated with mortality among patients with heart failure (HF). However, whether this reflects more severe disease or a greater co-morbidity or is independent of such risk factors is unclear.

Methods: OPERA-HF is an observational study enrolling patients hospitalized with heart failure. Inclusion criteria were: age > 18 years, hospitalized for or with HF and treated with loop diuretics and at least one of the following: left ventricular ejection fraction ≤ 40%, left atrial dimension > 4.0 cm or NT-ProBNP > 400 pg/ml (if in sinus rhythm) or > 1200 pg/ml (if in atrial fibrillation)). Depression was assessed by Hospital Anxiety and Depression Scale (HADS-D) questionnaire. Co-morbidity was assessed by the Charlson Comorbidity Index (CCI). Kaplan-Meier and Cox regression analyses were used to estimate the association between depression and all-cause mortality.

Results: Of 154 patients that completed the HADS-D questionnaire, 103, 27 and 24 patients had no-to-normal (score 0-7), mild (score 8-10) or moderate-to-severe (score 11-21) depression, respectively. Over a mean follow-up time of 302 days, 27 out of 154 patients died. In univariate Cox regression analysis, moderate-to-severe depression was associated with an increased risk of death (HR: 5.11; 95% CI: 2.39 to 10.93; P < 0.001) comparing to no-to-normal or mild depression. Moderate-to-severe depression remained a significant predictor of mortality after controlling for sex, age, hypertension and NT-proBNP (HR: 6.50; 95% CI: 2.19 to 19.32; P < 0.001); and changed little with the further inclusion of the CCI in the model (HR: 5.38; 95% CI: 1.84 to 15.67; P < 0.005). On the other hand, a low HADS-D score between 0 and 7 was associated with a decreased mortality risk (HR: 0.21; 95% CI: 0.09 to 0.46; P < 0.001).

Conclusion: This analysis suggests that depression is strongly associated with an adverse outcome in the year after discharge from a HF hospital episode and that it may not be explained by the severity of HF or co-morbidity. Recognition and management of depression might improve outcome. Appropriately designed randomized trials are required.

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Diabetes as a risk factor of stroke and death in heart failure patients in sinus rhythm - a nationwide cohort study

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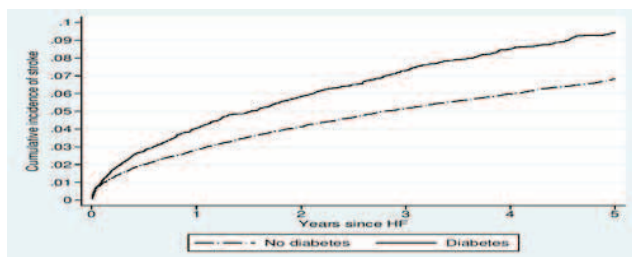
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Purpose: Stroke risk among heart failure patients with concomitant diabetes is poorly described. We conducted a large-scale observational study to evaluate the risk of stroke and death among heart failure patients in sinus rhythm and with diabetes.

Methods: Population-based cohort study of patients diagnosed with incident heart failure in sinus rhythm and not in therapy with a vitamin K antagonist during 2000-2012, identified by record linkage between nationwide registries in Denmark. Taking into account competing risks of death, we calculated relative risks of stroke and death after 1 and 5 years follow-up to compare patients with diabetes to patients without diabetes.

Results: 39,018 patients with an incident heart failure diagnosis were included, among which 17.8% had diabetes. At 5-years follow-up, diabetes was associated with a higher risk of stroke compared to patients without diabetes (crude relative risk [RR]: 1.38, 95% confidence interval [CI]: 1.26-1.51). This association persisted after adjustment for other cardiovascular risk factors (adjusted RR: 1.19, 95% CI: 1.07-1.33). Similarly, diabetes was associated with a non-significant increased risk of stroke at 1-year follow-up. When considering the endpoint of death, a significant increased risk was found among patients with diabetes both after 1- and 5-years follow-up (1- and 5-year adjusted RR: 1.23 and 1.20).

Conclusions: Among heart failure patients in sinus rhythm, a concomitant diagnosis of diabetes was associated with a higher risk of stroke after long-term follow-up and possibly also after short-term. Additionally, diabetes was associated with a higher risk of death both after short- and long-term follow-up. Increased focus on secondary prevention in patients with both diabetes and heart failure may be warranted.



Cumulative incidence of stroke

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Relationship between diastolic stiffness assessed by diastolic wall strain and cardiac toxicity from trastuzumab

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Purpose: Trastuzumab is a molecularly targeted anticancer agent that can induce reversible cardiac dysfunction and an increase in left ventricular mass (LVM). This study investigated the utility of diastolic wall strain (DWS) to assess diastolic stiffness in patients treated with trastuzumab.

Methods: We studied 156 consecutive breast cancer patients (all females; mean age, 57.1 ± 10.8 years) who received trastuzumab for more than 6 months. Echocardiography was performed before and after administration of trastuzumab, and the following parameters were calculated: left atrial diameter (LAD); LV diameter in diastole/systole (LVdD/s); LV end-diastolic volume (LVEDV); LV end-systolic volume (LVESV); interventricular septal thickness in diastole/systole (IVSTd/s); posterior wall thickness in diastole/systole (PWTd/s); LV ejection fraction (LVEF); ratio of early to late ventricular filling velocity (E/A); mitral annulus velocity (e'); E/e'; Tei index (TI); relative wall thickness (RWT); DWS (DWS=(PWTs-PWTd)/PWTs); LVM; LVM index (LVMi); diameter of the inferior vena cava (IVC); pulmonary artery systolic pressure (PASP); LV end-diastolic pressure (LVEDP) and systolic blood pressure (BPs). We

also analyzed the correlation between rate of change (%) in DWS (Δ DWS) and rate of change (%) in LVM (Δ LVM). We also investigated the correlation between DWS before administration of chemotherapy (DWSb) and the rate of change in various indices: Δ LAD, Δ LVdD/s, Δ LVED(S)V, Δ IVSTd/s, Δ PWTd/s, Δ LVEF, Δ E/A, Δ e', Δ E/e', Δ TI, Δ RWT, Δ DWS, Δ LVM(i), Δ IVC, Δ PASP, Δ LVEDP, and Δ BPs.

Results: Symptomatic heart failure was observed in five cases. No significant changes were observed in the indices of cardiac function, including IVSTd, PWTd, E/A, e' and IVC. After treatment with trastuzumab, significant increases were observed in LAD ($p < 0.01$), LVdD/s, LVED(S)V, E/e', TI, LVM, LVMi, PASP, LVEDP and BPs ($p < 0.001$), and a significant decrease was observed in IVSTs ($p < 0.05$), PWTs ($p < 0.01$), LVEF ($p < 0.001$), RWT ($p < 0.05$) and DWS ($p < 0.001$). There was an inverse relationship between Δ DWS and Δ LVM ($r = 0.3$, $p < 0.001$). Moreover, DWSb correlated with Δ PWTd ($r = 0.33$), Δ RWT ($r = 0.27$) and Δ LVM ($r = 0.18$) and inversely correlated with Δ DWS ($r = -0.45$), Δ PWTs ($r = -0.33$), Δ TI ($r = -0.21$) and Δ BPs ($r = -0.23$).

Conclusion: Administration of trastuzumab resulted in an increase in LVM, an increase of diastolic stiffness, a tendency towards eccentric hypertrophy, and induced heart failure with reduced ejection fraction. This tendency was more common in patients with higher DWS than in those with lower DWS before treatment of trastuzumab.

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Predictive value of cardiac troponins in the development of chronic anthracycline-induced cardiomyopathy

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Over the last decades, effective treatment markedly improved survival in many types of cancer. As a result, a number of anthracyclines (ANT)-exposed long term cancer survivors is dramatically growing which has intensified efforts to improve cardiovascular safety in this high risk population. Cardiac troponins (cTn) seem to be more sensitive for the detection of anthracycline cardiotoxicity than the currently recommended method of monitoring LV systolic function. The aim of this study was to evaluate the predictive value of cTns during the development of chronic ANT-cardiotoxicity on the validated model in rabbit. The study was carried out on two groups of rabbits: 1) daunorubicin (3 mg/kg, once weekly for 8 weeks), 2) control (saline in the same schedule). The experiment was terminated 2 weeks after the last dose. Blood samples were collected 2-168 hrs after the 1st, 5th and 8th drug administration. Plasma concentrations of cardiac troponins were determined using both hs cTnT (Roche) and hs cTnI (Abbott).

Echocardiographic examination (LVFS) as well as invasive examination of LV function (dP/dtmax) confirmed the significant systolic impairment of LV. While only a mild non-significant increase in both cTn levels occurred after the 1st daunorubicin dose, significant rise was observed after the 5th and 8th administrations. Unlike acute myocardial infarction, the first troponin increase occurred very early after daunorubicin dose (2 hrs), the maximal values were reached between the 4th and 6th hours and then gradually declined. Discrete cTn release continued even after cessation of the therapy. After the 1st clinically relevant ANT dose no predictive value of this examination has been established. However, a very strong correlation between dP/dtmax and AUCtotal5-10 (calculated from the 5th till the 10th week) for both cTnI and cTnT ($R = -0.857$, $p < 0.01$ and $R = -0.833$, $p < 0.01$; respectively) and LV FS ($R = -0.810$, $p < 0.01$ and $R = -0.833$, $p < 0.01$; respectively) were found. Furthermore, cmax for cTnI during the 5th and 8th weeks correlated with dP/dtmax ($R = -0.690$, $p < 0.05$, $R = -0.738$, $p < 0.05$). Similarly, cmax for cTnT during the 5th and 8th weeks correlated with dP/dtmax ($R = -0.683$, respectively $p < 0.05$, $R = -0.690$, $p < 0.05$).

Data presented in this work complete the results from previous clinical and experimental studies and significantly contribute to optimization of the examination of cTns in ANT cardiotoxicity settings, which can be very valuable from clinical point of view.

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Serial cardiac biomarker and echocardiographic evaluation for the early detection of antricycline + trastuzumab cardiotoxicity

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Background: HER2-positive breast cancer(BC)treatment with Anthracycline (ANT) followed by humanized monoclonal antibody Trastuzumab (TZB)is often complicated by an high incidence of non-reversible cardiotoxicity (CTOX). Early detection

and treatment of CTOX is an important determinant of the extent of cardiac function recovery.

Aim of this study: to evaluate the clinical and prognostic implications of serial cardiac biomarkers and Ecocardiographic (Echo) evaluation in patients (pts) treated with ANT+TZB.

Methods: Pts with early HER2-positive BC treated with Epirubicin (90 mg/m² for 3 or 4 cycles every 21 days) followed by adjuvant TZB (6 mg/kg for 12 cycles every 21 days) were enrolled. The presence of a known heart disease, previous ANT treatment and exposure to mediastinal irradiation were exclusion criteria. Echo evaluation and blood measurements of cTnI and NT-proBNP were performed at baseline, 1 week after each ANT administration and every two TZB cycles. In case of CTOX (decrease in LVEF% below the normal limit of 50%) treatment with enalapril was initiated and up-titrated to the maximum-tolerated dose. Plasma cTnI was determined using LOCI method on a Dimension Vista system(Siemens Healthcare Diagnostic); we considered elevated any value >0.05 ng/mL. For analyzing NT-proBNP behavior we calculated the critical difference between baseline and peak value ($CD = K \cdot \sqrt{CVa^2 + CVi^2}$; CVa = coefficient of analytical variation-in our Lab = 1.65%; CVi = coefficient of within subject variation-for NT-proBNP = 35%; K = factor dependent on the probability level selected-for $p < 0.05$, K = 2.77). Results. This preliminary analysis includes only the subgroup of pts who completed the first 3 months follow-up (n = 40; mean age 50 ± 9.8). No pts had an increase in cTnI during ANT treatment (mean cumulative dose 319.5 ± 45.94 mg/m²), while after the first two TZB cycles 7 pts showed a transiently elevation in cTnI that are normalized in all cases within 3 month. In 4 of these pts CTOX occurred: TZB treatment was transiently discontinued and treatment with enalapril was initiated. LVEF recovery was observed in 3 cases and TZB was reintroduced. The patient who did not recover from CTOX had a higher drop in LVEF, developed symptomatic HF, and was the only who had showed a persistent increase in NT-proBNP level during ANT treatment.

Conclusion: Serial cardiac biomarker and echocardiographic evaluation could be useful for early detection of ANT and TZB-induced CTOX. It is difficult to separate the cardiac effects induced by ANT from those due to TZB: the implementation of our series and data from long term follow-up, could provide us more information.

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Biventricular myocardial deformation in hematological malignancies explored by velocity vector imaging

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Purpose: Chemotherapy prolongs survival in patients with hematologic malignancies. Repeat left ventricular ejection fraction (LVEF) appraisal has been dedicated to detecting myocardial dysfunction. Myocardial deformation imaging is a sensitive means of identifying ventricular dysfunction. We aimed to investigate the potential hazardous effects of chemotherapy on biventricular function in patients with hematologic malignancies using myocardial deformation imaging.

Methods: Velocity vector imaging echocardiography was acquired from the apical views in 17 subjects with leukemia and lymphoma. Patients were on multiple chemotherapy protocols including mitotic inhibitors, alkylating and ancillary agents, anthracyclines, targeted and biologic therapy, and antimetabolites. All patients had baseline and at least 3 months follow up echocardiogram after chemotherapy. Both right ventricle (RV)/LV subendocardial borders were traced and tracked by the software along the border in order to achieve average global peak systolic longitudinal strain (GLS) and strain rate (SR).

Results: Mean age was 53 ± 18 years with 10 men (59%). No significant changes were noted in LVEF with chemotherapy. LV/RV peak systolic GLS and SR were not significantly changed post-chemotherapy in comparison to pre-chemotherapy values (TABLE).

Conclusions: The current report provides insights regarding safety of various chemotherapeutic agents in hematologic malignancies with little apparent risk. This might be due to our small cohort number to reach significance, utilization of multiple agents avoiding high dose long term cardiotoxic anthracyclines or disease specific with low predilection of cardiac involvement in hematologic malignancies. The significance of these findings and their potential application will warrant further work.

	Pre chemotherapy	Post chemotherapy	P value
LVEF (%)	62.5±5.2	61.7±8.3	0.34
LV strain (%)	-14.5±7.9	-16.5±2.6	0.24
LV SR (S ⁻¹)	-1.1±0.17	-1.1±0.15	0.18
RV strain (%)	-23.4±5.3	-22.4±5.7	0.18
RV SR (S ⁻¹)	-1.8±0.55	-1.6±0.49	0.09

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Cardiac toxicity associated to trastuzumab treatment in usual clinical practice

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Introduction and Purpose: Trastuzumab (TZ) is a monoclonal antibody, which has shown significant benefit in the adjuvant treatment of breast cancer (BC), with its widespread use nowadays. However, cardiac toxicity (CT) is a potential complication of such treatment. Our aim is to analyze the prevalence, characteristics and severity of CT associated with TZ by echocardiographic follow-up in usual clinical practice.

Patients and Methods: 21 women with BC received adjuvant treatment with TZ. Median age was 51 ± 9 years (range 38-80). BSA was 1.7 ± 0.16 m². Cardiovascular risk factors: diabetes mellitus in 0 %, smoking in 23.8%, hypertension in 23.8 %, dyslipidemia in 14.3%. The patients had received prior chemotherapy with various regimens, which included anthracyclines in 18 cases (85,7%). Periodical echocardiography was performed every 3 months, or sooner if occurrence of cardiac toxicity (mean 3.5 ± 1.3 echocardiograms / patient). Mean follow-up of 11 ± 4 months. HT was defined as decrease in left ventricular ejection fraction (LVEF) <50% or decrease > 15% over baseline LVEF.

Results: CT was observed in 7 patients (33.3%), of which 4 had mild systolic dysfunction (LVEF 40-50%) and 3 moderate dysfunction (LVEF 35-40%), in no case was severe dysfunction (LVEF <35%). Cardiac toxicity appeared in all cases in the first 6 months of treatment.

Generalized hypokinesia was observed in 6 patients with CT and in other single case, hypokinesia limited to septum. In 3 patients (14.28%) mild pericardial effusion was found, and in one case temporary severe mitral regurgitation was observed. No statistically significant trend consisting on initial diameters, volume and myocardial mass increase coinciding with the appearance of CT, and no significant concomitant decrease in stroke volume and cardiac output were observed. CT led to delay in the following doses of TZ (until improvement of LVEF) and in two cases stopping treatment was necessary because of persistent systolic dysfunction and onset of symptoms of heart failure (HF), in other cases there were no signs nor symptoms of HF. There were no cases of cardiovascular death.

Conclusions: The occurrence of CT associated to TZ is common in clinical practice and takes place at the beginning of treatment. However, with the usual measures of change in the treatment regimen, associated systolic dysfunction is limited to mild-moderate and usually asymptomatic.

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Heart failure as a consequence or in association with cancer

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Purpose: Cancer and heart failure both predominantly affect older people and may co-exist. Amongst patients with cancer who develop heart failure, it is not clear which is the more lethal condition.

Methods: We identified patients referred to a heart failure clinic who had a pre-existing diagnosis of cancer. Heart failure was defined as a clinical diagnosis supported by an NT-proBNP >125ng/L and treated with a loop diuretic. Cancer types were classified into breast, lung, gastrointestinal, urological, ovarian, skin, thyroid, haematological, multiple myeloma and cancer of unknown primary. Mortality and mode of death are reported.

Results: Of 3084 patients fulfilling the definition of heart failure, 112 had cancer. The most common cancers were urological (n=38; mostly bladder and prostate), gastro-intestinal (n =20), skin (n =19), haematological (n=12), breast (n=7), myeloma (n=6) and lung (n=5). During a median follow-up of 64 (IQR: 42-118) months, 74 patients (66%) died of which 34 (46%) were cardiovascular (CV), including eight from progressive heart failure. Only 16 deaths were classified as non-cardiovascular, mostly sepsis and pneumonia. Of 24 deaths that occurred out-of-hospital cause-uncertain (OOHCU) but 11 occurred in patients with evidence of advanced malignant disease and 13 may have been sudden arrhythmic deaths. Of 38 patients with urological cancer, 25 (66%) died of which ten (40%) were CV and six OOHCU. Of 20 patients with gastro-intestinal cancers, 14 (70%) died of which eight (57%) were CV and three OOHCU. Of 19 patients with skin cancer, 11 (58%) died, of which five were CV (45%) and five were OOHCU.

Conclusions: A relatively small proportion of patients referred to a heart failure clinic have cancer. This may reflect referral bias due to perceived need or the poor prognosis of some cancers that cause premature death. For some cancers, prognosis is driven by CV events but for others it is not. Many patients with cancer die at home of which half might be cardiac.

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Early changes in left ventricular diastolic function after chemotherapy predict subsequent NT-proBNP elevation in breast cancer patients

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Purpose: We aim to determine changes in echocardiographic parameters of diastolic function that occur after chemotherapy in patients (pts) with breast cancer and to evaluate their prognostic value.

Methods: Prospective study of patients diagnosed with breast cancer without evidence of structural heart disease or previous chemotherapy. Clinical, echocardiographic and laboratory evaluation with determination of NT-proBNP, were performed before the start of chemotherapy and at 1, 3, 6, 9 and 12 months of follow-up. The echocardiographic assessment included diastolic function parameters, with measurement of mitral inflow and tissue Doppler annular early (E') and late diastolic velocities, as well as measurement of left ventricular ejection fraction (EF).

Results: 92 women with a mean age of 53 ± 13 years, undergoing potentially cardiotoxic therapy (anthracycline: 77%, cyclophosphamide: 94%, trastuzumab: 31%) were studied. The median follow-up was 12 months. Overall, there was a gradual and consistent decrease in EF (68 ± 5% vs. 64 ± 5%, p = 0.008) and in 5 pts the EF was less than 55%. We detected a reduction in septal and lateral E' velocity (8.6 ± 2.9 vs. 7.56 ± 2.9 m/s; p = 0.014 and 11.4 ± 3.6 vs. 10.1 ± 3.2 m/s; p = 0.017, respectively), as well as an increase in E/E' ratio (8 ± 3 vs. 10 ± 4; p = 0.044). However those changes did not predict a subsequent decline in EF.

At 6 months, 12 pts (13%) had a NT-proBNP higher than 125 pg/mL. Those pts had a septal and lateral E' velocity significantly lower in the first month (9.7 ± 2.8 vs. 6.5 ± 2.1 m/s, p = 0.001; 13.1 ± 2.9 vs. 9.0 ± 2.3 m/s; p < 0.001, respectively), as well as a higher E/E' ratio (7.7 ± 1.9 vs. 10.7 ± 3.6, p = 0.002). The same was seen at 3 months after chemotherapy (8.2 ± 2.6 vs. 6.0 ± 1.5 m/s, p = 0.046; 11.5 ± 3.2 vs. 8.7 ± 1.9 m/s, p = 0.03; 9.2 ± 3.3 vs. 11.7 ± 3.0, p = 0.03; respectively). Septal and lateral E' velocities and E/E' ratio at 1 and 3 months showed an elevated accuracy in predicting the increase of NT-proBNP at 6 months after chemotherapy (1 month: AUC: 0.82, p = 0.002; AUC: 0.88, p = 0.001, AUC: 0.83, p = 0.003; respectively; 3 months: AUC: 0.75, p = 0.030; AUC: 0.75, p = 0.030, AUC: 0.73, p = 0.048; respectively).

Conclusion: The echocardiographic parameters of diastolic function, septal and lateral E' and E/E' ratio, have changed early after chemotherapy and allowed to predict the subsequent elevation of NT-proBNP. The prognostic implications of this fact should be evaluated in studies with longer follow-up.

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There are no differences in clinical picture of heart failure in patients with and without cancer

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Purpose: Cancer and cardiovascular diseases often coexist. The number of patients (pts) with cancer hospitalized in cardiology wards due to cardiovascular disorders has been increasing. The coexistence of cancer is regarded to cause many difficulties in dealing with cardiovascular diseases particularly with heart failure (HF). The study aimed to compare clinical picture of HF in pts with (Group A) and with no cancer (Group B).

Methods: There were 144 pts with cancer hospitalized due to cardiovascular disorders in our cardiology department in 2014, which constituted 9,3% of total hospitalized population (1549 pts). The reasons for hospital admission of cancer pts were: ACS-72 pts, AF-13 pts; PE-11 pts; HA-4 pts; other than AF arrhythmia/conduction disturbances-9 pts; syncope-3 pts; HCM-1 pt and HF in 31 pts which constituted 7,4 % of HF (432 HF and no cancer pts) and 2,0% of total hospitalized population. In all cases cancer disease was stable and fully controlled. Thirteen pts suffered from blood malignancies while other 21 from solid cancers. All received chemotherapy (21-containing anthracyclines); 7 radiotherapy according to the oncology recommendations.

Results: In group A 14 (43,8%) pts had MI in the past. In the other 18 ones no history of CAD or no significant changes in coronarangiography were revealed. In Group B 358 (83%) pts had ischemic aetiology of HF and it was the only statistically significant difference between group A and B (p < 0,05). Nine pts in Group A and 25 in Group B had LVEF > 50 % (HFpEF) (p > 0,05).

There were no differences between Group A and B as to clinical (age 69,7 ± 13,9 vs. 70,6 ± 13,4 [years]; sex M/F - 39 vs. 61; NYHA class 3,3 ± 0,7 vs. 2,9 ± 0,9); biochemical (GFR-50 ± 13 vs. 52 ± 13 [ml/m²/min], K-4,5 ± 0,8 vs. 4,3 ± 0,6 [mmol/l]; Na-140 ± 6,0 vs. 140 ± 4,0 [mmol/l]; INR-2,3 ± 3,6 vs. 1,5 ± 0,8; HgB-12,9 ± 2,6 vs. 13,2 ± 1,8 [g/dl]; WBC-9,1 ± 6,6 vs. 9,7 ± 3,9 [tys/ml]; PLT-223 ± 184 vs. 208 ± 81 [tys/ml]), echocardiographic (LVEF- 44 ± 19 vs. 41 ± 16 [%], LAD-44 ± 7 vs. 45 ± 8 [cm];

E/A-1,3 ± 0,6 vs 1,0 ± 0,6, E/E'-13 ± 11 vs 16,1 ± 8,3) characteristics; comorbidities (HA-68 vs. 80, DM-39 vs. 34, dyslipidemia-35 vs. 56, IHD/MI-45 vs. 49, infection-45 vs. 49, AF-32 vs. 38, CKD-32 vs. 39, COPD-3 vs. 7), in-hospital bleeding-0 vs. 1; in-hospital mortality (13 vs. 8), and treatment (ACE-I/ARA-68 vs. 77; beta-bloker-77 vs. 82; MRA-48 vs 49; diuretics-77 vs. 69; ivabradin-0 vs 1; statin-68 vs. 76) (P > 0,05).

Conclusion: Clinical picture of stable cancer patients hospitalized due to HF apart from aetiology of myocardium damage seems not to differ from those with HF and no cancer.

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Intrapericardial treatment with bleomycin in neoplastic pericardial effusion: our experience in the last 4 years

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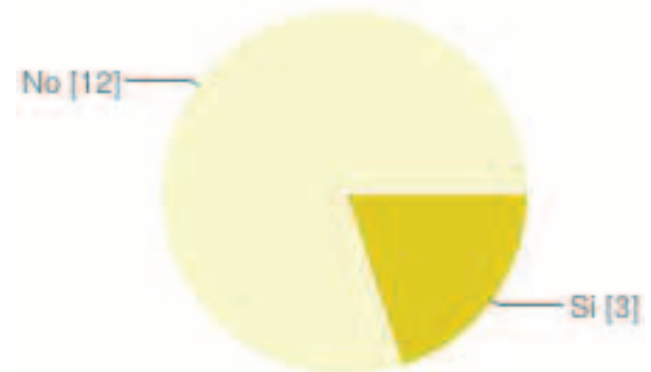
Introduction: Pericardial effusion and cardiac tamponade are complications of some advanced malignancies which carries poor prognosis and require cardiac intensive care management.

Percutaneous echo-guided pericardiocentesis is the initial technique in order to relief symptoms and restore normal cardiac function. Subsequent intrapericardial instillation of chemotherapy drugs may help to reduce effusion recurrences, which represents up to 40% of cases if only simple pericardial drainage is performed.

Methods: We analyzed 65 pericardial effusions in patients admitted in our Cardiac Intensive Care Unit between 2009 and 2013 with cardiac tamponade diagnosis. We determined incidence of neoplastic etiology, recurrences, and survival up to 12 months after bleomycin instillation.

Results: 15 of the 65 effusions had a neoplastic etiology (23%), being lung cancer the most frequent (67%). 13 were male (87%) and mean age was 61.8 (+/-17.7). Pericardial effusion recurrence occurred in 3 of the lung cancer patients (20%) within the first year. Two of the three patients had received bleomycin instillation. Overall survival at 12 months was 20%, staying alive only three patients.

Conclusion: Neoplastic pericardial effusion represented 23% of all pericardial effusions admitted in our unit. Pericardial involvement carries a poor prognosis in any malignancies, being lung cancer the most prevalent. The use of bleomycin do not impact on survival, but decrease recurrence rates, and therefore morbidity in this population who normally visit the hospital many times during the illness



Pericardial effusion recurrences

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Ultrafiltration therapy in patients with severe heart failure and resistance to diuretic treatments

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Purpose: analyze the effect of Ultrafiltration (UF) on the management of patients with heart failure (HF) and resistant to high dose of diuretics.

Methods: a consecutive series of 10 patients affected by severe HF (NYHA IV) and resistant to diuretic were treated with UF from 2009 until 2014. The fluid overload was removal in a single session of UF, for a total of 16 sessions. Ecocardiographic, laboratory, clinical and hemodynamics parameters were investigated before and 24 hours after the UF. The number of admissions and the admission's duration were compared one year before and after UF.

Results: fluid was removed at an average rate of 300 ml/h for 22.3 hours. On average, 3815.6 ± 1379.7 ml of ultrafiltrate and 1237.5 ± 637.8 ml of urine were removed during the UF. NYHA class significantly decreased in 7 patients. All patients had a clinical benefit showing a reduction of peripheral edema, dyspnea and weight (3.4 kg in av.). Serum creatinine and urea were increased while the GFR was reduced, although not clinically relevant. NT-proBNP was reduced. VTD and VTS were the only echocardiographic parameters statistically significant. No significant changes were seen in blood pressure and heart rate. The number of hospitalizations and the admission duration were reduced of 1.13 and 14.8 respectively. (Tab.1)

Conclusions: UF is an effective and safe therapeutic strategy for advanced HF patients resistant to diuretic, probably reducing hospital costs linked to the clinical management of these patients.

Table 1

	Baseline	After 24 hours	P-value
NYHA class IV	10	3	<0.001
Weight (Kg)	75.53 ± 17.97	72.11 ± 18.36	<0.001
Creatinine (mg/dl)	1.77 ± 0.74	2.04 ± 0.79	0.0309
Urea (mg/dl)	92.6 ± 56.80	101.5 ± 56.24	0.0164
GFR (ml/min/1.73 m ²)	47.25 ± 20.41	39.69 ± 17.23	0.0063
Sodium (mEq/l)	129.75 ± 6.02	129.06 ± 7.23	0.5613
Potassium (mEq/l)	3.81 ± 0.46	4.04 ± 0.78	0.2144
Ejection Fraction (%)	29.1 ± 10.64	28.8 ± 11.67	0.7381
Diastolic volume (ml)	189.60 ± 84.72	169.70 ± 70.70	0.0046
Systolic volume (ml)	140 ± 74.01	127.1 ± 66.77	0.0007

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Phenotypes of cardiorenal interrelations in patients with acute cardiac diseases

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Objective: Kidney damage is associated with higher all-cause and cardiovascular mortality. Large studies estimating the prevalence of cardiorenal syndromes in Russian population are limited. The aim of the study was to evaluate the prevalence, predictors and outcomes of cardiorenal interrelations in patients with acute cardiac diseases.

Methods: 566 patients (278 with acute decompensated heart failure (ADHF) and 288 with non-ST-elevation acute coronary syndrome (NSTEMI-ACS)), 46% male, 71 ± 11 years (M±SD), 28% smokers, arterial hypertension 91%, diabetes mellitus (DM) 28%, previous myocardial infarction (MI) 45%, admissions with ADHF 55%, ejection fraction <35% 15%, atrial fibrillation 35%, anemia 33%, blood pressure 142 ± 30/83 ± 16 mmHg were studied. Acute kidney injury (AKI) and chronic kidney disease (CKD) were defined according KDIGO Guidelines. Mann-Whitney test was performed. P < 0.05 was considered statistically significant.

Results: Different cardiorenal interrelations were revealed in 70% of patients. CKD was diagnosed in 46% of patients, AKI - in 40%, 30-50% increase of serum creatinine (SCr) from baseline was revealed in 35%. The following prevalence of different phenotypes of AKI was found: community-acquired/ hospital acquired 45%/55%, AKI on CKD/ AKI de novo 60%/40%, transient/ persistent 52%/48%. Patients with vs without AKI had higher rate of coronary artery disease (69 vs 54%), CKD (52 vs 41%), DM (34 vs 24%), acute heart failure (AHF) or ADHF (75 vs 61%), anemia (38 vs 30%), SCr >118 μmol/l (50 vs 22%), p < 0.01. Patients with ADHF with vs without AKI had higher rate of previous hospitalizations with ADHF (84 vs 70%), hyperhydration (72 vs 44%), the absence of outpatient therapy with beta-blockers (34 vs 9%), p < 0.01. Patients with NSTEMI-ACS with vs without AKI had higher rate of MI (83 vs 54%) and EF <35% (17 vs 8%), p < 0.01. Patients with acute cardiac diseases with vs without AKI had higher risk of hospital mortality (15 vs 4%), patients with ADHF with vs without AKI had higher risk of rehospitalizations (48 vs 37%), patients with NSTEMI-ACS with vs without AKI had higher risk of recurrent MI (11 vs 2%), p < 0.01.

Conclusions: Cardiorenal interrelations in patients with acute cardiovascular diseases are common and found in 70%. Coronary artery disease, CKD, DM, AHF or ADHF, anemia, baseline sCr >118 mmol/l are the main determinants of AKI in studied population. AKI is an independent negative prognostic factor and is associated with higher rate of in-hospital mortality and rehospitalizations in patients with ADHF or recurrent MI in patients with NSTEMI-ACS.

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Prevalence and outcomes in community-acquired versus hospital-acquired acute kidney injury in patients with decompensated heart failure

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Objective: Acute kidney injury (AKI) is a common problem in patients hospitalized with acute decompensated heart failure (ADHF) and occurs up to 70%. Little is known about AKI acquired in the community (CA-AKI) and how it differs from hospital-acquired AKI (HA-AKI). The aim of the study was to determine the prevalence of CA-AKI and HA-AKI in ADHF patients and to evaluate the impact on short-term (30-days mortality) and long-term (6 months rate of ADHF rehospitalizations) outcomes.

Methods: in 183 patients admitted with ADHF (125 male, 69 ± 9 years (M±SD), arterial hypertension (AH) 87%, ischemic heart disease (IHD) 56%, myocardial infarction (MI) 53%, atrial fibrillation 51%, diabetes mellitus (DM) 36%, known chronic kidney disease (CKD) 40%, ejection fraction 44 ± 15%) the prevalence of different variants of AKI was assessed. AKI was defined using 2012 KDIGO Guidelines. Depending on the timing of AKI, AKI was divided into CA-AKI, presenting on admission, and HA-AKI, that occurred after admission. Mann-Whitney and multiple logistic regression analysis were performed. P < 0.05 was considered statistically significant.

Results: 41% of patients developed AKI. CA-AKI was revealed in 56% of all AKI cases. Patients with CA-AKI versus HA-AKI were younger (65 ± 8 vs 71 ± 8 years, p < 0.01), had lower rate of previous ADHF-hospitalizations (71 vs 100%, p < 0.001). There was no difference in prevalence of main comorbidities, but there was tendency to higher rate of AH, IHD, DM, CKD and anemia in patients with CA-AKI. Patients with CA-AKI had higher risk of 30-days mortality (21 vs 12%, p < 0.05) and similar 6 months rate of ADHF rehospitalizations (48 vs 49%, p > 0.05).

Conclusions: CA-AKI was more frequent in ADHF patients and developed in 56%. Patients with CA-AKI had higher risk of 30-days mortality than HA-AKI and similar rate of long-term outcomes.

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Clinical characteristics of chronic kidney disease in patients hospitalized for acute decompensated heart failure

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Introduction: A large number of patients hospitalized for acute decompensated heart failure have some degree of kidney dysfunction.

Purpose: To evaluate prevalence and in-hospital characteristics of chronic kidney disease (CKD) in patients with acute decompensated heart failure in Internal Medicine Department.

Methods: A retrospective study was conducted on 112 patients admitted in Internal Medicine Department of an emergency clinical hospital for acute decompensated heart failure, from July to December 2014. Serum uric acid, sodium and potassium levels were monitored. BUN, serum creatinine and eGFR using MDRD equation were evaluated. Transthoracic echocardiography and abdominal ultrasonography were performed.

Results: 64% of patients were male (72) and 36% were female (40). Mean age was 77.86. Hypertension was the cause of hospitalization in 69.6% of cases, ischemic etiology in 30.4%. CKD was presented in 46.42% of patients (52): stage II in 5.7%, stage III in 69.23%, stage IV in 19.23% and stage V in 7.6% of patients. Pneumonia was presented in 23% of patients, urinary tract infection in 36.53%, atrial fibrillation in 32.69%, and COPD in 75% of patients with acute decompensated heart failure and CKD. Lower left ventricular ejection fraction (LVEF <45%) was measured by Simpson method on transthoracic echocardiography in 82.69% of cases. Small kidneys were seen at abdominal ultrasonography in 78.84% of patients. Worsening renal function in-hospital occurred in 28.84% of patients. Hyponatremia was diagnosed in 30.76% of patients at admission and hypokalemia in 71.15% of admitted patients.

Conclusions: Kidney dysfunction was often observed in patients hospitalized for acute decompensated heart failure. Older patients with lower LVEF had a high prevalence of kidney dysfunction and dyselektrolytemia.

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Differences in treatment intensity and outcomes of acute heart failure and the cardio-renal syndrome: a cohort study

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Purpose: To compare the treatment intensity and clinical outcomes of acute heart failure (AHF) between patients with or without Cardiorenal Syndrome (CRS).

Methods: This retrospective cohort study included data on 494 patients admitted to two tertiary care centers for AHF between July 2009 and June 2013.

Results: The mean age of the CRS patients was 61 years. CRS was observed in 30.8% (116) of the studied individuals. The frequencies of chronic heart failure and atrial fibrillation were the same between the studied groups, but hyperkalemia was higher among no CRS ones (Table 1). CRS individuals presented greater length of hospitalization and higher proportions of Intensive Care Unit admission, and use of furosemide and vasoactive amine. In this cohort, the death risk was approximately twice among CRS patients in comparison with no CRS individuals.

Conclusion: In this study, CRS appearance during hospitalization was associated with higher use of vasoactive amine and death. These findings suggest that CRS is an important marker for bad prognosis in patients with acute heart failure during the hospitalization phase.

General characteristics and prognosis				
	CRS	no CRS	P	Odds ratio
Male, % (n)	45.7 (53)	58.2 (152)	-	-
Mean Age \pm SD (range)	61.0 \pm 15.64 (22-91)	63.5 \pm 15.3 (20-93)	0.15	-
Hypertension, % (n)	29.0 (79)	36.7 (36)	0.158	1.99
Atrial fibrillation, % (n)	29.2 (31)	39.7 (87)	0.07	0.63
Diabetes, % (n)	33.3 (32)	30.3 (83)	0.58	0.31
Hyperkalemia, % (n)	27 (31)	8.9 (23)	0.001	3.8
Chronic renal failure, % (n)	27.8 (32)	21.3 (54)	0.17	1.4
Mean Length of stay (range)	18.0 (10-29)	10.0 (6.0-18)	0.001 [*]	-
Vasoactive amine use, % (n)	31.9 (37)	21.5 (56)	0.03	1.70
Furosemide, % (n)	94.7 (108)	21.3 (228)	0.004	2.5
Intensive Care Unit, % (n)	47.7 (55)	32.8 (85)	0.006	1.88
Death, % (n)	12.2 (14)	6.1 (16)	0.04	2.12

Data are expressed as frequency % (n) for categorical variables and median and interquartile range for continuous variables. * Mann-Whitney test. CRS, cardio-renal syndrome; OR, odds ratio. P-value < 0.05.

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Arterial wall remodeling depending on filtration renal function in patients with chronic heart failure and preserved ejection fraction

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Aim: to present some peculiarities of arterial wall remodeling in patients with chronic heart failure and preserved ejection fraction depending on eGFR.

Methods and materials: 30 CHF patients with preserved LV EF and stable angina were examined. Patients were divided into two groups based on eGFR (MDRD). The 1st group consisted of 16 patients with normal eGFR > 60 mL/min/1.73m². The 2nd group was of 14 patients with eGFR < 60 mL/min/1.73m². Average age was 61,78 \pm 4,20 yrs. Average FC of stable angina was 2,24 \pm 0,44, average CHF FC was 2,34 \pm 0,48. Sphygmoplethismography using VaSera VS-1000 was performed to evaluate shock-absorbing and conductive functions of arterial wall.

Results: patients between groups did not differ in risk factors, comorbidities, CAD and CHF therapy. In 2nd group PWVcf was reliably higher than in 1st one: 13,20 \pm 5,86 m/sec vs 8,36 \pm 2,44 m/sec (p=0,010). There was significant difference in CAVI1 between groups (p=0,032). Patients in groups differed in PWV both in aorta and carotids reliably: 6,50 \pm 1,41 m/sec vs 8,90 \pm 2,34 m/sec (p=0,002) and 3,70 \pm 1,29 m/sec vs 5,63 \pm 2,48 m/sec (p=0,011), respectively. Augmentation index R-AI was significantly higher in 2nd group, than in 1st: 1,17 \pm 0,11 vs 1,06 \pm 0,15 (p=0,032). There were no significant differences both in R- PWV and L-PWV between groups. Indirect reliable correlations between eGFR and CAVI1 (r=-0,51; p=0,012); between eGFR and PWVcf (r=-0,54; p=0,031); between eGFR and PWV aorta (r=-0,64; p=0,008); between eGFR and C-PWV (r=-0,69; p=0,003); between eGFR and R-AI (r=-0,48; p=0,041).

Conclusion: in patients with ischemic CHF and preserved LV EF arterial wall remodeling depends both on severity of CAD and CHF and on eGFR. Also, its characterized

with more evident increase of arterial wall stiffness and decrease of elasticity in patients with renal dysfunction.

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Heart and kidney damage in infective endocarditis

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Infective endocarditis (IE) is often associated with kidney and heart damage. However, cardiorenal relationships in IE have not been largely discussed until now.

Objectives: To assess the impact of impaired renal function on the course of IE.

Methods: The study included 122 patients [76 (52,8%) men] hospitalized with IE (Duke criteria 2009) during the period from January 2010 to January 2015. Mean age was 52,3 \pm 20,2 years, the proportions of patients with the history of drug use and alcohol abuse were 44 (36,1%) and 32 (26,2%), respectively. Patients with the history of structural kidney disease were not included in the study. Patients were divided into 3 groups by glomerular filtration rate (GFR,CKD-EPI) value: group 1 (GFR > 60 ml/min, n=62), group 2 (59-30 ml/min, n=43), Group 3 (<30 ml/min, n=17). Patient's history, types of IE, GFR, CRP, echocardiogram, class of heart failure (HF, NYHA), time to diagnosis and treatment period, clinical features, severity of proteinuria, microscopic hematuria, total in-hospital mortality were evaluated.

Results: Mean GFR value in Group 1 was 93,5 \pm 23,1 ml/min, in group 2 - 44,1 \pm 8,1 ml/min, in group 3 - 20,2 \pm 6,7 ml/min (p < 0,001). Fifteen (24%) patients in Group 1, 31 (72%) patients in Group 2 and 8 (47%) patients in Group 3 reported III-IV heart failure functional class symptoms (p < 0,05); acute kidney injury (AKIN, Increased SCr to \geq 1,5 baseline) was found in 18 (29%), 29 (67,5 %) and 13 (76,5 %) patients, respectively (p < 0,05). Overall inpatient mortality was higher among patients with low GFR: 9 (14,5%) in Group 1, 12 (27,9%) in Group 2, 10 (58,8%) in Group 3, p < 0,05. In all groups, left-sided native valve IE (p > 0,05) was predominant. There were no differences in other types of IE, echocardiography parameters, mean age and the period when IE was diagnosed. Proteinuria occurred in 46 (74,2%) in Group 1, in 31 (72,1%) in Group 2 and in 17 (100 %) in Group 3, microhaematuria in 26 (41,9%) vs. 25 (58,1%) vs. 9 (52,9%) respectively, but differences between the groups were not significant (p > 0,05).

Conclusion: Deteriorated kidney function in patients with IE is associated with more severe heart failure symptoms, higher risk of acute kidney damage and higher in-hospital mortality.

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Increased renal arterial resistances are independently associated to microalbuminuria in chronic heart failure outpatients

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The aim of the study was to evaluate the relationship between the renal resistance index (RRI), a parameter reflecting an altered renal blood flow, and the microalbuminuria in a group of CHF outpatients.

We enrolled 154 CHF outpatients in stable clinical conditions and in conventional therapy. Peak systolic velocity and end diastolic velocity of segmental renal artery was obtained by pulsed Doppler flow. Then RRI was calculated. Normalalbuminuria, microalbuminuria and macroalbuminuria were defined on the basis of the urinary albumin/creatinine ratio (UACR) of <30, 30 to 299, and \geq 300 mg/g.

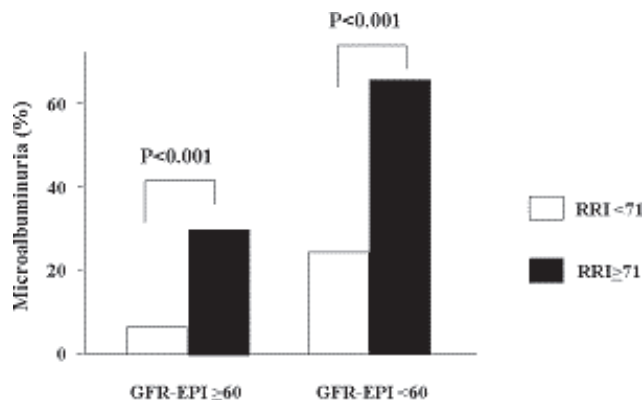
At the time of enrolment, all patients underwent a medical visit, an ECG, an echocardiographic examination and chemistry test. At the univariate regression analysis age (p < 0.001), diabetes (p: 0.029), NYHA class (p: 0.005), central venous pressure (CVP, p < 0.001), GFR-EPI (p < 0.001), NT-proBNP (p < 0.001) and RRI (OR 1.52; 95%CI: 1.31-1.76; p < 0.001) were significantly associated with microalbuminuria.

At the multivariate logistic regression analysis RRI (p: 0.017), GFR-EPI (p: 0.010), CVP (p: 0.016) and diabetes (p: 0.014) remained independently associated to microalbuminuria.

At ROC curve analysis, RRI showed an AUC of 0.75 (95%CI: 0.68-0.82) in predicting microalbuminuria. An RRI > 71 was the best cut-off with a sensitivity of 86% and a specificity of 56%.

Finally, using this cut-off, the prevalence of microalbuminuria was significantly higher in patients with high RRI both when patients with reduced and preserved GFR were considered (Figure).

In conclusions, the presence of an increased RRI is an independent determinant of microalbuminuria. This helps to better clarify the pathophysiological relevance of RRI and strengthens its potential utility in order to better characterise CHF outpatients.



Figure

VALVULAR HEART DISEASE (DIAGNOSIS, MANAGEMENT AND INTERVENTIONAL THERAPIES)

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Epidemiologic and clinical profile of the rheumatic mitral stenosis in Morocco

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Introduction: Rheumatic Mitral Stenosis(RMS);in clear decrease these last decades in the industrialized countries, still a frequent reason for admission in department of cardiology in Morocco. The aim of this study is to determine the epidemiologic and clinical profile of the RMS, in a department of Cardiology during the year 2014.

Methods: A cross sectional descriptive type study being spread out over one 10 months period starting from January 2014, including all the patients admitted at the department of Cardiology for RMS.

Results: The median age of 118 consecutively admitted patients (101 women: 85.6%; 17 men: 14.4%) was of 47.4 ±11.87 years. Almost all the patients were symptomatic (95.8%). An antecedent of rheumatic fever was noted at 30.5% of the cases. The mitral valves appeared calcified at 93.2% of the cases. The RMS was severe at 78.8% of the patients. It was about a pure MS in 22.9% of the case, associated with a mitral regurgitation or a significant aortic valvulopathy at 33.9% and 39% of the patients respectively, and of a mitral restenosis at 17% of the patients. Complications were noted at 70.3% of the patients of which primarily: an atrial fibrillation (65.3%), a dysfunction of the right ventricle (23.7%), an ischemic stroke (12.7%), a thrombus will intra left auricle (5.9%), an infective endocarditis (1.7%) and an ischemia of the members (1.7%). A mitral valve replacement and a percutaneous mitral dilation were indicated at 59.2% and 19.5% of the patients respectively.

Conclusions: The RMS remains in practice cardiologic significant problems hospital in Morocco, being presented at adult people, under advanced clinical tables, requiring interventional procedures. From where need for the strengthening of the preventive strategies primary and secondary of the rheumatic fever, in the structures of care of first line.

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Heart failure and galectin-3 (Gal-3) level at patients with mitral valve disease

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Objectives: To evaluate relationship between galectin-3 level and manifestations of heart failure at patients with mitral disease.

Methods and Results: 95 patients (mean (SD) age 57.4 ± 9,6 years) with mitral valve disease were included. Isolated mitral valve stenosis was detected in 40 patients, mitral insufficiency - in 48 patients, 7 patients had a combined valve lesion. 50 were male and 45 were female. 23 patients has NYHA class I-II heart failure and 72 patients has NYHA class III-IV heart failure. Plasma galectin-3 levels were assessed pre-operatively.

In patients with mitral stenosis level of Gal-3 was statistically significantly lower than in patients with mitral insufficiency: 19,4± 3,7ng / ml vs 25,7± 4,8 ng /ml (p < 0.05) respectively.

It was found that patients with I-II heart failure f.c. by NYHA had a lower level of Gal-3 - 16,4± 6,3 ng /ml in contrast with patients with III-IV f.c. by NYHA Gal-3 level - 24,4± 3.6 ng/ml (p < 0.05).

Also patients with I-II heart failure f.c. by NYHA has better results of test with a 6-minute walk test (330±93m) in contrast with patients of another group (182 ± 76m).

Conclusions: It was confirmed the dependence of galectin-3 level on the severity of heart failure in patients with mitral valve disease, as evidenced by the results of a 6-minute test.

Galectin-3 level at patients with mitral			
	All patients	Mitral stenosis	Mitral insufficiency
	22,3±3,1	19,4±3,7*	25,7±4,8*
NYHA I-II f.c.	16,4±6,3*	15.1±6.4	18.2±6.7
NYHA III-IV f.c.	24,4±3.6*	21.4±4.5	25.4±4.9

* - p < 0,05

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Left atrial reservoir function in symptomatic versus asymptomatic patients with moderate mitral stenosis

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Introduction: Determining the deformation of the left atrium (LA) during the reservoir phase achieves encouraging results for providing information about potential preclinical heart disease. However, insufficient data are available regarding LA reservoir function in valvular heart disease.

Objectives: To assess left atrial reservoir function in patients with moderate mitral stenosis (MS) and its relation to a patient's clinical status.

Methods: We studied 40 patients with isolated moderate MS in sinus rhythm (31 females and 9 males; mean age, 29.47 ± 19.1 years) who were classified into symptomatic (Group I) and asymptomatic (Group II) groups. All patients underwent a complete history, thorough clinical examination, and transthoracic echocardiography examination to assess MS severity, systolic pulmonary artery pressure (SPAP), mean pulmonary artery pressure (MPAP), left atrial maximal volume (LAV max), left atrial minimal volume (LAV min), and indices of left atrial reservoir function, including total left atrial emptying volume (Tot empVol), indexed Tot empVol, and total left atrial emptying fraction (LAEF).

Results: Symptomatic patients (Group I) showed a significantly higher mean LAV max (74.25 ± 19.12 vs. 70.65 ± 31.34, P < 0.05), LAV min (54.63 ± 16.68 vs. 47.1 ± 22.87, P < 0.05), Tot empVol (23.83 ± 5.33 vs. 18.4 ± 7.13, P < 0.05), indexed Tot empVol (14.73 ± 2.49 vs. 12.53 ± 3.18, p < 0.05), SPAP (44.35 ± 7.79 vs. 32.65 ± 10.6, P < 0.05), and MPAP (37.60 ± 10.78 vs. 30.46 ± 7.55, P > 0.05) and a significantly lower mean LAEF (30.40 ± 7.26 vs. 36.13 ± 6.37, P < 0.05). There were significant negative correlations between LAEF with SPAP, LAV max, and LAV min. Multivariate analysis revealed that the best predictors of symptoms were LAEF, Tot empVol, and Indexed Tot empVol.

Conclusion: LA reservoir function is impaired in symptomatic patients with moderate MS.

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Left atrial strain is highly predictive of pulmonary artery pressures with aortic stenosis

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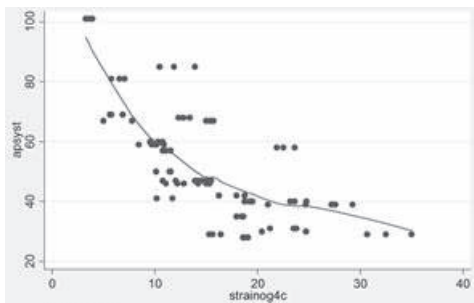
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Background: Pulmonary hypertension is one of the most powerful predictors of outcome in patients with severe aortic stenosis (AS). However, the mechanisms of PH occurring in the setting of AS are not fully understood.

Methods: We studied 30 consecutive AS patients referred for preoperative assessment. Echocardiographic assessment included left ventricular ejection fraction (LVEF) and mass (iLVM), mean aortic gradient (MAG), aortic valve area (AVA), mean E/E' ratio at the mitral annulus, TAPSE, indexed left atrial volume (iLAV), and left atrial longitudinal end systolic 2D strain using speckle tracking in the apical 4 (LAS-4C) and 2-chamber (LA-2C) views. All patients underwent right heart catheterization (RHC) with measurement of pulmonary artery pressures (systolic: sPAP, mean: mPAP) and pulmonary capillary pressure (PCWP).

Results: Patient age was 81 ± 8.8 years. MAG was 45 ± 16 mmHg, AVA was 78 ± 18 cm². Echocardiographic analysis yielded 63 ± 16% (range 24-87) for LVEF, 151 ± 45 g for iLVM, 18 ± 8 for E/E' ratio, 55 ± 36 for iLAV, 20 ± 6 mm for TAPSE, 16 ± 7% for LAS-4C and 17 ± 8% for LAS-2C. Feasibility was 100% for LAS-4C and 93% for LAS-2C. RHC showed: sPAP 51 ± 18 mmHg (range 28-101), mPAP 32 ± 11 mmHg (range 15-60), PCWP 19 ± 8 mmHg. sPAP correlated poorly with TAPSE and E/E', marginally with LVEF and MAG, and strongly with LAS-4C and LAS-2C (r = .72, 95% CI -2.5 -1.1, p < 0.001) (figure).

Conclusion: Left atrial strain measured by speckle tracking analysis is a simple parameter to acquire and is a strong predictor of pulmonary artery pressure in patients with severe AS. These results suggest that the increase in sPAP is tightly linked to the decrease in left atrial reservoir function. The prognostic value of LA strain should be further assessed.



figure

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Spectrum of associated cardiac lesions in isolated cleft of mitral valve

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Background: Isolated Cleft Of Mitral Valve (ICMV) is an uncommon congenital cardiac disease that may cause all degrees of mitral regurgitation; it can be isolated or associated to another congenital heart defect. The therapeutic options depend on the level of regurgitation and the type of associated cardiac defects.

Objectives: The aim of this study was to describe the profile of the associated cardiac lesions in Isolated Cleft Of Mitral Valve.

Methods: We conducted a retrospective descriptive study based on the congenital heart disease monocentric registry and on offline analysis of all echocardiography of patients with ICMV from December 2008 to November 2014. Patients who had an atrioventricular septal defect were excluded.

Results: Among 2177 patients with congenital heart disease, 22 had ICMV with a prevalence of 1%. Sex ratio M/F was 0,83. Consanguinity rate was 9,1%. Median age at the diagnosis was 5 years (6 days to 36 years). Nine patients (40,9%) had Down syndrome. One patient had anterior lateral cleft and 21 (95,5%) patients had anterior median cleft. The mitral regurgitation was severe in 5 patients (22,7%), moderate in 2 patients (9,1%), mild in 6 patients (27,3%), and 9 patients (40,9%) had no regurgitation. 17 patients (77,3%) had associated lesions; among them 11 patients (64,7%) had an accessory chordae in the LVOT with no obstruction, 15 patients (88,23%) had a VSD (Perimembranous=8, inlet=7), 3 patients had a secundum ASD, and 4 patients had a PDA. 13 patients who needed surgery but only 3 patients were operated on. The remaining patients were: waiting for operative date (n = 6), refused surgery (n = 1) or lost to follow up (n = 3). No death was recorded.

Conclusion: Our study showed that ICMV is rare and it is highly associated with Down syndrome. Also the Perimembranous VSD and accessory chordae of LVOT was the most common associated cardiac abnormalities.

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Transcatheter aortic valve implantation in patients with depressed left ventricular ejection fraction: results from a tertiary centre

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Purpose: Transcatheter aortic valve implantation (TAVI) has proven to be a feasible option for patients with aortic stenosis (AS) not suitable for surgery. A subset of these patients have ventricular dysfunction, which is known to be a risk factor for poor outcome after conventional replacement. The aim of our study was to evaluate the results of a series of patients with ventricular dysfunction undergoing TAVI.

Methods: 68 patients with AS and depressed EF were sent for TAVI. An echocardiogram was performed before hospital discharge and patients were followed up in the TAVI clinic. Data was recorded and analysed retrospectively.

Results: 52,9% were male and mean age was 82,19 (SD6,33). 19,1% were diabetic, 25% had chronic lung disease; 27,9% renal failure and 29,4% had concomitant coronary disease. 13 patients had a previous cardiac surgery. Mean EF was 43,28% (SD8,42), 20,6% having an EF<35%. The intervention was successful in all 68 patients with no deaths or major complications during the procedure. During hospital stay 4p(6,25%) died and 3(4,7%) needed reintervention. Most common complications were need for pacemaker implantation (40,62%), renal failure (14,7%) and major bleeding (8,8%). No patient presented neurological complications. An echocardiogram before discharge showed a mean improvement in EF of 11,38% (SD9,4); 15,09% for EF<35%; 12,43% for EF 35-45% and 8,25% for EF 45-55%. During a mean follow up of 247 days, 6 patients were lost, and 2 died for no cardiac

reasons. Clinical status was improved in most patients, with 86% being in class I-II in comparison with 22% before the procedure.

Conclusions: In our series TAVI was safe in patients with ventricular dysfunction, with low perioperative morbidity and an important improvement of functional capacity as well as a modest recovery in ejection fraction, specially in the group with severely depressed ventricular function. Longer follow up and larger studies will be needed, but given these results, TAVI appears to be a good option in this setting.

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Infective endocarditis: a comparison between community-acquired and health care-associated endocarditis

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Introduction and Purpose: Infective endocarditis (IE), an infection of the endocardium and heart valves, carries a poor prognosis and a high mortality. According to the mode of acquisition, IE can be classified as community-acquired IE or health care-associated IE. The last one includes nosocomial and non-nosocomial IE. The goal of this work is to describe and compare the clinical profile and in-hospital outcome between community-acquired IE (CA-IE) and health-care associated IE (HCA-IE).

Methods: We studied 65 cases of consecutive diagnosed IE in a tertiary center from July 2013 to July 2014. Data were collected from the electronic clinical process and registered in a uniform base. They were classified into two groups: CA-IE (38) and HCA-IE (25). In HCA-IE group, 9 were nosocomial and 16 were non-nosocomial. Two cases of intravenous drug abuse-associated IE were excluded.

Results: The groups were similar in gender (male sex CA-IE 68.4% vs. HCA-IE 52.0%) and mean age (CA-IE 62.8 ± 17.5 vs. HCA-IE 68.2 ± 15.3). Within the comorbidities studied, heart failure (CA-IE 18.5% vs. HCA-IE 57.9%, p=0.006) and in particular left ventricular dysfunction (CA-IE 8.6% vs. HCA-IE 37.5%, p=0.010) were more common in HCA-IE patients. No differences between groups were found concerning diabetes mellitus, chronic pulmonary disease or predisposing disease (rheumatic heart disease, congenital heart disease, mitral valve prolapse or degenerative heart disease). Echocardiographic features were not different as well. Staphylococcus aureus methicillin-susceptible (21.1%), coagulase-negative staphylococci (13.2%) and enterococcus spp. (13.2%) were the main causative microorganisms in CA-IE group. In the other group, staphylococcus aureus methicillin-resistant (20%) and staphylococcus aureus methicillin-susceptible (20%) were more often involved. Most of the complications studied, local or at distance, occurred with similar frequency between the groups, although systemic embolism was significantly more prevalent in CA-IE cases (CA-IE 34.2% vs. HCA-IE 4.0%, p=0.005). In-hospital mortality was significantly higher in the HCA-IE patients (CA-IE 18.4% vs. HCA-IE 44.0%, p=0.028).

Conclusion: In our study, preexisting heart failure and left ventricular dysfunction were more common in the HCA-IE patients. Among several complications, systemic embolism seems to be more frequent in CA-IE. As expected, HCA-IE was positively associated with in-hospital death.

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Ventriculo-vascular coupling index as a prognosticator in mild to moderate aortic stenosis

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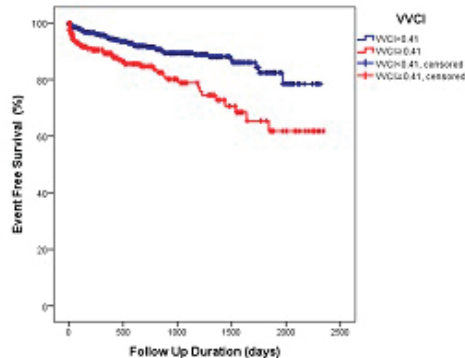
Purpose: Natural history of mild to moderate aortic stenosis (AS) remains poorly defined and only limited data have been available to provide risk stratification. We evaluated the natural history of mild to moderate AS and whether ventriculo-vascular coupling index (VVC) can be used as a prognosticator reflecting systemic hemodynamic load.

Methods: A total of 848 consecutive asymptomatic patients (mean age, 71 ± 12) with mild to moderate AS (aortic jet velocity >2.0 m/s) were retrospectively analyzed. We excluded the patients who have aortic valve area <1.0 cm² or ejection fraction <50%. Cardiovascular death, aortic valve replacement and admission for heart failure were regarded as clinical events.

Results: During mean follow up duration of 23 ± 21 months, 40 patients were died from cardiovascular cause, 25 patients experienced aortic valve replacement and 31 patients were admitted with heart failure. Estimated event-free survival was 93.0 ± 1.0% at 1 year, 86.0 ± 1.6% at 3 years, and 75.7 ± 3.0% at 5 years. In multivariate Cox regression analysis, BMI (adjusted HR 0.89 [95% CI 0.82-0.96], P=0.003), hemoglobin (adjusted HR 0.87 [95% CI 0.77-0.99], P=0.037), peak aortic jet velocity (adjusted HR 1.76 [95% CI 1.18-2.62], P=0.006) and VVC

(adjusted HR 5.39, [95% CI 1.85-15.66], $P=0.002$) were independent predictors of cardiovascular events. The patients with higher VVCI (≥ 0.41 ; the best cut-off value in ROC analysis) experienced clinical events more frequently (8.3% vs. 16.6%; OR 2.2 [95% CI 1.40-3.43], $P < 0.001$).

Conclusion: The actual cardiovascular event rate of mild to moderate AS is substantially high in real world. In addition to conventional parameters, BMI, hemoglobin and VVCI are also powerful independent predictors of clinical events in asymptomatic mild to moderate AS.



DEVICES / ARTIFICIAL HEART / CRT / ICD

P347

Is the implantation of CRT proarrhythmic?

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Introduction: CRT is an important device for the treatment of patients with HF. The relationship between biventricular pacing and the incidence of ventricular arrhythmias remains controversial. Some trials suggest that biventricular pacing might have a proarrhythmic effect because of reversing the direction of normal activation of the ventricle due to epicardial stimulation. The aim of this study was to identify potential proarrhythmic effect of CRT.

Methods: The study included 496 patients with HF, NYHA II-IV, $EF \leq 35\%$, who underwent implantation CRT-D or ICD only in primary prevention of sudden death according to guidelines. First appropriate therapy of defibrillator was end-point which was defined as antitachycardiac pacing or shocks for ventricular tachycardia/fibrillation.

Results: CRT-D devices were implanted in 277 patients (group A) and ICD in 219 patients (group B). Ventricular arrhythmias requiring appropriate therapy occurred in 58 patients (20.94%) in group A and in 50 patients (22.83%) in group B. There were no differences in the incidence of appropriate therapies ($p=0.61$). Kaplan-Meier analysis for arrhythmic events showed no significant differences in the patients with CRT-D compared to those with ICD only ($p=0.47$).

Conclusions: The incidence of appropriate therapy of defibrillator was similar in both groups. We did not find a potential proarrhythmic effect of CRT.

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Impact of QRS complex duration on mechanical systolic dyssynchrony in patients with heart failure

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Background: We investigated systolic mechanical dyssynchrony (MD) and its relation to different clinical, laboratory and echocardiographic parameters in adult patients with heart failure with reduced ejection fraction (HFrEF).

Methods: 59 consecutive patients with HFrEF and formal indications for cardiac resynchronization therapy (CRT) according to national and European guidelines were admitted to our hospital for any cause (64.4% males, 74.0 ± 12.1 years ($M \pm SD$), NYHA functional class II, III, IV 27.1, 50.8, 22.1%, respectively; median LV ejection fraction 28% (15-35)). Patients were prospectively evaluated using 12-lead electrocardiogram and complete echocardiographic examination including tissue Doppler imaging. Epidemiological, clinical and laboratory data were collected for each patient. Ischemic cardiomyopathy was reported in 53 (89.8%) patients. Comorbidities were hypertension ($n=49$; 83.0%), chronic kidney disease ($n=28$;

47.5%), atrial fibrillation ($n=23$; 39.0%), diabetes mellitus ($n=14$; 23.7%), chronic pulmonary diseases ($n=9$; 15.3%), anemia ($n=8$; 13.6%). Left and right bundle branch block were diagnosed in 56 (94.9%) and 3 (5.1%) patients, respectively. Median QRS duration was 140 ms (120-200 ms)

Results: MD was revealed in 90.0% of patients with HFrEF and formal indications for CRT. Atrioventricular (AVD), inter- (inter-VD) and intraventricular (intra-VD) dyssynchronies were present in 11 (18.6%), 32 (54.2%), and 47 (79.7%) patients, respectively. The most common variants of MD were (1) isolated intra-VD ($n=20$, 34%), (2) combination of AVD, inter-VD and intra-VD ($n=18$, 30.5%), (3) combination of inter-VD and intra-VD ($n=9$, 15.3%). Kruskal-Wallis and multiple comparison tests were performed ($p < 0.05$ were considered significant). Combination of AVD, inter-VD and intra-VD compared with inter-VD was associated with lower LV EF (median 22.5 vs 32.0%), BMI (median 22.4 vs 28.9 kg/m²), and greater QRS duration (median 160.0 vs 130.0 ms; $p < 0.05$ for all). Multivariable logistic analysis revealed that only QRS duration (odds ratio 1.21, 95% confidence interval 1.05-1.45; $p < 0.05$) could predict presence of combination of AVD, inter-VD and intra-VD. QRS duration of 170.0 ms identified combination of AVD, inter-VD and intra-VD with 33.3% sensitivity and 100.0% specificity.

Conclusions: Systolic inter- and intraventricular dyssynchronies are common in adult patients with HFrEF, and may be associated with some clinical characteristics. QRS duration is a specific marker of combination of AVD, inter-VD and intra-VD.

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Changes and predictive value of QRS duration for mortality in non-ischemic heart failure patients with cardiac resynchronization therapy

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Introduction: Cardiac resynchronization therapy (CRT) is an effective therapy in selected heart failure (HF) patients. Especially in HF patients with wide QRS of left bundle branch block and lower left ventricular ejection fraction, CRT effectively reduce HF progression and reduce mortality. Little is known about the relationship between changes of QRS duration (QRSd) and mortality in non-ischemic HF patients with CRT. The aim of this study is to evaluate the association between changes of QRSd before and after Cardiac resynchronization therapy (CRT) and mortality in non-ischemic HF patients with CRT.

Methods: This retrospective study included 196 consecutive non-ischemic HF patients (age, 60 ± 13 years; 133 men) who had newly undergone CRT implantation between 2000 and 2013. We evaluated QRSd before and one week after CRT implantation.

Results: During the mean follow-up period of 35 ± 27 months, 45 (23%) patients died from any cause. 79 (40%) patients with widening QRSd after CRT had significantly shorter QRSd before CRT than patients with narrowing QRSd after CRT (146 ± 21 msec vs. 187 ± 29 msec, $p < 0.05$). There is a tendency of the lower rate of patients with reverse remodeling in patients with widening QRSd after CRT than patients with narrowing QRSd (45% vs. 55%, $p < 0.10$). Multivariate analysis adjusted for age, gender, LVEF, previous sustained ventricular tachycardia or ventricular fibrillation, and beta-blocker use demonstrated that widening QRSd (HR: 3.79; 95% CI, 1.91-7.53; $P < 0.05$) and estimated glomerular filtration rate < 60 mL/min/1.73 m² (HR, 2.87; 95% CI, 1.45-5.68; $p < 0.05$) to be independently associated with mortality.

Conclusion: Our results suggest that widening QRSd is an independent risk of mortality in non-ischemic HF patients receiving CRT, regardless of LVEF or beta-blocker use. Change in QRSd may be an important predictor of mortality in HF patients receiving CRT. Management strategies for shortening the QRSd after CRT implantation warrant further discussion.

P350

B-type natriuretic peptide to predict and follow up response to cardiac resynchronization therapy

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Cardiac resynchronization therapy (CRT) is an established Therapy for patients with moderate-to-severe heart Failure, however, a lack of response to CRT has been reported in up to 30% of patients. A variety of parameters have been reported to be predictors of the CRT response, Brain natriuretic peptides (BNP) and its inactive amino terminal portion (NT-pro BNP), are neurohormones released by the ventricle in response to increase LV wall stress. Hence, BNP level may have valuable role for the assessment of cardiac dysfunction, particularly LV dysfunction, and for the monitoring of the response to cardiac therapy

Aim of study: evaluate the effect of CRT on plasma concentrations of β -type natriuretic peptide (BNP) and the value of BNP in predicting the clinical response to CRT, -and whether basal levels and/or change in neurohumoral activation during treatment are related to clinical efficacy of CRT

Methodology: we included 30 patients with CHF (27 males, mean age 57 ± 6 years)

undergoing CRT. Echocardiography and Plasma levels of (BNP) were evaluated before and 6 months after implantation.

Results: Responders (22 patients) at follow-up were defined by echocardiography (decrease in LV end systolic volume $\geq 15\%$). Responders and Non Responders had no significant difference regarding baseline BNP level, however Responders only showed a significant decrease in plasma BNP levels (229.64 pg/ml \pm 111.47) as compared to Non-Responders (468 pg/ml \pm 96.52) P value < 0.01 . A decrease of BNP value $\geq 12\%$ had a specificity of 87.5% and a sensitivity of 90.9% in predicting CRT response

Conclusions: Percentage change in plasma BNP levels from baseline to 6 months was the strongest predictor of response to CRT and may have potential to predict outcome.

P352

Cardiac MRI and phase analysis gated SPECT in evaluation of left ventricular scar burden and dys-synchrony in determining the outcome of cardiac resynchronization therapy

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Methods: Thirty patients underwent CRT implantation. Pre-implantation CMR was done to document scar burden and lateral wall involvement. Degree of dyssynchrony was assessed through LV phase analysis.

Results: Thirty patients received CRT (mean age 58.7 \pm 9.0, 24 males). CRT implantation had a favorable prognosis on cardiac functions (LVEF pre-implantation: 30 \pm 5% versus 37 \pm 7% post-implantation; P=0.017). Echocardiographic response, defined as relative decrease in LVES by $\geq 15\%$, was documented in 19 patients (63.3%). After adjusting for CMR scar burden, neither Histogram BW nor SD was correlated to LV remodeling. Applying ROC curve for CMR examination data for LV scar analysis showed that a cutoff value of 38.5% for global LV scar burden had a sensitivity of 72.7% and specificity of 68.4%. A cutoff value of 12% for lateral wall scar burden had a sensitivity of 81.8% and specificity of 68.4%.

Conclusions: Global and lateral scar burden of the left ventricle have unfavorable impact on CRT outcome. CMR is superior to gated SPECT in detection of scar burden and providing acceptable predictors for potential CRT non-responders. Mechanical dyssynchrony depends largely on underlying LV scar substrate.

P353

Various methods for selection of patients with non-ischemic cardiomyopathy for cardiac resynchronization therapy

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Aim: The aim of the study was to use various methods of selection of patients for cardiac resynchronization therapy (CRT) and to evaluate prospects of method implementation in clinical practice to increase treatment efficacy.

Materials and methods: The study comprised a total of 88 patients aged 32 to 75 years (55 \pm 12 years) with dilated cardiomyopathy (DCM), NYHA functional class III heart failure, left ventricular (LV) ejection fraction (EF) of 30.1 \pm 3.8%, 6-min walk test distance of 290.5 \pm 64.3 m, end diastolic volume (EDV) of 220.7 \pm 50.9 mL, intraventricular and interventricular dyssynchrony of > 120 ms. At the selection stage, patients were divided into three groups: group 1 (n=28) that received assessment of myocardial metabolism defect (MMD) by radionuclide methods, group 2 (n=24) that received assessment of tricuspid annular systolic velocity (TASV), and control group.

Results: One-year follow-up study showed that 69 patients (78.5%) clinically responded to CRT; 19 patients (21.5%) did not respond to CRT. Evaluation of the selection methods demonstrated that 3 (10.7%), 6 (25%), and 10 (27%) patients did not respond to CRT in group 1, 2, and 3, respectively. Group 1 included 25 responders (89.3%) whose MMD was $< 15\%$ prior to CRT; if initial MMD was $> 15\%$, patients did not respond to CRT. Group 2 included 18 responders (75%) whose TASV was > 10 cm/s (12.5 \pm 2.1 cm/s) (p = 0.0001).

Conclusions: (1) Preserved myocardial metabolism (LV MMD $< 15\%$) is a predictor of efficacious CRT in DCM patients. (2) Tricuspid annular systolic velocity is an independent predictor of response to CRT; TASV enables to identify CRT responders with sensitivity of 85% and specificity of 83% at the selection stage. (3) For selection of patients for CRT, the administration of all presented methods is rational in order to increase treatment efficacy.

P355

Safety and outcomes involved in upgrading devices to biventricular systems: a single centre experience

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Background: Upgrading bradycardia pacing (PPM) and/or defibrillator (ICD) systems to cardiac resynchronization (CRT) devices is increasingly common. We

present our experience of elective day case CRT upgrade procedures.

Methods: The UK centralised cardiac audit database identified cases and additional data were obtained from medical records and databases. Data from de novo CRT implants were used for comparison.

Results: Over 5yrs, 61 elective upgrades were performed (82% male; age 68 \pm 16yrs) with the majority (n=31) in the last 2yrs. Mean interval between index implant and upgrade was 60 months. $> 75\%$ of patients were discharged home on the procedure day. 23/61 patients were upgraded from ICD (index indication 2° prevention: n=21), and 38/61 patients were PPM upgrades (index indication 3° heart block: n=17, AF with bradycardia: n=18, AF with pace/ablate: n=2, and chronotropic incompetence: n=1). Indications for upgrade included symptomatic heart failure, ejection fraction (EF) $< 35\%$, and high prevalence of RV pacing (mean 70%, with 44/61 patients persistently RV pacing $> 40\%$ of the time). Venography identified $> 50\%$ subclavian vein (SCV) stenosis in 15/61 of cases; requiring venoplasty (n=2), very proximal SCV puncture (n=1), and a right-sided approach (n=1). Venous access complications were comparable to de novo implants: pneumothorax (n=1) and arterial puncture requiring an Angioseal device (n=1). Total procedure time (time in cath lab) was significantly shorter for upgrades compared to de novo cases (158 \pm 132 v 118 \pm 35 min; p=0.02), while screening time, radiation dose, and contrast use were similar for the two procedures (888 \pm 642 v 821 \pm 423 msec: p=0.5, 1770 \pm 4156 v 1779 \pm 5486 Gy: p=0.9, and 107 \pm 68 v 100 \pm 63ml: p=0.6 respectively). EF improved by $\geq 5\%$ in 45% of patients 6 months post upgrade. The greatest improvements in EF were observed in the 20 patients in whom there was evidence of progressive LV dysfunction following the index implant and in the patients with the highest prevalence of RV pacing.

Conclusions: Elective upgrade procedures can be performed safely on a day case basis with procedure times being significantly shorter than de novo implants. Venography is useful to identify potential venous access problems where in 5% a change in practice may be required. The greatest EF responses appear to be in patients with the greatest prevalence of RV pacing and in the patients with evidence of progressive LV dysfunction following the index device implant.

P356

Comparison between participants and non-participants of a randomized clinical trial on e-health in heart failure: the e-vita heart failure study

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Background: Selection bias in heart failure (HF) trials is a major concern, especially in e-health trials where an over-representation of young and educated patients is suspected.

Purpose: To compare patient characteristics of participants with non-participants from a trial on e-health in HF.

Methods: We included 900 eligible HF patients registered at a HF clinic for more than 3 months; 450 participants from the e-Vita heart failure trial and 450, randomly selected, from the patients who did not choose to participate.

Data was collected from 9 participating hospitals in the Netherlands.

Differences between the two groups at baseline will be compared using independent sample T-test or Mann-Whitney U tests for continuous and chi-square test for categorical variables. The comparison will include patient characteristics such as age, gender, smoking status, socioeconomic status, comorbidities (prior myocardial infarction, PCI, CABG, valvular heart disease, arrhythmia, diabetes mellitus, renal dysfunction, depression, COPD), NYHA class, and body mass index.

Results: Mean age of the 450 participants was 66.3 (SD 11.0) years, and 74% were male. Details of the non-participants are currently collected and analysed.

Conclusions: This study will provide important information on whether participants differ from non-participants in a study on e-health in patients with HF. These data provide information on generalizability of results of studies with e-health in HF patients.

P357

Evaluation of ReDS-guided patient management in ambulatory heart failure patients at-risk for rehospitalization

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Introduction: Pulmonary congestion is the most common cause of worsening Heart Failure (HF) symptoms and HF hospitalization. Accurate and remote monitoring of lung fluid volume may inform optimal treatment and prevent rehospitalization. Remote dielectric sensing (ReDS) technology, based on low power electromagnetic signals, is a quantitative non-invasive method for measuring absolute lung fluid

volume in patients with fluid management problems, including HF patients. We present data from the first outcome study using ReDS technology.

Methods: Patients hospitalized for HF, regardless of LVEF, were enrolled and followed at home for 3 months post-discharge using ReDS. Daily ReDS readings were obtained using a wearable vest (Sensible Medical Innovations LTD), in addition to standard of care monitoring and follow-up including daily weights and routine clinical follow-up visits. ReDS measurements were used as an adjunct to clinical assessments to guide HF therapy towards maintaining pulmonary fluid content within the targeted normal range. ReDS was utilized throughout a 3-month follow-up period or until one of two events: ADHF readmission or patient death from any cause. Patients were blinded to ReDS values. Daily ReDS data were sent to the treating cardiologist via secured website to consider appropriate action when ReDS readings were out of the normal range. The number of events in the 3 months following ReDS-guided management was collected, for comparison.

Results: Forty-seven patients were enrolled, and followed at home for 76 ± 27 days. Patients were 74.8 ± 10.1 years old, 42% had LVEF above 40%, and 40% were women. Patient and clinician adherence to ReDS measurement and the study treatment protocol was excellent. During active ReDS-guided management there were only 4 events (2 HF readmissions and 2 deaths) in 4 patients. In the 3-months post-ReDS study period, there were significantly more events, 10 events (8 readmissions and 2 deaths) in 5 patients (Hazard Ratio 4.38; 95% CI [1.20-15.92], $p = 0.025$).

No device-related adverse events were noted. Final study visits are pending for a number of patients.

Conclusions: Current findings suggest that ReDS-guided management may reduce HF readmissions in patients recently discharged following HF hospitalization.

P358

Telemonitoring is associated with reduced mortality in newly diagnosed heart failure patients

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Background: Heart failure (HF) is a complex clinical syndrome associated with high mortality and high rate of hospital readmissions. Telemonitoring (TM) is a promising strategy for improving HF outcomes but there is a need to identify those patients in whom a TM approach might provide benefit. We wanted to determine if TM in patients with recently diagnosed HF and ejection fraction <45% reduces the risk of re-admission from any cause or death from any cause in a "real world" setting.

Methods: Retrospective study of 124 patients (78.2% male; aged 68.6 ± 12.6 years; 56.5% ischaemic etiology) who underwent TM and 345 patients (68.5% male; 70.2 ± 10.7 years; 56.3% ischemic etiology) who underwent the usual-care (UC), between 2009-12. All patients had a recent diagnosis of HF, NYHA class II-III and ejection fraction <45%. The TM-group were assessed daily by body weight, blood pressure and heart rate using electronic devices with automatic transfer of data to an online database. There were no differences between the two groups in the treatment with beta-blockers, ACE inhibitors/angiotensin receptor blockers and aldosterone antagonists (83%, 85%, 62% in the TM-group; 79%, 82%, 59% in the UC-group, respectively). Follow-up was 12 months.

Results: Death from any cause occurred in 8.1% of the TM-group and 19% of the UC-group, $p = 0.002$. The TM-group and the UC-group did not differ significantly in the number of patients admitted for any cause 63.7% vs. 62.5% respectively, $p = 0.8$. The number of readmissions/patients was also similar in the two groups, 1.3 ± 1.7 in the TM-group and 1.4 ± 1.7 in the UC-group ($p = 0.9$). There was no difference in the number of days in hospital (8.1 ± 12.8 days in TM-group and 9.5 ± 17.3 in UC-group; $p = 0.4$). Readmissions for HF occurred in 13.6% of patients in the TM-group and 12.7% of patients in the UC-group ($p = 0.9$), while 0.8% of patients in the TM-group and 15.5% in the UC-group experienced admission for renal failure ($p = 0.0002$). Readmissions for ischaemic heart disease and arrhythmias occurred in 13.6% and 12.8% in the TM-group and 17.9% and 11.5% in the UC-group, respectively. There was a significantly greater number of days alive and out of hospital for the patients in the TM-group at 348.3 ± 5.5 days compared with 329.9 ± 4.6 days in the UC-group ($p = 0.0001$).

Conclusions: In patients with a recent diagnosis of HF and reduced left ventricle systolic function, TM is associated with lower any-cause mortality. Furthermore TM has the potential to reduce number of days lost to hospitalization and death.

P359

First steps to implement a customer relationship management process (crm) in the field of health care, a software tool for coordination and monitoring of heart failure patients

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Purpose: Focusing on the implementation of ICT tools in the Basque Health System (Osakidetza), a CRM platform has been included within its technological infrastructure.

CRM is a computer program created to support and improve company-customer relationship management for marketing and sales purposes. CRM programs are not usually used in the healthcare sector, although CRM functionality, development and widespread use of information becomes an attractive element for healthcare organizations.

We are adapting a commercial CRM for management of Heart Failure (HF).

Methods: Osakidetza's CRM architecture (modules):

Data management: includes administrative data (all patients in the healthcare system).

Tele-monitoring: incorporates external data obtained from patients at home or from clinical records (manually or automated).

Workflow automation: manages different tasks (appointments, blood studies, radiological tests) as well as generates alerts based on rules and trends.

Reporting: in-process measuring function (indicators).

We identify processes in HF which can be considered as standard models for different patient types.

The workflow includes clinical tasks, non-face-to-face phases (telephone contacts, tele-health alarms, etc.) visits (home, GPs' clinics and community nurses) and alerts management. Our work approaches also the modelling of the application itself to suit patients and professionals needs (easy access, interaction between CRM and medical record or notes).

Results: We have identified 3 clinical pathways to use CRM.

Follow-up after hospitalization discharge (350 patients included): Phone health-questionnaire at 72 hours done by a contact-centre nurse whom segments patients to visit nurse or GP at home or in health clinic, from 24 hours to 8-10 days later and in 9% less than 24 hours.

Remote monitoring of HF patients and alerts management according to blood pressure, heart rate, weight, oxygen saturation and clinical questionnaires. (42 patients included)

Patients with repeated hospital admissions for HF (in process).

Conclusions: CRM platform can be used by health systems as remote monitoring, disease management and database management system.

We have considered hospital discharged for HF patients a clinical situation that can be managed by CRM, after the definition of clinical pathways according to the risk profile of patients.

The CRM allows coordinated tracking of telemonitored HF patients and early nursing care for patients at high risk of readmission

P360

A novel algorithm for left ventricle capture check in cardiac resynchronization therapy. Results from the DREAM (CRT device left capture confirmation through an electrogram's analysis model) study

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Purpose: A biventricular pacemaker (CRT-P) or defibrillator (CRT-D), with an effective stimulation percentage greater than 90%, is recommended for heart failure patients. Not all models of modern devices offer an auto-threshold system which regulates spike's energy in right (RV) and left (LV) ventricle channels. Remote Monitoring System (RMS), moreover, offers many benefits to the patient's safety and represents an important alternative to the current standard of care. The purpose of this study was to develop an automatic algorithm to off-line check of LV capture in CRT devices by analyzing the electrograms (EGMs) from RMS.

Methods: Seventy-eight signals were analyzed in 19 patients (15 men (79%) and 4 women (21%)) enrolled at the implant or during an in-office follow-up. The algorithm verified beat-to-beat the LV capture by analyzing the recorded signals in the frequency domain in order to check if specific frequency components characterize the capture stimulus condition. All parameters calculated were elaborated using a particular classifier algorithm (k-NN).

Results: An automatic tool of k-NN software calculates sensitivity, specificity and accuracy for all LV tested configurations. The worst case was observed for standard bipolar pacing and sensing configuration, values was respectively 83%, 86% and 85%. Better configurations were observed for all unipolar pacing configurations where calculated values were 100% for all parameters.

Conclusions: The algorithm that we implemented is a new and reliable clinical tool based on the EGM analysis that appears to be sensitive, specific and accurate to identify a loss of LV capture in patients with CRT devices.

impairment of FEV1 ($-9 \pm 3\%$, $p < 0.016$) and FVC ($-18 \pm 3\%$, $p < 0.001$) despite of a mean decrease in both PCW and PAP of 16 ± 2 mmHg ($p < 0.0001$). Mean time to RFT-2 was 626 ± 65 days, when there was no further significant decrease in PCW or PA. Compared to post-implantation values, FEV1 did not show significant differences, but FVC increased by $17 \pm 3\%$, $p < 0.004$. Both mean FEV1 and FVC values at RFT-2 remained lower than pre-implantation studies, but didn't show significant differences ($p < 0.16$ and $p < 0.39$ respectively). 42% of the patients with normal baseline FEV1 had impaired levels in the last test and only 17% of the patients with pre-implantation impaired FEV1 achieved normal values. The degree of FEV1/FVC impairment, both post-implantation and long term, were independent of the history of smoking, previous lung disease or weight. RFT pre or post-implantation were not correlated with global survival rate or post heart transplant survival rate.

Conclusion: unexpectedly, RF after implantation of a LVAD is significantly impaired despite of a significant decrease in pulmonary pressures and does not improve even after long term support. This suggests that unloading the pulmonary congestion in heart failure patients is not enough to improve their lung function. Other factors that need further study may play a role.

P365

A matter of weight in bridge to transplantation with centrifugal continuous-flow ventricular assist devices

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Purpose: obesity is a predictor of poor outcomes in heart transplantation. After a left ventricular assist device (LVAD) implantation, reduced congestion and increased exercise activity should lead to weight loss. However, increased appetite and quality of life may have the opposite effect. Regarding the "bridge to weight-loss" strategy with a LVAD, conflicting results have been published with different devices. We present a retrospective study of weight and Body Mass Index (BMI) in patients with a third generation LVAD implanted as a bridge to transplant.

Methods: we analysed the weight and BMI of 66 patients with a centrifugal continuous-flow LVAD, at baseline (pre-LVAD) and after 3 months, 6 months, 1 year and long-term LVAD support. Subgroup analyses were performed according to baseline BMI <30 (Group A) or BMI >30 (Group B).

Results: preLVAD mean weight was 80.7 ± 13.5 Kg and BMI 26.1 ± 4.9 . At 3 months follow-up, mean weight significantly decreased to 77.2 ± 13.6 ($p < 0.0001$) and BMI to 25 ± 4.5 ($p < 0.001$). The BMI drop was more prominent in Group A (-0.7 ± 2.3 , $p < 0.015$) than Group B (-2.4 ± 3.5 , $p < 0.029$) (A vs B: $p < 0.045$). 6 months after implant both mean weight and BMI were back to baseline levels ($p < 0.8$ and $p < 0.7$). At that moment, Group A was stable compared to baseline ($p > 0.4$), while group B still showed a remarkable BMI decrease of 2.1 ± 2.9 ($p < 0.04$) (A vs B: $p < 0.009$). One year and long term (910 ± 408 days) follow up showed a mean weight increase from baseline of 2.1 ± 9.1 Kg ($p < 0.009$) and 4.6 ± 9 Kg ($p < 0.003$) respectively, with corresponding BMI rise of 1.1 ± 3.2 ($p < 0.027$) and 1.6 ± 3.2 ($p < 0.003$). At 1 year, BMI had increase in Group A by 1.5 ± 3.4 ($p > 0.013$) while those with baseline BMI >30 only showed a decrease of 0.6 ± 1 from preLVAD value ($p > 0.1$) (A vs B: $p > 0.004$). Group A BMI at long term follow up again showed a significant rise from baseline, 1.9 ± 3 ($p < 0.0001$), whereas Group B BMI remained similar to preLVAD level ($p = 1$). The proportion of Group A patients that increased their BMI over 30 while on LVAD support at 6 months, 1 year and long term follow up, was 4%, 6% and 12% respectively. Among Group B patients, only 15% achieved a BMI <30 at their last follow up.

Conclusions: weight and BMI significantly decrease 3 months postLVAD implantation but progressively increase afterwards exceeding preLVAD levels at 1 year. A significant proportion of LVAD patients with normal weight reach the obesity range during follow up. Those with a baseline BMI >30 experience a higher initial weight loss and lower long term BMI increase. However, the "bridge to weight loss" strategy is frequently unsuccessful despite of long support

P366

Analysis of echocardiographic predicting parameters of right ventricular function in patients with LVAD implantation

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Background: There is still an important risk of RV worsening in short term after LVAD device implantation (9 - 44% in latest publications). The aim of our study was to analyze the echocardiographic predicting parameters of RV failure described in last years by reason authors and compare them with our, Zabrze data.

Material and Method: Our group consisted of first 21 patients with mean age 47,6 years and mean LVEF 16,9%, LV diameter 71,3mm and diastolic volume 306,3ml, with successfully implanted continuous flow pumps (16 Heart Ware and 5 Heart-Mate II). All patients meet in preoperative TTE most of parameters which

confirmed the preserved RV function as FAC (fractional area change) with normal value >20%, TAPSE (tricuspid annulus plane systolic excursion) higher than 15mm, RV diameter < 50mm, RV/LV (right-to-left ventricle) ratio in 4ch view below 0,73 - 0,75 in reson publications, RVSP (right ventricle systolic pressure) lower than 37mmHg and degree of TR (tricuspid regurgitation). Postoperatively hemodynamic parameters were measured every 2 hours during first 12 hours by using Swan-Ganz catheter and thermodilution method for assessing CI parameter. We also measured CVP and PAM. The parameters were mentioned as CI 1, CI 2 and so on.

Results: The mean preoperative value of FAC was 29,23 (21 - 44%), TAPSE 16,7 (11 - 23mm) in 2 patients below 15mm, RV diameter 49,3 (42 - 60mm) in 7 patients above borderline 50mm, RV/LV ratio 0,62 (0,45 - 0,73) in 2 patients 0,72 and 0,73, RVSP 44,7 (33 - 58mmHg) and TR 2/3 degree (0 - 4) in 2 patients 4th degree. 20 patients alived postoperative and in-hospital period with evident improve of haemodynamic parameters, functional capacity and drop of NT-proBNP level. 1 patient died because of multiorgan disfunction. Post implantation all patients had adequate CI and not elevated CVP and PAM. Only RV/LV ratio correlates significantly with CI, CVP and PAM in first 3 measuring points

Conclusions: Despite borderline preoperative echocardiographic parameters of RV in a few of 21 cases all patients meet most of criterias prognosed the good pooperative RV function and it was confirmed by patient's pooperative status. In our observation not TAPSE or the RV diameter alone (larger than 50mm in 53,8% of patients) but combination of parameters, especially the RV/LV ratio established by Kukucka at all as 0,72, Kormos (0,73) or Matthews (0,74) and Vivo as 0,75 strongly correlates with preserved postoperative RV function and our data.

P367

Exercise tests by a patient supported with the carmat bioprosthetic heart

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Introduction: The electro-hydraulically driven Carmat total artificial heart (TAH) is a single-unit biventricular system designed for long-term use as an alternative to heart transplant. It contains bioprosthetic blood-contacting surfaces with 4 biological valves and produces 3-9 l/min pulsatile flow. Pressure sensors located inside the ventricles of the TAH provide an indication of pre-charge and post-charge pressures in the patient. We report the first results of exercise tests done by a patient supported with this recently introduced device.

Methods and materials: A 68 year-old male patient (180cm, 76kg) with irreversible biventricular heart failure and not eligible for transplantation was implanted with the Carmat TAH. During six-minutes walk tests with fixed cardiac output, we analyzed intraventricular right diastolic pressure (IRDP) and intraventricular left systolic pressure (ILSP). A bicycle exercise test performed at 2 months post-implant was analyzed also.

Results: The patient started mobilizing in the first week post-operatively. The device cardiac output was 5.1 l/min at the first month and 5.4 l/min thereafter. Six-minute walk distances at 1, 2, 3 and 4 months improved gradually to 228, 298, 360 and 394 meters respectively. The IRDP increased from -6mmHg (median; range -10 to -2) at baseline to 7.5 (5-10) mmHg during the tests and restored to pre-test values after 4.5 (2-8) minutes. The ILSP increased from 144.5 (140-145) mmHg to 152 (143-165) mmHg during the test and to 172 (140-180) mmHg after two minutes; return to pre-test values took 22.5 (17-30) minutes. The bicycle exercise test at 2 months post-implant showed an anerobic threshold 7 mL/min/Kg reached after 8 minutes, a VO₂ peak 10mL/min/Kg, a respiratory exchange ratio 1.14, a VE/VCO₂ slope 51, a ventilatory reserve 32% and a maximum charge of 49W at 10 minutes. During this exercise test, the IRDP increased from 8 to 10 mmHg, returning to 8 mmHg 15 minutes after resting. The ILSP increased from 140 to 180 mmHg at maximum effort and returned to 140 mmHg 25 minutes after resting.

Conclusion: Exercise tests performed by a patient supported with the Carmat TAH with fixed pump output were well tolerated. The intraventricular right diastolic and left systolic pressures rose during the tests, indicating a compensatory physiological vascular resistance increase in response to higher oxygen demand with fixed cardiac output. The next generation device-operating software for the Carmat TAH includes self-regulating algorithms allowing adaptation of flow according to the patient's needs.

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An analysis implementation of ventricular assistant device in Brazil

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Introduction: Heart failure is a major problem associated with high mortality and morbidity. Medical therapy and some devices, as resynchronization therapy, have improved the survival of many heart failure patients. A significant group of patient remains, despite optimized medical therapy, unable to live an ordinary life with a very poor prognosis. For the patients with advanced heart failure, not responding the medical therapy, heart transplantation is the treatment of choice. However, this is a scarce resource, limited by low donor available globally. Left ventricular assist device is rapidly evolving and is being increasingly used to treat patients with advanced heart failure.

Objectives: The purpose of this study is to describe the initial results of the implementation of a Ventricular Assisted Device in Brazil. **Methodology:** The data were collected in the archives from all patients that received any ventricular assist device in a quaternary cardiology hospital in Brazil from January to November 2014.

Results: Eighteen devices were implanted during the period of analysis, 61% were men, and seventeen were from Brazil and one was from England. The primary diagnosis at admission was acute myocardial infarction. The median time of hospitalization was 120 days, and the general hospital survival was one-third. The temporary support used was extracorporeal mechanical oxygenation (30%) and Centrimag (70%). Half of the patients that survived the acute illness went to heart transplantation, and the other half was implanted Heartware.

Discussion: The survival of the studied population is almost the same of those described in the literature. As a pioneering implementation, it needs training of all of the stakeholders, including nurses, physiotherapists, and physicians. One of the challenges consists of the new introduction to the medical group of some old diseases, as an example: coagulation disorders and sepsis.

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Gastrointestinal bleeding and left ventricular assist devices: pre-operative risk factors and outcome in a minority population

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Background: Continuous flow left ventricular assist devices (CF-LVADs) have become a valuable therapeutic option to a growing population with end-stage systolic heart failure. Gastrointestinal bleeding (GIB) is among the most common adverse events after device implantation. The risk factors for GIB, timing of bleeding events and outcomes among minority populations remain unclear.

Methods: Between September 2009 and June 2014, 51 consecutive advanced heart failure patients underwent CF-LVAD implantation at a single tertiary care center. Electronic medical records were reviewed to determine demographic characteristics, co-morbidities and GIB episodes. Univariate and multivariate regression analyses were conducted to identify pre-operative risk factors.

Results: Seventeen of the 51 patients (33.3%) had at least one episode of GIB. Recurrent GIB was present in 13.7% of the population. African Americans represented the majority (n=29, 56.9%) followed by white (n=13, 25.5%). There was no statistical difference among races and incidence of GIB (p=0.873). Body mass index was significantly lower in the GIB group (30.04 ± 8.5 vs 31.16 ± 5.07, p=0.032). Patients with peripheral artery disease (30% vs 70%, p=0.051) had less episodes of GIB. There were no deaths attributed to GIB.

Conclusions: GIB is a frequent cause of morbidity for patients with CF-LVAD support although it does not impact survival. Race does not influence the rate of GIB, whereas peripheral artery disease and body mass index may be protective. Larger epidemiological studies will be required to confirm such associations and better stratify bleeding risk.

DISEASE MANAGEMENT PROGRAMMES

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Different management of patients admitted with loss of consciousness between different clinical services of a central hospital

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Loss of consciousness (LC) had several differential diagnoses, including syncope. The precise etiology requires expertise evaluation by different medical specialties.

Methods: Retrospective analysis of patients hospitalized for LC in different clinical services of a central hospital, after initial evaluation in the emergency room, during 2013 (12 months).

Results: There were admitted 168 patients, with a mean of 71 ± 16 years and 61% were male. There were admitted 58% in the Internal Medicine service (IM); 30% in Cardiology (C), 5% in Neurology (N), 4% in Surgery (S) and 3% in Intensive Care unit (ICU). Patients admitted in the IM were older (mean age 78 ± 5 years) than in C (70 ± 11 years) or in N (41 ± 04 years). There were 23% diabetic patients, 62% hypertensive, 34% with heart disease, 15% had neurological disease. 43% were medicated with vasoactive drugs.

The exams most frequently performed in IM were electrocardiogram (ECG) (97%), brain CT (74%) and echocardiography (TTE) (68%), 24- Holter monitoring (33%) and electroencephalogram (EEG) (32%). The most common diagnosis was reflex syncope (31%), non-syncopal LC (28%), unexplained LC (21%) and cardiogenic syncope (19%). In C, 47% patients admitted had heart disease. All patients performed ECG, 90% ETT, 22% electrophysiological study and 31% cardiac catheterization. The most common diagnosis was cardiogenic syncope (69%). In N, 13% of patients had neurological pathology. Although the ECG examination has been performed in all patients and ETT in 50% patients, the neurological examination was much more common than in the other services, brain CT (88%), EEG (75%) and brain MRI (38%). The most frequently diagnosed was non-syncopal LC (50%), although the majority of patients with LC attributed to cerebrovascular disease having been hospitalized in the Medicine (65%) and not in Neurology (12%); 38% had reflex syncope and 13% unexplained syncope. In S there were similar number of patients with reflex syncope, LC (non- syncope) and unexplained syncope (29%), none with cardiogenic syncope.

Conclusion: Initial clinical evaluation in the emergency room often defined the correct hospitalization unit. There was however a diversity of specialties that evaluate patients with LC. For this, is essential to implement ESC-based guidelines protocols in diagnostic evaluation in the emergency and all units to achieved better yields in workup exams and to reduce the unexplained causes of LC at discharge.

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Seamless heart failure care program promotes referral of patients to primary care

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Purpose: In 2014 a heart failure program using several protocols has started in Netherlands connecting care givers from primary, secondary and tertiary care to provide seamless heart failure care. One of the goals of the program was to transfer care given by secondary and tertiary caregivers to the primary care. Those patients eligible for heart failure care given by the general practitioner were predefined and included the patients who had complete recovery of myocardial function, patients with stable heart failure without comorbidity and those patients with endstage heart failure.

Methods: Data were collected retrospectively from 2013 about alle patients out of the region of Alphen a/d Rijn admitted with heart failure in an Hospital. Using our seamless heart failure program we investigated which of these HF patients were referred to their GP's for their heart failure care according to predefined criteria. These data were compared to data collected from 2000 until 2012.

Results: In the years 2000 until 2012 before starting our seamless heart failure program 209 patients in total were referred back to the GP. From the 162 admitted patients in 2013 43 patients died. 27 patients were referred back to primary care for the following reasons. Six because of complete recovery of myocardial function, 2 because of stable heart failure without comorbidity and 8 patients because of end stage heart failure. Another 9 patients were referred to the GP because of frailty or at their own request.

Conclusion: Starting a seamless heart failure program in the Alphen a/d Rijn region resulted in a substantial increase in the number of patients being referred to primary care for heart failure care. Significant part of this group entails endstage heart failure patients. This transfer of care request both training of GP's in delivering this care as well as being available for back-up of secondary care in case of problems and or questions.

Expectations are that this transfer of care will expand and future data might show effects of this program on mortality, morbidity, quality of life and costeffectiveness. Data will be collected prospectively.

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Baseline measurements of a dutch seamless heart failure care program

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Purpose: In 2014 a Heart failure program has started connecting care givers from primary, secondary and tertiary care in the region Alphen a/d Rijn to obtain seamless heartfailure care. To get baseline information about the way care was given before starting this program, information about patient contact before their admission in hospital in 2013 was collected from general practitioners and secondary care givers in this region.

Methods: From all patients originating from the Alphen a/d Rijn region and being admitted with heart failure at the Rijnland hospital Leiderdorp in 2013, information was collected from the heart failure outpatient clinic and their GP's. This included data about contact with the GP or GP assistant in 2013 and additional investigations done like recording of EKG or (NT-pro)BNP measurements.

Results: Totally 182 admissions for heart failure including 20 re-admissions were recorded in the Alphen a/d Rijn region. 84 patients were newly diagnosed with heart failure, 50 admitted patients were known at the heart failure clinic, 49 patients were known with heart failure elsewhere. Of 53 out of 84 new heart failure patients data were collected from the GP. 5/53 did not have any contact with the GP before admission, 48/53 did contact their GP before admission. Number of contact ranged from 0-18. Totally in 27 patients either EKG(10), (NT-pro)BNP(17) or both(5) were recorded. 27 out of 50 patients known at the heart failure outpatient clinic contacted the heart failure nurse before admission. Of the remaining 23 patients 12 patients contacted their GP. Largest number of contacts of this group involved end stage heart failure patients.

Conclusion: Before the start of our heart failure program more than half of all patients were admitted with newly diagnosed heart failure. Relatively many patients had contacted their GP before admission for heart failure. In a small number of patients either EKG or (NT-pro)BNP was recorded as a way to diagnose heart failure. Furthermore, of those patients known at the heart failure outpatients clinic, a significant number also contacted the GP particularly in the end stage of heart failure. In the near future our heart failure program might change the way in which care for HF patients is shared between all lines of care which might lead to a decrease in heart failure admission particularly for those patients with newly diagnosed heart failure. Data will be prospectively collected.

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The new method of programming individualized physical rehabilitation for heart failure patients

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Purpose: to estimate efficiency of individualized approach to the development of more precisely physical rehabilitation program in HF patients with III FC.

Methods: We evaluated 48 hospitalized patients 40-68 years old, mean age 55+/-1.8, 33 men, with HF NYHA class III, ejection fraction (LVEF) 37,8+/-0,3%. All patients performed a symptom-limited cardiopulmonary exercise test (CPET) on a treadmill with gas exchange system "Oxycon Pro" initially and after 6 months. We measured oxygen uptake at lactate threshold (VO₂LT), pH-threshold (VO₂pH-T) and at exercise peak (VO₂peak). The cubital venous catheter was installed in all subjects before exercise test. Blood samples were taken at baseline and at 1-minute intervals during test. PH, lactate and HCO₃⁻ concentration were estimated using analyzer i-STAT, cartridge CG4 (Abbot, USA). LT and pH-T were determined by changes in pH and lactate level. 48 patients were divided into two groups: 38 patients of main group (MG), who underwent physical rehabilitation program (PRP) based on lactate threshold and pH-threshold, that characterized the biological reserves of adaptation to physical activity; and 10 HF patients control group (CG), who performed usual PRP. HF patients in both groups were matched in age, sex, LVEF and BMI.

Results: At the study beginning CPET Results: VO₂LT, VO₂pH-T and VO₂peak were similar in MG and CG, 8.7 of +/- 0.5, 11.0+/-0.8, 13.5+/-0.9 ml/min/kg and 8.9 +/- 0.9, 11.5+/-1.3, 13.6+/-1.2 ml/min/kg, respectively (pVO₂LTMG-CG=0,08, pVO₂pH-TMG-CG=0,07, pVO₂peakMG-CG=0,09). First three month patients of MG were trained 40 minutes every day on treadmill with exercise intensity that was observed at LT, every month after control CPET exercise intensity was increased gradually. Other three month patients of MG were trained 35 minutes every day on treadmill with exercise intensity that was observed between LT and pH-T, every month after control CPET exercise intensity was increased gradually. Patients of CG were made training walking at 40% of VO₂peak three times a week. After 6 months VO₂LT, VO₂pH-T and VO₂peak were better in MG than in CG: 10.1 of +/- 0.6, 12.8+/-0.5, 16.7+/-1.1 ml/min/kg and 9.3 +/- 1.0, 12.1+/-1.1, 14.6+/-1.2 ml/min/kg, respectively (pVO₂LTMG-CG<0,01, pVO₂pH-TMG-CG<0,05, pVO₂peak MG-CG<0,01).

Conclusions: physical rehabilitation program, calculated based on individualized approach of exercise physiological stages, improves the biological reserves of adaptation to physical activity and exercise capacity in HF patients with III NYHA class more than usual PRP.

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30-day re-hospitalization reduction with a specific outpatient consultation that supports post-discharge heart failure patients

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Background: Heart failure (HF) is the main cause of hospital admissions in patients over 65 years in developed countries. The incidence of re-admissions in the first 30 days after being discharged with the diagnosis of HF is 20-30%, which accounts for a significant increase in health budget. Several hospital strategies to lower re-admission rates have been developed. However, the magnitude of these strategies has been rather modest, with an absolute reduction around 2-3% (relative 10-15%). Moreover, those patients routinely not attended in the Cardiology Department and followed in specific Units show the highest rate of re-admissions.

Objectives: 1) To reduce 30-day readmission rate in those patients not routinely attended in the Cardiology Department. 2) To facilitate the transition from hospital care to Primary Care physicians (GPs).

Methods: Those patients admitted into the hospital due to HF, mainly in the setting of Internal Medicine or Geriatric Unit wards or other non-Cardiology wards were referred to a specific 30-day consultation. Risk of readmission was calculated with the CORE HF risk readmission score (Yale) at first visit. Patients were attended by specialized HF nurses and physicians, both GPs and geriatricians, within 3-5 days after discharge. An educational intervention was performed by nurses and a visually friendly drug prescription sheet was supplied. During the 30 day period patients were visited as many times as necessary, and then were referred to the GP for a close visit via e-notification together with a written medical report and the drug prescription sheet. IV diuretic treatment was administered if required.

Results: During the first 9 months of the consult 141 patients have been attended (mean age 81.5 ± 9.6 years, 25% were ≥88 years-old; 58.2% women). Mean calculated readmission risk was 26.3% ± 5.1 and 28% of them had a risk ≥30%. Mean time to first visit from discharge was 4.9 ± 4.8 days. Mean number of performed visits was 3.9 ± 2. HF 30-day readmission rate was 9.9% (6.4% through the Emergency Department and 3.5% directly from the consult). All-cause readmission rate was 16.3%. That represents a relative reduction of 38% and an absolute reduction of 10% on what was estimated with the CORE score.

Conclusions: A specific consultation that supports post-discharge HF patients achieved near to 40% relative reduction of all-cause readmissions at 30 days in an elderly population. Readmission due to HF was only 9.9%.

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Inpatient and outpatient heart failure management: evidence from the russian hospital heart failure registry (RUS-HFR)

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Purpose: The aim of RUS-HFR was to obtain real-life contemporary analysis of the HF management and 1.5-year outcomes of inpatients with chronic systolic HF in Russian clinical practice.

Methods and Results: The RUS-HFR is a prospective, multicentre, observational study conducted in 3 Centers. Inclusion criteria were NYHA I-IV, EF≤40%, age 18-75 years. From Oct 2012 to Jan 2014, 524 patients were enrolled. CRT and ICD have been previously implanted with 4.5% and 5.2% of patients. RAS blockers, β-AB, and MRAs were used in 82.3-87.3%, 76.3-95.8%, and 65.9-81.1% of patients. The rate of prescription of these drugs prior admission was: RAS blockers 12.6-58.7%; β-AB 11.1-70.7%; MRAs 4.4-53.3%. Diuretics prior to admission were not taken in 55%, 23%, 24% of patient with NYHA II, III and IV, respectively. 80.7-94.6% of patients were on diuretics at hospital discharge. The median duration of hospital stay for HF decompensation was 18 days (interquartile range 13-26). 100% patients were informed about Internet resources in Russian. Indications for implantation of ICD and/or CRT were determined at 21.2% and 4.6% of CHF patients. Indications for heart transplantation were identified to 17 patients. Dose reduction of basic drugs recommended for the treatment of HF was observed after 1.5 years. Ambulatory patients with HF were under the supervision of a cardiologist and therapist in the 43-72% and 15-42% cases, respectively, and 7-17.7% of patients did not visit a doctor at all. The all-cause death and hospitalization for HF decompensation within 1.5 years were 11.6-26.2% and 16.1-47.3%, respectively.

Conclusion: The RUS-HFR showed that the proportion of patients receiving RAS blockers, β-AB and MRAs is comparable with European registers. The mortality and re-hospitalization in 1.5 years due to decompensated HF in Russia remained high. The main drugs recommended for outpatient HF were used insufficiently. High-tech methods of treatment in patients with HF NYHA II-IV were not often enough recommended. The greatest number of inconsistencies recommendations for obligatory drug therapy was detected in patients with HF NYHA II. Oral diuretics were not prescribed for the clinical manifestations of HF in 23-55% of cases, which is unacceptable. Outpatient CHF management in Russia still present the most problematic item depending on many factors, one of the way to improve is to organize network of HF clinics throughout the country.

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Prevention of exacerbation of chronic heart failure: psychological aspects

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Taking care of psychological support is essential during the management of patients with severe heart failure (HF). Low quality of life (QoL) and prevalence of negative emotions have impact on patients' clinical status and reduce their adherence to following the recommendations of physician which is one of the most reasons of HF decompensation. Really important thing to remember of is psychological state of the relatives of patient. It is important to keep in mind that the patient is part of a family who is affected by the HF experience and related worse psycho-emotional status and QoL. Since family support can positively impact the patient's clinical status, QoL, depression, providing care to families should not be overlooked.

Objectives: to evaluate factors related to psycho-emotional status and QoL in patients with chronic HF.

Methods: a total of 248 patients aged 69 (65-74) yrs with stable NYHA FC II- IV HF were given the Minnesota Living with Heart Failure questionnaire and Hospital Anxiety and Depression Scale (HADS). Depression was defined as a score on the HADS of 11 and more.

Results: the mediana of QoL was 30 (20-44), in severe HF patients - 31,5 (22-48). Main factors of low QoL were clinical congestion symptoms leading to recreational pastimes or hobbies difficult and making patients feel they are a burden to their family or friends; polypragmasia ($r=0,24$, $p=0,014$) or low functional capacity ($r=-0,34$, $p<0,001$). A total of 22,8% HF patients scored as depressed. Depressed patients scored significantly worse than non-depressed patients on all components of the questionnaire measuring QoL and tended to have more severe HF symptoms ($r=-0,26$, $p=0,004$). Decline in activities of daily living, dissatisfaction with affairs and occupations earlier bringing pleasure to patients, lack of support and understanding from patient's relatives were associated with HF progression and worse psycho-emotional status. Patients with more severe HF often had absence of the family and emotional support compared with mild HF ($p=0,008$). There was an relationship between the loneliness of the patient and disease severity ($p=0,009$, $r=0,16$).

Conclusions: keeping the family informed about the patient's disease and depression is important. Patient's relatives should receive additional teaching and support from doctors or nurses about care management ways to reduce patient's isolation, helping family opens channels of communication and identify the strengths and resources to provide family care, which may indirectly lead to an improvement in the patient's psycho-emotional status and QoL.

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Re-admission patterns in patients following first admission for heart failure: heart failure with preserved ejection fraction as compared with heart failure with reduced ejection fraction

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Purpose: Despite significant advances in heart failure therapies, re-admission rates following hospitalisation for heart failure remain high. The objective of this study was to document re-admission patterns of patients with HF-pEF and HF-rEF managed in a dedicated disease management programme.

Methods: Patients admitted to a University Hospital between November 1998 & April 2014 with a diagnosis of decompensated heart failure were included in this study. All patients were entered into a disease management programme. We

identified the re-admission pattern over the 8 month period following the index hospitalisation.

Results: There were 1266 (58.6% male, mean age 72.2yrs) index hospitalisations for heart failure (410 (32.3%) HFpEF, 856 (67.7%) HFrEF). All-cause readmission rates at 0-2, 2-4, 4-6 and 6-8 months are shown in table 1. The readmission rates for recurrent heart failure at 0-2, 2-4, 4-6 and 6-8 months were 7.3%, 3.1%, 2.1% and 3%. In the first two months following discharge, 102 patients (102/410, 24.8%) with HFpEF and 191 patients (191/856, 22.3%) with HFrEF were readmitted. All-cause and HF readmission rates at 0-2, 2-4, 4-6 and 6-8 months were similar in both groups.

Conclusions: Nearly one quarter of patients discharged following an index HF hospitalisation require early readmission. A significant number of admissions are due to noncardiovascular causes. HFpEF and HFrEF demonstrate similar re-admission patterns.

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Clinical impact of a multidisciplinary heart failure program in colombia

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Heart Failure is a major cause of morbidity and mortality worldwide. Multidisciplinary Heart failure programs are available in Europe and North America, however they had not been implemented in many countries of Latino America despite of the increase in the prevalence of this disease.

Objective: to evaluate the impact of a multidisciplinary heart failure program in functional class, emergency service visits and readmissions to the hospital in a population of patients treated in a multidisciplinary heart failure program in Colombia using the resources of our health care system.

Methodology: a retrospective cohort study was performed. The clinical, demographic characteristics of the patients, admissions rate to the hospital, emergency room visits and the health care expenses were analyzed one year before and after they were admitted to multidisciplinary program that included cardiology consult, nurse evaluations, cardiac rehabilitation, an educational program and psychology follow up.

Results: The study included 511 patients, with a mean age of 64 +/- 14.3 years, 58.7% were males. After 12 months of follow up an statistical significance increase in ejection fraction was found 27,4% +/-12 vs 38,72 +/- 14,4 ($p<0.005$). The NYHA functional class presents an improvement with more patients in NYHA I (20,6% vs 28,2%), the percentage of NYHA II patients were (50,7% vs 50%) and there were less patients in more advanced functional NYHA functional class (NYHA III 23,8% vs 19,8% and NYHA IV 4,9% vs 2%). The emergency room visits decreased in 29.3%, Admissions to the hospital decreased in 66,8% (Mean, SD: 0.96 +/- 1,01 vs 0.51 +/- 0.83 $p<0.000$) and the length of stay decrease in 37.5% (Mean and SD 5.09 days +/- 9.2 vs 3.1 days +/- 7.4 $p<0.003$). Total mortality was 4% and only 2% of the patients required a heart transplant. The costs driven by admissions to the hospital and emergency room visits decrease in a 50% after the patients were admitted in the program.

Conclusion: the multidisciplinary follow up in heart failure program is feasible in Colombia with our health care system resources, it improves the functional class, the ejection fraction and decreases admissions to the hospital and emergency room visits with less cost to the health care system. This experience can be reply in many other countries of Latino-America

Table 1: 61497

Heart failure admission per patient during 8 months after discharge by patient type				
Time after discharge	0 - 2 months	2 - 4 months	4 - 6 months	6 - 8 months
All patients	92/1266 (7.2%)	38/1188 (3.2%)	24/1106 (2.2%)	31/1030 (3%)
HF-pEF	28/410 (6.8%)	13/381 (3.4%)	16/354 (4.5%)	12/327 (3.6%)
HF-rEF	64/856 (7.4%)	25/807 (3%)	8/752 (1%)	19/703 (2.7%)
Admission per patient during 8 months after discharge by admission type				
Time after discharge	0 - 2 months (n = 1266)	2 - 4 months (n = 1188)	4 - 6 months (n = 1106)	6 - 8 months (n = 1030)
All admissions	293 (23%)	153 (12.8%)	106 (9.5%)	109 (10.5%)
Heart Failure	92 (7.2%)	38 (3.2%)	24 (2.2%)	31 (3%)
Cardiovascular	50 (3.8%)	26 (2.1%)	18 (1.6%)	13 (1.2%)
Non-cardiovascular	151 (12%)	89 (7.5%)	64 (5.7%)	65 (6.3%)

Hospital readmissions in the 8 months following discharge by patient type and admission type

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Burden and depressive symptoms associated with adult-child caregiving for individuals with heart failure

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Purpose: The primary purpose of this study was to investigate adult-child caregiver burden in heart failure (HF) patients. Secondary purpose of the study was to identify the possible influencing factors for caregiver burden and depressive symptoms in a young adult-child caregiver group.

Methods: A total of 138 adult-child caregivers and 138 patients with HF participated in this study. Caregivers' burden, depressive symptoms, and anxiety levels were assessed by using Zarit Caregiver Burden Scale (ZCBS), Beck Depression Inventory, and State-Trait Anxiety Inventory (STAI), respectively.

Results: Mean age of the patients was 66.36 ± 12.71 (63 were male). Mean ejection fraction was 36.6%. Approximately two-thirds of the patients were in NYHA classes III and IV. Mean age of adult-child caregivers was 37.13 ± 11.57 years. Majority of adult-child caregivers were female (65.2%). Mean caregiver time was 44.36 ± 34.79 months. All adult-child caregivers had severe caregiving burden (ZCBS ≥ 17) and female caregivers had significantly higher ZCBS scores compared to male caregivers. One-third (34.8%) of the adult-child caregivers had at least mild depressive symptoms (BDI ≥ 14). There was no significant difference in terms of severity of depressive symptoms between male and female adult-child caregivers. On the other hand, female adult-child caregivers had significantly higher anxiety scores on both STAI-1 and STAI-2 subscales. Adult-child caregivers with primary educational level (≤ 8 years) have significantly higher levels of caregiver burden compared to adult-child caregivers with educational level > 8 years (40.37 ± 7.46 versus 34.09 ± 6.86 , $p = 0.001$). There were positive correlations between caregivers burden and caregiving time period ($r = 0.327$, $p < 0.001$). There were significantly higher levels of caregiver burden in adult-child caregivers of patients with longer (> 36 months) caregiving time period ($p = 0.001$). There was positive correlation between depressive scores of caregivers and caregiver burden ($r = 0.410$, $p < 0.001$). We detected negative correlation between educational levels of caregivers and perceived caregiver burden ($r = -0.31$, $p < 0.001$). Linear regression analysis revealed that age, socioeconomic level, and marital status of HF patients were affecting factors for depressive symptoms in adult-child caregivers. Among adult-child caregiver characteristics, gender, marital status, and ZCBS scores seem to influence the depression in caregivers.

Conclusions: The study findings suggest significant levels of burden and depressive symptoms even in adult-child caregivers of HF patients.

DIURETICS AND FLUID STATUS MANAGEMENT

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Experience with tolvaptan in patients with chronic heart failure

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Purpose: our aim is to describe the experience with the compassionate use of tolvaptan in patients with chronic heart failure and hyponatremia resistant to conventional treatment.

Methods: from January 2010 to December 2014 we managed tolvaptan to 44 patients admitted for congestive heart failure and, in addition, hyponatremia resistant to conventional treatment. We ask each patient a special permit for administration because our country is not approved its indication in patients with heart failure.

Results: the mean age was 61.8 ± 13.1 years, and 68% were men, with an average of admissions for heart failure during last year of 1.47 ± 1.5 . Patients presented different etiologies: 25% dilated cardiomyopathy, 22% ischemic heart disease, 27% valvular heart disease, 15% previously heart trasplant, 7% hypertrophic heart disease and 2% congenital heart disease. Mean LVEF was 41.7 ± 20.1 . Most patients were treated with high dose diuretic drugs: 95% with furosemide > 60 mg/day, 68% with spironolactone or eplerenone, and 59% with thiazides diuretics. In addition 47% were treated with ACE inhibitors or Angiotensin II receptor antagonists and 38% with beta blockers. The starting dose of tolvaptan was 15 mg/day in 59% patients, 30 mg/day in 41% and 60 mg/day in the rest. We observed that there was a significant increase in serum sodium values (mean 122.8 ± 5 mEq/L before tolvaptan vs 131.7 ± 6 mEq/L after, $p < 0.001$) with no significant changes in renal function (creatinine level 1.79 ± 1 mg/dL vs 1.89 ± 1 mg/dL, $p = 0.55$; glomerular filtration by MDRD: 50.7 ± 31 mL/min vs 46.8 ± 33 mL/min,

$p = 0.3$) or serum potassium values (4.3 ± 1 mEq/L vs 4.1 ± 1 mEq/L, $p = 0.16$). Furthermore, we observed a significant decrease in weight between admission and discharge (73.1 ± 13.1 kg vs 69.56 ± 11.7 kg, $p = 0.001$) and an increase in urine output (2151.5 ± 105 mL before tolvaptan vs 3113.6 ± 351 mL at 24 hours later, $p = 0.005$; or vs 3261.2 ± 388 mL at 48 hours later, $p = 0.005$). The mean time to achieve eunatremia was 15.8 ± 14 days and until hospital discharge was 10.5 ± 6 days (some patients continues treatment with tolvaptan after hospital discharge). We observed hospital mortality in 9 patients (20.5%) and 18 patients died in the follow-up (40.9%). Finally, we observed readmission for heart failure within 30 days in 10 patients (22.7%).

Conclusions: use of tolvaptan is an alternative because improves serum sodium values and urine output without worsening renal function, in patients with advanced heart failure that needing treatment with high dose of diuretics.

P381

The combination therapy of mineral corticoid receptor antagonists and vasopressin receptor antagonist is useful for hospitalized heart failure patients

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Purpose: Vasopressin receptor antagonists represent an interesting class of drugs for the treatment of hyponatremia and congestion. Several studies have investigated the efficacy of tolvaptan for heart failure (HF), and tolvaptan is effective for maintaining cardiac output and preventing worsening renal function. But there are no data about the interaction of tolvaptan with other therapeutic drugs for HF. We assessed the interaction of tolvaptan with those drugs and examined an effective use of tolvaptan.

Methods: We investigated 133 hospitalized HF patients who had taken tolvaptan for congestion, and clinical data including other concomitant drugs just before and after administration of tolvaptan were obtained. Changes in urine volume (ΔUV) were observed during next 24 hours after tolvaptan treatment on the first day. We analyzed the correlation between ΔUV and other clinical factors by multivariate analysis.

Results: Baseline patients characteristics were as below; mean age, 75.1 ± 13.5 years old; male, 82 (61.7%); mean dose of tolvaptan, 5.5 ± 3.0 mg/day; mean systolic and diastolic blood pressure, 111 ± 21 and 57 ± 10 mmHg; mean heart rate, 76 ± 15 bpm; mean serum Cre level, 1.6 ± 1.4 mg/dl; mean serum Sodium level, 137 ± 5.9 mEq/L; mean serum and urine osmolality, 289 ± 21 and 387 ± 142 mOsm/L; mean left ventricular ejection fraction, $42.4 \pm 16.1\%$. Urine volume were significantly increased by administration of tolvaptan (1287 ± 788 to 1610 ± 992 ml/day, $p < 0.01$) and patient's symptoms were improved. ΔUV were correlated with usage of mineral corticoid receptor antagonists ($p < 0.05$) and inotropic agents ($p < 0.01$), and were not correlated with usage of any other concomitant drugs or baseline clinical characteristics of patients. In multivariate analysis, both mineral corticoid receptor antagonists and inotropic agents were correlated with the increase of urine volume independently ($p < 0.01$ and $p < 0.01$).

Conclusions: Mineral corticoid receptor antagonists and inotropic agents have an important role on efficacy of tolvaptan. The combination therapy of mineral corticoid receptor antagonists and tolvaptan is useful strategy for decongestion of hospitalized heart failure patients.

P382

Quality of life in advanced heart failure is improved by chronic intermittent renal replacement therapy

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Background: Renal replacement therapy (RRT) may be an efficient alternative method of decongestion in advanced stage heart failure patients with resistance to diuretics. However, there is not enough data concerning the impact of chronic intermittent RRT on patients' quality of life.

Patients and Methods: During the past 7 years, 58 patients in advanced heart failure with signs and symptoms of congestion and resistance to diuretics underwent chronic intermittent RRT. Resistance to diuretics was defined as congestion despite optimal medical treatment including furosemide dose ≥ 250 mg daily. Out of the 58 patients, thirty two (55%) survived for more than 6 months. These patients underwent a program of outpatient, extracorporeal fluid removal sessions (1-3 per week) aiming at maintenance of a stable body weight without signs and symptoms of congestion. Patients' quality of life and performance status were evaluated before and 6 months after RRT initiation with Minnesota Living With Heart Failure Questionnaire and NYHA class evaluation performed by attending physicians.

Results: Baseline characteristics of the 32 patients (survival for more than 6 months) were as follows: mean age 62.4 ± 10.7 years, ischemic cardiomyopathy in 31.6% as the cause of heart failure, mean left ventricular ejection fraction $27.5\% \pm 7.9\%$, mean serum creatinine 2.2 ± 1.2 mg/dl, mean hemoglobin levels 12.3 ± 4.9 g/dl,

mean serum sodium concentration 134 ± 5 mEq/L, mean systolic blood pressure 98 ± 13 mmHg, mean right atrial pressure 17 ± 6.9 mmHg, mean PCWP 23.9 ± 5.2 mmHg, mean cardiac index 1.7 ± 0.6 L/min/m², mean levels of BNP 2120 ± 1250 pg/ml and mean per os furosemide daily dose 624 ± 175 mg/24h. After 6 months of intermittent RRT, a significant improvement of quality of life (from 78 ± 14 to 41 ± 17 , $p < 0.001$) and of NYHA class (from 3.5 ± 0.5 to 2.6 ± 0.7 ($p < 0.001$)) was evident.

Conclusions: Intermittent RRT implementation in advanced stage heart failure patients results in significant improvement of their quality of life and functional capacity.

P383

Correlation between aldosterone levels and oedema score in a series of patients admitted with acutely decompensated heart failure - a preliminary investigation

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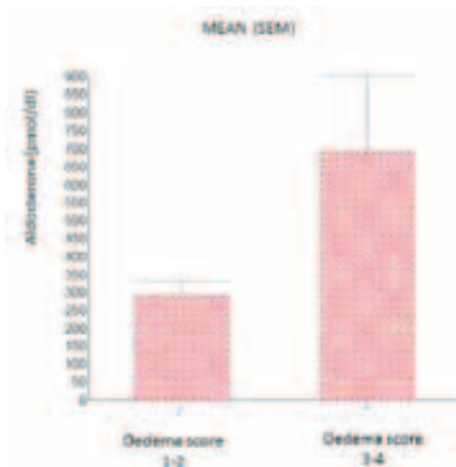
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Purpose: Patients with acutely decompensated chronic heart failure (HF) present with variable degrees of peripheral oedema. Although aldosterone is known to be elevated in patients with HF, it is not yet established if aldosterone levels affect clinical presentation. This study aimed to establish the degree of variation in baseline aldosterone and any relation between aldosterone levels and extent of peripheral oedema.

Methods: We enrolled 29 patients admitted to a cardiology ward with acutely decompensated chronic HF (Framingham criteria). Aldosterone was measured on the first morning after admission. Serum creatinine and BNP were measured simultaneously to control for renal function (eGFR) and overall severity of HF. The extent of oedema was assessed using a standard scoring system (levels 1 to 4, with 4 being the most extensive).

Results: All had moderate or severe impairment of left ventricular function and were either NYHA class 2 (n=8) or 3 (n=21). The mean age was 76 (range: 43-90). Aldosterone levels varied widely (mean: 496; range 60 - 2775 pmol/dl) and there was no correlation between aldosterone and BNP ($R^2 = 0.02$) or between aldosterone and eGFR ($R^2 = 0.13$). Aldosterone levels were higher in patients with oedema score grade 3 to 4 than in those with oedema score 1 to 2 (mean: 688 vs 289 pmol/dl; $p = 0.04$ one tailed unpaired t test). See figure.

Conclusion: Aldosterone levels vary widely in patients presenting with acutely decompensated HF, but appear to be highest in those with gross peripheral oedema. These findings need to be confirmed in a larger cohort, but may have implications for guiding diuretic therapy including targeted use of MRA's at higher doses than currently prescribed.



Aldosterone level vs oedema score

P384

Decongestion efficacy of "nitrate centered" and moderate "diuretic centered" strategies in acute decompensated heart failure (ADHF)

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Background: Our purpose was to compare effects of prolonged optimal-dosed nitrate continuous infusion plus low doses of i.v. diuretics («nitrate centered strategy» - NC) and moderate doses of i.v. diuretics plus short intermittent nitrate infusion («diuretic-centered strategy» - DC) on congestion symptoms and signs, mitral E/E' and NT-pro-BNP.

Methods: In single-blind parallel-group study pts with «wet-warm» ADHF were randomized 1:3 into 2 groups. NC group (per protocol n=19, age 59.4 ± 1.1 yrs) received optimal-dosed NTG continuous infusion ≥ 72 hrs plus low doses of i.v. diuretic (≤ 80 mg pd for furosemide), while DC group (per protocol n=48, age 62.1 ± 1.7 yrs) - moderate doses of i.v. diuretic (41-120 mg pd for furosemide) plus short intermittent (<10hrs pd, ≤ 3 days) NTG.

Endpoints were relative 24hrs body weight (BW) loss and CVP at days 4-6 (D 4-6), dyspnoe by Borg scale, mitral E/E' (TDI) and plasma NT-pro-BNP (ELISA) at D 4-6 and discharge (Dsc).

Results: Furosemide total 1st week dose in NC group was 192 ± 20.9 mg, in DC group - 396 ± 15.3 mg, duration of NTG infusion - 3.2 ± 0.3 vs 0.76 ± 0.07 days ($p < 0.001$). Symptomatic hypotension occurred in 3 (23%) and 2 (3.4%) pts, correspondingly, transfer to p.o. diuretics was in 7.3 ± 1.3 and 8.5 ± 1.7 , Dsc - in 9.6 ± 1.3 and 11.7 ± 1.5 days (both $p < 0.05$). Pts in NC and DC groups didn't differ in relative 24 hrs BW loss at D1 ($2.4 \pm 0.17\%$ vs $2.2 \pm 0.15\%$, $p > 0.05$), but at D4-6 it increased in both groups ($p < 0.01$), yet more significantly in NC ($4.8 \pm 0.32\%$ vs $3.0 \pm 0.22\%$, $p < 0.01$). Nevertheless mean BW was similar not only at admission (85.6 ± 7.4 vs 83.9 ± 6.4 kg), but at Dsc (77.4 ± 7.0 vs 76.2 ± 5.2 kg, $p > 0.05$). Other endpoints see in table.

Conclusion: In ADHF patients «nitrate centered» strategy compared to moderate intensive «diuretic centered» one is associated with more pronounced and more early clinical decongestion, as well as mitral E/E' and NT-pro-BNP lowering.

P385

Clinical significance of the combined therapy with aquaretic and natriuretic agents for fluid managements in hospitalized heart failure patients

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Background/Purpose: In hospitalized heart failure (HHF), congestion, especially organ congestion, caused by water and sodium retention, is an important therapeutic target. But the differences in aquaresis and natriuresis are not clarified. Therefore, we evaluated the effects of the combined therapy with tolvaptan (TLV) plus furosemide (F) and the F monotherapy on both extra-cellular water volume (ECW) and intra-cellular water volume (ICW) measured by multifrequency bioimpedance.

Methods: Ten HHF patients were prospectively enrolled and randomly administered TLV+F (n=5) or F (n=5). The changes in both ECW and ICW were examined by a bioimpedance device (InBody S10) for 5 days from pre-administration. The patient characteristics, urine output, and % change from baseline of ECW and ICW were compared between both therapies.

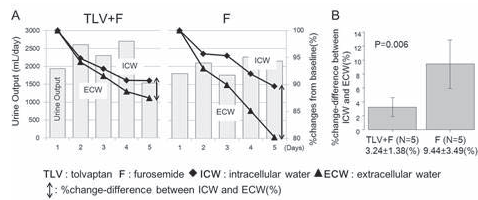
Results: The patient characteristics including age (TLV+F: 72 ± 12 , F: 71 ± 20 years), sex, etiologies, cardiac function, and comorbidities were not different. The effects of aquaresis were shown in the left of A and those of natriuresis in the right of A. The balances of removing excess ECW and ICW were markedly different between TLV+F and F (B in the figure), although the changes in body weight were not different between both therapies (T+F: 5.61 ± 3.74 vs F: 5.00 ± 2.36 kg, $P = 0.766$).

Conclusion: The present study demonstrated that a dual therapies with aquaretic and natriuretic agents were effective to remove equally excess ECW and ICW,

Groups	CVP, M \pm m, mm H ₂ O			Dyspnoe, M \pm m (Borg)			Mitral E/E'			NT-pro-BNP, M \pm m, pg/ml		
	D1	D4-6		D1	D4-6	Dsc	D1	D4-6	Dsc	D1	D4-6	Dsc
NC	194 \pm 14,7	78 \pm 5,28**#		7,8 \pm 0,4	4,1 \pm 0,25***#	2,2 \pm 0,13***##	19,6 \pm 1,85	16,8 \pm 1,27***##	14,5 \pm 1,2***##	1238 \pm 342	871 \pm 244**#	747 \pm 128**#
DC	186 \pm 12,9	97 \pm 5,89**		7,1 \pm 0,36	5,23 \pm 0,3**	2,8 \pm 0,17***	20,1 \pm 1,56	19,2 \pm 1,48	17,7 \pm 1,25*	1172 \pm 304	1061 \pm 271	871 \pm 249**

*- $p < 0,05$, **- $p < 0,01$ compared to D1; #- $p < 0,05$, ##- $p < 0,01$ compared to Group DC

suggesting that additional TLV administration might be more effective for organ decongestion compared with F monotherapy.



figure

P386

Survival following ultrafiltration in patients with diuretic-resistant decompensated heart failure

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Purpose: Patients with diuretic-resistant acute decompensated heart failure (DR-ADHF) have a poor prognosis. Veno-venous ultrafiltration (UF) may effectively treat congestion and reduce rehospitalisation rates in patients with decompensated heart failure, but in a randomised controlled trial it was associated with worsening renal function. Whether UF has an impact on mortality is uncertain. The aim of this single-centre observational study was to assess factors associated with mortality.

Methods: Data was recorded on consecutive patients undergoing UF for DR-ADHF. The latter was defined by failure to achieve 1Kg weight loss with 250mg of intravenous frusemide. Patients were followed up and mortality recorded. Survival analysis was performed using multivariate Cox proportional hazard models to identify independent factors associated with mortality.

Results: 20 patients (84% male, age 66 ± 13 years, estimated glomerular filtration rate (eGFR) 41 ± 22ml/min, LV ejection fraction (LVEF) 33 ± 15%, heart rate 80 ± 16bpm, albumin 21 ± 5g/l, tricuspid annular plane systolic excursion (TAPSE) 1.2 ± 0.4cm, peak pulmonary artery systolic pressure (PASP) 61 ± 18mmHg) underwent UF via central venous access. The mean duration of UF was 94 ± 45 hours, with 11 ± 5l fluid removed and mean weight loss of 8 ± 4kg. At the end of UF there was a significant mean decrease in eGFR of 5 ± 13ml/min.

Patients were followed up for a median of 728 (IQR 550-785) days. During this period 14 patients (70%) died. Amongst those who died, median survival was 121 (IQR 63-306) days.

A multivariate Cox regression model that included LVEF, PASP, TAPSE, HR, albumin, haemoglobin, baseline eGFR and change in eGFR was constructed. This demonstrated that the only covariate associated with death in this cohort of patients with DR-ADHF was a decrease in eGFR (HR 1.16, CI 1.02-1.32, p=0.02), such that for every 5ml/min reduction in eGFR at the end of UF the risk of death increased by 210%.

Conclusions: Patients with DR-ADHF have a poor prognosis, and a fall in eGFR with UF was associated with increased risk of mortality. Larger studies are required to confirm these findings.

P387

Treating diuretic resistance in heart failure patients in daily practice

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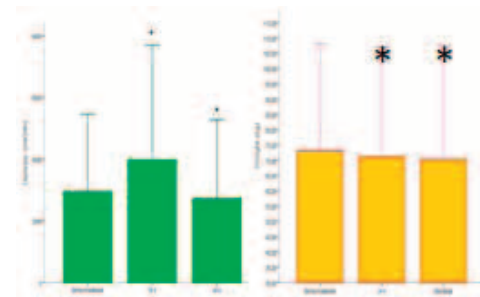
Purpose: Loop diuretics (LP) remain the first-line therapy for decompensated heart failure (DHF). Diuretic resistance (DR), defined as weight gain and lower diuresis rate secondary to the reduction of efficacy of LP, is a major problem in patients treated chronically with diuretics. In those cases, hydrochlorothiazide (HTZ) or ameride association may be useful. We aimed to assess the efficacy of this association in daily clinical practice.

Methods: We retrospectively reviewed patients admitted for DHF treated with LP who developed DR so were treated with ameride and HTZ. Sodium (Na), potassium (K), creatinine (Cr), glomerular filtration rate (MDRD) and weight were evaluated before administration, 24 h after and at discharge. Diuresis rate was evaluated at 24 and 48 h after administration.

Results: Forty-three patients were included (26 male) with a mean age of 73 ± 13. Ischemic and valvular heart disease were the most prevalent etiologies (33% vs 42%), being the 54% in NYHA III. Fifteen were in concomitant treatment with aldactone and one with tolvaptan. Diuresis increased significantly at 24 hours and 48 hours (2780 ± 1128 before vs 3550 ± 1645 at 24 h vs 2600 ± 1260 at 48 h; p = 0,001) which correlated with a corresponding significant weight loss (73,2 ± 16,4

before vs 69,5 ± 22,1 at 24 h vs 70,5 ± 17,5 at discharge p = 0,001) (figure 1). We didn't find statistically significant changes of Cr at 24 hours (1,2 ± 0,4 before vs 1,3 ± 0,4 at 24h vs 1,4 ± 0,5 at discharge p = 0,001) neither of MDRD. None of them developed electrolytic disturbances.

Conclusions: In our experience, use of ameride and HTZ was safe and effective in increasing diuresis rate without electrolytic nor renal function changes.



Weight and Diuresis changes

DRUG THERAPY, OTHER

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Short-term efficacy and safety of high-intensity statin therapy in patients with very high cardiovascular risk

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Objective: Dyslipidemia is recognized as a prominent risk factor for cardiovascular (CV) disease. The recent cholesterol guidelines recommend aggressive statin therapy in patients with high cardiovascular risk. The aim of the study was to investigate the efficacy and safety of short-term high-intensity statin therapy in patients with high cardiovascular risk.

Methods: In 72 patients with history of clinically evident cardiovascular disease and fasting low-density lipoprotein cholesterol (LDL-C) > 1.8 mmol/l or non-high-density lipoprotein cholesterol (non-HDL-C) > 2.6 mmol/l (63.9% male, 60.8 ± 8.6 (M ± SD) years, current smoking 40.3%, abdominal obesity 63.9%, arterial hypertension 86.1%, myocardial infarction 73.6%, percutaneous coronary intervention 58.3%, coronary artery bypass surgery 12.5%, non-hemorrhagic stroke 29.1%, diabetes mellitus 22.2%, symptomatic peripheral arterial disease 6.9%, atrial fibrillation 14%, chronic heart failure NYHA II 54%, left ventricular ejection fraction 48 ± 8%, chronic kidney disease 11.1%, estimated glomerular filtration rate 72 ± 13 ml/min/1.73 m², high-sensitivity C-reactive protein (hsCRP) mediana 5.3 mg/dl (min; max 0.5; 97.9), hsCRP > 2.0 mg/dl 41.7%, total cholesterol (TC) 5.58 ± 1.63 mmol/l, HDL-C 1.09 ± 0.32 mmol/l, LDL-C 3.49 ± 1.33 mmol/l, triglycerides (TG) 2.16 ± 1.40 mmol/l, very LDL-C (VLDL-C) 0.88 ± 0.37 mmol/l, non-HDL-C 4.52 ± 1.51 mmol/l, previous statin therapy 73.6%) efficacy and safety of 1 month of high-intensity statin therapy (atorvastatin 80 mg/day) was assessed. Wilcoxon test was performed. P < 0.05 was considered significant.

Results: 29 (40.3%) patients achieved target LDL-C level < 1.8 mmol/l, 31 (43.5%) patients achieved target non-HDL-C level < 2.6 mmol/l, 14 (19.4%) achieved both target levels after 1 month of therapy. Atorvastatin 80 mg/day decreased lipids significantly in the group with achieved target LDL-C-level: TC from 4.81 ± 1.1 to 3.33 ± 0.36 mmol/l; LDL-C from 2.83 ± 1.12 to 1.57 ± 0.23 mmol/l; VLDL-C from 0.91 ± 0.52 to 0.63 ± 0.33 mmol/l; non-HDL-C from 3.75 ± 0.89 to 2.2 ± 0.26 mmol/l; TG from 1.98 ± 1.13 to 1.38 ± 0.72 mmol/l, (p < 0.05 for all trends). Changes of HDL-C were insignificant. No hepato-biliary and musculoskeletal adverse events were observed.

Conclusion: Short-term high-intensity statin therapy is effective only in 40.3% of patients with high cardiovascular risk but is well-tolerated.

P389

Medium-term follow up of hospitalized patients with systolic heart failure undergoing early treatment with beta-blockers more ivabradine: a randomized study

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Introduction and objectives: Heart rate is a parameter with prognostic value in patients with heart failure with depressed ejection fraction (HF-dEF) and sinus rhythm, having shown that the value of heart rate at 28 days of starting treatment predicts long-term mortality. Our objective is to analyze the effect on heart rate at 28 days of discharge after admission for heart failure in patients with HF-dEF, sinus rhythm, HR>70bpm and EF>40% and evaluate the functional class, BNP values and combined death or hospitalization at 4 months of admission for heart failure of 2 protocols: only Betablockers (Bb) or Betablockers+Ivabradine (Bb+Iv) after 24 hours of admission.

Methods: Comparative, randomized comparing treatment with Bb only against Bb+Iv, with the usual dose titration regimen.

Results: We studied 49 consecutive patients who met the inclusion criteria (28 patients in Bb group, 21 in Bb+Iv group). Both groups were homogeneous in relation to age, sex, BNP, renal function, comorbidities and treatment with diuretics, ACEI or ARBs and MRA. Heart rate at discharge was $73,97 \pm 10,45$ bpm in Bb group vs $70,13 \pm 10,60$ in Bb+Iv group (NS). The heart rate at 28 days was lowest in Bb+Iv group ($64,29 \pm 7,75$ vs $70,28 \pm 9,37$ bpm, $p=0,016$). Regarding functional class at 4 months follow-up, there is a tendency to better functional class in Bb+Iv group without reaching statistical significance (86% vs 73,1% in FC I-II, $p=0,29$ NS). Not find differences between groups in the values of BNP at 4 months of monitoring ($281,18 \pm 90,46$ in Bb+Iv group vs $390,20 \pm 106,48$ in Bb group, $p=0,47$ NS) or combined death or hospitalization (4 in Bb+Iv vs 5 in Bb group, NS).

Conclusion: Co-administration of Bb+Iv immediately after admission in patients with HF-dEF, SR and HR at 70 bpm or higher is feasible, safe and produces a significant decrease in HR at 28 days in comparison to Bb alone. This reduction in HR appears to be associated with a trend towards improvement in functional class but didn't reach statistical significance. It is required a larger number of patients and a longer follow-up to see if this trend reaches statistical significance and whether differences appear in terms of long-term morbidity and mortality.

P390

The effect of ivabradine on improving exercise tolerance in chronic obstructive pulmonary disease patients

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Background: Diastolic dysfunction (DD) is common in COPD patients and can be responsible for worsening of functional capacity. Tachycardia due to increased sympathetic tone and use of bronchodilators increases severity of DD and worsens functional capacity.

Aim: To study the short term effect of heart rate lowering drug ivabradine on clinical status and exercise capacity in COPD patients.

Methods: COPD patients with sinus heart rate ≥ 90 beats/min with evidence of diastolic dysfunction on echocardiography were included. Patients with evidence of ischemic heart disease or left ventricular systolic dysfunction were excluded. All included patients were subjected to complete history and clinical examination including subjective assessment of dyspnea using modified Borg scale, electrocardiogram, chest X-ray, transthoracic echocardiography, pulmonary function tests and six minute walk distance (6MWD). The patients were randomized for either taking 14 days ivabradine 7.5 mg twice plus regular COPD medications versus continuing on regular COPD medications alone followed by reassessment of symptoms and 6MWD.

Results: Drug group (40 patients) versus control group (40 patients) were age and sex matched. No significant difference was found between both groups regarding degree of airway obstruction measured with FEV1 ($p=0.32$). No significant difference between both groups regarding severity of diastolic function ($p=0.23$). No difference in pulmonary artery systolic pressure between both groups ($p=0.48$). The patients who received ivabradine showed significant improvement in 6MWD (from 192.6 ± 108.8 m at baseline to 285.1 ± 88.9 m at the end of study) compared with control group (230.6 ± 68.4 at baseline and 250.4 ± 65.8 m at the end of study) ($p < 0.001$). This improvement in the drug group was associated with significant improvement of dyspnea on Borg scale ($p=0.007$).

Conclusion: Lowering heart rate with ivabradine in COPD patients could improve diastolic function, an effect that can help in improving their clinical status and exercise capacity.

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The impact of low dose carperitide administration for reducing worsening renal function (WRF) and in-hospital stay in acute decompensated heart failure

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Background: Some clinical studies have demonstrated Carperitide, a recombinant form of alpha-human atrial natriuretic peptide (hANP), might have a favorable effect in acute decompensated heart failure (ADHF); however, the detail of its clinical effect remains unclear.

Purpose: The purpose of this study is to investigate short-term and long-term clinical outcomes of ADHF patients according to the Carperitide usage.

Method: A total of 135 non-hemodialysis ADHF patients admitted from Jan. 2010 to Dec. 2011 followed-up at least for 1 year were retrospectively reviewed. They were divided into 2 groups according to Carperitide usage, Carperitide group ($n=83$), and non-Carperitide group ($n=52$). Worsening renal function (WRF) was defined as occurrence of 25% or 0.3 mg/dL increase in serum creatinine levels during hospitalization.

Result: Baseline characteristics of age and sex were not different in each group except blood pressure at admission was significantly higher in Carperitide group than non-Carperitide group. Average dose of Carperitide was $0.024 \mu\text{g}/\text{kg}/\text{min}$. Left ventricular function and BNP levels at admission were not different. The occurrence of WRF was significantly lower in Carperitide Group than non-Carperitide group (30% vs 56%, $p < 0.05$). The length of in-hospital stay was significantly shorter in Carperitide group (14.5 vs 18.9 days, $p < 0.05$). Survival rate at 1 year is tended to be lower in non-Carperitide group (82% vs 71%), but not significantly different. In Carperitide group, estimated glomerular filtration rate (eGFR) levels at admission, discharge, and 1 year (48.8, 46.2, and $45.8 \text{ ml}/\text{min}/1.73 \text{ m}^2$, n.s.) were not different. On the other hand, eGFR levels were significantly decreased at 1 year compared with admission in non-Carperitide group (66.3, 55.4, and $36.1 \text{ ml}/\text{min}/1.73 \text{ m}^2$, $p < 0.05$). **Conclusion:** Low dose administration of Carperitide to ADHF patients was effective to prevent WRF in this study. Also, favorable long-term renal protective value with reduction of in-hospital length was observed in Carperitide group.

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Comparison of enalapril-amlodipine and captopril-indapamide combinations in the management of hypertension patients with metabolic syndrome

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Background: Hypertension is a strong contributor to cardiovascular disease in patients with the metabolic syndrome. It has been shown to not only be an independent risk factor, but it also contributes to the development of other risk factors for cardiovascular disease. Over the last few decades, a number of classes of anti-hypertensive drugs have been used to treat hypertension, with the ultimate goal of reducing the incidence of endpoints such as heart attacks and stroke. Some of the broad categories of antihypertensives include diuretics, angiotensin-converting enzyme inhibitors (ACEIs) and calcium channel blockers (CCB).

Aim: To compare the efficacy and tolerability of enalapril 10 mg + amlodipine 5 mg combination (EN+AM) versus captopril 50 mg + indapamide 2.5 mg (CP+IN) combination.

Material and Methods: We have investigated 97 outpatients who have hypertension and metabolic syndrome with mild-to-moderate arterial hypertension not adequately controlled by a monotherapy with ACE inhibitors or calcium channel blockers or diuretics entered this work, randomized, parallel-group study. After a 2-week placebo run-in, all patients with sitting diastolic (D) blood pressure (BP) > 95 mmHg and/or sitting systolic (S) BP > 160 mmHg were randomized to receive either EN+AM (52 patients) or CP+IN (45 patients) once daily for 12 weeks. Main outcome measure was sitting DBP and SBP values at the end of active treatment. The response rate was defined as the proportion of patients with either a final sitting DBP < 90 mmHg or decreased by at least 10 mmHg or a sitting SBP < 150 mmHg or decreased by at least 20 mmHg from baseline.

Results: The DBP and SBP values obtained with EN+AM were, respectively, 2.7 and 3.7 mmHg lower than those obtained with CP+IN (both $p < 0.001$ vs. CP+IN). The response rate in the EN+AM group (92.6%) was better than that observed in the CP+IN group (85.1%, $p=0.004$). The incidence of adverse events was similar with the 2 treatment regimens (17.5% for both).

Conclusions: These data suggest a higher antihypertensive efficacy of the fixed combination EN 10 mg+AM 5 mg as compared with CP 50 mg+IN 2.5 mg.

P393

Effect of tolvaptan on congestive heart failure patients with reduced stroke volume

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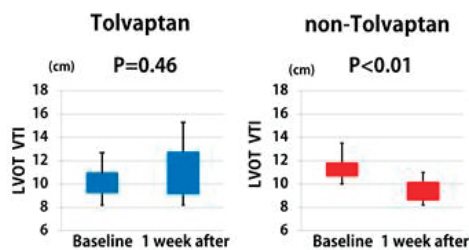
Background: Despite the effect on relief of congestion in patients with acute heart failure syndrome, traditional diuretic therapy would often induce patients presenting

with reduced LV stroke volume to lower cardiac output and renal impairment. We sought to determine the short-term hemodynamic effects of tolvaptan (TLV) in this high risk population.

Methods: We assessed the clinical course of congestive heart failure patients with reduced stroke volume, comparing between TLV group (n=9) and non-TLV group (n=10). Reduced stroke volume is defined on the basis of left ventricular outflow tract velocity time integral (LVOT VTI) <15cm in ESC guideline. The therapeutic effects were compared with respects to vital sign, signs of congestion, echocardiographic parameters and laboratory data during 1 week.

Results: EF and LVOT VTI at baseline were not significant difference (TLV vs. non-TLV, 40 ± 16 vs. $38 \pm 17\%$, $p=0.81$; 10.2 ± 1.5 vs. 11.5 ± 1.2 cm, $p=0.14$). Between at baseline and 1 week after, similar reductions in body weight were observed (3.7 ± 2.4 vs. 3.4 ± 2.0 kg, $P=0.86$), moreover, improvements in physician-assessed signs of congestion (dyspnea, lower limb edema and pulmonary congestion), HR and BP were not significant difference between two groups during 1 week. However, 1 week after, LVOT VTI in TLV group maintained significantly ($P=0.23$), differentiated from non-TLV group (Figure). Additionally, reduced LVOT VTI during 1 week had associated with elevated creatinine ($r = -0.57$, $P < 0.05$).

Conclusions: TLV has the potential to maintain cardiac output in congestive heart failure patients with reduced stroke volume in spite of similar improvements in congestion, compared with traditional diuretic therapy.



Effect of Tolvaptan on LVOT VTI

P394

The effectiveness of glutathione on the immunological status of patients with dilated cardiomyopathy

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The Aim: To evaluate the effectiveness of immunomodulatory drug glutathione and safety of its usage with standard therapy of CHF in patients with dilated cardiomyopathy (DCM).

Methods: The study involved 96 pts with DCM of both genders (m/w 56/40), mean age 37.6 ± 1.1 years old. Examination included the ECG Holter ECG, EchoCG 6-minute walking test (6MWT) immunological study of blood. In the whole group 6MWT was 252.5 ± 8.7 m, which corresponds to an average of NYHA class 3, 1 ± 0.1 . I gr was on glutathione application (n=24), II gr. (n=22) treated by only ST of CHF. The control gr included 29 healthy volunteers aged 18 to 55 years. The daily dose of glutathione was 600 mg / day

Results: the state of cellular immunity had the following characteristics: CD3 + $50.6 \pm 0.6\%$ (control gr. - 59.4 ± 1.5); CD4 + $25.5 \pm 0.3\%$ (33.8 ± 1.1); CD8 + $24.1 \pm 0.5\%$ (18.4 ± 0.05); CD16 + $21.1 \pm 0.3\%$ (18.4 ± 1.1); CD20 + $21.9 \pm 0.2\%$ (19.6 ± 0.5); CD95 + $23.6 \pm 0.3\%$ (22.3 ± 1.02); IRI (CD4 / CD8) - 1.15 ± 0.02 (1.5 ± 0.05), ie it was revealed a statistically significant suppression of the general population (CD3) and helper (CD4) T cell activity, and a significant increase of suppressor (CD8) and killer (CD16) T-lymphocyte activity, as well as some increase in cell apoptotic factor (CD95) (all $p=0.01$). Due to the significant increase in T-suppressor and oppression of T-helper lymphocyte activity it was determined a statistically significant reduction of IRI compared with the control group ($p < 0.001$). On the background of the combined treatment with glutathione it was revealed a normalization of cellular and humoral immunity. Revealed positive changes in cellular immunity characterized by increased levels of CD3 + 3.3% (up to $52.2 \pm 1.1\%$, $p < 0.05$), CD4 + 9.1% (up to 27.8 ± 0.5 ; $p < 0.01$) and CD8 + 2.1% (up to 23.2 ± 1.01 ; $p > 0.05$), reducing the killer activity in CD16 + 2.9% (up to 20.5 ± 1.1 ; $p > 0.05$) and apoptotic factor to 20.6 ± 0.7 ($p > 0.05$). In this case, the main indicator of immunity IRI increased on 18.2% ($p < 0.01$). At the same time, the analyzed indicators of immunity in patients with DCM who were only under ST of CHF remained virtually unaltered (CD3 + $49.6 \pm 1.2\%$; CD4 + $24.9 \pm 1.2\%$; CD8 + $24.8 \pm 1.1\%$; CD16 + $22.6 \pm 1.3\%$; CD95 + $22.9 \pm 1.08\%$; IRI - 1.1 ± 1.1 , large CEC - 26.5 ± 1.5 , small CEC - 44.8 ± 1.1) compared with the outcome.

Thus, the usage of glutathione at a dose of 600 mg / day for a month with standard therapy of CHF having immunomodulatory properties leads to normalization of cellular and humoral immune response with a reduction in both large and small CEC.

P395

Pharmacokinetics, safety and tolerability of serelaxin in patients with severe renal impairment or end-stage renal disease

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Purpose: Serelaxin, a recombinant human relaxin-2, is currently in clinical development for treatment of acute heart failure (AHF). As patients with AHF often have accompanying renal insufficiency or experience worsening of renal function during hospitalization, this study was primarily aimed at evaluating the pharmacokinetics (PK) of serelaxin in patients with severe renal impairment or those with end-stage renal disease (ESRD) on haemodialysis.

Methods: This open-label parallel-group study enrolled patients with severe renal impairment (Group 1; n=6) or ESRD on haemodialysis (PK assessed on the day of dialysis [Group 2; n=6] or during dialysis-free interval [Group 3; n=6]) and matched healthy subjects (Group 4; n=18) to evaluate the impact of renal impairment and haemodialysis on serelaxin PK after a single 4h intravenous infusion (10 µg/kg). Primary PK parameters (area under serum concentration-time curve [AUC]_{0-28h}, AUC_{last}, AUC_{inf}, and maximum serum concentration post-dose [C_{max}]) were compared between patient groups (Groups 1-3) and matched healthy subjects. Immunogenicity, safety and tolerability of serelaxin were also evaluated.

Results: Detailed results to be presented. In brief, a moderate decrease in serelaxin systemic clearance (37%-52%) and an increase in its exposure (30%-115%) were observed in all patient groups (Groups 1-3) compared with healthy subjects. The mean terminal elimination half-life of serelaxin ranged between 6.50-8.81h in all study groups. During the 4h haemodialysis in ESRD patients, 30% of serelaxin was removed from the blood with dialysis clearance constituting about 52% of the total systemic clearance. No anti-serelaxin antibodies were detected and serelaxin was well tolerated with no deaths, serious adverse events (AE), or AE-related discontinuations.

Conclusions: Overall, there were moderate differences in serelaxin PK with moderately increased exposure in patients with severe renal impairment or ESRD compared with healthy subjects. Based on the wide therapeutic window of serelaxin the observed differences are not considered to be of clinical relevance. Therefore no dosage adjustments are warranted for serelaxin in these patients.

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The proportion of patients suitable for ARNI treatment before and after optimal therapy in HFrEF

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Background: The PARADIGM-HF trial, that randomized >8000 patients (pts) with HFrEF to treatment with LCZ696 or enalapril on top of other evidence-based therapies, showed a huge drop in the primary outcome in favour to the new drug. After the success of the trial, the new CCS guidelines update has already made a room for use of Angiotensin-Receptor-Nepriylsin inhibitor (ARNI) in HFrEF. But still there are questions in sense of the practical use of ARNI in a real-life population. One of the main question is at what rate is it necessary to change ACEi to ARNI.

Aim: To assess the proportion of pts suitable for ARNI according to the criteria of the PARADIGM-HF trial (NYHA II-IV; LVEF ≤ 35%; systolic blood pressure (SBP) ≥ 100mmHg; eGFR ≥ 30ml/min/1.73m²; serum potassium (seK) ≤ 5.2mmol/l; tolerated dose of an ACEi/ARB equivalent to at least 10 mg of enalapril twice daily; elevated level of BNP), before and after treatment optimization (TO) in real-life conditions.

Patients and Methods: The primary cohort (PC) included 596 consecutive HFrEF pts who were followed prospectively at our heart failure outpatient clinic (LVEF: $29.8 \pm 7.9\%$; NYHA: 3.1 ± 0.7 ; blood pressure: $126.6 \pm 23.3/80.2 \pm 13.3$ mmHg; ischemic etiology: 46.8%; diabetes: 34.4%; male: 75.5%; age: 62.7 ± 25.4 years; eGFR: 54.1 ± 25.1 ml/min/1.73m²). Treatment at baseline: ACEi/ARB in 36.1% (at target doses (TD) - equivalent to at least 10mg enalapril twice daily - 18.5% of pts of PC), BB in 35.2%, MRA in 30.7%, CRT-P/CRT-D in 7.5%, ICD in 1.6%. The proportion of pts suitable for ARNI was examined before and after TO. BNP's measurement was not available at the time of the analysis.

Results: At baseline, 78 of 596 pts (13.1%) were suitable for ARNI. The main reason of the unsuitability was the low dose of ACEi/ARB treatment. After TO, the proportion and doses of guideline recommended therapy, ACEi/ARB (91.6%, at TD: 60.4% of PC), BB (92.3%, at target doses: 60.9% of PC), MRA (53.9%), the use of CRT-P/CRT-D and ICD (16.6%; 2.8%, i.e.) increased significantly. The proportion of pts suitable for ARNI was to 11.4% (68pts). The pts were unsuitable for ARNI

after TO because of the improvement in NYHA (30.7% of PC), change in LVEF (45.3% of PC), SBP<100mmHg (22.8% of PC), eGFR<30ml/min/1.73m² (30.7% of PC), seK>5.2mmol/l (12.4% of PC), because of the tolerated dose of an ACEi/ARB (31.2% of PC).

Conclusions: Treatment with ARNI may be an important, new possibility for the management of pts with HFREF. Among real-life HFREF pts the proportion of pts suitable for ARNI according to the PARADIGM-HF trial criteria seems to be moderate.

P397

Patiromer lowers serum potassium and prevents recurrent hyperkalemia in patients with heart failure and CKD when treated with RAAS inhibitors: results from OPAL-HK

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Purpose: Patients (pts) with heart failure (HF) and chronic kidney disease (CKD) are at risk for hyperkalemia (HK), especially when treated with renin angiotensin aldosterone system inhibitors (RAASi). Patiromer, the active moiety of which is a nonabsorbed potassium (K⁺)-binder, was previously shown in clinical trials to lower serum K⁺ (s-K⁺) with good gastrointestinal tolerability. This was a two-phase multi-center international study in 243 pts with HK and an eGFR 15- $<$ 60 mL/min/1.73m² with/without HF on RAASi. This prespecified subgroup analysis presents the findings in CKD pts with (n = 102) and without HF (n = 141).

Methods: Phase 1, a 4-wk single-blind treatment study, assessed patiromer for HK treatment. Phase 2, an 8-week placebo-controlled randomized withdrawal study, assessed whether chronic patiromer treatment prevented recurrent HK. Primary outcomes were change from baseline in s-K⁺ (Phase 1) and the between group difference in change in s-K⁺ from Phase 2 Baseline to Phase 2 Wk 4 (Phase 2). Secondary outcomes included the proportion with s-K⁺ in the target range (Phase 1) and the proportion with recurrent HK (Phase 2).

Results: The mean (\pm SE) change in s-K⁺ from baseline to week 4 was -1.06 ± 0.05 mEq/L (95% CI, -1.16 to -0.95 , p < 0.001) in pts with HF and -0.98 ± 0.04 (95% CI, -1.06 to -0.90 , p < 0.001) in pts without HF (p value for interaction, 0.22). Serum K⁺ was controlled (3.8- $<$ 5.1 mEq/L) at the end of Phase 1 in 76% of HF and 75% of non-HF pts. Primary endpoint results for Phase 2 are shown in the Table. Significantly (p < 0.001) more placebo than patiromer pts (HF, 52% vs 8%; non-HF, 66% vs 23%) developed recurrent HK (s-K⁺ >5.5 mEq/L) during Phase 2. Patiromer was well tolerated; constipation (none severe) was the most common adverse event with patiromer in both pts with/without HF (11% and 4% in Parts 1 and 2, respectively).

Conclusions: Patiromer provided effective s-K⁺ control and, compared to placebo, decreased HK recurrence in CKD pts with and without HF, with a well-tolerated safety profile that may allow continuous management of s-K⁺ in HF pts with HK on RAASi.

Phase 2: Primary Endpoint Results

	Median Change in Serum K ⁺ from Phase 2 Baseline to Phase 2 Week 4	Between-Group Difference in Medians, 95% CI (p-value)	Interaction p-value	
	Placebo	Patiromer		
Heart Failure Present (n = 49, 46%)	0.74 mEq/L	0.10 mEq/L	0.64 mEq/L, 95% CI: 0.29, 0.99 (p < 0.001)	0.50
Heart Failure Absent (n = 58, 54%)	0.78 mEq/L	-0.05 mEq/L	0.83 mEq/L, 95% CI: 0.42, 1.24 (p < 0.001)	

BETA BLOCKERS

P398

Performance evaluation indicators carvedilol beta-adrenoreceptors in patients with chronic heart failure

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The purpose of the study, evaluation of the effectiveness of carvedilol on the density of beta-blockers in patients with chronic heart failure (CHF).

Material and methods: The study included 56 male patients, aged 40 to 55 years with postinfarction cardiosclerosis (PICS). All the patients were divided into two groups of functional class (FC) of CHF according to the NYHA: the first group consisted of 30 patients with CHF FC II and the second group - 26 patients with CHF III FK.NYHA. The control group consisted of 20 healthy volunteers. The density of beta2-adrenergic receptors of erythrocytes in patients with CHF was determined using reagent kit « β -APM-AGAT». Activity was determined by erythrocyte adenilattsiklazymogenatov procedure Solomon (1979). All took nonselective beta blockers, has α 1-, β 1- and β 2- blocking properties - carvedilolputem slow dose titration with 3.125 up to 25-50 mg / day target dose.

The results of the study. In patients with class II heart failure initial density of erythrocyte beta2-adrenergic (β 2-AR) in patients with class II heart failure exceed the value of the control group by 2.4 times amounting to $27,7 \pm 1,4$ conv, whereas in patients with FC III CHF this figure exceeds the value of the control group by 2.9 times amounting to $30,8 \pm 1,3$ conv (p < 0,001). Analysis of the results of the study showed that when the carvedilol in the complex therapy after six months in patients with class II, a decrease density of β 2-AR to 15,7% (p < 0,01), and in patients with FC III to 22,7% (p < 0.01) from baseline. Thus, in patients with CHF state erythrocyte beta2-adrenergic receptors is characterized by an increase in their density and desensitizatsiyadenilattsiklaznoy systems which are most pronounced in patients with FC III CHF and chronic treatment with carvedilol reduces the density of beta-adrenergic receptors.

P399

Heart rate or beta-blocker dose? Association with outcomes in ambulatory heart failure patients with systolic dysfunction: results from the HF-ACTION trial

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Background: Data has shown that Heart Rate (HR) is an important modifiable factor in reducing mortality in heart failure (HF). It has also been shown that titrating doses of Beta-blockers (BBs) improves outcomes in chronic HF with reduced ejection fraction (EF). We compared whether reduced HR or higher BB dose affected outcomes to a greater extent in the HF-ACTION trial population.

Methods: HF-ACTION was a randomized trial enrolling 2331 ambulatory HF patients with systolic dysfunction (NYHA class II-IV, LVEF <0.35) randomized to exercise training vs. usual care, with median follow-up of 2.5 years. BB dose and HR were analyzed as a continuous variable and by discrete groups (higher/lower dose; higher/lower HR). The relationship of BB dose, HR and the primary endpoint of all-cause mortality or all-cause hospitalization, and other cardiovascular secondary endpoints were determined before and after adjustment for potential confounders in the HF ACTION cohort.

Results: There was a significant inverse relationship between BB dose (higher better), HR (lower better) and all-cause death or hosp in unadjusted analysis; however, for the endpoint of all-cause mortality, only BB dose was significant for improved outcomes. After adjustment for other prognostic predictors, only BB dose remained significant for improving all-cause death or hosp. BB dose, but not HR, was associated with improved outcomes on other CV endpoints in unadjusted analysis, but did not remain significant when adjusted.

Conclusion: Higher BB dose was associated with more improved outcomes than lower HR, suggesting that titrating BB doses may confer a greater benefit than reducing HR in such patients.

	Unadjusted		Adjusted	
	p-value	HR [95% CI]	p-value	HR [95% CI]
All Cause Death at All Cause-HF				
BB (high vs low dose)	<0.001	0.77 (0.71, 0.86)	0.03	0.87 (0.77, 0.99)
HR (≥ 70 vs HR < 70)	0.01	1.14 (1.03, 1.24)	0.09	1.11 (0.98, 1.24)
All Cause Death				
BB (high vs low dose)	0.027	0.75 (0.64, 0.87)	0.57	0.94 (0.75, 1.17)
HR (≥ 70 vs HR < 70)	0.82	0.97 (0.806, 1.204)	0.26	0.89 (0.72, 1.09)
CV Death				
BB (high vs low dose)	0.098	0.80 (0.62, 1.04)	0.60	0.95 (0.71, 1.27)
HR (≥ 70 vs HR < 70)	0.54	0.93 (0.72, 1.19)	0.32	0.81 (0.63, 1.05)
CV Death or CV Hosp				
BB (high vs low dose)	0.001	0.62 (0.48, 0.81)	0.37	0.86 (0.61, 1.19)
HR (≥ 70 vs HR < 70)	0.15	1.08 (0.872, 1.307)	0.8227	1.02 (0.86, 1.11)
CV Death or HF Hosp				
BB (high vs low dose)	0.001	0.77 (0.60, 0.98)	0.2480	0.99 (0.747, 1.29)
HR (≥ 70 vs HR < 70)	0.026	1.19 (1.03, 1.36)	0.89	1.06 (0.9, 1.24)

P400

Discharge but not admission usage of beta blockers is associated with improved long term survival in patients admitted to hospital with heart failure and preserved ejection fraction

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Background: Previous registries have shown beta blocker (BB) use at hospital discharge is associated with lower mortality for patients with heart failure and preserved ejection fraction (LVEF > 45%). We sought to determine if admission use of beta blockade modified this relationship.

Methods: We utilized a prospective population-based disease-specific registry to identify all consecutive individuals hospitalized in a province of Canada with a diagnosis of HF between October 15, 1997 and July 1, 2003. Registry patients were included if they had a documented LVEF ≥ 45% within 60 days. Cox proportional hazard ratios were calculated to estimate the independent association of BB therapy at admission/discharge and mortality at 5 years follow up.

Results: There were 12,590 records identified. Of these, 2090 (16.6%), patients had a documented EF ≥ 45%. In this group, 55% were female, the mean age was 72 years, serum creatinine 127 µmol/L and LVEF was 54%. Of these, 1061 were taking BB on admission (51%) and 1483 were prescribed BB at discharge (71%). Use of BB was discontinued in 117 patients while initialization occurred in 539. Discharge prescription of BB was associated with lower mortality (HR 0.730, 95% CI 0.63, 0.86, p < 0.0001) while on admission was not (HR 1.01, 95% CI 0.95, 1.07, p = 0.74). Mortality was lowest in patients who started BB while in hospital (HR 0.65, 95% CI 0.59, 0.71, p < 0.01).

Conclusions: Prescription of BB on hospital discharge, but not admission, is associated with lower long term mortality for patients discharged from hospitals with HF and LVEF < 45%. Patients initiated on BB while in hospital experienced the lowest mortality. Further studies are required to determine the impact of beta blockade administration in acute heart failure

P401

The effect of genetic polymorphism on the dose and tolerability to beta-blocker therapy in Turkish heart failure population

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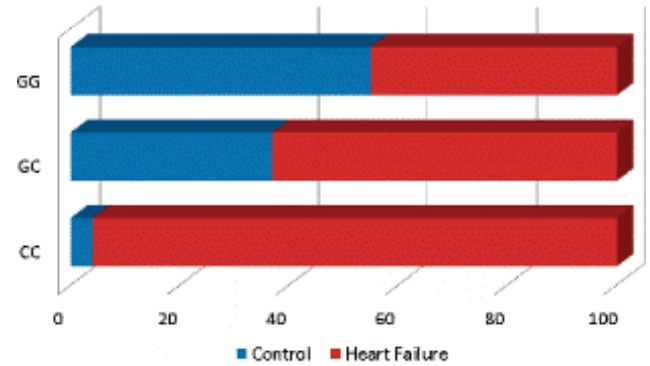
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Background: Genetic factors can influence the response of beta-blockers (BB) in patients (pts) with heart failure (HF). The aims of this study were: 1- determine the frequency of polymorphism of beta-adrenergic receptor in Turkish HF subjects, 2- evaluated the influence of Arg389Gly polymorphism and CYP2D6 genotype in response to beta-blocker therapy.

Methods: One hundred and sixty-two patients (mean age: 59 ± 11 yrs, male: 74 %) with systolic heart failure (LVEF: ≤ 45%, NYHA functional classification II-III) were prospectively enrolled. The Arg389Gly and CYP2D6 genotypes were measured before initiation of beta-blockers which identified by PCR and RFLP polymorphism analysis. The tolerability and response to therapy were compared with the Arg389Gly and CYP2D6 genotypes.

Results: The 43% of patients (pts) had history of ischemic etiology of HF. The rate of Arg389Gly polymorphism was higher in pts with HF (p < 0.0001). The frequency of the polymorphism of CYP2D6 was the similar in each group (p > 0.05). The 47,8% of pts reached the maximum target dose of BB and 83% reached the half dose. The main causes of intolerance was hypotension. The Arg389Gly polymorphism and CYP2D6 genotype were not influence the response to BB therapy (> 0.05).

In Conclusion: However the frequency the Arg389Gly beta1-adrenoceptor gene polymorphism was higher in our study population nor adrenergic receptor neither CYP2D6 polymorphism was not associated with dose and tolerability to BB therapy.



RENIN-ANGIOTENSIN-ALDOSTERONE ANTAGONISTS

P402

The impact of dose of the angiotensin-receptor blocker valsartan on the post-myocardial infarction ventricular remodeling (VALID study)

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Purpose: Recent guidelines advocate the use of high dose angiotensin-converting enzyme (ACE) inhibitors or angiotensin-receptor blocker (ARB) after acute myocardial infarction (MI), as used in major clinical trials. However, those trials did not provide the optimal dosing or risk-benefit assessment of different doses. This study aimed to identify whether the recommended high dose of valsartan (titrated up to 320 mg/d) is more efficacious than usual dose (80 mg/d) in retarding or reversing post-MI left ventricular (LV) remodeling.

Methods: This was a randomized, single-blinded, multicenter study in which 495 patients with acute ST-elevation MI (STEMI) and subnormal LV ejection fraction (<50%) were grouped in 2:1 fashion into high dose (n=333) or usual dose valsartan (n=162). Primary objective was the changes of echocardiographic parameters of LV remodeling from baseline to 12 months after discharge. Genetic polymorphism of neurohormone component was analyzed to detect potential interaction between genetic variance and pharmacological effect. Clinical adverse effects were collected to obtain safety profile.

Results: The mean age of study subjects was 59.1 years and 23.0% of patients were female. Baseline characteristics including concomitant medications were comparable between two groups. During 12 months period, diastolic LV dimension (LVIDd) decreased significantly in usual dose group (from 87.3 ± 20.7 mL to 80.1 ± 26.1 mL, P = 0.01) while the change in high dose group was minimal (from 87.3 ± 20.7 to 87.0 ± 24.2 mL, P = 0.79). The magnitude of LVIDd change was not significantly different between two groups. (-3.50 ± 15.5 vs 0.42 ± 20.0, P = 0.08). LV ejection fraction (LVEF) rose significantly in both groups (from 47.9 ± 7.2 to 57.3 ± 10.7%, P < 0.001; from 47.3 ± 7.2 to 54.2 ± 9.8 %, P < 0.001). The amount of LVEF change was similar in both groups (8.45 ± 9.2 vs 6.07 ± 8.3 %, P = 0.08). The difference in LVIDd change was significant in patients with specific genotypes, which include ACE insertion/deletion ID heterozygote and type 1 angiotensin receptor A1166C AA homozygote. Drug-related adverse effects occurred significantly less frequently in usual dose group than in high dose group (0.69 vs 7.96 %, P < 0.001).

Conclusions: The use of high dose valsartan did not exhibit greater effect on reversing post-MI LV remodeling, and led more frequent occurrence of adverse effects.

Usual dose valsartan appeared more beneficial in patients with specific genotype. Judicious selection of valsartan dose rather than routine high dosing should be considered in post-MI circumstance, especially in Asian patients.

P403

Comparative efficacy of renin-angiotensin system modulators on prognosis, right heart and left atrial functional parameters in patients with severe systolic chronic heart failure

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The aim of study was to compare efficacy of ramipril (R, 10 mg), spironolacton (S, 50 mg), valsartan (V, 320 mg) and aliskiren (A, 300 mg) long-term therapy on prognosis, right ventricular (RV), right (RA) and left atrial (LA) parameters, BNP and hsCRP levels in pts with III-IV NYHA FC systolic CHF.

Methods: 148 pts (age 57.4±0.4) were randomly assigned to groups A (n=38, receiving only R), B (n=37, receiving S), C (n=37, receiving V) and D (n=36, receiving A) in addition to R, diuretics, beta-blockers and digoxin. RV ejection fraction (EF), fractional area change (FAC), tricuspid annulus plane systolic excursion (TAPSE), RA and LA functional index (FI), fractional contribution (FC), relation of pulmonary vein (PV) systolic and diastolic fraction (S/D), systolic contribution (SC), difference between duration of reversal atrial flow (Ar) and late (A) transtricuspid filling, pulmonary artery ejection (PAET) times, BNP and CRP levels were assessed at baseline, 3, 6, 12, 24 and 36 months.

Results: 1-, 2- and 3-year mortality (%) were 31.6, 44.4 and 55.6 in groups A, 21.6, 27 and 37.8 in B; 29.7, 40.5 and 51.4 in C and 16.7, 22.2 and 33.3 in D. Survival analysis revealed lower probability (RR reduction, %) of 1-(at 31.6 and 47.2), 2- (at 38.6 and 50) and 3-year mortality (at 32 and 40.1) in pts, treated with S (p<0.05) and A (p<0.01), respectively, compared to group A. R use significantly improved (% from baseline) BNP at 30.6, CRP at 28.9, LA FI at 80.9, PV SC at 41.7, RA FI and FC at 75 and 38, PAET at 7.7 after 6 months, RV EF at 27.5, TAPSE at 38, LA FC at 23.5, S/D at 41.4, Ar-A at 28.5 after 12 months. R+S significantly changed BNP at 32.1 after 3 months, CRP at 29.2, RV EF at 26.1, FAC at 22.9, TAPSE at 41.4, PAET at 7.4, RA and LA FI at 71.4 and 77.3, RA and LA FC at 39.5 and 39.2, PV SC at 45.5, S/D at 42, Ar-A at 27 after 6 months. R+V improved CRP at 29.4, BNP at 31.2, RV EF at 26.3, TAPSE at 36.2, PAET at 7.2, RA and LA FI at 77.3 and 78.3, RA FC at 39.3 and PV SC at 45.3 after 6 months, RV FAC at 31.8, FC at 34.7, S/D at 48.6, Ar-A at 30 after 12 months. R+A use changed BNP at 35.3, CRP at 28.9, RV EF at 26, FAC at 20.1, TAPSE at 35.9, RA and LA FI at 70 and 71.4, FC at 37.5 and 26.1, PAET at 6.6, PV SC at 50.2, S/D at 38.2, Ar-A at 27.7 after 3 months.

Conclusions: 1) Decrease of BNP ≥50%, CRP and Ar-A ≥40% and increase of RA and LA FC at ≥40%, TAPSE and PV SC ≥50% and RA and LA FI ≥80% identified pts with cardiac events reduction. 2) A use associated with lower mortality due to strongly expressed improvement of right heart and LA functional parameters, neurohormonal and inflammation status.

HORMONES / NEUROHUMORAL REGULATION

P404

Effect of recombinant human parathyroid hormone (1-34) on heart in postmenopausal women with osteoporosis

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Purpose: Treatment with teriparatide (recombinant human parathyroid hormone [1-34]) reduces the risk of fractures and increases bone mineral density (BMD) in patients with osteoporosis, but its effects on heart are less well known. We hypothesize that teriparatide improves cardiac structure and function in postmenopausal women with osteoporosis.

Methods: We recruited 13 postmenopausal women (age 77 ± 7 [SD] years, plasma B-type natriuretic peptide levels 32 ± 24 pg/ml, serum parathyroid hormone levels 48 ± 20 pg/ml) with osteoporosis and vertebral or hip fractures. Teriparatide was administered at 20 µg daily subcutaneous injections. We obtained repeated measurements of BMD and transthoracic echocardiography after a median of 24 months of treatment.

Results: Within-subject percent change in lumbar spine BMD was significantly increased (9.1 ± 6.1%, P < 0.001). Left ventricular end-diastolic dimension and stroke volume were significantly increased, and posterior wall thickness and relative wall thickness were significantly decreased (11.2 ± 11.1%, 26.4 ± 24.5%, -9.5 ± 10.8% and -9.9 ± 7.9% [absolute change], P < 0.01, respectively), with no change in left ventricular mass, left atrial diameter, mitral inflow pattern and estimated left ventricular filling pressure. The percent change in lumbar spine BMD was correlated with the percent change in left ventricular end-diastolic dimension and stroke volume (r = 0.63 and 0.64, p = 0.02, respectively).

Conclusions: In postmenopausal women with osteoporosis, once-daily administration of teriparatide can induce beneficial changes in cardiac structure and function without obvious adverse effects on heart.

P405

Salt taste threshold in patients with chronic heart failure shows no correlation with plasma neurohormones

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Background: Dietary sodium restriction is a recommended lifestyle intervention in patients with Chronic Heart Failure (CHF) due to left ventricular systolic dysfunction (LVSD). However, achieving this reduction in salt intake is challenging and one explanation for this may be that systemic neurohormonal factors lead to salt craving and may also reduce their ability to taste salt in food. Little is known about salt appetite in CHF patients and few studies have examined the neurohormonal effects of dietary sodium restriction.

Methods: Twenty six subjects were studied: nine healthy volunteers, seven patients with stable angina and normal LV function (CAD) and ten with CHF due to LVSD. Participants were studied at four time points: baseline, two, four and six weeks. Prior to the third visit participants were asked to observe a low-salt diet (<3g/day) with return to a normal diet prior to the final visit. At each visit salt appetite was assessed using a salt taste-threshold test (STT) plasma aldosterone, renin and cortisol were measured and salt intake was assessed using a questionnaire.

Results: At baseline salt taste threshold was lower in healthy volunteers than in patients with both CAD and LVSD although not significantly so (1.4 ± 0.91 mol/L vs 2.44 ± 1.44 vs 2.89 ± 1.77 respectively p > 0.05 in all cases). Low salt diet lowered salt taste threshold in CAD (2.44 ± 1.44 vs 1.95 ± 1.34) and LVSD (2.89 ± 1.77 vs 2.44 ± 1.97, p > 0.05) although these differences were not significant. On a low salt diet, salt intake was non-significantly lowered in CAD (22.43 ± 13.75 vs 15.17 ± 6.67g/wk, p > 0.05) and LVSD (26.6 ± 13.82 vs 19.90 ± 19.9, p > 0.05) patients with no change in healthy volunteers. When compared to the subjects with preserved LV function, LVSD patients had higher cortisol (275.1 ± 33.16 vs 234.1 ± 21.64 mmol/l, p > 0.05) Renin (417.1 ± 658.9 vs 45.83 ± 55.93mmol/L, p > 0.05) and Aldosterone (428.3 ± 184.1 vs 190.0 ± 28.97, p > 0.05) at baseline although none of these differences were significant nor were they changed by a low salt diet.

Conclusion: Whilst limited by sample size, our data suggest that patients with LVSD have a poorer ability to taste salt. This is associated with neuro-hormonal activation and may contribute to the salt and water retention that typifies CHF. Confirmation of these findings in a larger study may allow salt taste threshold to be targeted therapeutically in the future.

HEART FAILURE IMAGING

P406

Pulmonary artery to aorta ratio and right ventricular hypertrophy for detecting pulmonary hypertension by cardiac magnetic resonance imaging in heart failure with preserved ejection fraction

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Objective: Previous work shows that dilatation of the pulmonary artery (PA) by itself or in relation to the ascending aorta (PA:Ao ratio) predicts pulmonary hypertension (PH) in patients with pulmonary disease. Furthermore, right ventricular septomarginal trabeculation (SMT) mass has been identified as a cardiac magnetic resonance (CMR)-derived marker of PH. In the present study we aimed to evaluate the prognostic power of PA diameter, PA:Ao ratio and SMT size by CMR for the prediction of PH in patients with heart failure and preserved ejection fraction (HFpEF).

Methods: 111 consecutive HFpEF patients (70.0 ± 9.3 years; 67.4% female) were prospectively enrolled and underwent CMR and right heart catheterization within two weeks. Moderate and severe PH was defined as mean pulmonary artery pressure (mPAP) ≥ 30 mmHg.

Results: By invasive assessment 64% of patients suffered from moderate/severe PH. Significant differences between patients with and without moderate/severe PH were observed with respect to PA diameter (30.9 ± 5.1mm versus 26 ± 5.13mm, p < 0.001), PA:Ao ratio (0.93 ± 0.16 versus 0.78 ± 0.14, p < 0.001), and SMT diameter (4.6 ± 1.5 mm versus 3.8 ± 1.2; p = 0.008). The strongest correlation with mPAP was found for PA:Ao ratio (r = 0.421, p < 0.001). In addition, PA:Ao ratio measurements showed excellent inter-observer agreement (Intra Class Correlation Coefficients of

0.815). By Receiver Operating Characteristic analysis the best cut-off for the detection of moderate/severe PH was found for a PA:Ao ratio of 0.83.

Patients were followed for 13.5 ± 11.5 months. By Kaplan Meier analysis event-free survival was significantly worse in patients with a PA:Ao ratio ≥ 0.83 (log rank, $p = 0.001$). By multivariable Cox-regression analysis PA:Ao ratio was independently associated with event-free survival (HR 16.1 [CI 2.5-105.4], $p = 0.004$).

Conclusion: PA:Ao ratio is an easily measurable noninvasive indicator for the presence and severity of PH in HFpEF, and it is related with outcome.

P407

FDG-PET imaging for the management of suspected inflammatory cardiomyopathies beyond cardiac sarcoidosis: a single center initial experience

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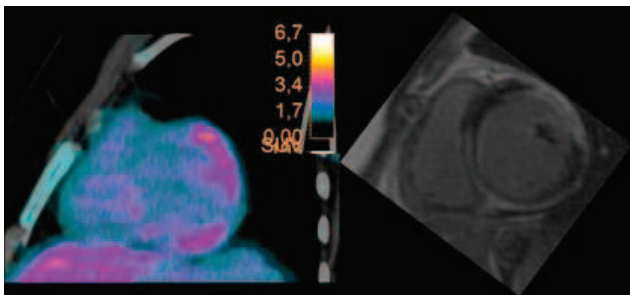
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Purpose: FDG-positron emission tomography (PET) has high diagnostic accuracy in cardiac sarcoidosis (CS). Beyond CS, the non invasive diagnosis of inflammatory cardiomyopathies (IC) is challenged by a lower diagnostic performance of usual tools as magnetic resonance imaging (MRI).

Methods: 17 consecutive patients with suspected IC had a FDG-PET to detect myocardial inflammation. From all clinical data including PET, we classified patients in either CS or non-CS and respective PET data were compared. The clinical impact of adding PET in the non-CS group was evaluated by comparing diagnosis and management proposed by an expert blind to PET with final diagnosis and management actually held in practice.

Results: 6 patients had CS, all with positive PET. In the 11 non-CS patients, 7 had a positive PET. All had MRI late gadolinium enhancement in FDG uptake areas, suggesting a true positivity of PET for the presence of inflammation. PET data were all significantly different between CS and non-CS patients with positive PET. In non-CS patients, 2 were classified as certain IC, 2 as excluded IC, and 7 as possible IC by an expert blind to PET. Adding PET in clinical practice, IC was excluded for 5 of the 7 patients with possible IC, 2 patients remained with a possible IC diagnosis and the 2 certain IC were confirmed. PET did not change patient management in terms of endomyocardial biopsy or immunosuppressive therapy.

Conclusion: Some patients with suspected IC had a positive FDG-PET in favour of myocardial inflammation, with a different pattern from that observed in CS. Adding PET to usual diagnostic tools led to a decrease of possible IC diagnosis that turned in excluded IC. These preliminary data suggest a potential role of PET for the non-invasive diagnosis of IC that will need further investigations.



FDG uptake concordant with MRI-LGE

P408

Angiographic follow-up of Marfan syndrome patients after aortic root replacement: what can we expect?

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Introduction: Marfan syndrome (MFS) is an autosomal dominant disease caused by mutations in the gene encoding fibrillin-1 that manifests in cardiovascular (CV), skeletal and ocular tissues. The leading cause of death is acute dissection of the ascending aorta, but surgery has improved life expectancy. However distal aortopathy seems to be an important issue after aortic root replacement (ARR). The aim of this work was to compare the prevalence and clinical relevance of distal aortic disease in MFS patients (pts) with or without AAR.

Methods: Data were obtained from 46 MFS pts followed in a reference center.

Twenty pts underwent AAR between 1991 and 2012, the majority of cases (60%) due to aortic root aneurysms and the remaining (40%) to acute dissections. Clinical data was collected from medical records and angiographic evaluation was performed with magnetic resonance (MRA) or computed tomography (CTA). Dimensions of aorta segment were compared in the operated (OP) vs non-operated (NOP) pts using t-test and evaluation of dilation in the two groups was compared using χ^2 test.

Results: The majority of pts were male ($n = 16$, 61.5% non-operated; $n = 13$, 65% operated) and the mean age was similar in OP and in NOP (45.7 ± 11.3 years vs 34.8 ± 13.4 years, $p = 0.56$) at the time of angiographic evaluation. The mean age at the time of surgery was 34.4 ± 12.7 years. Family history of MFS was found in 74%, (28% OP, 46% NOP). The prevalence of CV risk factors was not different in the two groups with the exception of diabetes mellitus, more frequent in the OP group ($n = 4$, 20% vs $n = 0$, 0%; $p = 0.03$). After intervention all pts remained on medical treatment (22% on beta-blockers, 28% on ARA II and 50% on both) until the latest angiographic follow-up (9.0 ± 6.8 years from surgery in OP pts). Aortic dilation was present in 63% (46% thoracic, 2% abdominal, 15% thoracoabdominal), being more prevalent in OP pts ($n = 17$, 85%) than in NOP pts ($n = 12$, 46%; $p = 0.01$). Aneurysms were noted in 9(45%) OP pts, predominantly in the thoracic aorta, while they occurred in only 3(12%) NOP pts. Dissection de novo in the descending aorta occurred and was fatal in 3 patients, all of them with prior AAR. No patient died secondary to complications related to AAR.

Conclusions: It is well known that MFS pts have an increased risk of aortic events in the ascending but also in more distal aorta. Although medically treated pts presented with some cases of distal aortopathy, this risk seems significantly higher in OP pts, reinforcing the need of close angiographic surveillance of distal aorta, especially in this population of MFS pts.

P409

A new parameter of 123I-metaiodobenzylguanidine (MIBG) to assess the risk of major cardiac events in patients with heart failure

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Background: Prevention of sudden cardiac death (SCD) is the most important goal in patients (pts) with heart failure (HF). Malignant ventricular arrhythmias constitute the most common mechanism of SCD. Sympathetic denervation of the myocardium is also thought to play an evident role in the development of life-threatening ventricular arrhythmias and sudden arrhythmic death. ICD represents the therapy of choice for pts at risk of malignant ventricular arrhythmias, ICD has also been established for primary prevention in high risk pts. Iodine-123 Meta-Iodobenzylguanidine (MIBG) scan represents a safe and reliable method to evaluate this risk. ADMIRE-HF study establishes that myocardial uptake of MIBG measured as a heart to mediastinum (H/M) ratio is an indicator of sympathetic function [$H/M \leq 1.6$]. Another parameter is Late Summed Score (LSS) when it is lower than 26 indicates low risk of ventricular arrhythmias. But LSS results difficult to calculate for the effect of extracardiac activity on external segments of polar map.

Methods: From 2010 to 2014 we evaluated prospectively 170 patients (age 64.2 ± 0.8 years old; 81,6% males) admitted to our hospital with diagnosis of HF (left ventricular ejection fraction $\leq 35\%$; NYHA class II, III and IV) 69 patients with non-ischemic dilated cardiomyopathy and 101 pts with post-ischemic HF. They underwent to 123I-MIBG. Planar images were analyzed and early and late H/M ratio were obtained. Data from seventeen segments were semi-quantified using the 5-point visual scoring model of tracer uptake (0, normal - 4, absent), as recommended by AHA and ASNC. LSS was obtained by MIBG SPECT myocardial receptor images.

Results: We obtained an important result from the weighted analysis of segments. The third medium of septal wall represents the best predictor for malignant ventricular arrhythmias with an AUC of 0.81.

Conclusion: Mid septal wall is the parameter that is less influenced by extracardiac activity and it shows to be reliable to identify HF pts at high risk of SCD that may benefit of ICD.

P410

Perfusion and metabolic scintigraphy in prognosis of cardiac resynchronization therapy in patients with non-ischemic cardiomyopathy

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Purpose of the study was to study perfusion and metabolism of the left ventricular (LV) myocardium in patients with non-ischemic cardiomyopathy (NICMP) and to identify the scintigraphic predictors of the efficacy of cardiac resynchronization therapy (CRT).

Methods: The study comprised 63 patients with NICMP and NYHA class III-IV chronic heart failure. Before CRT, all patients received scintigraphy with ^{99m}Tc-MIBI and with ^{123I}-BMIPP for evaluation of myocardial perfusion and metabolism, respectively. Before CRT and six months after, all patients underwent echocardiography study to estimate intracardiac hemodynamics.

Results: Patients were divided into two groups 6 months after CRT: (1) responders - LV ESV decreased by $\geq 15\%$ ($n=39$); (2) non-responders - LV ESV decreased by $< 15\%$ ($n=24$). Correlation analysis demonstrated the presence of significant association ($r=0.37$, $p<0.5$) between the sizes of metabolic defect and changes in the values of LV ESV after 6 months the implantation of CRT device. Before CRT, LV pumping function didn't significantly differ between groups. Significant differences were found in the following preoperative scintigraphic parameters: myocardial perfusion defect size and metabolic defect size. Metabolic scintigraphy showed higher diagnostic efficacy in determination of indications for CRT compared with perfusion scintigraphy (AUC 0.722 and AUC 0.612, respectively). The best metabolic defect size threshold value of 7.35% predicted CRT efficacy with the sensitivity and specificity of 77.8% and 66.7%, respectively. To increase diagnostic efficacy of the metabolic scintigraphy in detection of potential responders and non-responders to CRT, we performed multiple regression analysis. The equation of the dependence of postoperative LV ESV dynamics on the original values of stroke volume (SV) and metabolic defect size (BMIPP-score,%) on early scans is $\Delta\text{ESV}' = -59.14 + 1.44 \cdot \text{BMIPP-score} + 0.3 \cdot \text{SV}$. The multiple regression equation enables to predict CRT outcomes even more accurately than the isolated metabolic scintigraphy results (AUC = 0.972).

Conclusions: The results of myocardial metabolic scintigraphy with ^{123I}-BMIPP may be used as the secondary criteria for selection of patients for CRT and for prediction of the efficacy of this interventional treatment modality in patients with NICMP.

P411

The ways of revascularization influence in the acute period of myocardial infarction on the structural and functional remodeling of the left ventricle

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The aim of the research was to study the most efficient ways of revascularization influence in the acute period of myocardial infarction (MI) on the structural and functional remodeling of the left ventricle (LV).

Methods: After a time period of one year 101 STEMI patients were performed echocardiographic research to analyze the dynamics of the disease. The age group of the patients was 56 ± 9.99 years, 81.9% out of them were men. All the patients were subdivided into three groups according to availability and the way of revascularization in the acute MI period: the 1st group ($n=28$; 27.7%) consisted of the patients with thrombolytic therapy (TLT); the 2nd group ($n=42$; 41.6%) included patients with percutaneous coronary intervention (PCI), and the 3rd group ($n=31$; 30.7%) consisted of patients with no myocardium revascularization.

Results: The patients of the 2nd group demonstrated reliable positive dynamics in the form of SPWMD thickness reduction ($r=0.000$), IVMD ($r=0.010$), the decrease of LVMI ($r=0.035$), the reduction of a wall relative thickness index ($r=0.0007$), the increase of exertion index by the volume ($r=0.045$), the fraction of LV emission (LVEF) (0.000) and VE/VA MK ($r=0.028$). All the above proves the regress of the LV hypertrophy (LVH), as well as the improvement of systolic and diastolic functions. The dynamics in the 3rd group of the patients was characterized by the increase of IKDR ($r=0.000$), IKDO ($r=0.049$), LVMI ($r=0.000$), MS ($r=0.000$), LVEF ($r=0.049$), the indicator of the impactive emission ($r=0.003$), VE/VA MK ($r=0.020$), which demonstrate the LVH progress, deterioration of the systolic and diastolic LV functions. As to the patients of the 1st group, it should be noted that they had a lack of reliable changes of the systolic and diastolic LV functions, structural characteristics of the heart chambers, but the level of the intergroup changes was reliable.

Conclusions: The PCI performance in the acute period of the disease promoted the regression of structural and functional LV remodeling, i.e. the reduction of hypertrophy expressiveness, and improvement of systolic and diastolic function. Thus, it proves to be the most efficient method for MI treatment. Performance of TLT only did not result in reliable dynamics of structural and functional LV indicators after a year time period. In the patients without revascularization in the acute MI period progression of hypertrophy, deterioration of systolic and the diastolic LV function were observed.

P412

Global right and left atrial performance in hematological malignancies explored by velocity vector imaging

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Purpose: We investigated the potential effects of chemotherapy on left & right atrial (LA/RA) function in patients with hematologic malignancies.

Methods: Velocity vector imaging echocardiography was acquired from the apical 4 chamber view in 17 patients with leukemia and lymphoma pre and at least 3 months post chemotherapy. Patients were on multiple chemotherapy protocols including mitotic inhibitors, alkylating & ancillary agents, anthracyclines, targeted & biologic therapy, and antimetabolites. The atrial subendocardium was traced to obtain RA/LA volumes and dynamic function.

Results: Mean age was 53 ± 18 years with 10 men (59%). No significant changes were noted in LA/RA dynamic function and ejection fraction as well as left ventricular ejection fraction with chemotherapy (TABLE).

Conclusions: The current cohort delivers an overview concerning safety of chemotherapy in hematologic malignancies with seemingly insignificant risk. This is presumably due to small study population, use of multiple protocols to minimize cardiotoxic anthracyclines or low predilection of cardiac involvement in hematologic malignancies.

	Pre-chemotherapy	Post- chemotherapy	P-Value
LEFT ATRIUM			
EJECTION FRACTION (%)	65.4±7.9	66.1±12.5	0.34
RESERVOIR FUNCTION			
1-Filling Volume (ml)	45.6±29.5	39.1±9.9	0.15
CONDUIT FUNCTION			
1-Passive emptying (%) of total emptying	44.9±29.6	38.4±9.9	0.15
BOOSTER PUMP FUNCTION			
1- Active emptying (%) of total emptying	17.3±11.9	18.2±8.9	0.34
RIGHT ATRIUM			
EJECTION FRACTION (%)	57±13.8	57.9±12.1	0.49
RESERVOIR FUNCTION			
1-Filling Volume (ml)	29.2±14.2	26.3±12.3	0.28
CONDUIT FUNCTION			
1-Passive emptying (%) of total emptying	28.5±14.4	25.5±12.4	0.27
BOOSTER PUMP FUNCTION			
1- Active emptying (%) of total emptying	12.6±8.7	12.4±4.8	0.49

P413

Comparative analysis of two-dimensional strain and strain rate imaging of the left and right heart in prosthetic heart valve thrombosis before and after thrombolytic therapy

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Purpose: Thrombolytic therapy (TT) is effective for the treatment of prosthetic heart valve thrombosis (PHVT). The potential effects of TT in patients with PHVT to right and left heart deformations have not been studied.

Methods: We studied 71 patients (49 female, 47 mitral; 21 aortic; 1 mitral and aortic; 2 tricuspid valve, 38% with atrial fibrillation; 47% obstructive PHVT; mean age: 49 ± 14) with PHVT before and early after TT. Speckle tracking derived left ventricle (LV), right ventricle (RV), left atrial (LA) and right atrial (RA) global longitudinal peak systolic strain (S) and strain rate (SR) were measured from apical four, two and three chamber views. Peak systolic atrial longitudinal S and SR were measured during atrium reservoir phase.

Results: TT was successful in 68 patients (95.7%). Only peak systolic S at left atrium (LA) reservoir phase increased significantly in successfully thrombolysed

Table 1.	Deformation Parameters	Mean ± Std (pre TT vs. post TT)	P value
Obstructive Aortic PHVT	LV-S-4CH	-14.32±2.34 vs. -16.88±3.28	0,012
LV-SR-4CH	-0.92±0.14 vs. -1.12±0.20	0,010	
LV-S-2CH	-12.34±2.56 vs. -13.56±2.88	0,001	
LV-SR-2CH	-0.83±0.19 vs. -0.88±0.19	0,019	
LV-S-3CH	-12.99±2.60 vs. -14.72±3.49	0,017	
LV-S-GLOBAL	-13.21±2.26 vs. -15.02±2.81	0,001	
LA-S	18.03±2.85 vs. 20.72±4.91	0,013	
Obstructive Mitral PHVT	LA-S	21.87±5.85 vs. 23.05±5.97	0,029
RV-S	-20.84±4.36 vs. -22.07±3.94	0,018	
RV-SR	-1.17±0.22 vs. -1.26±0.28	0,023	

patients (19.6±9.0 vs. 18.7±8.6 p=0.009). Subgroup analysis showed that, LV 4-chamber S and SR, LV 2-chamber S and SR, LV 3-chamber S, LV global S and LA peak systolic longitudinal S differed significantly following TT in patients with obstructive prosthetic aortic valve thrombosis. Similarly, there was a significant difference between RV-S, RV-SR and LA peak systolic longitudinal S before and after TT in patients with obstructive prosthetic mitral valve thrombosis (Table 1). **Conclusion:** Successful thrombolysis of obstructed aortic and mitral valves may result in a significant improvement in LV, LA and RV, LA deformation parameters respectively.

P414

Indications, safety and usefulness of exercise stress echocardiography in patients with impaired left ventricle ejection fraction

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Background: Exercise Stress Echocardiography (ExE) usefulness and safety in patients with impaired left ventricle ejection fraction (LVEF) still remains a concern. We ought to present the experience of a tertiary hospital.

Methods: We evaluated 301 consecutive patients referred for ExE in a tertiary hospital (June 2012 - May 2013). Patients with abnormal LVEF were analysed. Indications and ExE results were reviewed. Revascularization, admittance in a Cardiology ward and death during the follow up were analysed.

Results: We found 49(16%) patients with abnormal LVEF: 26 (9%) LVEF 54-50% (borderline-group B) and 23(8%) LVEF<50% (impaired LVEF-group I). We did not find differences between groups regarding cardiovascular risk factors except diabetes (56% vs 17%,p=0,006). History of myocardial infarction was also similar (62% vs 61%, p=n.s). In 45 patients (91,8%) ExE was performed (Table). Complications related to ExE were not found. In both groups, the most frequent reason to request an ExE was to diagnose ischemia in symptomatic patients (46% vs 56%, ns); a positive ExE was more frequent in group I (10% vs 39%, p = 0,12) and in both groups it was followed by invasive angiography except in 1 patient (group I). The second most frequent indication was to guide treatment in patients with known obstructive coronary disease (46% vs 30%,ns). Among these patients revascularization was not performed if ExE failed to demonstrate ischemia, only 1 patient (7%, group B) required hospitalization and 1 patient died (7%, group I) during follow up (14,2±7 months). Less frequent indications were to assess for ischemia in asymptomatic patients (4% vs 4%,ns) and to assess valvulopathies (0% vs 4%,ns). A positive ExE was not found to be a predictor of future cardiologic hospitalization or death in a multivariate model (a bigger sample or a longer follow-up might have shown a significant association).

Conclusions: ExE is a test feasible and safe in patients with borderline and impaired LVEF. Our data suggest that ExE is useful in diagnosing ischemia and guiding revascularization in patients with abnormal LVEF.

table (ExE)

	BORDERLINE	IMPAIRED	
METs	7,3±3	6,7±2	p=0,06
ExE positive	10(44%)	8(36%)	p=0,63
Extensive ischemia	9 (39%)	5(23%)	p=0,24

P415

Atrial electromechanical coupling times in patients with repaired tetralogy of fallot

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Objectives: After repair of Tetralogy of Fallot (rTOF), dilation and dysfunction of the right ventricle (RV) due to chronic pulmonary regurgitation is very common. The manifestations of global and regional systolic RV functions are well documented, but few studies focused on atrial electromechanical coupling times (AEMCT). We aim to assess the AEMCT in patients with repaired TOF.

Methods: 50 patients with repaired TOF and 20 normal controls were involved and underwent echocardiography in our study. The time intervals (adjusted by heart rate) from the onset of P wave on ECG to the onset of late diastolic A wave were recorded from the septal annulus (Septal pA'), lateral annulus (Lateral pA') and tricuspid annulus (Tricuspid pA'). The right AEMCT (Septal pA'- Tricuspid pA'), left AEMCT (Lateral pA'- Septal pA') and inter AEMCT (Lateral pA'- Tricuspid pA') were calculated.

Results: Groups were similar for age (mean age: 31.9±13.9y vs 34.4±12.8) and gender (male: 48% vs 50%). Left ventricular ejection fraction (LVEF) was decreased but still in normal range in patients with rTOF compared with normal controls. Tricuspid pA' was significantly prolonged (p<0.01), inter-atrial AEMCT and right AEMCT was significantly decreased (both p<0.01) in patients with rTOF compared with normal controls (Table1). Tricuspid pA' was correlated with tricuspid annulus A velocity (r=-0.262, p=0.016).

Conclusions: There is a time delay in the RA compared to LA between the onset of electrical conduction and mechanical activity in atrial contraction, which may be a reflection of the RA and LA electromechanical mis-coupling in patients after TOF repair.

Table Atrial coupling times in 2 groups

	Normal (n=20)	rTOF (n=50)
LVEF (%)	71.25±10.26	57.65±11.65*
RA valume (ml)	28.05±13.89	47.66±25.45*
RV A velocity (m/s)	10.26±3.30	7.04±2.13*
Septal pA'(ms)	51.30±2 11.10	49.05±15.58
Lateral pA'(ms)	67.46±14.71	60.09±20.05
Tricuspid pA'(ms)	49.76±14.18	66.59±40.71*
left AEMCT (ms)	16.16±15.06	11.04±22.55
Inter-atrial AEMCT (ms)	17.70±16.70	-6.50±40.67*
Right AEMCT (ms)	1.54±12.51	-17.54±39.37*

*: P <0.05 compared with normal controls.

P416

Echocardiographic assessment in patients with chronic heart failure

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Purpose: Heart failure is a major global public health problem. Echocardiography remains an important means in its diagnostic, etiologic, therapeutic, and prognostic management. This study aimed to evaluate the echocardiographic parameters and their evolution in patients with chronic heart failure.

Method: A descriptive study was conducted from May 2006 to September 2014. 1,614 patients followed in our chronic heart failure unit were included. Echocardiographic parameters were recorded at the first admission and during follow-up.

Results: Mean left ventricle ejection fraction(LVEF) was 35.72 +/- 11.12 % ; 11.54% of our patients had preserved ejection fraction and 10.68 % had right ventricular dysfunction. Diastolic cardiac dysfunction accounted for 28.3 % and 48.9 % had a dilated heart cavities. 55.3 % had wall motion abnormalities and 8.36% had mitral regurgitation > grade II. During follow-up, LVEF increased by 2.61%.

Conclusion: As new biomarkers are increasingly used, echocardiography remains an accessible and essential means in the management of heart failure.

P417

Correlation between left ventricular systolic function by longitudinal speckle tracking and Simpson method

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Introduction: Expression of left ventricular systolic function in term of ejection fraction by m- mode, Simpson's method or by subjective eyeball has multiple limitations and marked inter and intra observer variability. Average global strain (AGS) by longitudinal speckle tracking may provide easy, reproducible and accurate assessment of LV systolic function.

Aim of work: expression and grading of left ventricular systolic function in term of average global strain (AGS) by longitudinal speckle tracking.

Methods: sixty individuals including 20 normal and 40 post MI patients were enrolled in the study. EF% by Simpson's method and AGS by longitudinal speckle tracking were measured for all individuals. Correlation and grading LV of systolic function by the 2 methods were done.

Results: There was a highly significant correlation between LV EF% by Simpson's method and AGS by speckle tracking ($p < 0.0001$). Normal LV EF% i.e. $\geq 55\%$ was consistent with AGS $\leq -20\%$. Fair LV EF% i.e. between 50-55%, was consistent with AGS between -15.1 and -20% . Mildly impaired EF % i.e. 40-50% was consistent with AGS -14.1% and -15.1% . Moderately impaired EF% i.e. 30-40 % was consistent with AGS between -9% and -14.1% . Severely impaired EF% i.e. $<30\%$ was consistent with AGS $> -9\%$.

Conclusion: Expression of LV systolic function in term of AGS by speckle tracking may be considered as a new reliable method for assessment of LV systolic function.

P418

Impact of the EAS index in acute coronary syndrome

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Background: Tissue Doppler imaging (TDI) to detect left ventricular (LV) systolic and diastolic myocardial functions. In patients with acute coronary syndrome did not studied.

Purpose: Our aim was to investigate the prognostic value of patients (p) admitted with a myocardial infarction with ST elevation (STEMI) according to their EAS index ($E'/A' \times S'$).

Methods: We realized a prospectively cohorts study and included 80 P with STEMI undergoing primary angioplasty from September to December 2012. Pulsed-wave TDI (PWTDI), including average of peak systolic (S'), early (E') and late diastolic (A') velocities from mitral annular sites was evaluated. PWTDI was also calculated to create a combined index (EAS index) of diastolic and systolic performances. Also we evaluate the incidence mayor cardiovascular events defined as death, recurrent ischemia, revascularization and stroke during admission and follow-up.

Results: 86 % are men, 22% were active smokers, 11% with previous history of CAD, 42% hypertensive, 14% obese and 8% were nephropathy. The mean age of patients was 67 ± 11 years. Based on the filling pattern: 85,4% showed $EAS < 10$ and 14,6% $EAS \geq 10$. Baseline characteristics were similar in all groups. There were no significant differences in symptom onset-to-balloon time or door-to-balloon time and performed treatment. EAS index ≥ 10 was associated had more cardiovascular events (6,25% vs 3,75, $p = 0.04$), independent the systolic ventricular function and diastolic function. A After 300 days, patients with EAS index < 10 had a survival free events 88% vs 60% of patients with EAS index ≥ 10 (long Rank: 3.912, $p = 0.07$).

Conclusions: The EAS index reflects systolic and diastolic performances, is a highly effective means of differentiating patients with STEMI with worse prognosis.

P419

Assessment of myocardial viability using pulsed tissue doppler mitral annulus velocity during dobutamine stress echocardiography

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Background: Assessment of viability could be of significance in ischemic and heart failure patients before deciding for revascularization. The use of Dobutamine stress echocardiography has the disadvantage of subjective visual evaluation of regional wall motion.

Aim: to evaluate the value of Pulsed wave tissue Doppler (TDI) mitral annulus velocity with dobutamine echocardiography in assessment of myocardial viability and prediction of functional recovery of wall motion abnormalities after revascularization in patients with coronary artery disease.

Patients and Methods: The study group included 40 patients, with coronary artery disease as proved by diagnostic coronary angiography and recommended for potential coronary revascularization. Each patient underwent baseline transthoracic echocardiography, in addition to low dose dobutamine echocardiography using TDI at mitral annulus in 6 different walls. All patients were subjected to revascularization (30 by PCI and 10 by CABG) then followed up after 6 months by transthoracic echocardiography to assess improvement in EF and SWMA.

Results: In order to relate the results of TDI, The 16 segments were reevaluated into 6 walls per patient. Using this method, 240 walls were studied. 19 walls were excluded due to technical difficulties in assessment of TDI. Pulsed wave TDI demonstrated that dysfunctional areas had lower systolic velocities compared to areas considered as normal. However, There was no significant difference in the mean TDI at rest for viable and non-viable walls as detected by dobutamine stress echocardiography. But the increase in TDI velocity with peak dobutamine was significantly more in viable (1.97 ± 0.44) vs. non-viable (1.14 ± 0.54) walls, with $p < 0.0001$.

Using TDI method, 115 (79.3%) walls were diagnosed as viable by this method, while 30 walls were nonviable (20.7%). 80 walls (55.2% of total studied walls) were detected to be viable by both dobutamine conventional 2D echocardiography and dobutamine TDI echocardiography (systolic wave). On the other hand, 27 walls (18.6% of total studied walls) were detected to be non-viable by both methods. However, 38 walls (26.2% of total abnormal walls) showed discordance between the two methods. The improvement of 74 walls of 80 combined TDI& DSE positive walls, making a sensitivity of 90.2%, similarly 24 of 27 concordant TDI & DSE negative walls did not improve, making a specificity of 92.3%.

Conclusion: the current study confirmed the importance of using TDI in different mitral annular sites, as an objective tool in detecting myocardial viability, and to improve the sensitivity and specificity of DSE.

P420

Mid-term impact of manual thrombus aspiration on left ventricular remodeling: the echocardiographic substudy of the randomized physiologic assessment of thrombus aspiration in patients with ST-segment

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Background: It has been reported that index of microcirculatory resistance (IMR) is lower in STEMI patients who underwent thrombus aspiration before stent implantation compared to those treated with conventional primary PCI. The aim of this study was to evaluate impact of improved myocardial perfusion by manual thrombus aspiration assessed by IMR on left ventricular remodeling in STEMI patients at mid-term follow-up.

Method: The total of 115 patients entered the echocardiography substudy of the PATA STEMI (randomized Physiologic Assessment of Thrombus Aspiration in patients with ST-segment Elevation Myocardial Infarction) trial which evaluated efficacy of manual thrombus aspiration using Eliminate3 catheter (Terumo Europe, Leuven, Belgium). Echocardiography was done within the first 24 hours after the index procedure and after 4 months. End-diastolic and end-systolic left ventricular (LV) volumes, ejection fraction (EF), cardiac sphericity index (CSI) and regional wall motion score index (WMSI) were calculated.

Results: In baseline characteristics, in patients with thrombus aspiration compared to those with conventional primary PCI, total ischemic time tended to be longer $246,7 \pm 181,8$ vs. $200,9 \pm 110,1$ min, $P = 0,09$ and AUC CK was smaller 40090 ± 26158 U/L vs. 52676 ± 32013 U/L, $P = 0,026$. Also, corrected IMR was lower in thrombus aspiration group $27,5 \pm 16,8$ vs. $39,9 \pm 32,7$ U/L, $p = 0,039$, while coronary flow reserve ($1,68 \pm 0,81$ vs. $1,61 \pm 0,67$, $P = 0,6$) and mean coronary wedge pressure ($20,4 \pm 6,6$ vs. $21,4 \pm 7,8$ mmHg, $P = 0,5$) were similar. End-diastolic and end-systolic LV volumes per body surface area, EF, CSI volume and WMSI were similar between the thrombus aspiration and conventional PCI group at baseline and at follow-up. At follow-up, percent change in WMSI tended to be greater in thrombus aspiration group (decrease in WMSI 8,2% vs. increase in WMSI 0,8%, $P = 0,094$). The rate of major adverse events (death, myocardial infarction, stroke or hospitalization for heart failure) at 12 months follow-up was similar between thrombus aspiration and conventional PCI group: 4,6% vs. 11,1%, $P = 0,20$.

Conclusions: Improved myocardial perfusion assessed by IMR has no impact on left ventricular remodelling rate in STEMI patients at mid-term follow-up.

2D strain parameters							
Characteristics	Long global S	Long basal S	Long medium S	Long apical S	Apical Ratio: Long apicalS/ basal+medium	Long S	Rad global S
Controls (n = 15)	-19,86±2,7	-18,74±5,8	-19,69±2,4	-21,04±2,9	0,56±0,1		27,7±6,2
Amyloidosis (n = 23)	-7,87±2,9 a,b	-4,92±2,2 a,b	-6,73±2,6 a,b	-11,8±5 a	1,08±0,5 a,b		10,59±6,3 a,b
Hipertrophic cardiomyopathy (n = 51)	-12,57±3,8 a,b	-12,53±3,7 a,b	-10,99±4,2 a,b	-14,2±6,1 a	0,61±0,2		20,21±6,5 a,b

a. p < 0.05 compared to controls; b. p < 0.05 between CA and HCM.

P421

Value of myocardial deformation parameters for the differential diagnosis between cardiac amyloidosis and hypertrophic cardiomyopathy

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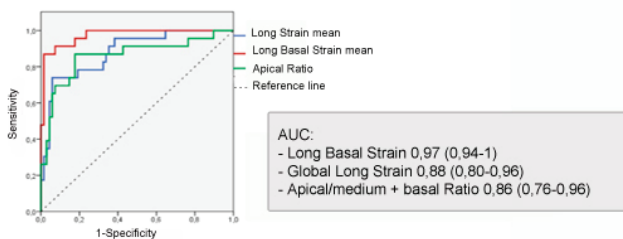
Cardiac amyloidosis (CA) and hypertrophic cardiomyopathy (HCM) are entities to be considered in the differential diagnosis of left ventricular hypertrophy. 2D Strain parameters can provide additional value in doubtful cases.

Objective: To describe regional patterns of longitudinal (LongS) and radial (RadS) strain in the CA and test its usefulness.

Methods: 23 patients with CA, 51 patients with HCM and 15 controls were included. Echo images were obtained at 4, 3, and 2 chambers and basal and medium short axis. We analyze the LongS and RadS curves in 16 individual segments. Apical ratio was calculated.

Results: The LongS and RadS VI values are severely reduced in patients with CA, particularly in the basal segments. The Apical ratio is clearly higher in the CA. The ROC curves showed that a value of the LongS basal segments > - 9% has a sensitivity of 96 %, specificity of 83% and negative predictive value of 97.7 % for the diagnosis of CA.

Conclusion: CA is characterized by longS values globally decreased, with particular involvement of basal segments. This pattern is easily recognizable, reproducible and useful in differentiating this two entities. With its systematic application, and the clinical relevance of this disease, an earlier diagnosis of CA could be performed.



ROC curves

BIOMARKERS

P422

Influence of statin on inflammatory status and hospital readmissions in acute decompensated heart failure with preserved ejection fraction

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Background: Inflammation is an important process in the development of heart failure. The objective of this prospective study was to evaluate whether statin therapy helps improving the life quality and decrease the readmissions due to aggravated heart failure patients with preserved ejection fraction (HFPEF).

Methods: The study included 78 patients hospitalized with a first diagnosis of heart failure with preserved ejection fraction (HFPEF), in sinus rhythm. The diagnosis of

heart failure was based on clinical, echocardiographical (left ventricular ejection fraction ≥45%, E/E' ratio ≥15) and biological (plasma BNP ≥150 pg/ml) parameters. 64% were women, the mean age was 66 years.

Results: The treatment of patients consisted in betablockers (91%), angiotensin converting enzyme inhibitors (55%), angiotensin receptor blockers (32%), diuretics (68%) and statins (61%). At the 1 year re-assessment, we found that 41% of the patients have had rehospitalizations. 19% due to heart failure aggravation. The latter were predominant females, older, had higher values of BNP, NT-proBNP and TNF-a at admission. Regarding to treatment, those with readmissions received more frequently angiotensin receptor blockers (p=0.013) and diuretics (p=0.008), but more rarely statins (p=0.027). Statin treatment determined a significant reduction of the inflammatory marker TNF-a (p < 0.0001) after 1 year.

Conclusions: These results suggest that reducing the inflammatory status by statins may improve the outcome of HFPEF patients, reducing rehospitalizations due to heart failure aggravation.

Correlations between HFPEF biomarkers

	BNP	NT-proBNP	MLHFQ	6MWT
Baseline	r = 0.652	r = 0.434	r = 0.415	r = 0.424
TNF-α	p < 0.001	p < 0.001	p < 0.001	p < 0.001
AT 1 year	r = 0.718	r = 0.579	r = 0.352	r = 0.436
TNF-α	p < 0.001	p < 0.001	p = 0.004	p < 0.001

HFPEF: heart failure with preserved ejection fraction, BNP: brain natriuretic peptide, NT: N-terminal, TNF: tumor necrosis factor, MLHFQ: Minnesota evaluation of life quality in heart failure, 6MWT: 6 minutes walk test.

P423

Analytical performance of the new aspect-PLUS ST2 test and comparability with the presage ST2 assay

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Purpose: For optimal clinical utility new in vitro diagnostic tests should be significantly comparable with existing tests. The Presage[®] ST2 Assay, which is an ELISA format, provided the first fully validated assay for the cardiac biomarker ST2. The new Aspect-PLUS[™] ST2 Test utilizes the same antibodies as the Presage[®] ST2 Assay. This assessment evaluates the analytical performance of the Aspect-PLUS[™] ST2 Test and it's comparability with the established Presage[®] ST2 Assay.

Methods and Results: The Aspect-PLUS[™] ST2 Test is a quantitative fluorescent lateral flow format assay. The standard analytical and clinical performance characteristics were evaluated including analytical sensitivity, linearity, precision, hook effect and interfering substances. The two assay formats were also evaluated for comparability using Passing-Bablok regression and correlation analysis. Table 1 summarizes the basic test and analytical performance characteristics of the two assay formats.

Comparability of the two assay formats was also assessed by Passing-Bablok regression testing. A set of 60 EDTA plasma specimens were measured in duplicate using the Aspect-PLUS[™] ST2 Test and with three different lots of Presage[®] ST2 Assay's. This analysis showed no significant deviation from linearity (p=0.75, y = 1.01x + 5.8). And a correlation coefficient (R) of 0.92.

Conclusions: The new Aspect-PLUS[™] ST2 Test is comparable to the established Presage[®] ST2 Assay and meets the requirements for IVD analytical performance.

Assay Characteristics and Performance		
Parameter	Presage® ST2 Assay	Aspect-PLUS™ ST2 Test
Limit of Quantitation (LoQ)	2.4 ng/ml	12.5 ng/ml
Linearity Limit	200 ng/ml	257 ng/ml
Intra-Assay Precision	4.0%	10.4%
Inter-Assay Precision	6.4%	13.6%
Hook Effect	No hook effect up to 200 ng/ml	No hook effect up to 2000 ng/ml
Interfering Substances	no effect observed from 5 endogenous and 49 therapeutic substances	
Specimen	EDTA or heparin plasma, serum	EDTA plasma
Specimen volume	0.020 ml	0.035 ml

P424

Impact of blood urea nitrogen on in-hospital mortality in Japanese patients with acute heart failure

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Purposes: Cardio-renal syndrome was demonstrated to be important in management of heart failure in 2012 ESC heart failure guidelines. In acute heart failure, several studies have reported that elevated blood urea nitrogen (BUN) is associated with adverse outcomes. This purpose is to assess the effect of BUN on in-hospital outcomes compared with other biomarkers in Japanese patients with acute heart failure.

Methods: Objectives were 352 cases with acute heart failure admitted in our ICU (77 ± 11 years old, Male 189) from 2007 through 2010, in which ischemic heart disease, valve disease, cardiomyopathy, hypertension, tachycardia, bradycardia and others were 147, 47, 47, 46, 27, 9, and 29 cases. Re-admission was 149 cases (42.3%). The relationships between in-hospital outcomes and hemodynamics, anemia, renal function, serum electrolytes, lipid, neurohormonal factors at admission, pre-hospital medication were evaluated retrospectively.

Results: In all objectives, systolic blood pressure, heart rate, were 152 ± 37mmHg, 101 ± 31bpm. Hemoglobin, BUN, serum creatinine, uric acid, total cholesterol were 11.9 ± 2.4mg/dl, 28.7 ± 18.5mg/dl, 1.35 ± 0.91mg/dl, 7.1 ± 2.5mg/dl, 172 ± 42mg/dl. Median of plasma aldosterone concentration (PAC), plasma rennin activity (PRA), BNP were 5.85pg/ml, 1.70ng/ml/h and 1149.3 ± 1326.3pg/ml. Median of admission period was 19 days. Death in hospital was 30 cases (8.5%). Non-survivors had significantly lower systolic blood pressure (135 ± 44 vs 154 ± 36mmHg, p < 0.01), higher BUN (52 ± 33 vs 27 ± 15 mg/dl, p < 0.01), higher serum creatinine (1.84 ± 0.90 mg/dl vs 1.30 ± 0.90, p < 0.01), higher uric acid (9.4 ± 3.8 vs 6.9 ± 2.3mg/dl, p < 0.01), lower total cholesterol (156 ± 42 mg/dl vs 174 ± 42, p < 0.01) and higher PAC (21.9 ± 23.9 vs 10.2 ± 24.9, p < 0.05), higher PRA (13.2 ± 15.5 vs 4.3 ± 8.2 ng/ml.h, p < 0.01), higher BNP (1942.1 ± 2076.0 vs 1075.4 ± 1212.4 pg/ml, p < 0.05) than survivors in-hospital. Clinical scenario, medication of allopurinol and diuretics before admission were significantly different between survivors and non-survivors in hospital. In Cox's proportional hazards analysis, BUN > 23mg/dl (median) was an independent predictive factor of in-hospital death (HR 1.133, 95%CI 1.046-1.386, p < 0.001). Age, systolic blood pressure, serum creatinine, uric acid, total cholesterol, PAC, PRA, log-BNP, medication of pre-admission were not independent predictive factor of in-hospital death.

Conclusions: These results may suggest that BUN > 23mg/dl is the independent high-risk marker of in-hospital mortality in Japanese patients with acute heart failure.

P425

Use of procalcitonin for predicting repeated hospitalisations in patients with acute heart failure

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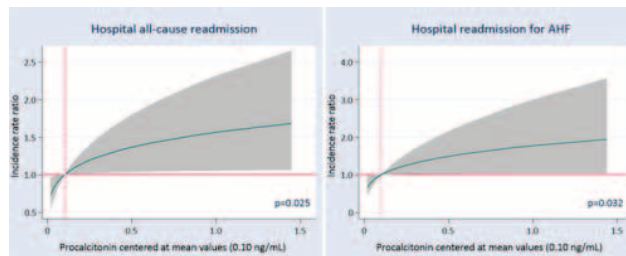
Purpose: Risk of readmission after an episode of acute heart failure (AHF) remains prohibitively high. Despite contemporary heart failure programs and institutional initiatives recognize reduction in the rate of readmissions as a main target; there are not well-established risk factors for identifying patients at maximum risk. PCT has

emerged as a promissory biomarker for risk stratification in heart failure setting, PCT has shown to be associated to higher risk of mortality; nevertheless, the relationship with risk of readmission has not been reported. In this regard, we aimed to evaluate PCT value to predict the risk of all-cause and HF readmissions.

Methods: We measured at admission PCT in 261 consecutive patients admitted for acute heart failure (AHF) after excluding active infection diagnosis. Multivariable negative binomial regression method was used to evaluate the association between PCT and recurrent rehospitalizations at a median follow-up of 2 years.

Results: Patients who died during admission or lacked of any follow-up were excluded, leaving a sample of 243 patients. We accounted 170 all-cause rehospitalizations and 96 AHF-rehospitalizations. In an adjusted analysis, the logarithm of PCT was associated to all-cause rehospitalizations (IRR=1.22, 95% CI: 1.02-1.44; p=0.025) and AHF-rehospitalizations (IRR=1.28, 95% CI: 1.02-1.61; p=0.032). In a same sensitivity analysis forcing white blood cells, CRP, endotoxin and interleukins into the final model, logPCT remained related to all-cause rehospitalization (HR=1.27, CI 95%:1.05-1.52; p=0.013). and HF-rehospitalization (HR=1.27, CI 95%:1.01-1.59; p=0.042).

Conclusion: In patients with AHF and no evidence of infection, PCT was independently and positively associated with the risk of long-term recurrent rehospitalizations.



P426

Copeptin as a prognostic biomarker in patients admitted for acute coronary syndrome

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Purpose of the study was to evaluate the prognostic significance of copeptin in patients with acute coronary syndrome (ACS) in real clinical practice

Methods: 74 patients (66 (59;74) years old) admitted to the emergency department for ACS were involved in the prospective cohort study. Follow-up period was 12 months. The primary end point (PEP) was the composite of cardiovascular (CV) mortality and rehospitalization (RH) due to worsening of CV symptomatic. Copeptin and Gal-3 were measured by commercially available ELISA kit. Blood samples were collected at admission. Gal-3 threshold level was accepted as 17.8 ng/mL.

Results: The rate of reaching primary end point was 28.4%: CV mortality - 10.8% and RH - 17.6%. Gal-3 threshold was exceeded in 54.1%. In patients who did not reach PEP copeptin concentration was lower than in patients who reached PEP (moda 0-2 pmol/ml in 30% vs 2-4 pmol/ml in 13%, p > 0.05). Compared with patients with copeptin concentration less than upper quartile, those with copeptin concentrations exceeding this level were not more likely to reach the PEP with HR 0.54 (CI 0.22; 1.36).

Copeptin levels in patients with acute myocardial infarction and unstable angina were of non-significant difference (2.19(1.16; 3.62) pmol/ml vs 2.51(1.77;4.09) pmol/ml, p=0.144). After sex and diagnosis adjustment positive correlations of copeptin level and in-hospital, and 6 months after discharge death probability (R=0.51 and 0.61, p < 0.05) were detected.

Copeptin concentration addition to age, troponin, Gal-3, BMI, glucose, RBC, platelets and creatinine significantly increased ROC AUC of life without adverse cardiovascular event duration (0.937 vs 0.760).

Conclusion: Copeptin seems to be a promising biomarker for the complex evaluation of emergency patients with acute coronary syndrome. Isolated assessment of copeptin level was not useful in both diagnostic and prognostic decision-making in real clinical practice. Copeptin, Gal-3 and troponin are complementary prognostic markers for CV death and RH in patients admitted for ACS.

P427

The prognostic value of renal dysfunction and NT-proBNP levels in chronic heart failure patients

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The aim was to evaluate the effect of renal dysfunction on a plasma N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels and a prognostic impact of NT-proBNP and estimated glomerular filtration rate (eGFR) in patients with heart failure (HF).

Methods: 84 patients (mean age 54 ± 8.1 years, 89.3% males) with impaired systolic function (LVEF <40%) and symptomatic HF (NYHA class II-IV) were recruited. During the study patients were treated by optimal medical therapy according to the national guidelines. NT-proBNP levels were measured by CARDIAC proBNP assay with a measurement range from 60 to 3000 pg/ml. Renal function was classified into 6 categories (≥ 90 , 60-89, 45-59, 30-44, 15-29, and <15 mL/min/1.73 m²) by eGFR using the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) formula. Serial blood samples were obtained at baseline. The primary end point was defined as unplanned hospitalization due to HF or death related to HF decompensation.

Results: During the follow-up time (follow-up median 18 months), 33 patients (39%) had primary end point (33 hospitalizations due to HF including 6 lethal cases). eGFR ($p < 0.001$), creatinine ($p < 0.001$), NT-proBNP ($p < 0.001$) levels differed significantly between groups. NT-proBNP levels increased with a decrease eGFR. We analyzed the end point onset frequency depending on the NT-proBNP level and eGFR. Analysis of the NT-proBNP concentration and eGFR in relation to clinical condition of patients revealed that 33 patients had primary end point. 16 of these patients had NT-proBNP level more than 3000 pg/ml at baseline visit. 25 patients had eGFR less than 45 mL/min/1.73 m² and frequency end points increased with a decrease eGFR ($p = 0.001$). We investigated the OR of adverse events depending on NT-proBNP plasma level and eGFR. NT-proBNP level higher 3000 pg/ml at baseline increases the OR of end point onset (OR 95% 2.8 (1.1 - 7.0), $p = 0.033$), eGFR from 45 to 59 mL/min/1.73 m² increases the OR of end point onset (OR 95% 2.6 (1.03 - 6.34), $p < 0.044$) and eGFR from 30 to 44 mL/min/1.73 m² increases the OR of end point onset several more (OR 95% 5.8 (1.09 - 30.6), $p < 0.004$).

Conclusion: Renal dysfunction increases the concentrations of NT-proBNP. Utilization of the effect of renal dysfunction and NT-proBNP may improve interpretation for diagnosis and monitoring. This strategy allows identify high-risk patients for more intensive monitoring and more aggressive therapy.

P428

Persistently elevated serum levels of the heart failure marker osteopontin predict mortality in critically ill patient

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Introduction: Heart failure, as well as inflammatory, autoimmune and metabolic disorders have been associated with alterations in Osteopontin (OPN) serum levels. We therefore analyzed OPN serum-concentrations in a large cohort of critically ill medical patients.

Methods: A total of 159 patients (114 with sepsis, 45 without sepsis) were studied prospectively upon admission to the medical intensive care unit (ICU) as well as after three days of ICU treatment and compared to 50 healthy controls. Clinical data, various laboratory parameters as well as investigational inflammatory cytokine profiles were assessed. Patients were followed for approximately one year.

Results: We found strongly and significantly elevated serum levels of OPN at admission to the ICU and after three days of treatment in critically ill patients compared to healthy controls. OPN concentrations were further related to disease severity and significantly correlated with established prognosis scores and classical as well as experimental markers of inflammation and multi-organ failure. In the total cohort, OPN levels decreased from admission to day 3 of ICU treatment. However, persistently elevated OPN levels (especially $>2.5 \mu\text{g/mL}$) at day 3 of ICU-treatment were a strong independent predictor for an unfavorable prognosis and indicated mortality with higher diagnostic accuracy than routinely used markers of organ failure and prognostic scoring systems such as SAPS2 or APACHE-II score.

Conclusion: Persistently elevated OPN serum concentrations are associated with an unfavorable outcome in patients with critical illness. Besides a possible pathogenic role of OPN in critical illness, our study indicates a potential value for OPN as a prognostic biomarker in critically ill patients during the early course of ICU treatment.

P429

Prognostic value of myeloperoxidase in patients with acute myocardial infarction treated with primary percutaneous coronary intervention

The project was funded by the National Science Centre, Poland, grant no. N N402 497340M Kacprzak¹; M Zielinska¹

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Inflammation plays an important role on every stage of atherosclerosis. Myeloperoxidase (MPO), a leukocyte-derived enzyme, probably is involved in many stages of atherothrombosis. According to the recent studies, MPO is related with unfavorable outcome in patients with chest pain and acute coronary syndromes. However, there are no large studies evaluating significance of MPO levels in patients with ST-segment elevation myocardial infarction (STEMI) treated in accordance with current standards.

The aim of the study was to assess if elevated MPO level is a predictor of long-term major adverse cardiovascular events (MACE) in patients with STEMI treated with primary percutaneous coronary intervention (pPCI).

Material and Methods: We investigated data of all consecutive patients hospitalized in our clinic with the diagnosis of STEMI treated with pPCI within two years. Patients with the history of previous MI, known chronic or acute inflammatory disorder or admitted after 12 hours from symptom onset were excluded from the analysis. Plasma levels of MPO collected on admission and the 3rd-4th day of hospitalization were measured by ELISA.

Method: C-reactive protein (CRP) and N-terminal prohormone of B-type natriuretic peptide (NT-proBNP) were also determined. All patients were followed-up prospectively for the occurrence of MACE defined as unscheduled coronary revascularization procedure, stroke, reinfarction or all-cause death.

Results: Our cohort consisted of 127 patients, aged 58 (54; 66) years. After 14 months of follow-up 20% of patients developed MACE. There were no significant differences in the concentration of MPO on admission to hospital between patients who developed MACE compared to uneventful survivors ($p = 0.1179$). However patients who experienced MACE had significantly higher MPO levels assessed in the 3rd - 4th day ($p = 0.00007$).

Elevated MPO levels collected on the 3rd-4th day of STEMI proved to be the strong predictor of death ($p = 0.0039$), reinfarction ($p = 0.0332$), the need for coronary revascularization ($p = 0.0067$) and all adverse events taken together (AUC = 0.770, $p = 0.00007$). In univariate logistic regression analysis also CRP and NT-proBNP concentration assessed in the 3rd-4th day of hospitalization predicted MACE ($p = 0.0262$ and 0.0206 respectively). MPO was significantly better predictor of MACE than NT-proBNP (AUC = 0.770 vs. 0.531; $p = 0.0123$). In multivariate analysis, only MPO and CRP levels assessed on the 3rd-4th day of hospitalization revealed to be significant predictors of MACE ($p = 0.003$ and $p = 0.0227$).

Conclusions: Myeloperoxidase is a prognostic marker in patients with STEMI treated with pPCI.

P430

Glycoprotein CA125 as short and long term prognostic biomarker in heart failure

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Purpose: Serum Carbohydrate Antigen 125 (CA 125) is a high-molecular-weight glycoprotein secreted in response to inflammation and production of interstitial fluid, as a marker of mesothelial cells stress. In Heart Failure (HF), it is secreted in response to fluid overload and higher venous pressure. CA 125 correlates with clinical, hemodynamic and echocardiographic parameters in HF patients. In this study we sought to analyse short and long-term prognostic information yielded by serum CA125 in patients admitted for acute heart failure (AHF). We also analysed whether changes in serum CA 125 correlate with prognosis.

Methods: We have included patients consecutively admitted for AHF to Internal Medicine Department of a teaching hospital between 2013-2014. Ethical Committee had approved the study and all patients gave informed consent to participate. Clinical and analytical data were collected. CA 125 serum levels were obtained in the first 48 hours after admission, 48 hours prior to discharge and one month after it. Patients were grouped according to changes in CA125 concentration between admission and discharge. Increased CA125 concentration (group 1), no change (group 2) or decreased (group 3). Mortality and readmissions at one, six and twelve month after discharge was recorded.

Results: Two hundred patients have been included, (50,5% men, mean age 79 years (CI 95% 78-80,4)). Mean CA125 concentrations were $92,57 \pm 7,73$ U/ml at admission; $97,34 \pm 8,73$ U/ml prior to discharge and $54,98 \pm 7,18$ U/ml one month after discharge, in stable patients. Admission CA125 significantly correlated with mortality at one ($p = 0,004$), six ($p = 0,001$) and twelve months (all-cause mortality $p = 0,02$ and HF-mortality $p = 0,005$). A cut-off point of 60 U/ml of serum CA125 indicates a higher mortality rate (at one $p = 0,016$; six $p = 0,043$ and twelve months (global $p = 0,048$ and HF-mortality $p = 0,013$)). Admission CA125 did not correlate with readmissions. Patients with an increase of serum CA125 between admission and discharge (group 1) had higher mortality at one ($p = 0,04$) and six months ($p = 0,008$) and higher readmission rates at one month ($p = 0,034$).

Conclusions: The concentration of CA125 at admission has a direct correlation with short (one month) and long-term (one year) HF and all-cause mortality, being 60 U/ml the optimal cut-off at which mortality is higher. In addition, patients with a

rise in serum CA125 between admission and discharge are at special risk of severe complications in follow-up and should be carefully monitored after discharge.

P431

Admission and discharge values of soluble ST2-receptor are predictive for short-term prognosis in patients with acute decompensated heart failure

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Purpose: to evaluate the significance of soluble ST2-receptor (sST2) activity during the hospitalization in determining the short-term (90 days) prognosis in patients (pts) with acute decompensated heart failure (ADHF).

Methods: In a prospective single-center trial included 113 pts with ADHF III-IV FC NYHA. Blood sampling to determine the sST2 concentration were taken at the admission before the first dose of diuretic and at discharge from the hospital. The primary end point of the trial was total cardiovascular events for 90 days follow-up period that included cardiovascular (CV) death, hospitalization due to HF, and episodes of HF deterioration needed additional i/v diuretics.

Results: All pts have had elevated sST2 concentrations. At admission sST2 concentrations in high risk pts (who have CV events) were significantly higher compared with low risk pts (without CV events): 68.76 [59.80; 117.7] ng/ml vs 52.56 [36.25; 76.24] ng/ml ($p < 0.05$), as well as at the day of discharge: 48.44 [34.34; 57.50] ng/ml vs 31.28 [21.35; 48.44] ng/ml ($p < 0.05$). sST2 concentration over 59.26 ng/ml at the admission ((82,1% vs 17,9%), with 55,7% sensitivity and 83,3% specificity (HR 5,61 [1,52-20,77], $p = 0,009$), and over 38,31 ng/ml at discharge ((82,1% vs 17,9%), with 76,5% sensitive and 67% specific, (HR 6,26 [1,87-21,02], $p = 0,002$)) significantly associated with the 90-days primary end point. The area under the ROC curve for primary end point for sST2 was 0,69 at the admission and 0,69 at the discharge. Changes in sST2 concentration during the period of pts hospitalization have had no prognostic significance. At the admission and discharge sST2 significantly correlated with NT-proBNP ($r = 0.56$ and $r = 0.52$, respectively, $p < 0,001$).

Conclusion: The values of soluble ST2-receptor over 59.26 ng/ml at the admission, and 38.28 ng/ml at the discharge from the hospital reflects the adverse short-term prognosis in patients with ADHF. The degree of sST2 concentrations changes during the period of hospitalization have had no additional predictive information in ADHF pts.

P432

Which biochemical and clinical parameters are associated with high galectin-3 levels in heart failure?

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Purpose: Elevated Galectin-3 levels has been associated with decompensated heart failure (HF) which is a complex mechanical and neurohormonal syndrome. Many clinical and biochemical factors have been implicated in the pathophysiology of HF. In a group of patients who are referred to emergency clinic for HF, Galectin-3 levels and their association with various clinical and biochemical parameters were determined.

Methods: Decompensated HF, cardiogenic shock, hypotension, 2.and3. degree AV block, pregnancy, serious valvular disease, renal failure (creatinine $> 3,5$ mg/dL) and severe chronic obstructive pulmonary disease were exclusion criteria. Our control group consisted of 25 young healthy people. The study protocol was approved by the local research ethics committee. Galectin 3 levels were measured with an automated enzyme-linked fluorescent assay.

Results: Our study group consist of 70 patients (33 woman and 37 men) and 25 healthy controls. All 70 patients had at least Class II or higher levels of HF according to NYHA criteria. Galectin-3 were significantly higher in the patients group (17,98 vs. 10,24 ng/mL; $p < 0,001$). 53 patients had atherosclerotic heart disease 14 patients had intracardiac cardioverter-defibrillator implantation (ICD), 37 patients had atrial fibrillation and 25 patients had type 2 diabetes mellitus. Low levels of cloremia, low rdw, as a low blood count parameter low MHCH and higher age were associated with elevated levels of Galectin 3. Statistical analysis has shown that galectin-3 were significantly associated with chloride ($p = 0,002$), MHCH ($p = 0,002$), rdw ($p = 0,009$).

Conclusion: Age, hyponatremia and anemia are clinically relevant indices of decompensated HF associated with high levels of Galectin 3.

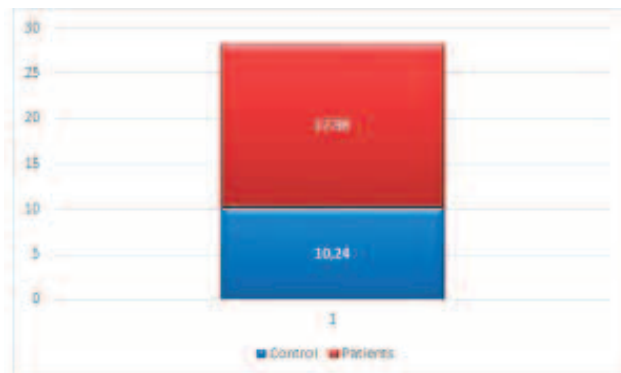


Figure 1. Comparison of gal3 in two groups

P433

Galectin-3 is the most relevant independent predictor of microalbuminuria in chronic heart failure outpatients

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Galectin-3 (Gal-3) is a novel biomarker reflecting inflammation status and fibrosis which has been demonstrated to be strictly related to both chronic heart failure (CHF) and renal dysfunction. The aim of this study was to better clarify this last relationship by evaluating the association between Gal-3 serum levels and microalbuminuria in a group of CHF outpatients.

We enrolled 149 outpatients (82% males, 64 ± 13 years, NYHA class 2.4 ± 0.6 , left ventricular ejection fraction, LVEF $33 \pm 10\%$, GFR EPI 69 ± 27 ml/min $^{1.73}$ m 2) with CHF (ESC criteria) due to left ventricular systolic dysfunction, in stable clinical conditions (> 1 month) and in conventional therapy. All patients underwent a clinical evaluation, a routine chemistry and an echocardiogram. Normalalbuminuria, microalbuminuria and macroalbuminuria were defined as the 24 h urinary albumin/creatinine ratio (UACR) of < 30 , 30 to 299, and ≥ 300 mg/d.

Patients with microalbuminuria, when compared to patients with normoalbuminuria, showed significantly higher levels of Gal-3 serum levels (20 ± 8 vs 14 ± 6 pg/ml). At univariate regression analysis Galectin 3, GFR EPI, LVEF, log NT-proBNP and diabetes were associated with the presence of microalbuminuria.

As shown in the table, in a stepwise forward regression analysis Gal-3 was the first determinant of microalbuminuria, followed by NT-proBNP and diabetes.

In conclusion, our findings demonstrate the independent association between Gal-3 and microalbuminuria in CHF outpatients, thus strengthening the potential clinical usefulness of this biomarker because reflecting the pathophysiological status underlying the progression of cardiorenal syndrome in heart failure patients.

Table

Forward stepwise regression analysis for prediction of microalbuminuria

Variable	OR (95%CI)	p
Gal-3	1.26 (1.06-1.49)	0.009
Log NT-proBNP	1.23 (1.04-1.46)	0.018
Diabetes	1.17 (1.01-1.36)	0.043

Multivariate regression analysis to assess independent predictors of microalbuminuria

P434

Osteopontin levels in adult patients with repaired coarctation of the aorta

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Introduction: Osteopontin (Opn), although minimally expressed in healthy myocardium, is involved in the inflammatory process of atherosclerosis and, may be considered as a reliable biomarker for heart failure (HF). Adult patients with congenital heart diseases (CHD), present with a pattern of neurohormonal and immune activation which is also found in chronic HF patients. Adult patients with

coarctation of aorta (CoA) even late after repair, show complications (hypertension, aneurisms, coronary artery disease) which may be related to an inflammatory process. The role of Opn in patients with repaired CoA has never been studied. Our aim was to evaluate Opn levels in adults with repaired CoA and investigate their relation to surrogate markers of cardiovascular function.

Methods: We enrolled 21 adult patients (9 male) with repaired CoA (mean age 23.3±9.1y, 16.1±9.4y after repair) and 23 matched healthy controls (11 male, mean age 26.8±8.5y). From transthoracic echocardiography (Vivid7, GE, USA) we measured the systolic (ASd) and diastolic diameter (ADd) of the ascending aorta and we calculated aortic distensibility as $[2 \times (ASd - ADd) / ADd \times (SBP - DBP)]$ and stiffness index as $\log [SBP \times (ASd - ADd) / (DBP \times ADd)]$. We measured left ventricular end-systolic and end-diastolic dimensions, LV ejection fraction and posterior wall thickness in systole and diastole. Arterial applanation tonometry (SphygmoCor 2000, AtCor Medical, Australia) was used to measure augmentation index (AI%) and augmented pressure (AP) of the central aortic pressure and strain gauge plethysmography to measure forearm blood flow (FBF) as an index of endothelial function of peripheral arteries. Finally, we measured plasma Opn levels using Sandwich Elisa method (R&D Systems, Minneapolis, USA).

Results: Patients with repaired CoA had statistically significant higher plasma Opn levels (ng/ml) compared to healthy controls (272.6 ± 48.07 vs 215.03 ± 40.95 , $p = 0.0001$). Opn levels were not related to the elastic properties of the aorta (AD, SI), the arterial applanation tonometry and plethysmography indices (AI%, AP, FBF), the echocardiography indices and the blood pressure. Opn levels were only related to the years after repair ($r = -0.31$, $p = 0.009$).

Conclusions: This is the first study to demonstrate increased Opn plasma levels in patients with repaired CoA. This is independent of other cardiovascular function parameters, making Opn a possible early biomarker of disease progression. Further investigation is needed to clarify the role of Opn in patients with repaired CoA and other CHD.

P435

Retinal vascular tortuosity: a novel marker in heart failure

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Purpose: The retinal vasculature provides a window to systemic microvascular health and cardiovascular risk. However retinal microvasculature has not been studied in heart failure (HF). We aimed to examine the association between HF and retinal microvascular abnormalities.

Methods: Retinal photography was prospectively performed in consecutive HF cases (88% men; aged 55±10y) in a population-based study. Retinal microvascular parameters (tortuosity, calibre, branching angle, and fractal dimension) were compared with 131 age- and sex-matched community-based controls.

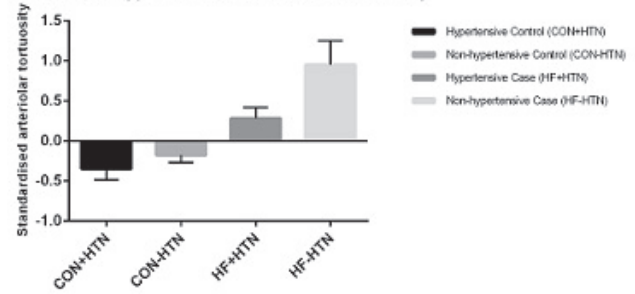
Results: HF cases had higher vascular tortuosity and lower fractal dimensions than controls (Table). Adjusting for cardiovascular risk factors, increased retinal arteriolar tortuosity remained independently associated with presence of HF (adjusted OR per SD: 6.2; 95% CI 1.8 - 21.4). Retinal arteriolar tortuosity was negatively related to systemic hypertension (Figure) and did not correlate with carotid stiffness.

Conclusion: Retinal arteriolar tortuosity may be a novel marker in HF indicating the presence of microvascular abnormalities beyond systemic large artery stiffness.

Retinal microvascular abnormalities & HF		
Retinal Markers	Cases (HF)	Controls (Non-HF)
Retinal arteriolar calibre	126.73±12.92	127.27±11.34
Retinal venular calibre	193.95±16.96	192.10±19.71
Arteriovenous ratio	0.66±0.05	0.66±0.05
Total fractal dimension*	1.43±0.05	1.46±0.04
Arteriolar fractal dimension*	1.21±0.05	1.24±0.05
Venular fractal dimension*	1.21±0.06	1.24±0.05
Arteriolar tortuosity*#	0.81±0.17 (x10 ⁻⁴)	0.71±0.13 (x10 ⁻⁴)
Venular tortuosity*	1.06±0.29 (x10 ⁻⁴)	0.92±0.18 (x10 ⁻⁴)
Arteriolar branching asymmetry ratio	0.80±0.08	0.77±0.10
Arteriolar branching angle	76.36±10.63	78.95±11.46
Venular branching asymmetry ratio	0.69±0.09	0.68±0.11
Venular branching angle	80.47±9.47	78.33±9.08

*significant association in univariable analysis #significant association in multivariable analysis

Influence of hypertension on arteriolar tortuosity



Figure

P436

MicroRNA signatures differentiate preserved from reduced ejection fraction heart failure

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Aims: Differentiation of heart failure with reduced (HFrEF) or preserved (HFpEF) ejection fractions independent of echocardiography is challenging in the community. Diagnostic strategies based on monitoring circulating microRNA (miRNA) levels may prove to be of clinical value in the near future. The aim of this study was to identify a novel miRNA signature that could be a useful HF diagnostic tool and provide valuable clinical information on whether a patient has HFrEF or HFpEF.

Methods and Results: miRNA biomarker discovery was carried out on 3 patient cohorts; no heart failure (no-HF); HFrEF; HFpEF, using Taqman miRNA Arrays. The top 5 miRNA candidates were selected based on differential expression in HFpEF and HFrEF, and their expression levels were also different between HF and no-HF. These selected miRNAs were further verified and validated in an independent cohort consisting of 225 patients. The discriminative value of B-type natriuretic peptide (BNP) as a HF diagnostic could be improved by use in combination with any of the miRNA candidates alone or in a panel. Combinations of 2 or more miRNA candidates with BNP had the ability to significantly improve predictive models to distinguish HFpEF from HFrEF compared to using BNP alone (AUC >0.82).

Conclusion: This study has shown for the first time that various miRNA combinations are useful biomarkers for HF, and also in the differentiation of HFpEF from HFrEF. The utility of these biomarker combinations can be altered by inclusion of natriuretic peptide. miRNA biomarkers may support diagnostic strategies in sub-populations of patients with HF.

P437

Chronic kidney disease and acute coronary syndrome: the effects of cardiac biomarkers

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Purpose: Cardiac biomarkers are an important part in the diagnosis and risk stratification of Acute Coronary Syndrome (ACS). It is well known that Chronic Kidney Disease (CKD) is associated with persistently elevated markers. This makes it challenging to interpret and assess their significance in these patients. This study evaluates differences in troponin, myoglobin and brain natriuretic peptide (BNP) values based on degree of CKD severity in patients admitted for ACS.

Methods: A retrospective study of 1054 patients admitted for ACS was performed. Clinical and analytical parameters were evaluated. Patients were divided according to CKD severity determined by estimated creatinine clearance calculated using the MDRD (Modification of Diet in Renal Disease) formula. All cases of acute kidney injury were excluded from the study population. Statistical analysis was performed using SPSS and considered significant when $p < 0.05$.

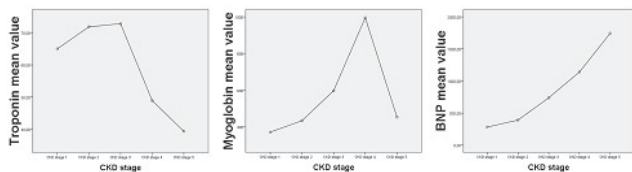
Results: The study consisted of 1054 patients, 68.8% male, with a mean age of 69.10 ± 12.65 years.

ANOVA test was used to compare the mean values of the selected biomarkers within each stage of CKD severity. A statistically significant difference was found

when evaluating myoglobin ($p=0.001$) and BNP ($p<0.001$) values. However, no difference was observed when analyzing troponin values ($p=0.169$).

Conclusion: When comparing cardiac biomarkers in patients with CKD admitted for ACS:

1. Troponin values were not significantly different between the different stages of CKD severity.
2. Regarding myoglobin levels, a statistical difference was observed in CKD stage 1 through 4, with higher values in stage 4.
3. As for BNP, there is a significant difference between the various stages, showing higher values in CKD of greater severity.



CKD and Biomarkers

P438

Serial soluble ST2 and galectin-3 measurement and its association with LV systolic and diastolic function in chronic heart failure patients after acute decompensation

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Purpose: to evaluate the significance of serial myocardial fibrosis biomarkers measurements (sST2 and galectin-3) and changes in systolic and diastolic function in pts with chronic heart failure (CHF) after acute decompensation.

Methods: In a prospective single-center trial were included 113 pts with CHF discharged from hospital after acute decompensation. Blood sampling to determine the sST2 and galectin-3 concentrations were collected at discharge from the hospital, 3 and 6 months after discharge. Parameters of LV systolic and diastolic function were assessed also at discharge from the hospital, 3 and 6 months after discharge.

Results: At the time of discharge from the hospital and CHF symptoms compensation, pts sST2 concentration remained elevated - 32,16 (21,91; 50,0) ng/ml. Positive correlations were found between sST2 and LA volume ($r=0.46$, $p<0,0001$), E/A ($r=0.35$, $p<0,05$), E/E' ($r=0.41$, $p=0,014$) and negative with LVEF ($r=-0.3$, $p=0,008$). Significant correlations between Gal-3 and parameters of LV remodeling and diastolic dysfunction were not revealed. After 3 months of treatment sST2 concentration correlated positively only with E/E' ($r=0.44$, $p<0,05$). Again any significant correlations of Gal-3 and pts parameters of LV remodeling and diastolic function were found, and appeared only with E/A ($r=-0,45$, $p<0,05$) after 6 months of follow-up. After 6 months of treatment correlations went on staying positive between sST2 and E/E' ($r=0.6$, $p<0,0001$), and negative with LVEF ($r=-0.43$, $p<0,02$). During the period of follow-up $\Delta\%$ sST2 also correlated closely with $\Delta\%$ LVEF ($r=-0.56$, $p=0,002$) and especially with $\Delta\%$ E/E' ($r=0.75$, $p=0,0001$). $\Delta\%$ Gal-3 have had more weak correlation with $\Delta\%$ LVEF ($r=-0,36$, $p=0,009$) and $\Delta\%$ E/E' ($r=0,4$, $p<0,05$), compared with sST2.

Conclusion: sST2 concentration changes during serial measurement more strongly associated with changes in LV diastolic and systolic function in CHF pts compared with galectin-3.

P439

The value of copeptin serial measurement in the assessment of LV systolic and diastolic function in chronic heart failure patients after acute decompensation

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Purpose: to evaluate the significance of serial copeptin measurements in comparison with NT-proBNP and changes in systolic and diastolic function in pts with chronic heart failure (CHF) after acute decompensation.

Methods: In a prospective single-center trial were included 113 pts with CHF discharged from hospital after acute decompensation. Blood sampling to determine the copeptin and NT-proBNP concentrations were collected at discharge from the hospital, 3 and 6 months after discharge. Parameters of LV systolic and diastolic function were assessed also at discharge from the hospital, 3 and 6 months after discharge.

Results: At the time of discharge from the hospital and CHF symptoms compensation, pts copeptin and NT-proBNP median concentration remained elevated: 2196,0 (1027,0; 4215,0) pg/ml and 29,25 (19,95; 37,45) pmol/ml respectively. Weak but significant correlations were found between NT-proBNP and end-diastolic LV volume ($r=0.26$, $p=0,01$), end-systolic LV volume ($r=0.3$, $p=0,03$), LVEF ($r=-0.38$, $p<0,0001$), LA volume ($r=0.37$, $p=0,004$) and moderate with E/E' ($r=0.6$, $p<0,0001$). Relationship copeptin with LVEF was very weak ($r=-0.25$, $p<0,04$). As NT-proBNP, copeptin have had more strong association with diastolic parameters: LA volume ($r=0.35$, $p<0,02$), E/A ($r=0.4$, $p<0,0001$), E/E' ($r=0.57$, $p<0,0001$). After 3 months follow-up were revealed the same correlation between NT-proBNP and E/E' ($r=0.42$, $p=0,017$), as well as between copeptin and LA volume ($r=0.42$, $p<0,02$) and E/E' ($r=0.5$, $p=0,018$). At the end of the study both NT-proBNP and copeptin have had more strong correlation with parameters, reflected diastolic function (as well as filling pressure): with LA volume, respectively $r=0.5$, $p=0,001$ and $r=0.47$, $p<0,004$; and E/E', respectively $r=0.6$, $p<0,0001$ and $r=0.65$, $p<0,0001$. During the period of follow-up (6 months) copeptin and NT-proBNP concentration changes ($\Delta\%$) have had practically the same moderate association with LV volume changes ($\Delta\%$), and strong negative correlation with $\Delta\%$ LVEF (respectively $r=-0.72$, $p<0,0001$ and $r=-0.6$, $p<0,0001$), and positive with $\Delta\%$ E/E' (respectively $r=0.7$, $p<0,0001$ and $r=0.67$, $p=0,0001$).

Conclusion: copeptin concentration changes during serial measurement strongly associated with changes in LV diastolic and systolic function in CHF pts, comparable to the NT-proBNP.

P440

Somatostatin correlates with central venous pressure and cardiac output in patients with advanced heart failure

The present study was financed with a grant from the Research Fund at Copenhagen University Hospital, Rigshospitalet, Copenhagen L. Balling¹; K Rossing¹; S Boesgaard¹; JP Goetze²; F Gustafsson¹

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Purpose: Somatostatin is a well-known regulator of the gastro-intestinal system and a potent arterial vasoconstrictor of the splanchnic blood flow in patients with cirrhosis. It is unknown if somatostatin is associated with hemodynamic measures in patients with heart failure (HF).

Methods: Consecutive HF patients ($n=50$) with a left ventricular ejection fraction (LVEF) $<45\%$ referred for evaluation for heart transplantation or LVAD. A right heart catheterisation was performed in all patients. Blood analyses were measured after an overnight fast.

Results: Fifty patients were included (mean age 53 ± 12 years, 82 % male). All patients were in NYHA-class III-IV and mean LVEF was $18 \pm 8\%$. Mean somatostatin levels were 18.9 ± 10 pmol/L and mean NT-proBNP levels were 572 ± 806 pmol/L. An elevated level of somatostatin (≥ 18 pmol/L) was present in 26 (52 %) patients. In univariate regression analysis, log(somatostatin) was associated with increased central venous pressure (CVP) ($r^2=0.17$, $p=0.0031$) and a reduced cardiac output (CO) ($r^2=0.10$, $p=0.02$) (Figure 1). When adjusted for important clinical variables (age, gender, LVEF and NT-proBNP), log(somatostatin) remained a significant predictor of CVP ($r^2=0.20$, $p=0.0057$), but not of CO ($r^2=0.26$, $p=0.08$). Log(somatostatin) did not correlate with age, gender or LVEF ($p>0.05$ for all), but somatostatin did correlate with renal function estimated by estimated glomerular filtration rate (eGFR) ($r^2=0.22$, $p=0.0007$).

Conclusions: Somatostatin is associated with elevated right-sided filling pressure in patients with advanced HF. The pathophysiological release mechanism may be related to congestion and/or hypoperfusion of the intestine. Hence, somatostatin may be a novel biomarker for the degree of intestinal congestion in patients with advanced HF.

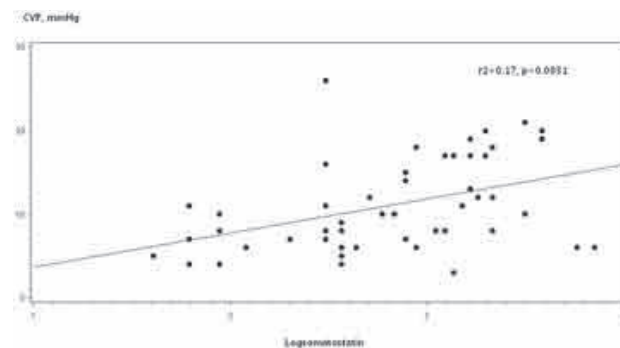


Figure 1

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Sex differences in biomarkers of different pathophysiological domains in acute heart failure

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Sex differences in the pathophysiology and outcome of heart failure can be characterized by biomarkers. We analyzed sex differences of various established and novel biomarkers of different pathophysiological domains in acute heart failure. We used the 2033 patients (33% women) hospitalized for acute heart failure of the PROTECT trial for propensity score matching of women with men on 40 clinical characteristics evaluating 180-day mortality. Sex differences in 48 established and emerging biomarkers were analyzed. The propensity score matched 501 men to 501 women (mean age 72.0 vs. 72.9 years) with no relevant difference in clinical characteristics and outcome. Women showed significantly lower levels of procalcitonin, PSAP-B, NTpro-CNP, hemoglobin, creatinine, and blood urea nitrogen, whereas platelet count and total cholesterol were higher compared to men (all $P < 0.001$). Multivariate outcome analyses showed higher risk of hypoalbuminemia in women over men (Pinteraction = 0.019). Analyses of multi-marker effects relative to established clinical predictors showed that adverse outcome was associated with troponin I, interleukin-6 and estimated glomerular filtration rate in men, and with RAGE, VEGFR, BUN and albumin in women. The incremental value in risk discrimination of these biomarkers over clinical predictors was higher in women than men (Table 1).

In AHF, Women had lower biomarker levels in several pathophysiological domains. Different biomarkers were related to adverse outcome in both sexes with higher incremental risk discriminative value of biomarkers in women than men.

Incremental value of biomarkers by sex		
	Model derived in men Age, SBP Biomarkers: Troponin I, eGFR, Interleukin 6	Model derived in women Age, SBP, Edema, History of Diabetes Biomarkers: RAGE, VEGFR, Albumin, BUN
clinical AUC (95% b.s. CI)	0.672 (0.598 - 0.727)	0.670 (0.589 - 0.735)
+ biomarker AUC (95% b.s. CI)	0.715 (0.635 - 0.770)	0.747 (0.674 - 0.806)
Δ AUC (95% b.c. CI)	0.042 (0.003 - 0.010)	0.077 (0.028 - 0.144)
P-value (test equality of AUCs)	0.082	0.010
IDI (95% b.s. CI)	0.053 (0.017 - 0.106)	0.082 (0.038 - 0.150)
event IDI (95% b.s. CI)	0.044 (0.013 - 0.085)	0.071 (0.033 - 0.129)
non-event IDI (95% b.s. CI)	0.009 (0.003 - 0.021)	0.011 (0.004 - 0.023)
cNRI (95% b.s. CI)	0.550 (0.272 - 0.804)	0.550 (0.316 - 0.858)
event cNRI (95% b.s. CI)	0.268 (0.005 - 0.457)	0.205 (0.056 - 0.442)
non-event cNRI (95% b.s. CI)	0.281 (0.170 - 0.427)	0.344 (0.233 - 0.458)

b.s. means 1000 times bootstrapped; CI means confidence intervals

NURSING

P442
Remote monitoring in heart failure patients: nursing management

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In recent years, the implantable cardioverter defibrillator implantation (ICD) with cardiac resynchronization therapy (CRT) in patients with heart failure has increased significantly in our hospital.

This group of patients, by their illness requires a more specific attention of a multidisciplinary team that cares because of its decompensation, fluid accumulation and alerts. A key tool for control these devices is the home remote monitoring telemedicine.

Objective: Reporting our remote monitoring system experience in patients with CRT ICD's and assess the nurses role in the scheduled and unscheduled transmissions follow up, of these patients.

Methodology: Descriptive, retrospective study of ICD in the period 2008-2014.

Results: Of all the devices implanted, there are currently 117 ICD's with remote monitoring, 53 are CRT devices. In our center of the 1373 total transmissions, 701 were CRT devices. There were 60 OptiVol alerts, 4 patients were detected with a left ventricle threshold up to 5 volts and 6 patients were less than 80% biventricular stimulated and all patients with a daily activity less than an hour were detected.

Conclusions: Remote monitoring is reliable and clearly accepted by patients.

The nursing is a mainstay within the multidisciplinary team for the control and monitoring of these patients

All transmissions control by nursing and good education of patients allows early treatment, avoiding unnecessary journeys and Hospital income.

P443

The opinion of heart failure patients on their legal rights-can some rights be infringed with their consent ?

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Purpose: The patients right to choose their treatment or doctor is fundamental and represents a measure of our respect for one's autonomy. In Romania these rights are guaranteed by the Patients Rights Act (PRA) of 2003, which is based on the Anglo-Saxon judiciary system. Our study aims to evaluate the knowledge of heart failure (HF) patients and their families about the PRA, its existence and the rights it guarantees because HF is a chronic condition with multiple hospitalizations.

Methods: The study group included 42 patients with HF (age > 18, 36% males and 64% females, average age 57.7 ± 13.3) who signed the informed consent. Patients and their family members were asked to complete a semistructured questionnaire about PRA. The study design was approved by the Ethics Committee. SPSS ver.16 was used for statistical analysis.

Results: The existence of the PAR is known by most patients (87.5%), regardless of gender, age, background, marital status and education; sources were: media (71.4%), doctors (19%) and family members (9.5%). Only 26.3% of patients believe PRA has helped them. On the contrary, 80% of family members know about PAR and 83.3% of them believe it didn't help them. Surprisingly, 45.5% of patients and 40% of family members believe doctors should not obtain an informed consent before performing diagnostic procedures (invasive or noninvasive), which is against the law. 13.3% of patients and 6.7% of family members believe doctors must obtain an informed consent only for invasive procedures (biopsies, CT scans etc), probably because they are more recent (thus less known) procedures, more invasive and more painful than blood sample or performing ECG (tests that are more familiar to patients). It is also worth noting that although the „paternalist” model is ubiquitous in Romania, patients and family members are not afraid to refuse a test (90.9% vs 64.3%) or a treatment (63.6% vs 66.7%), believing the doctor would consider it as a „patient's right”. 73.9% of patients and 86.7% of family members say they would ask for a second opinion, however only 62.5% of patients and 53.3% of family members have actually done it. On the topic of concealing the diagnosis from the patient, 4.2% of patients responded "always" (only family members know it) while 16.7% of patients responded "depending on the patient (scared or depressive) or the diagnosis (serious condition / terminal stage)" - which is a clear violation of the PRA.

Conclusions: Although HF patients and their family members know about the PRA, they lack a complete understanding of it and often disagree with it.

P444

Prognostic implications of sleep disorders in chronic heart failure

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Sleep disorders have been associated with increased risk of heart failure (HF) and contribute to poor quality of life in HF patients (pts). Although insomnia is highly prevalent in HF pts, the prognostic implications of sleep disorders in HF pts has not been addressed.

To assess the clinical implications of insomnia, 68 HF pts, followed in a heart failure unit, were studied. Pts were asked whether they were having difficulty initiating sleep, maintaining sleep or having poor sleep quality. Need for worsening HF hospitalization or death during follow-up was recorded.

Pts mean age was 68 ± 12 years, 59% were men. HF etiology was non-ischemic cardiomyopathy in 25 pts (37%), coronary artery disease in 27 pts (40%), valve disease in 7 (10%) and other 9 pts (13%). Atrial fibrillation was present in 30 pts (44%), chronic pulmonary disease in 37 (54%), sleep apnea corrected with CPAP in 21 (31%) and DM in 28 (41%). Mean ejection fraction (EF) was $42 \pm 16\%$, with 19 pts having preserved EF (28%). NYHA functional class 2 was present in 35 pts (51%) while functional class 3/4, in 33 (49%). Medical therapy included ACEI/ARA in 56 pts (82%), beta-blockers in 47 (69%) and aldosterone antagonists in 47 (69%). During follow-up (mean 5 ± 3 months), 2 pts died and 5 required a new hospitalization for worsening HF.

Sleep disorders were present in 33 pts (48.5%). Of those, difficulty initiating sleep was present in 14 pts (42%), difficulty maintaining sleep in 26 (79%) and having poor sleep quality in 18 (54%). Presence of the 3 parameters was detected in only 9 pts (13%). Sleep disorders were more prevalent in pts in NYHA functional class 3/4 than in pts in functional class 2 (64% vs. 34%, $p=0.01$).

Sleep disorders were associated with higher incidence of events (death or HF hospitalization) during follow-up (21% vs. 0%, $p<0.005$). Of the three parameters, the difficulty initiating sleep was significantly associated with events (55% vs. 5%, $p<0.05$), while there was a trend towards significance with difficulty maintaining sleep or having poor sleep quality.

In **Conclusion:** 1/ The prevalence of sleep disorders is high in HF patients, 2/ Sleep disorders are associated with worse prognosis, 3/ Of the three parameters analyzed, the difficulty initiating sleep was the most relevant associated with new events during follow-up. 4/ Larger studies are needed to assess the implications of sleep disorders in HF prognosis.

P445

Safety and effectiveness of drug up titration by nurses specialized in heart failure patients, ETIFIC project, design of a multicenter randomized trial

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Introduction: Heart Failure (HF) causes multiple hospital admissions and the risk of premature death, which are reduced with the administration of Beta-Blockers (BB), Angiotensin Converting Enzyme Inhibitors (ACEI), Angiotensin II Receptor Blockers (ARB) and Mineralocorticoid Receptor Antagonists (MRA) to HF patients with Ejection Fraction (E.F.) $\leq 40\%$ (Level of Evidence A). The effect is dose-dependent. Nevertheless, current dosages are often suboptimal. European Guidelines 2012 recommend close monitoring and up-titration of these drugs by HF nurses. Although this role of HF nurses have been widely named in the literature, trials are needed to evaluate its effectiveness and safety.

Purpose: Main Objective: To compare achieved doses (% relative to target doses) of BB, by patients in 4 months in the intervention group (HF nurse) and in the control group (cardiologist).

Secondary Objectives: To compare achieved doses (% relative to target doses) of ACEI, ARB II and MRA by patients in 4 months in the intervention group (HF nurse) and in the control group (cardiologist), adverse events, E.F., NYHA, 6 min. walking test, quality of life, Nt-proBNP, readmissions and mortality. Hypothesis: Non-inferiority.

Methods: Design: Multicenter randomized controlled trial.

Participants: 628 Hospitalized New ("de novo") HF patients with Ejection Fraction $\leq 40\%$, NYHA II-III at discharge, without contraindications to BB of 17 experienced Spanish hospitals will be included. Major exclusion criteria are contraindications to BB, living in a long-term residence and short life expectancy.

Intervention: The cardiologist will prescribe drugs and the HF nurse, driven by protocol, will implement the up-titration. Safety will be protected by a checklist and a safety committee. In the control group doses will be decided by the cardiologist, clinical support and education to patients being provided by nurses.

Variables: mg.(%) of drug, age, sex, education, psycho-social level, cardiovascular risk factors, NYHA, E.F., ischemic cardiopathy, Charlson Index, Nt-proBNP, 6 minute walking test, creatinine/glomerular filtration, haemoglobin, blood pressure, heart rate, Self Behaviour Scale, quality of life, MLHF, EQ-5D.

Ethical considerations will be taken into account.

Expected Results: If our hypothesis were confirmed, evidence would be provided on the effectiveness and safety of this healthcare model, that could improve current drug suboptimal dosing and would be economically evaluated in future studies.

P446

The relationship between social support and quality of life in patients with heart failure

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Introduction: Social support can improve the low quality of life (QoL) of patients with HF in order to properly manage the symptoms of the disease, maintaining the physical and emotional well-being of people with HF

Aim: The main purpose of this research study was to investigate the relationship between social support and QoL in patients with HF

Methods: It is a descriptive correlation study. The population of the study is comprised from 117 patients with HF who were hospitalized in the cardiology departments and patients who visited the outpatient clinics staging NYHA I-IV, during the period 2010 to 2013. The data were collected by completing the Greek versions of the questionnaires «Multidimensional scale of perceived social support» (MSPSS) and «Minnesota Living with Heart Failure Questionnaire» (MLHFQ). Pearson tests were conducted and as well as Hierarchical Regression Analysis. This study is part of the research project MEETinCY

Results: The total score of MSPSS has a moderate negative correlation with the total score of MLHFQ ($r = -0.31$ $p < 0.01$). Lower values of QoL are associated with higher rates of Social support, which means that people with better QoL tend to report greater perceived social support. Furthermore, the overall rating of MSPSS are significantly associated with the physical ($r = -0.36$ $p < 0.05$) and emotional dimension ($r = -0.24$, $p = 0.05$), but not with the social dimension of QoL ($r = 0.05$, $p = 0.98$). The hierarchical regression analysis showed that the gender ($p = 0.042$) and NYHA staging affect the relationship between social support and QoL.

Conclusions: The current results indicate that the lack of social support has a negative impact on the QoL of patients with HF

P447

Impact of acute hyperglycemia after primary percutaneous coronary intervention treatment

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Background: Hyperglycemia has been shown to be a powerful predictor of worse outcome after ST segment-elevation myocardial infarction (STEMI).

The aim of this study was to investigate the relationship between acute hyperglycemia and angiographic and clinical outcome after primary or rescue angioplasty for STEMI.

Methods: We retrospectively included 618 patients who underwent revascularization for STEMI: 534 primary angioplasty and 84 rescue angioplasty, plasma glucose was measured at hospital admission. Acute hyperglycemia (HG) was defined as plasma glucose of 11mmol/L (198mg/dL), regardless of the diabetic status.

Results: Among the 618 patients with STEMI included in the study, 285 (46.1%) patients had acute hyperglycemia. There was no difference among the two groups with regard to clinical characteristics, cardiovascular risk factors and hemodynamic parameters. Angioplasty success, TIMI 3 flow and ST segment resolution were significantly lower in acute HG group. On multivariate regression, HG was not found to be an independent predictor of angioplasty success ($p = 0.08$; OR = 0.9; 95%CI [0.92-1]) or of ST resolution, however diabetes was independently associated with ST segment resolution after achieving TIMI 3 flow (OR = 3.2; 95% CI [1.02 - 8.1]; $p = 0.014$). The in-hospital mortality rate was significantly higher in patients with acute hyperglycemia than in patients without (18.4% versus 5%, $p < 0.003$). By multivariate analysis, independent in-hospital mortality predictors were: heart failure (OR: 8.9; 95% CI [3.4 - 23]; $p < 0.0001$), acute hyperglycemia (OR: 3.8; 95% CI [1.4 - 9.8]; $p = 0.005$), renal insufficiency (OR: 6.5; 95% CI [2.3-18]; $p < 0.001$), and anemia (OR = 4.7, 95% CI [1.9 - 11.6], $p = 0.001$). Among the HG patients, mortality predictors were: glycemia level (OR = 1.13; 95% CI [1.03-1.23]; $p = 0.005$), Killip class (OR: 2.14; 95% CI [1.36 - 3.35]; $p = 0.001$), blood hemoglobin level (OR: 0.69; 95% CI [0.53 - 0.9]; $p = 0.007$), and angioplasty success (OR: 0.25; 95% CI [0.08-0.82]; $p = 0.022$).

Conclusion: Acute hyperglycemia in patients with STEMI is an important predictor of mortality with an increasing mortality risk even beyond 11mmol/l but diabetes is a better predictor of ST resolution after TIMI 3 restoration. These results suggest the usefulness of glycemia assessment in the setting of STEMI and the beneficial effect of strict glycemic control.

P448

Multimorbidity, self-care and frailty: important considerations in anticoagulation in heart failure with atrial fibrillation

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Background: Chronic heart failure (CHF) and atrial fibrillation (AF) are common, yet complex cardiogeriatric syndromes, mediated by physical, psychological and social factors. Thromboprophylaxis is an important part of avoiding adverse events, particularly stroke.

Purpose: This study sought to: (1) describe the clinical characteristics of a cohort of individuals hospitalised with CHF and concomitant AF; (2) document the rate and type of thromboprophylaxis; (3) examine practice patterns of therapy prescription; and (4) determine the predictors of adverse events.

Design: Prospective cohort study.

Methods: Prospective consecutive participants with CHF and concomitant AF of any type and aetiology admitted to a cardiology ward were enrolled during April - October 2013. Socio-demographic and clinical characteristics including medical history, frailty, medication adherence, self-care behaviour and thromboprophylaxis prescription were assessed at index hospitalization. Participants were followed-up by telephone at 12 months to collect the following outcome data: all -cause rehospitalisation and mortality, stroke or transient ischaemic attack, and bleeding.

Results: All-cause rehospitalisation was frequent (68%) and 12-month all-cause mortality was high (29%). Prescription of anticoagulation at discharge was statistically significantly associated with lower mortality at 12 months [23% vs. 40%, $p=0.037$, HR 0.506, 95% CI 0.267-0.956], but was not associated with lower rates of rehospitalisation among individuals with CHF and AF. 66% of participants were prescribed an anticoagulant at discharge from hospital. Worse self-reported heart failure self-care behaviour and participants identified as 'not for CPR' were associated with not receiving anticoagulation at discharge. Whilst statistical significance was not achieved, those who were assessed as frail or having greater comorbidity, were less likely to receive anticoagulation at discharge.

Conclusion: This study highlights multimorbidity, frailty and self-care to be important considerations in thromboprophylaxis decision making. Further, results demonstrate that whilst the CHA2DS2VASc and HAS-BLED schemata are useful in practice to risk stratify stroke and bleeding. It is problematic simply to use these tools in isolation to guide treatment decisions. Whilst helpful, they lack ability to provide a comprehensive assessment. Shared-decision making with patients and caregivers offers promise to potentially improve treatment knowledge, adherence and outcomes in this group of individuals with complex care needs.

P449

The influence of frailty syndrome using the tilburg frailty Indicator (TFI) on the assessment of self-care abilities assessed with european heart failure self-care behavior scale (EHFScBS) in elderly

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Introduction: Heart failure (HF) is a chronic condition with a dynamic course. It requires the patient to adapt to numerous limitations and to actively participate in treatment. Frailty syndrome and self-care capabilities, the evaluation of which in elderly patients with cardiovascular conditions is increasingly frequent, are especially important in HF patients. Concurrent frailty syndrome and decreased self-care capabilities are an indication for interventions aiming at improving the physical, psychological and social functioning of HF patients.

Purpose of the study. To assess the influence of frailty syndrome on self-care capabilities in patients with chronic heart failure.

Material and methods: The study included 110 patients (51 female and 59 male) diagnosed with chronic heart failure, hospitalized in the Cardiology Clinic. Two standardized research instruments were used: the Tilburg Frailty Indicator (TFI) - a questionnaire for evaluating frailty syndrome, and the European Heart Failure Self-care Behavior Scale (EHFScBS), evaluating patients' self-care capabilities. Correlations and differences at $p < 0.05$ were considered statistically significant.

Results: The frailty syndrome FS occurred in 75.1%. Mean TFI score in the study group was $M \pm SD = 7.45 \pm 3.02$ points. Mean self-care scale score was $M \pm SD = 27.6 \pm 7.13$ points.

The correlation analysis showed that the social component score in TFI has a statistically significant influence on the level of self-care ($p = 0.006$).

Conclusions: Lower TFI scores are correlated with better self-care capabilities in HF patients.

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Recruitment and retention challenges of examining cognitive dysfunction in older adults hospitalized for acute heart failure

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Background: Recruiting and retaining older adults, age 65 and above, in clinical research can be challenging. This is especially true for community-dwelling older adults living with a diagnosis of chronic heart failure (HF) and for older adults hospitalized in a critical care unit. Barriers include intrusiveness of the study, transportation availability, lack of time, lack of family availability for consent and family unwillingness to consent. However, less is known about challenges of recruiting and retaining older adults hospitalized for acute HF.

Purpose: To describe the recruitment and retention challenges of a recent study examining cognitive dysfunction in older adults hospitalized for acute HF

Methods: A cross-sectional descriptive design was used to examine the relationship between acute HF symptoms and cognitive dysfunction in older adults hospitalized for acute HF. Nurse screeners were used to identify potential participants using daily census and study inclusion criteria. Data were collected on inpatient acute HF units of a Midwest hospital that annually treat 800 HF patients.

Results: The original plan was to assess serial changes in cognitive function over time, but issues arose that prevented the collection of data beyond one time point. Sixty-two patients who voiced interest to screeners refused to participate when approached by the study team for reasons ranging from being too tired to the length of the informed consent document; 11 potential participants were deemed ineligible; and 27 participants who completed the initial data collection session refused to participate in further data collection because they were too tired, were being discharged on the day of data collection or because they had already been discharged prior to the next data collection day. To compensate for these issues and to augment recruitment, nurse screeners were asked to confirm potential participants' interest in meeting with the study team; recruitment units were expanded from one to three and recruitment time was expanded by 12 weeks. Despite these efforts only 53 older adults with acute HF were recruited.

Conclusions: Multiple barriers to the recruitment and retention of older adults hospitalized for acute HF were identified. Strategies are needed to augment recruitment and retention efforts, including reducing the length of voluminous informed consent documents, expanding the number of data collection sites and allocating sufficient financial and human resources to support efforts to improve recruitment and retention of older adults hospitalized for acute HF.

POPULATION STUDIES / EPIDEMIOLOGY

P451

Correlations between heart failure- related quality of life and in-hospital heart failure parameters in STEMI patients on mid-term follow-up

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Purpose: ST-elevation myocardial infarction (STEMI) is one of the most severe causes of heart failure and early percutaneous coronary intervention (PCI) is crucial for outcomes after STEMI. The present study aims to evaluate the heart failure - related quality of life following PCI in STEMI patients and to identify the in-hospital predictors in this high risk population

Methods: A questionnaire based study analysed a total of 317 consecutive STEMI patients treated by primary PCI in a single centre. Median follow up was 2,33 years. We had 2 questions addressing heart failure symptoms - one regarding physical autonomy and the other regarding exertion capacity. The first question was designed to evaluate the level of patients' autonomy from self-care skills to more complex activities, while the second one evaluates the exertion capacity using as a parameter the number of floors the patients were able to climb without experiencing heart failure symptoms.

Results: The mean age of the study group was 62,55 years (IQR: 56 - 70) and there were more men (221; 69,7%). We had a mean follow-up time of 2,33 years (IQR: 2 - 3; STDEV = 0.809). The prevalence of smoking was 37,5 % and 68,1% were hypertensives. 24,9% had diabetes mellitus and 53,9% had dislipidemia. 46,7% of the patients had an anterior myocardial infarction and the discharge mean LV(left ventricle) ejection fraction was 43,19% (IQR: 38 - 50). A linear regression model was performed regarding physical autonomy and physical exertion capacity, as described by the patients, and various parameters from admission (Killip class, heart rate, blood pressure and LV ejection fraction, etc). The only significant correlation ($p = 0.003$) was between physical autonomy and ejection fraction. Exertion capacity was not correlated to any parameter.

Conclusions: The LV ejection fraction is well known to be an independent predictor of late prognosis after acute myocardial infarction. Our study showed that in STEMI patients LV ejection fraction is also associated with physical autonomy. More data will be needed to differentiate between heart failure symptoms.

P452

New insights on the roma ethnic community: hidden heart failure - looking for diastolic dysfunctionD Bartos¹; E Tintea¹; C Japie¹; A Daraban¹; E Badila¹¹Clinical Emergency Hospital Bucharest, Internal Medicine, Bucharest, Romania**Objective:** To describe the cardiovascular (CV) risk profile of the heart failure (HF) patient with diastolic dysfunction (DD) in a Roma ethnic community.**Methods:** 400 adult subjects from the Roma urban community regardless of medical history were included and screened for major CV disease and CV risk factors in 2013. From these, 117 pts were diagnosed with HF with DD using echocardiography. We recorded anthropometric data, presence of major CV risk factors, blood pressure measurements, the presence of left-ventricular (LV) hypertrophy on echocardiography, peripheral artery disease (PAD) based on the ankle-brachial index (< 0.9 in either leg), diabetes mellitus (known or newly diagnosed - glycemia >126mg/dl) and hyperuricemia (>6mg/dl in females; >6,8mg/dl in males). eGFR was estimated using CKD-EPI study equation and chronic kidney disease stage >3 was considered at eGFR <60ml/min/1.73m².**Results:** See table.**Conclusions:** There were significant differences in the prevalence of CV risk factors between sexes in this HF group. Even if Roma women are more frequently hypertensives, diabetics and dyslipidemics, men are much more affected by myocardial infarction, LV remodelling and PAD. The grave CV burden in this ethnic community is once more made obvious along with the major differences between the sexes in terms of CV risk factors.

Diastolic dysfunction HF patients characteristics	Total	Males (M)	Females (F)	p (M vs F)
No pts	117	45	72	
Average age (yrs)	58.35±9.4	55.93±9.7	59.86 ±8.95	
Arterial hypertension	59	10	49	0.01
Myocardial infarction	15	11	4	0.05
Left-ventricle remodelling	61	37	24	0.01
Peripheral artery disease	24	15	9	0.01
Diabetes mellitus	17	6	11	ns
Chronic kidney disease stage≥3	3	1	2	ns
Dyslipidemia	44	15	29	ns
Hyperuricemia	11	8	3	0.01
Obesity	39	20	19	0.05

HF, Heart Failure

P453

Heart failure with preserved ejection fraction in 400 never-treated romanian hypertensivesL Livia Popescu¹; H Balan¹¹University of Medicine and Pharmacy Carol Davila, Bucharest, Romania**Purpose:** Heart failure with preserved ejection fraction (HFpEF) is common, increasing in prevalence, causes substantial morbidity and mortality. Patients with HFpEF experience similar rates of HF re-hospitalization and functional decline to patients with HF with reduced EF (HFrEF) and have a significantly higher risk of death compared with age-matched controls. HFpEF appears to be more common in elderly, female gender, hypertension, diabetes and obesity, and unfortunately despite multiple randomized controlled trials, no disease-specific therapy exists to improve prognosis. The aim of this study was to assess the prevalence of HFpEF among 400 never-treated Romanian hypertensives.**Methods:** We enrolled 400 consecutive never-treated hypertensives with normal EF (>=45%) and sinus rhythm, without diabetes and obesity. We retrospectively analysed the clinical features (breathlessness, orthopnoea, gallop rhythm, pulmonary crepitations, etc) and transthoracic echocardiographic parameters compared with a control group of 50 healthy subjects.**Results:** 32.5% of the enrolled hypertensives (mean age 54 ± 10 years; 52.5% women) presented HFpEF. Only 24.25% of hypertensive had normal LV morphological aspect. 58.75% had left ventricular hypertrophy (LVH) and 17% concentric remodeling. 78.5% of hypertensives had relaxation abnormalities, and 21.5% had normal / pseudo-normal pattern. We did not found restrictive pattern probably because only 6% of hypertensive patients were in grade 3. HFpEF was more frequently in women than in men (36.19% vs 28.42%), and in hypertensives with LVH than without LVH (77.87% vs 19.39%). HFpEF was correlated with higher values of

systolic and diastolic BP. Even if the elderly were few (16%), they had HFpEF more frequently than young hypertensives (75% vs 24.40%).

Conclusions: HFpEF is common in hypertension, reaching 32.5% of never-treated patients. Women and elderly hypertensives are more affected. Left ventricular hypertrophy was one of the risk factors for HFpEF.

P454

Fenetylline use could be a cause for dilated cardiomyopathy and heart failureA Abdelfatah Elasar¹¹Prince Salman Heart Center, King Fahad Medical City, Riyadh, Saudi Arabia**Purpose:** Fenetylline tablets (an amphetamine like substance) are a stimulant drugs which are widely used in the Arabian Peninsula. The aim of this study was to evaluate the possible etiological relationship between Fenetylline abuse and the incidence of dilated cardiomyopathy and subsequently heart failure.**Methods:** It is a prospective case control study for all consecutive patients with dilated cardiomyopathy and acute heart failure syndrome presented to emergency department in our tertiary care center from September 2009 to October 2013. Patients were divided into 2 groups: group I were Fenetylline users and group II were Fenetylline non-users. Fenetylline use was elicited mainly by history taking on admission. Patients with coronary artery disease or any other known cause of heart failure were excluded.**Results:** We included 580 patients in 2 groups; group I were Fenetylline users and included 140 patients (24%) and group II were Fenetylline non-users and included the remainder 440(76 %) patients. Fenetylline users were younger (mean age of 26 ± 12 vs 36 ± 9 years) and almost all of them were male (99% vs 73%). Fenetylline users were more frequently using alcohol (44% vs 8 %) and more frequently to be smokers (88 % vs 38%). Overall, Fenetylline users had higher risk of in-hospital death (9 % vs 5%, p value <0.05), cardiogenic shock (18% vs 9%, p value <0.05), pulmonary tuberculosis (7% vs 1%, p value <0.05) and recurrent admission with heart failure in one year (35% vs 24%, p value <0.05). After adjustment for baseline variability, Fenetylline use was found to be an independent risk factor for the development of dilated cardiomyopathy and also a risk factor for higher mortality and recurrent admission in patients presented with cardiomyopathy and acute heart failure.**Conclusions:** Fenetylline use was found to be an independent risk factor for the development of dilated cardiomyopathy and death and other morbidities in patients presented with cardiomyopathy and acute heart failure. Our study underscores the importance of improving education concerning the cardiac risks of Fenetylline use.

P455

Prediction of cardiovascular disease related readmission or death risk within 90 days after discharge: data from the Korean Heart Failure (KorAHF) registryHY Hyun-Young Park¹; MC Cho²; SE Lee³; NK Lim¹; BH Oh³¹Korea National Institute of Health, Department of Cardiovascular and Rare Diseases, Cheongju, Korea, Republic of; ²Chungbuk National University College of Medicine, Cheongju, Korea, Republic of; ³Seoul National University Hospital, Internal Medicine, Seoul, Korea, Republic of**Purpose:** Readmission or death of patients after acute heart failure hospitalization are very common and costly in the Korean population. But data for readmission or death after discharge are lacking. We derived substantial risk factors for death and readmission and developed the prediction models to estimate the risk of cardiovascular disease specific 90-day death or readmission after hospital discharge.**Methods:** 4,961 patients discharged alive and had at least one follow-up visit were analyzed from the of Korean Heart Failure (KorAHF) registry database. We excluded those who had malignant tumor as the past medical history and incomplete covariate. Finally, 4,136 participants were selected for analysis. During the follow-up period (mean follow-up was 4.8 month), 690 (16.7%) patient were died or re-hospitalized by cardiovascular disease within 90 days after discharge. Multiple logistic regression analysis was used to assess the risk factors and to calculate the estimated risk of 90-day death or readmission. The accuracy of the model was assessed by the c-statistics and Hosmer and Lameshow's goodness-of-fit test.**Results:** The mean age was 67.7 ± 14.7 years (64.6 men and 71.1 women) and 53.2% of the patients were men. Prediction model included age, past medical history (presence of diabetes mellitus, HF, idiopathic dilated cardiomyopathy, and chronic renal failure), New York Heart Association (NYHA) class, hospitalization period, systolic blood pressure, use of beta blocker (see Table). The model showed good calibration (Hosmer-Lemeshow's goodness-of-fit test, P=0.9593) and had moderate discrimination ability (c-statistics = 0.67).**Conclusion:** We presented a simple prediction model without laboratory test or echocardiographic measurements that it can be used to discriminate subjects at high risk for cardiovascular disease specific readmission or death within 90 days after discharge.

Table. Results for logistic regression

variables	Levels	OR (95% CI)	p-value
Age, years NYHA	- Class 1 or 2	1.02 (1.01-1.03)	<0.0001
Hospitalization period	Class 3 or 4 -7 days	Reference 1.57 (1.21-2.50)	0.0008 - 0.0094
SBP, mmHg	≥120	Reference 1.27	0.0023
Use of beta blocker	100	Reference 1.27	<0.0001
Past medical history	<120 <100 No vs Yes Diabetes Mellitus Heart Failure IDCP Chronic Renal Failure	(1.06-1.53) (1.13-1.68) (1.26-2.16) (1.10-1.54) (1.20-1.70) (1.38-1.97) (1.09-1.93) (1.30-2.04)	<0.0001 0.0105 <0.0001

NYHA, New York Heart Association; OR, odd ratio; CI, confidence interval; IDCP, idiopathic dilated cardiomyopathy

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Heart failure awareness is improved in Turkish HFREF patients

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Purpose: Heart failure (HF) is a complex syndrome with several dimensions. Turkish Society of Cardiology has been working on improving HF awareness in the population.

Methods: Turkish Research Team-HF (TREAT-HF) is a network which has been undertaking multicentric observational cohort studies in HF among HF centers. TREAT-HF network has been testing a questionnaire to investigate several aspects of HFREF outpatients. Herein, a questionnaire based comparison of validation cohort (n=324) with a derivation cohort (n=503 patients, in year 2013) was presented.

Results: There were 223 males and 101 females in the validation cohort vs. 362 males and 141 females in the derivation cohort (p=0.332) respectively. Patients in the validation cohort were older (63.9 ± 12.4 vs. 59.1 ± 14.3 years, p < 0.001).

Although they were older, there were more patients in the validation cohort who were graduated from a university than those in the derivation cohort (9.9% vs 5.6%, p=0.020). There were more patients in the validation cohort who made more than one additional doctor visit after initial diagnosis compared to those in the derivation cohort (86.5% vs 79.6%, p=0.017). Patients in the validation cohort stated more frequently that they were informed by their doctors about their disease compared to derivation cohort (95.2% vs 76.6%, p < 0.001). Patients in the validation cohort stated more frequently that their relatives know what to do in case of an emergency compared to those in the derivation cohort (53% vs 45.4%, p=0.037). Along with this, patients in the validation cohort were more concerned about their disease compared to patients in the derivation cohort (66.6% vs 56.4%, p=0.004). Furthermore, patients in the validation cohort consult on alternative medicine less frequently than patients in the derivation cohort (6.2% vs 10.1%, p=0.05).

Conclusion: Along with the comparison of two different cohorts, it seems HF awareness is improving in Turkey.

P457

Clinical characteristics and current treatment modalities in Turkish heart failure population: data from REALITY HF Study

This study is supported by Servier Y Cavusoglu¹; O Kozan²; A Temizhan³; S Kucukoglu⁴

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Purpose: Clinical profile of heart failure (HF) population shows regional differences. Evidence-based guidelines recommended therapy improves survival in HF, however

the gap between guidelines and practice seems to be greater in some countries. REALITY HF (Resting Heart Rate and Real Life Treatment Modality in Outpatients with Left Ventricular Systolic Dysfunction) data were analyzed for the evaluation of clinical characteristics and current treatment modalities used for systolic HF in Turkish population.

Methods: REALITY HF was a multicenter, prospective, national registry which represents the largest systolic HF population in Turkey and was designed to evaluate HF patients' clinical characteristics, currently applied treatment modalities and resting heart rate (HR) and enrolled 1251 patients from 16 centers who were admitted to the outpatient clinic with the diagnosis of chronic HF, LVEF <40% and >18 years of age.

Results: Mean age of HF population was 61 ± 12 years which is lower than that of the Western countries. 75.5% of the patients were in sinus rhythm and 24.5% had atrial fibrillation. In patients with sinus rhythm, mean resting HR was 76 ± 14 bpm and 68% of the patients had a resting HR ≥ 70 bpm. Mean EF was 30 ± 7%, NT-proBNP was 2300 ± 3451 pg/mL, creatinine level was 1.19 ± 0.78 and hemoglobin level was 13.4 ± 2 gr/dL. 22.3% of patients were in NYHA I, 40.1% in NYHA II, 29.5% in NYHA III and 8.2% in NYHA IV. Kansas City Cardiomyopathy Questionnaire (KCCQ) clinical summary scores were <25 in 6.9% of patients, 26-49 in 19.1%, 50-74 in 30.8% and >75 in 43.2% of patients. Comorbidities were coronary artery disease (CAD), previous MI, previous stroke, hypertension, diabetes, chronic obstructive pulmonary disease and chronic renal disease in 72%, 68.6%, 6%, 32.8%, 36%, 19.9% and 6.1% of the cases respectively. Etiological reasons for HF were reported as CAD (72%), primary cardiomyopathy (17.8%), valvular heart disease (5.8%), hypertension (2.9%) and other reasons (1.3%). At the time of enrollment, 93% of patients were receiving evidence-based HF medication and 82% were on ≥ 2 drug therapy. The use of beta blocker, ACEI/ARB, MRA, diuretic, ivabradin and digoxin were 79.1%, 68.7%, 34.8%, 67.2%, 6.1% and 19.2% respectively.

Conclusions: These results suggest that mean age of the systolic HF population in Turkey is lower than that of Western countries, two-thirds have a resting HR ≥ 70 bpm, one-third were in NYHA III-IV and almost half has impaired quality of life. In current practice, the use of evidence based medication was reasonable but needs to be adopted more vigorously in clinical practice.

P458

Effect of cardiovascular comorbidities on the mortality risk associated with serum potassium

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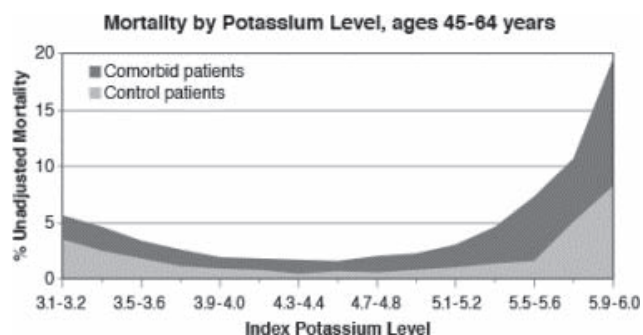
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Purpose: Hypo- and hyperkalemia are associated with an increased mortality risk. Serum potassium (K⁺) levels associated with these risks and relationships to comorbidity, however, are not well defined. We evaluated the odds of death in patients with and without comorbid conditions, stratified by K⁺ level.

Methods: De-identified medical records (2007-2012) from a large US population aged ≥ 5 years with 2 or more K⁺ readings were evaluated. Patients aged 45-64 years with comorbidities of CKD stages 3-5, heart failure, diabetes, hypertension, and cardiovascular disease (n=231,070) were identified by ICD-9 codes and biochemical data, excluding those with acute kidney injury or end stage renal disease, and compared with controls without these conditions (n=146,645). A separate analysis of patients aged ≥ 65 years was conducted. Index K⁺ value was defined as the last reported value prior to a pre-determined cut-off date. Mortality was evaluated through hospital discharge records and Social Security registry information.

Results: Patients with cardiorenal comorbidities aged 45-64 years and index K⁺ levels <4.1 mEq/L and >4.6 mEq/L had a significant increase in mortality (Figure). This finding was also observed in patients aged ≥ 65 years. The general pattern remained after adjustments for demographic characteristics (sex, race) and comorbidities associated with the propensity to develop hypo- and hyperkalemia.

Conclusions: Our results confirm that patients with hypo- or hyperkalemia are at greater risk for mortality than those with normal K⁺, and that mortality risk is significantly higher in patients with cardiorenal comorbidities and is independent of demographic characteristics. The increased mortality in patients with comorbidities occurs even at K⁺ levels within the usual normal laboratory range.



EXERCISE TESTING & TRAINING

P459

Effects of cardiac rehabilitation program on exercise capacity and chronotropic variables after heart valve surgery

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Purpose: Heart valve repair or replacement surgery remains the mainstay for valvular heart disease treatment. After surgery, recovery may take a few weeks to several months and can be challenging. The aim of this study was to evaluate the impact of a hospital-based cardiac rehabilitation program (CRP) on exercise capacity and chronotropic variables, after heart valve surgery.

Methods: Included 15 patients that participated in our CRP, less than 6 months after heart valve surgery, between 2009 and 2014. Patients underwent a supervised aerobic moderate exercise training protocol, 2 times/week during 2 to 3 months. Patients were evaluated with treadmill stress test before and 3 and 12 months after CRP. Functional capacity (expressed in metabolic equivalents - METs), chronotropic reserve (CR), chronotropic response index (CRI) and heart rate recovery (HRR) 1 and 2 minutes after cessation of exercise, were evaluated.

Results: Among the 16 patients included, 12 (80%) were submitted to heart valve replacement surgery mainly due to severe aortic stenosis (47%) or severe mitral valve regurgitation (40%) and 2 patients were also submitted to coronary artery bypass graft surgery. Most patients were male (67%), median age was 61 years old (IQR 56 - 63 years) and 15 had normal left ventricular systolic function. Patients started CRP within a median time of 60 days (IQR 34 - 83 days) after surgery. There was a significant improvement in exercise capacity 3 months after beginning CRP (8 ± 1.9 vs 9.7 ± 2 METs, $p=0.001$) and the benefit remained after one year (8 ± 1.9 vs 10 ± 2.7 METs, $p=0.003$).

At 3 months, there was a significant increase in HRR 2 minutes after exercise (23 ± 15 vs 27 ± 19 seconds, $p=0.033$), but no change in HRR in the 1st minute. There was also an improvement in CRI one year after beginning CRP ($70 \pm 39\%$ vs $79 \pm 26\%$, $p=0.028$) and a non significant trend to increased CR (59 ± 28 vs 78 ± 30 seconds, $p=0.069$).

Conclusion: In our group of patients submitted to heart valve surgery, there was a significant improvement in functional capacity and chronotropic variables with prognostic value, after CRP.

P460

The effect of low-carbohydrate diet and exercise on clinical status in chronic stable heart failure patients

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Background: The positive effects of nonpharmacologic treatment, diet and exercise have been informed on the clinical status of heart failure (HF) patients. However, there are not evaluations demonstrating it.

Purpose: to evaluate the effects of low-carbohydrate diet and exercise on clinical status of chronic stable HF patients.

Material and Method: In a randomized controlled clinical trial at the Instituto Nacional de Ciencias Médicas y Nutrición "Salvador Zubirán" (INCMSZ). One hundred twenty-three ambulatory patients were assigned to: A group (n=18), which received a low-carbohydrate diet (40% carbohydrates, 40% lipids and 20% proteins) and exercise training; B group (n=45), which received a low-carbohydrate diet (40% carbohydrates, 40% lipids and 20% proteins); C group (n=21), with a

conventional diet (50% carbohydrates, 30% lipids and 20% proteins) and exercise training; D group (n=39) with a conventional diet (50% carbohydrates, 30% lipids and 20% proteins) during four months. Eligible patients were men and women aged 18 years or older. The diagnosis of heart failure was classified according to the European Society of Cardiology (ESC). The subjects were stable in New York Heart Association functional classes II to III. Clinical evaluation, arterial blood pressure, heart rate, handgrip strength and 6 minutes walk test were made at the beginning and each month during the follow-up.

Results: After two months of follow-up we found a decrease in the diastolic blood pressure in the A group (71.5 ± 2.98 vs. 62.5 ± 1.70 mmHg, $p=0.03$) and C group (71.76 ± 2.31 vs. 64.69 ± 1.9 mmHg, $p=0.04$). Also at two months of follow, the A group and B group improve the 6 minute walk test (270.37 ± 11.39 vs 301.78 ± 7.02 , $p=0.08$ and 345.77 ± 22.32 at 370.07 ± 26.15 , $p=0.05$). With respect to other variables, non-significant differences were observed between the groups.

Conclusions: Exercise independent of carbohydrate in the diet has effect in diastolic blood pressure and low-carbohydrate diet has effect in functional capacity.

P461

Effects of a cardiac rehabilitation program in patients with severe left ventricular dysfunction: can all benefit?

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Introduction: Cardiac rehabilitation programs (CRP) after ST elevation myocardial infarction (STEMI) provide patients exercise, optimal medical treatment, education and counselling. Our objective was to analyze the functional impact of a CRP in this population and identify subgroup with more or less benefit.

Methods: We made an observational retrospective study including severe LVSD patients after STEMI admitted to a CRP in our institution between 2006 and 2014. Physical training, nutritional education, optimal medical treatment and medical counselling were supplied according to the CRP for 8 to 10 weeks. Left ventricular systolic function and functional capacity were tested before and after the CRP in accordance with the NYHA Functional Classification, besides a treadmill stress test (TST). Exercise capacity was reported in terms of estimated metabolic equivalents of task (METs).

Results: A total of 156 patients were included in our study, mean age 56.19 ± 12.22 years, male 90.4%. Prevalence of hypertension was 50.6%, diabetes 27.9%, dyslipidemia 55.8%, obesity 28.1%, current smoker 59%, chronic kidney disease (CKD) 5.1%, chronic obstructive pulmonary disease (COPD) 6.5% and cerebrovascular disease (CD) 1.9%. The NYHA class previous CRP was I 46.5%, II 43.7%, III 9.9%. Mean initial left ventricular ejection fraction (LVEF) was $29.93 \pm 5.14\%$. As to TST results before the CRP, medium METs were 6.46 ± 2.98 and 5.9 ± 2.69 minutes was the mean exercise time (ET). After CRP, LVEF was $42.32 \pm 10.52\%$ (LVEF improvement compare to baseline, $12.41 \pm 9.52\%$; $p < 0.001$). The NYHA class was I 79.7%, II 19.5%, III 0.8%. Medium METs were 10.04 ± 2.98 (METs improvement 3.52 ± 2.06 ; $p < 0.001$) and mean ET was 8.65 ± 2.50 minutes (ET improvement 2.62 ± 2.90 minutes; $p < 0.001$). We did not find statistically significant differences in functional capacity or LVEF improvement according to sex, age, cardiovascular risk factors profile, CKD, COPD or CD.

Conclusions: Severe LVSD patients enrolled in a CRP after suffering a STEMI improve functional capacity and LVEF regardless their previous cardiovascular risk factors profile, CKD, COPD and CD.

P463

Clinical characteristics of acute heart failure patients compared with acute myocardial infarction patients with cardiopulmonary exercise testing

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Purpose: Cardiopulmonary exercise testing (CPX) is one of the common assessment tools with acute heart failure (AHF) and acute myocardial infarction patients (AMI), but clinical characteristics of those patients have not been well described.

Methods: We have enrolled 91 Japanese patients with CPX from March 2014 to December 2014. We compared the baseline clinical characteristics and CPX variable in patients with AHF (n=44) and those with AMI (n=47).

Results: The patients with AHF were older than those with AMI (65.3 ± 10.0 vs. 72.7 ± 9.8 years of age; $p < 0.01$). They were more likely to have various co-morbidities; atrial fibrillation (45.5% vs. 2.1%; $p < 0.01$), cardiomyopathy (18.2% vs. 0%; $p < 0.01$), valvular disease (36.4% vs. 2.1%; $p < 0.01$), and chronic kidney disease (50.0% vs. 14.9%; $p < 0.01$). There was no significant difference in gender of male, body mass index, the prevalence of stroke, hypertension, diabetes or chronic obstructive pulmonary disease between AHF and AMI patients (77.3% vs. 87.2%; $p=0.21$, 22.7 ± 3.6 vs. 23.7 ± 3.3 ; $p=0.18$, 9.1% vs. 4.3%; $p=0.35$, 79.6% vs. 79.7%; $p=0.92$, 36.4% vs. 34.8%; $p=0.88$, 9.1% vs. 4.3%; $p=0.35$, respectively). Patients receiving the prescription of oral diuretic drugs were more in AHF

patients (81.8% vs. 17.0%; $p < 0.01$). There was no significant difference in the prescription of ACE inhibitors/angiotensin receptor blockers, calcium antagonists or beta blockers between AHF and AMI patients. In patients with AHF, peak VO_2 was significantly lower (14.4 ± 4.1 vs. 13.7 ± 2.8 ml/kg/min; $p < 0.01$). There was no significant difference in systolic blood pressure (sBP) at rest (113.4 ± 21.9 vs. 120.8 ± 19.0 mmHg; $p = 0.08$), but sBP at peak was lower in patients with AHF (159.7 ± 35.3 vs. 182.2 ± 27.1 mmHg; $p < 0.01$).

Conclusion: The patients with AHF were older and had more co-morbidities than those with AMI. The patients with AHF were lower physical function than those with AMI.

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Usefulness of RPE scale for exercise intensity in elderly patients with heart failure

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Background: Different rating scales have been validated in healthy adults, such as Borg 6-20 rated perceived exertion (RPE) scale, Borg category-ratio scale (CR-10). However deconditioned elderly persons with heart failure showed no constant relationship between RPE and HR, dyspnea or distance during the course of the submaximal test such as 6-minute walk test (6MWT). The aim of this study is to investigate usefulness of RPE scale for submaximal exercise intensity in elderly patients with chronic heart failure (CHF).

Method: The subjects were ambulatory patients with CHF. Each patient performed 6MWT using 2 RPE scales (Borg 6-20 RPE scale and CR-10) and cognitive impairment using the mini-mental state examination (MMSE). We checked the objective serum NT-proBNP level at same test time. Finally, 12 males over 70 years (mean age; 74 years) and 16 females over 70 years (mean age; 75 years) were enrolled. Results: A total 28 subjects with NYHA class II/III heart failure were analyzed. Proportion of patients with valvular heart disease, cardiomyopathy and ischemic heart disease were respectively 22%, 64% and 14%. The mean 6MWT distance, Borg 6-20 RPE scale, CR-10, MMSE and NT-proBNP were 345.42 ± 106.69 , 11.0 ± 1.29 , 1.95 ± 1.09 , 25.58 ± 3.39 , 5882.42 ± 11167.87 respectively. The MMSE scores were lower than might be expected. In retrospective medical record review, 12 patients had the neurological abnormalities due to cerebrovascular accidents (CVA). But cognitive levels are not significant different whether patient had a CVA or not. There were not significant relationship among physiological factors, 2 RPE scales and MMSE except resting diastolic blood pressure and MMSE (correlation coefficient $r = 0.58$, $p = 0.047$). However, NT-proBNP showed a significant correlation with BMI ($r = -0.71$, $p = 0.013$), resting systolic blood pressure ($r = -0.63$, $p = 0.038$) and resting heart rate ($r = 0.733$, $p = 0.01$). Although the distance walked during the 6MWT is an important prognostic marker in CHF, it was not significant correlation with all the other parameters.

Conclusions: The RPE could be associated with HR as a useful tool for monitoring and prescribing exercise in adults. However, it seems that the RPE-heart rate relationship or RPE-physical performance relationship is less pronounced in physically deconditioned elderly patients with heart failure. The objective NT-proBNP can reflect physiological condition of HF. But this parameter does not apply to description of exercise intensity. Therefore, a new subjective or objective scale to describe exercise intensity for elderly patients with CHF will be need to be looked at.

P465

Correlation between resting end-tidal carbon dioxide and cardiac index in patients with congenital disease

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Objectives: Cardiopulmonary exercise testing (CPET) variables have shown to provide valuable prognostic information. In patients with systolic heart failure, resting end-tidal carbon dioxide partial pressure (PETCO₂) is related with cardiac index. The purpose of the present study is to assess the association between PETCO₂ and cardiac index (CI) in our patients with congenital heart disease (CHD), as well as its ability to predict cardiac-related events in this population. **Methodology:** A total of 58 consecutive patients with CHD underwent CPET in our institution from July 2011 to July 2014. Resting PETCO₂ was determined immediately prior to the exercise test. Cardiac index was measured with magnetic resonance imaging (MRI), so we excluded patients without this test. Fontan and complex cyanotic lesions were also excluded because the poor precision in the CI calculation. We also observed clinical adverse events (death and hospital admissions).

Results: 14 patients were finally analysed. Mean age was 33 ± 10 years, with 42,9% of males. Etiologies were simple lesions in 1 (7,1%), valvular lesion in 2 (14,3%), repaired tetralogy of Fallot (TOF) in 10 (71,4%) and ebstein anomaly in 1 (7,1%). All patients had a New York Heart Association (NYHA) Class \leq II. Our mean follow up

period was of 17 months (interquartile range [IQ]: 8,5-18,25 months). Median resting PETCO₂ was 36 mmHg (IQ: 32-36,5). Mean cardiac index and beat volumen were $5,7 \pm 1,8$ l/min and $78,6 \pm 22,6$ ml, respectively. No correlation was found between resting PETCO₂ measure and CI measure by MRI ($r = 0,414$, $p = 0,159$). During the follow up, there was only one hospital admission for heart failure. We can not evaluate the relationship between resting PETCO₂ and clinical events.

Conclusion: Regarding these results, an association between cardiac index and resting end-tidal carbon dioxide partial pressure could not be stated in patients with CHD. The small size of our sample and the stable clinical situation of the patients (NYHA I-II and only one clinical event) probably influenced these findings. Further studies are mandatory to validate these results.

P466

Efficacy of the physical training in patients with heart failure after myocardial infarction

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The **Aim:** To study the efficacy and safety of the program of physical training (PT) on the clinical condition, cardiac contractility and quality of life (QOL) in patients (pts) with coronary artery disease and heart failure (CHF) II-III functional class (FC) NYHA.

Material and methods: The study included 40 men aged 39 to 60 years (mean age 54.9 ± 4 years), after myocardial infarction, which was complicated by the development of congestive CHF II-III FC (left ventricle ejection fraction (LV EF) $\leq 45\%$). Pts were randomized into two groups: Group (gr) 1 ($n = 20$) Program-PT 3 times a week and 2 group ($n = 20$) - control (pts seen by the attending physician). CHF NYHA class III was in 7 (35%) pts in group 1 and 6 (30%) pts of the 2 gr. In 12 (60%) pts in 1 gr and 9 (45%) pts of the 2 gr had chronic cardiac aneurysm.

Specially designed program PT with a graded approach for pts with FC II by NYHA (EF 35-45%) and pts with FC III by NYHA (EF $< 35\%$) has been used.

Period of observation in the study was 6 months. A physical working capacity (PWC) indicators at ECG stress test, echocardiography, QOL have been studied. The training program included exercises affecting motor reflexes segments of the spinal cord at the level of C3-C4 and L1-L8 (20 min) and exercise on a stationary bike with 50% of the individual maximal load capacity (25 min).

The Results. After 6 months, in 1 gr aerobic power (by 16%, $p < 0.001$) and its duration (by 23%, $p < 0.001$) increased respectively. In the control gr, on the contrary, aerobic power decreased by 13% ($p < 0.001$) and length of the load by 20% ($p < 0.001$). After PT LV EF increased by 2.6% ($p < 0.05$) and total peripheral resistance (TPR) decreased by 11% ($p < 0.01$). In the control gr was no dynamic of echocardiography parameters. At baseline, in both groups patient's QOL, estimated by Minnesota questionnaire, was low. In the 1 gr after the PT QOL improved by 28% ($p < 0.001$), less fatigue experienced by 42% of pts, dyspnea during PA by 80%, difficulty in relationships with loved ones by 37%, in the sexual sphere by 58%, anxiety by 32% of pts. In the control gr the QoL deteriorated (by 26.9%, $p < 0.001$). Pts have experienced fatigue by 80% ($p < 0.05$), dyspnea during PA by 95% ($p < 0.05$), difficulties in relationships with relatives by 60% ($p < 0.05$), in the sexual sphere by 70% ($p < 0.05$), anxiety by 70% ($p < 0.05$). In 2 gr, these figures have significantly deteriorated.

Conclusion: PT program for 6 months effects beneficially on the physical performance, has stabilized contractility and heart remodeling, improved psychological status and quality of life of pts with good safety.

P467

Relationship between cycle length in exercise and pulmonary artery hypertension in patients with heart failure and exercise oscillatory ventilation

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Background: Exercise oscillatory ventilation (EOV) is a noninvasive parameter that has prognostic value in patients with heart failure (CHF). Oscillations in ventilation (VE) during exercise have a characteristic cycle length (CL) and amplitude (an irregular breathing) defined EOV. CL is strongly related to circulation time, but amplitude is influenced by circulation time and other contaminating factors.

Aim: The aim of this study was to investigate the relationship between CL and hemodynamics in HF patients with EOV.

Methods: We evaluated 28 consecutive hospitalized patients with systolic HF and EOV and who completed both right heart catheterization and cardiopulmonary exercise test. Pulmonary arterial hypertension was defined as mean pulmonary arterial pressure (mPAP) > 25 mmHg. Pulmonary vascular resistance (PVR) = (mPAP - mean pulmonary capillary wedge pressure (PCWP))/cardiac output. EOV was defined as ≥ 3 consecutive, regular oscillations in VE during exercise, with VE oscillation amplitude $> 25\%$ of average VE, persisting for 60% of exercise duration.

Results: EOV CL was 63.7 ± 20.2 sec. Of 28 HF patients with EOV, 15 patients had pulmonary artery hypertension. EOV CL was associated with peak VO_2 ($r = -0.39$, $p = 0.02$) and VE/VCO_2 ($r = 0.44$, $p = 0.01$). EOV CL was correlated with PVR ($r = 0.47$, $p = 0.02$), but not cardiac index ($r = -0.38$, $p = 0.08$), mean PAP ($r = -0.002$, $p = 0.90$) or PCWP ($r = -0.14$, $p = 0.52$).

Conclusion: Half of our patients had pulmonary arterial hypertension. EOVC was related to PVR in HF patients with systolic HF and EOVC.

P468

Evaluating the feasibility of a supervised physical exercise program in patients with systolic heart failure in primary care

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Purpose: Supervised Physical Exercise Programs (SPEP) are scarcely implemented in Primary Care (PC). We assess the feasibility and safety of a SPEP in systolic heart failure (HF) patients, conducted in PC.

Methods: Randomized clinical trial 1:1 into two groups: EFICAR (SPEP + optimised usual care) and control group (optimised usual care). Inclusion criteria: age <80 years, LVEF <50%, stable NYHA class II-III, physically and mentally able to attend an exercise program. Therapy titration and stress test (ST) were performed before randomization. SPEP included 36 sessions of progressive exercise program (3 hours/week for 3 months) with an aerobic (cycle ergometer), and a strength component (weights and resistance bands work).

Results: 1492 patients were screened. 982 patients (65.8%) had an exclusion criteria (281 had LVEF >50%, 215 were >80 years old, 145 were not physically or mentally capable, 139 were in NYHA class I, 41 were not located by telephone, 161 for other causes). 304 patients (20.4%) refused to participate in the study (135 were not interested, 120 lived far from exercise program centre, 11 did not attend the first appointment, 10 argued no time for an exercise program, 28 for other causes). Of the 206 patients (13.8% of the total screened) that initially accepted, 26 (12.6%) discontinued voluntarily during the titration phase and 29 (14%) were excluded after ST (23 did not reach 4 METS and 6 had a clinically/electrically positive test). Finally, 150 patients (10% of the total screened) were randomized into two well balanced groups (mean age 67.4 ± 10.1 years; 77.3% men; 46.7% ischemic aetiology; mean LVEF 37.4 ± 7.9%). During follow up, 16 patients (21.3%) of the EFICAR group abandoned the SPEP (5 due to musculoskeletal problems, 3 arguing work reasons, 2 were not more interested after they started the sessions, 6 due to other causes). There were no serious adverse events in all exercise program [84.114 minutes of exercise (2031 full sessions, 41 partially completed sessions)].

Conclusions: Implementing a SPEP in PC is not exempt of a large number of difficulties. Age, co-morbidities, LVEF and lack of motivation are the main barriers to start an exercise training program in patients with HF in this environment. However, SPEP can be carried out safely in PC.

PROGNOSIS

P469

Mortality scores in ACS patients requiring invasive mechanical ventilation

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Introduction: The need for invasive mechanical ventilation (IMV) is a possible complication from acute coronary syndrome (ACS). This requires extra care, and usually transfer to a specialized unit. However, its impact is still not clearly defined and existing diagnostic tools do not distinguish this situation.

Objectives: To evaluate which of mortality scores currently used best predicts mortality in patients with ACS in need of IMV.

Methods: We identified all patients admitted for type1 ACS, on a single center between 01/07/2011 and 07/31/2013, that during hospitalization required IMV. The GRACE, SAPS2, apache2 and SOFA scores at 24 hours from admission were calculated. These various scores were compared with in-hospital mortality, using the Student t test, and the area under the curve (AUC) of the respective ROC curves.

Results: In the period under analysis, were recorded 19 cases that met the inclusion criteria, 78.9% male, 61.8 ± 15.7 years. 89.5% were MI with ST elevation, and 68.5% underwent primary PCI, 20.9% rescue PCI, 5.3% scheduled PCI and the remaining 5.3% did no reperfusion technic. Mortality rate was 52.6%.

The means, and areas under the curve of Scores SAPS2; apache2; SOFA and GRACE are represented in table 1.

Discussion and Conclusion: In spite the small size of this population, the absence of statistically significant differences in risk Scores demonstrates there imperfection. The idea stands that systemic scores like Apache2 and SOFA are probably better

predictors of mortality that the GRACE score. This is probably due to the survival impact of other systems, rather than cardiovascular, in patient undergoing IMV, such as immunological and respiratory system.

In the studied population, the SAPS2 score showed no prediction power.

It also highlights a high mortality rate in patients in need of IMV. Thus, although it is a rare event, the need for it should perhaps be considered as a variable to be included in future in-hospital mortality scores.

Means and AUC of diferent scores

	Global average	Deceased average	Survivors average	Student T-Test	AUC from ROC curve
SAPS2	52,9±13,9	55,4±17,6	50,4±7,9	0,51	0,491
Apache2	28±6,3	30,63±7,6	25±2,4	0,08	0,750
SOFA	7,5±3,3	8,6±3,7	6,4±2,7	0,19	0,723
GRACE	149±31	155,6±33,3	141,9±28,9	0,35	0,634

P470

Acute heart failure: evaluation of hemodynamic, biochemical and clinical deterioration predictors of adverse outcomes

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Purpose: Although there are known prognostic factors for unfavorable evolution of patients admitted for acute heart failure (AHF), there are very few parameters and validated scores that help in the decision to institute more aggressive treatments like inotropic support, which is known to increase mortality. Therefore we aimed to evaluate which parameters at admission, in patients with AHF could predict an unfavorable outcome in order to select a more aggressive therapeutic approach.

Methods: Retrospective study in a cohort of patients (P) admitted for AHF between Jan/2007 to Dec/2013. At admission we assessed basal characteristics of P, systolic blood pressure (SBP), left ventricle ejection fraction (LVEF), haemoglobin (Hb), creatinine, sodium, urea, troponin I, and BNP. Patients with acute variation of troponin I or highly elevated values were excluded. Then we compared these between groups who needed inotropic support (Group A) or not (Group B).

Results: From 284P, 143 (50,4%) needed inotropes. Mean age was 66,9y in group A and 70,1y in group B (p=0,014). In group A 73,4% of P were male (p=0,3618). Concerning etiology, 51% of P in the group A had dilated cardiomyopathy of non coronary cause, 51,7% had new onset HF and 64,3% were in class IV of NYHA (p=0,478, p=0,006 e p=0,001). The mean SBP was 113mmHg in group A versus 147mmHg in group B (p < 0,0001). At admission, in the group A there was a mean Hb of 12,03 g/dL, creatinine of 1,56 mg/dL, sodium of 135,24 mmol/L, urea of 8,76 mg/dL, troponin I of 0,183 pcg/mL and BNP of 5541,78 pcg/mL. The mean LVEF was 28% (comparing to 40% in the group B). There was a significant difference between groups regarding the values of creatinine, sodium, urea and also LVEF (p=0,00017, p=0,00064, p=0,02, p < 0,0001, respectively). Regarding global mortality, there was 17 deaths in the group A, comparing to only 1 patients in group B (p=0,0001).

Conclusions: Besides hemodynamic profile at admission, other parameters can predict an unfavorable clinical course for patients with AHF and the need for more aggressive therapies. Patients younger than 67yo, with new onset heart failure, in NYHA class IV, with renal failure - assessed by creatinine and urea - low blood sodium and with more severe left ventricle systolic dysfunction (LVEF below 28%) needed a more aggressive approach, as rescue therapy. Therefore, patients with a combination of these parameters at admission can benefit from more active surveillance in dedicated units and more aggressive therapies in order to preclude the need for inotropic therapy which similarly to other studies, correlated with worse outcomes.

P471

Clinical outcomes after transcatheter aortic valve implantation in patients with pure native aortic valve regurgitation

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Transcatheter Aortic Valve Implantation (TAVI) has become an alternative to surgical treatment in patients with severe aortic stenosis and high surgical risk, however, in patients with native and inoperable severe aortic regurgitation remains limited. The aim this study was to evaluate the use of TAVI in patients with pure native aortic valve regurgitation and comparing them with patients with aortic stenosis.

Methods: From April 2008 to December 2014, the CoreValve prosthesis was implanted in 10 consecutive high-risk surgical patients with symptomatic severe aortic regurgitation (AR) and in 431 patients with aortic stenosis (AS).

Results: The mean age and logistic EuroSCORE were similar in both groups (AR vs. AS) 79.2 ± 4.9 vs. 79.2 ± 6.8 years, $p = 0.993$ and $15.3 \pm 8\%$ vs. 17.7 ± 12 , $p = 0.552$ respectively. There were significant differences in measurement of annulus and ascending aortic size (24.5 ± 1.7 vs. 22.1 ± 1.8 mm, $p < 0.001$ and 34.1 ± 2.8 vs. 31.6 ± 4.1 mm, $p = 0.005$, respectively). Implantation of a TAVI was performed successfully in all patients with AR and the post-procedure aortic regurgitation grade was: absent in 5 patients, middle-moderate in 4 patients, and moderate-severe in one patient.

The NYHA functional class improved from 3.2 ± 0.6 to 1.6 ± 0.5 and remained stable at one year. The mortality at 30 days was 10% in patients with AR compared to 3.7% in patients with AS, $p = 0.307$ and there was no significant differences with late mortality (11.2% vs. 15.2%, $p = 0.736$) after a mean follow-up of 30.5 ± 20 months. The patients with AR had more acute kidney injury after procedure and lower occurrence new onset left bundle branch block than patients with AS 40% vs. 15.3% [OR = 3.68 (95% CI 1.01-13.4), $p = 0.037$] and 11.1% vs. 47.8%, [OR = 0.96 (95% CI 0.92-0.99) $p = 0.030$], respectively.

Conclusions: TAVI with the CoreValve prosthesis for patients with aortic regurgitation and a high surgical risk is a safe and efficient option resulting in a medium-term clinical improvement

P472

Impact of permanent pacemaker implantation after transcatheter aortic valve implantation impact on late clinical outcomes and left ventricular function

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Very few data exist on the clinical impact of permanent pacemaker implantation (PPI) after transcatheter aortic valve implantation. The objective of this study was to assess the impact of PPI after transcatheter aortic valve implantation on late outcomes in a large cohort of patients. **Methods and Results:** A total of 401 consecutive patients without prior PPI undergoing transcatheter aortic valve implantation were included. Of them, 97 patients (24.2%) required a PPI within the first 30 days after transcatheter aortic valve implantation, median time 48 hours (24-216 hours) and 8 patients required a PPI after. At a mean follow-up of 53.6 ± 39 months, there was a tend more mortality in patients with PPI (22.9% vs. 14.9%, $p = 0.061$), but no association was observed between the need for PPI and all-cause mortality (hazard ratio, 1.49; 95% confidence interval, 0.906-2.4601.30; $P = 0.116$), cardiovascular mortality (hazard ratio, 0.69; 95% confidence interval, 0.237-2.022; $P = 0.520$), and rehospitalisation for heart failure (hazard ratio, 1.93; 95% confidence interval, 0.804-4.647; $P = 0.141$). There were 4 cases of unexpected (sudden or unknown) death was observed in 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 60.7 ± 14 mmHg to 63.4 ± 11 mmHg after TAVI and decreased to 60.6 ± 10 mmHg at 1 years and 59 ± 6 mmHg at 4 years (p for post-TAVI trend 0.034). **Conclusions:** The need for PPI was a frequent complication of transcatheter aortic valve implantation, but it was not associated with any increase in overall or cardiovascular death or rehospitalization for heart failure after a mean follow-up of 2 years. However, new PPI did have a negative effect on left ventricular function over time.

P473

The long-term prognostic impact of moderately impaired left ventricular ejection fraction following ST-elevation myocardial infarction

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Purpose: Significant number of patients have moderately impaired left ventricular ejection fraction (LVEF) following ST-elevation myocardial infarction (STEMI) in the primary percutaneous coronary intervention (pPCI) era, but there are limited data on its long-term prognostic impact. The aim of this study is to analyse the prognostic impact of moderately impaired LVEF on 5-year all-cause mortality and major adverse cardiovascular events-MACE (cardiovascular mortality, reinfarction, ischemic stroke and target vessel revascularization) in patients with STEMI treated with pPCI.

Method: we analysed 1157 consecutive STEMI patients without previous cardiovascular disease. Echocardiographic examination was performed after pPCI. According to LVEF (biplane Simpson's method) patients were divided into three groups: (1) preserved LVEF $\geq 50\%$, (2) moderately impaired LVEF 40-49% and (3) severely impaired LVEF $< 40\%$. Patients presenting with cardiogenic shock were excluded.

Results: Out of a total of 1157 patients, 94 patients (8.1%) had LVEF $< 40\%$, 405 patients (35%) had LVEF 40-49% and 658 (56.9%) patients had LVEF $\geq 50\%$. In comparison with patients with preserved LVEF, patients with impaired LVEF were older and presented more often with heart failure; they were more likely to have diabetes, reduced kidney function, 3-vessel coronary disease and postprocedural flow TIMI < 3 . Five-year mortality rates were 37.22%, 8.45% and 3.28% and ($p < 0.001$) and 5-year MACE rates were 42.52%, 14.15% and 8.45% ($p < 0.001$) in patients with severely impaired, moderately impaired and preserved LVEF, respectively. The highest mortality and MACE rate was observed in the first 30 days in all patients. Patients with severely and moderately impaired LVEF had increased late mortality and MACE rate (> 30 days) as compared with patients with preserved LVEF (mortality 8.25%, and 4.72% vs 2.22%, $p < 0.001$, respectively; MACE 13.20% and 10.53% vs 7.62% $p = 0.015$, respectively). Moderately impaired LVEF was an independent predictor of 5-year mortality and MACE: Mortality: HR 2.08 (95%CI 1.12-3.83), $p = 0.021$; MACE: HR 1.98 (95%CI 1.13-2.25), $p = 0.034$. The risk for 5-year adverse events was increased with further worsening of LVEF. Other independent predictors of 5-year mortality and MACE were (older) age, heart failure at admission, renal dysfunction and postprocedural flow TIMI < 3 .

Conclusion: Moderately impaired LVEF (40-49%) following STEMI is an independent predictor of 5-year mortality and MACE. Patients with LVEF 40-49% have around 2-fold increase in 5-year mortality and MACE rates as compared with patients with preserved LV systolic function

P474

Predicting survival in patients with heart failure based on variables used in the MAGGIC model

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Background: The Meta-analysis Global Group in Chronic Heart Failure (MAGGIC) model is based on historical data from several trials and registries including 39,372 patients with heart failure (HF). Thirteen risk predictors were identified that stratified 3-year mortality from 10% to 70%.

Aims: To investigate the prognostic utility of the MAGGIC variables in a contemporary real-world patient population and the potential additional value of amino-terminal pro-brain natriuretic peptide (NT-proBNP).

Methods: Demographic measurements, symptoms, signs and blood tests were collected routinely from patients referred with suspected heart failure from the local community between 2000 and 2014. Consenting patients with heart failure, defined as a clinical diagnosis, treatment with a loop diuretic and confirmed by an elevated NT-proBNP were included. The 13 highly significant predictors in the MAGGIC model, including creatinine, diabetes, ejection fraction (EF), beta-blocker, NYHA class, BMI, HF duration > 18 -months, systolic BP, current smoker, COPD, sex, age, ACE/ARB, with an interaction between age and EF and an interaction between systolic BP and EF, were explored in this analysis.

Results: Of 2548 patients, the median (IQR) age was 75 (68-81) years and 64% were men. The median follow-up was 2.9 (IQR: 1.2-5.6) years. A multivariate Cox regression model identified only the following as independent predictors of all-cause mortality: age, creatinine, current smoker, NYHA class $\geq III$, diabetes, severity of left ventricular impairment (LVI), not taking beta-blockers, lower BMI and male sex (c -statistic = 0.67). Lower systolic BP was a significant predictor in the main effects model. The model discrimination was improved by adding NT-proBNP (c -statistic = 0.69).

Conclusions: This analysis suggests that NT-proBNP adds substantially to the MAGGIC risk model, even though patients with a low NT-proBNP were excluded. Some variables that were powerful predictors in the MAGGIC model did not predict outcome possibly due to differences in population characteristics or treatment utilization.?

P475

Prognostic significance of heart rate in patients with chronic heart failure with reduced ejection fraction

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Background: Elevated heart rate (HR) is associated with higher mortality and morbidity in patients with heart failure. This study is aimed to evaluate the clinical significance of heart rate in predicting the prognosis in patients with chronic heart failure.

Methods: We enrolled 1581 consecutive chronic heart failure (mean age 68.1 years) registered in the therapeutic unit of chronic heart Failure. We divided the patients into 2 groups: group 1 with HR ≤ 70 bpm, group 2 with HR > 70 bpm.

The relationships between HR and the prognosis of chronic heart failure patients were determined.

Results: Elevated HR was associated with male sex, hypertension, diabetes, stroke attack and ischemic heart disease, but the association was modest with obesity. chronic heart failure patients with NYHA grade III/IV had higher HR than those with NYHA grade I/II with a good correlation.

High HR correlated with increased cardiac decompensation and hospitalizations, elevated filling pressure. Also, There were statistical differences in atrial fibrillation between the group 1 and 2. Furthermore, β -Blocker therapy and Ivabradine were associated with reduced HR ($p < 0.0001$).

We also observed negative correlations between HR and hemoglobin, glomerular filtration rate were also found.

Conclusions: Elevated HR was associated with increased cardiac decompensation and hospitalization. It may have good clinical predictive value in patients with chronic heart failure and should be a distinct therapeutic target.

P476

Resting heart rate and survival in patients with advanced cancer

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Purpose: Patients with advanced cancer have been shown to suffer from cardiovascular impairment that leads to reduced exercise capacity and quality of life. Using patients' electrocardiograms, we sought to determine whether resting heart rate (HR) and other assessable variables have prognostic value.

Methods: From 2005 through 2010 we enrolled 145 patients with histologically confirmed cancer (age 59 ± 10 years, 56% men, body mass index [BMI] 24 ± 5 kg/m², UICC tumour stage [Union Internationale contre le Cancer] I/II/III/IV 11.0/10.3/32.4/46.3%) and 59 controls (age 60 ± 11 years, 54% men, BMI 26 ± 4 kg/m²). Patients were followed up until the database was censored in February 2014 or until death. The cancer group consisted of 36 patients with colorectal, 72 with pancreatic, and 37 with non-small cell lung cancer. At baseline, a thorough cardiac investigation was performed including a resting and 24 hour electrocardiogram, a full blood count and clinical chemistry. Electrocardiograms were analysed using the Welch Allyn Software and validated by two reviewers.

Results: Control subjects' mean resting HR was 70.1 ± 13.0 , that of cancer patients 79.5 ± 14.2 beats per minute (bpm, $p < 0.0001$). In total, 45.5% of all cancer patients presented with a resting HR > 80 bpm. This was the case in 13.6% in controls. Subgroup analysis of patients with colorectal, pancreatic, and non-small cell lung cancer showed a mean heart rate of 75.3 ± 12.9 , 78.0 ± 12.3 and 86.5 ± 16.6 bpm (ANOVA $p < 0.0001$). During a mean follow-up of 27.4 months, 82 patients died from any cause. Using single predictor Cox proportional hazard analysis, we found that resting HR, tumour stage, cancer diagnosis, presence of metastatic disease, BMI, surgical intervention, haemoglobin, ferritin, leukocytes, lipids, liver function tests, potassium, medication with anticoagulants, number of ventricular extrasystoles and ventricular tachycardia all predicted survival (all $p < 0.05$). Resting HR remained an independent predictor of survival after adjusting for all parameters deemed clinically relevant including tumour stage, surgical intervention, haemoglobin and beta-blocker use (hazard ratio 1.015, 95% CI 1.001-1.030, $p < 0.05$).

Conclusion: Resting heart rate is an independent predictor of survival in patients with advanced colorectal, pancreatic and non-small cell lung-cancer cancer.

P477

Six minute walk test: predictor of hospital readmission in patients with chronic heart failure

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Background: Patients with chronic heart failure are frequently readmitted to the hospital due to disease progression. Although a shorter 6-minute walk distance (6MWD) is correlated with poor prognosis, 6MWD is not considered a clinical indicator for predicting hospital readmission.

We investigated whether 6MWD predicted readmission due to heart failure in CHF patients.

Methods: We enrolled 814 patients admitted to the therapeutic unit of chronic heart failure from 2006 to 2013 as follow: 6MWD < 300 m ($n = 740$), 300 $<$ 6MWD $<$ 450 m ($n = 54$) and 6MWD > 450 m ($n = 20$).

Clinical characteristics, 6MWD and readmission due to heart failure were evaluated.

Results: The mean of age was 63 years old, 65% males. The mean 6MWD in groups were 131.4, 349 and 512m respectively.

6MWD was shorter in readmitted patients than non-readmitted patients and was a significant predictor of readmission ($P < 0.0001$).

6MWD measured is a predictor of hospital readmission in CHF patients for clinical or echocardiographic cardiac decompensation ($p = 0.01$)

Conclusions: In systolic heart failure outpatients, 6MWD demonstrated utility as predictors for hospitalization for cardiac decompensation.

P478

The novel index of contractile function of the heart can predict the rate of hospitalizations

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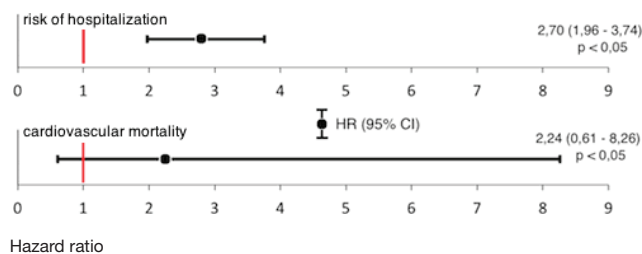
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Purpose: To examine the ability of myocardial contractile reserve (MCR) assessment to predict the rate of hospitalizations.

Methods: 162 patients with structural heart disease were studied during exercise stress echocardiography with characterization of MCR by Doppler imaging. During the stress test with the help of continuous wave Doppler the blood flow in the ascending aorta was registered. Value of cardiac output (CO) during the stress test was calculated every 10-20 bpm increase. Patients were divided into two groups: group A, normal ejection fraction of left ventricle (EF) and normal MCR defined as an increment of CO up to submaximal heart rate (HR) and monophasic dynamics of CO ($n = 36$) and group B, reduced EF and depressed MCR (biphasic dynamics of CO) ($n = 126$).

Results: 21 (58%) patients of group A and 93 (74%) patients of group B had clinical signs of heart failure ($p > 0.05$). Framingham risk score was $16.8 \pm 9.5\%$ in group A and $17.0 \pm 8.6\%$ in group B ($p > 0.05$). Long-term follow-up was done after 3-10 years, median 8 years. At the end of follow-up, rate of hospitalizations became significant (group A 53%; group B 78%; $p < 0.05$). Cardiovascular mortality was similar in both groups (11% and 19%, respectively). After subgroup analysis risk for subsequent hospitalization was increased in the patients with depressed MCR and reached maximal HR $<$ 120 bpm during stress test (hazard ratio 2.70; 95% confidence interval 1.96-3.74; $p < 0.05$; fig. 1).

Conclusions: MCR is a measure of the ability of the myocardium to increase its contractility with stress. The normal response is an increase CO up to submaximal HR in the shape of monophasic curve of CO. Risk of subsequent hospitalizations was increased in patients with depressed MCR.



P479

Prognostic significance of hyponatremia among ambulatory patients with heart failure

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Background: Hyponatremia - lowering of sodium in blood serum below 135 mmol/l - is a frequent disorder of electrolyte metabolism in patients with chronic heart failure. It is an established predictor of adverse outcomes in hospitalized patients with reduced ejection fraction.

Our aim was to evaluate the incidence of hyponatremia in ambulatory patients diagnosed with chronic heart failure in order to establish a correlation with the risk factors, evolution and prognosis.

Methods: We examined the prevalence, risk factors, and long-term outcomes of hyponatremia (serum sodium ≤ 135 mEq/L) in ambulatory HF with reduced EF. The cohort consisted of 1240 admitted in the therapeutic unit of heart failure (TUHF) between 2006 and 2014.

Results: Hyponatremia was present in 19.6%. Mean serum levels of natremia and were 131.3 meq/l. Hyponatremia was associated with male sex, diabetes, stroke attack, coronary heart disease. Compared with normonatremic patients, those with hyponatremia had lower systolic blood pressure and lower functional capacity during six - minute walk. Also, hyponatremia was associated with cardiac decompensation, diastolic dysfunction ($p = 0.014$), severe renal insufficiency and higher doses of diuretics ($p < 0.0001$); whereas, beta-blockers were inversely associated ($p < 0.0001$).

Conclusion: Patients with heart failure and hyponatraemia on showed a higher risk of long-term morbidity than patients without.

P480

Prognostic power of heart failure phenotypes in a population-based cohort study of outpatients with isolated hypertensive etiology

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Background: Prognostic stratification in heart failure (HF) is crucial to guide clinical management and treatment decision-making. However, there is paucity of information on HF patients presenting systemic hypertension (SH) as isolated etiology factor.

Objectives: To evaluate predictive factors of mortality in HF population with SH as isolated etiology taking into account different LVEF phenotypes (LVEF \leq 40% - HF-rEF, LVEF 41-49% - HF-bEF, LVEF \geq 50% - HF-pEF).

Methods: We analyzed patients with SH and HF enrolled from November 2009 to October 2013. HF patients with SH as isolated etiology factor (HF-SH) were defined as having a history of hypertension in absence of significant coronary artery disease/inducible ischemia and primary moderate-to-severe valvular, myocardial and congenital heart disease. Only case with available LVEF were included in the analysis. Clinical variables of study population were derived from the E-data chart for Outpatient Clinic collected in a regional Data Warehouse.

Results: HF was identified in 2610 out of 14110 (28%) patients with SH. After exclusion of 1974 patients affected by other cardiac diseases, HF-SH was diagnosed in 636 cases, 24% (mean age 77 \pm 9 years, 55% males, 16 % NYHA III-IV). Among HF-SH patients, 121 (19%) were identified as HFrEF, 88 (14%) as HFbEF, 427 (67%) as HFpEF. Patients with HFpEF were older, more frequently female, less symptomatic and with more frequent atrial fibrillation. Target HR \geq 70 bpm in SR patients was satisfied in 203 (32%). Moreover, ACE-I/sartans and antialdosteron treatments were less frequent in HFpEF, while betablocker were similarly prescribed (around 50%) across HF phenotypes. During a median follow-up of 24 \pm 9 months, 93 (15%) died. The independent predictors of mortality by Cox regression multivariate analysis were male sex, higher mean age and degree of renal dysfunction, along with lower body mass index (BMI). In addition to this, HF phenotypes were confirmed as independent predictors of outcome with HFpEF phenotype independently associated with survival.

Conclusions: In the subset of HF-SH population, different HF phenotypes were characterized by some different clinical characteristics and treatment. Along with demographic (age) and clinical factors (renal function and BMI), HFpEF phenotype (as compared with HFrEF) maintains its independent and favourable prognostic power. In the ‘real world’ of therapy for HF-SH patients there seems to be large room for improving prescription and titration of evidence-based HF treatments.

P481

Pre-discharge evaluation in heart failure: additive predictive value of the 6-minute walking test to clinical scores

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Purpose: Risk stratification in heart failure (HF) has largely evolved over the last decade. A considerable number of risk models and multivariable scores have been proposed to improve assessment of the disease progression, optimize treatment and promote more effective use of therapy. While some risk models include assessment of functional capacity by peak VO₂ during cardiopulmonary exercise testing, the more recently developed “real world oriented” scores are based on simple clinical variables. The aim of the present study was to investigate the predictive value of a pre-discharge evaluation combining an easy-to-obtain measure of functional capacity, such as the 6-minute walking test (6MWT) to two updated clinical scores.

Methods: We evaluated 466 patients who had pre-discharge data on the 11 and 13 items required for computing the 3C-HF (Cardiac and Comorbid Conditions) and the MAGGIC (Meta-analysis Global Group in Chronic Heart Failure) score and were able to complete a pre-discharge 6MWT. Cox regression models were used to assess the association between predictors and all-cause mortality.

Results: The 12-month event rate was 7.7%. Both the two scores and 6MWT were predictive for all-cause mortality ($p < 0.0001$ for all), with HR of 2.650 [95%CI 1.879-3.737], 2.754 [95%CI 1.870-4.056] for each one SD increase in the 3C-HF and MAGGIC respectively and of 0.481 [95%CI 0.374-0.618] for each one SD increase in the meters walked. The addition of 6MWT to both the 3C-HF and MAGGIC scores significantly improved predictive discrimination (c-index 0.793 [95% CI 0.722-0.864] and 0.802 [95% CI 0.733-0.871], respectively) and risk classification (integrated discrimination improvement 0.052 [95% CI 0.024-0.101] and 0.046 [95% CI 0.020-0.102], respectively). According to a distance walked $<$ or $>$ 376 meters, mortality was respectively 12.2% vs 4.1% ($p = 0.1$) and 24.3% vs 4.7% ($p = 0.0003$) in the intermediate and high risk strata for the 3C-HF, and 14.3% vs 0.9% ($p = 0.0002$) and 21.9% vs 8.4% ($p = 0.015$) in the intermediate and high risk strata for the MAGGIC score.

Conclusions: In HF patients, a pre-discharge evaluation combining the 6MWT to one updated clinical score substantially improves prediction of 12-month mortality.

PATHOPHYSIOLOGY

P482

I123-MIBG prognostic value in a selected patients population with idiopathic cardiomyopathy candidate to AICD implant: update of a pilot study

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Background: Chronic heart failure is characterized by a high percentage of arrhythmic cardiac sudden death. Guidelines recommend AICD implant to the patients with an optimal medical therapy, EF $<$ 35%, functional NYHA class II-III and at least 1 year of life expectancy. A high percent among them will never utilize the device or it will operate in a inappropriate manner with increased costs.

The MIBG scintigraphy demonstrated to be useful about prognostic stratification ability in these Patients. More trials have enrolled patients with extremely heterogeneous features both with CAD and idiopathic CMP.

Methods: Our pilot study has selected an homogeneous group of 32 patients with idiopathic dilatative cardiomyopathy (EF $<$ 35% in optimal medical therapy at least from 3 months). Diagnostic angiography excluded coronary disease. They were all candidates to the AICD implant. We have studied cardiac innervation after MIBG scintigraphy through the Heart/Mediastinum late rate, the wash-out rate background and evaluating a possible correlation with the left ventricular diameter and the left atrium sizes. The aim of our study is to verify if these collected data could be connected with arrhythmic events which had request the AICD intervention and to identify a cut-off in H/M late and wash-out rate.

Results: We have highlighted a medium H/M rate late about 1.62, a medium wash-out rate background corrected 34.6. After a 28 months follow-up, we have observed 3 ventricular fibrillation episodes treated with shock and 1 sustained ventricular tachycardia resolved by overdrive stimulation (ATP). Ventricular sizes seem to have a good proportional correlation with the H/M late rate and with the cardiac events. This correlation isn't so reliable with the atrium sizes.

Patients with arrhythmic events showed a late H/M late ratio respectively around 1.48, 1.31, 1.35 and 1.23; a ventricular diameter around 70 mm and a wash-out rate bkg corrected respectively of 32.27, 40.15, 47.8, 38.2. Other 28 patients with a regular clinical course showed an H/M late ratio $>$ 1.4 and ventricular diameters $<$ 65mm. Using ADMIRE cut-off (H/M late 1.6), we observed no events in Patients group with H/M late $>$ 1.6, while 4 arrhythmic events occurred in Patients with H/M late $<$ 1.6.

Conclusion: Our experience seems to endorse the prognostic validity of this method and it's comparable with ADMIRE study data where an H/M late $>$ 1.6 identify a group of patients with a low risk of arrhythmic events. In these patients it should be possible procrastinate AICD implant, while an H/M late $<$ 1.6 should identify a group with an high arrhythmic risk.

P483

Pathophysiological mechanisms of tolerance to physical loading decreasing in patients located at different stages of a cardiovascular continuum

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Purpose: to investigate the pathophysiological mechanisms decreasing of Tolerance to Physical Loading (TPL) in patients located at the different stages of cardiovascular continuum.

Methods: We studied 168 patients were at different stages of a cardiovascular continuum: 28 had hypertension stage I-III, 43 had the metabolic syndrome (MS), 53 - myocardial infarction (MI), 29 - end-stage of chronic heart failure (CHF) required the Heart Transplantation (HT) and 15 patients after HT. The age of patients with hypertension was 45,3 \pm 10,9 years, with MS - 45,3 \pm 10,2, with MI - 51,1 \pm 7,5, with CHF before HT - 44,3 \pm 12,7, after HT - 42,3 \pm 11,5 years ($p > 0,05$). Gas analysis, metabolism and TPL were estimated in the conditions of Spiro Bicycle Ergometry Test (spiroBET) starting from 25 Wt increased on 25 Wt every 3 minutes until maximal achieved dyspnoea appeared.

Results: The less value of TPL - 68,1 \pm 3,1 Wt was revealed in patients with end-stage CHF before HT, the greatest TPL 123,2 \pm 39,0 Wt was diagnosed at patients had only hypertension who were located at the initial stage of cardiovascular continuum. TPL in patients with MS (had not only hypertension but also obesity, hyperglycemia and/or dyslipidemia) was 110,0 \pm 49,1 Wt, in patients with MI it was significantly less - 84,4 \pm 20,3 Wt ($p < 0,05$), after HT TPL significantly increased up to 90,0 \pm 10,0 Wt (in comparison to value before HT $p < 0,05$). We established that even patients with hypertension and MS located at the initial stages of cardiovascular continuum had decreasing of TPL in comparison to age-expected. Mechanisms of TPL decreasing were different at different stages of cardiovascular continuum and depended on compensatory reserves safety. Decreasing of TPL was followed by decreasing of aerobic physical working capacity and of Maximal

Oxygen Consumption (VO₂max): the less level had patients with end-stage CHF (12.2 ± 0.5 ml/kg/min, patients with MI - 13.7 ± 4.0, with MS - 13.9 ± 5.2, with hypertension - 14.7 ± 4.9 ml/kg/min, the greatest value of VO₂max had patients after HT - 15.7 ± 0.9 ml/kg/min. Not only TPL but also VO₂max decreasing caused by existence not only cardiac, but also respiratory disturbances. We revealed that only patients with end-stage of CHF had disturbances of tissue mechanisms of oxygenation diagnosed according to spiroBET markers of high risk of a cardiovascular mortality (carbon dioxide production relationship, respiratory exchange ratio, the ratio of physiologic dead space over tidal volume at the rest and at the maximal level of loading).

Conclusion: spiroBET allowed to reveal main mechanisms of TPL decreasing.

PULMONARY HYPERTENSION

P484

The surprising results of the inhaled combination budesonide/formoterol in patients with chronic obstructive respiratory disease

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Purpose: Chronic obstructive respiratory disease (COPD) is a major health problem being, worldwide, the fourth leading cause of death and its prevalence tends to increase. We aim to evaluate the influence of therapy with full-dose inhaled combination budesonide/formoterol 320/9µg on heart remodeling and pulmonary hypertension studied by echocardiography in patients with COPD.

Methods: 21 patients with COPD (3 females and 18 males), mean age 61 ± 9.8 years, functional class I-III WHO, were included in a 12 weeks study with budesonide/formoterol 320/9µg (2 sprays a day). At baseline and after 12 weeks of therapy we assessed by transthoracic echocardiography: anterior-posterior diameter (APD) of right ventricle (RV), end systolic and diastolic volumes (ESV and EDV), ejection fractions (EF) by Simpson's Rule of RV and left ventricle (LV), systolic pulmonary artery pressure (SPAP), early and late diastolic tricuspid flows (E and A waves), index of eccentricity and TAPSE.

Results: At baseline all patients were characterized by increased right and decreased left heart chambers and systolic function of RV accordingly to elevated SPAP. 12 weeks of treatment with budesonide/formoterol resulted in significant elevation of EF of ventricles (EF RV % 60.04 ± 1.92 versus 53.10 ± 3.46, p < 0.05; EF LV % 70.31 ± 1.81 versus 64.36 ± 1.89, p < 0.05), diastolic function of RV (1.17 ± 0.09 versus 0.98 ± 0.06, p < 0.05) and reliably decrease in SPAP (50.37 ± 10.14 versus 56.43 ± 9.30, p < 0.05). Eccentricity index decreased from 1.7 to 1.3 and TAPSE increased from 12.3mm to 17.8mm (p < 0.05). All included patients noticed good tolerability.

Conclusions: The 12 weeks treatment with budesonide/formoterol had effect on heart remodeling, with the improvement of systolic and diastolic function and decreased pulmonary hypertension. Further studies are needed to confirm this data.

P485

Clinical experience with the use of sildenafil in patients with severe pulmonary hypertension due to left heart disease in a tertiary hospital

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Purpose: Guidelines do not recommend pulmonary vasodilators to treat patients with pulmonary hypertension (PH) due to left heart disease (group II). However, some studies have shown beneficial effects of sildenafil in this group of patients with high transpulmonary gradient (TPG). Our objective was to analyze the change of systolic pulmonary artery pressure (PAP), tricuspid annular plane systolic excursion (TAPSE) and clinical outcomes in these patients after sildenafil treatment in a real world setting.

Methods: We selected a cohort of 31 patients with chronic heart failure and PH treated with sildenafil from the Heart Failure Unit of a tertiary hospital. Most of them had a previous pulmonary catheterization that confirmed severe PH and high TPG. We compared differences in PAP and TAPSE before and after treatment with the student t-test for paired samples.

Results: Median age was 64 years, 58% male, 74% had systemic hypertension and 58% diabetes. Heart failure etiologies were ischaemic (39%), valvular (23%) and dilated (19%). 70% of patients were in NYHA class III-IV, with a median glomerular filtration rate of 47ml/min and median NT-proBNP of 2240pg/mL. Indication for sildenafil was pre-heart transplant (3%), post-heart transplant (23%) and refractory CHF in 74% of cases. Median dose of sildenafil achieved was 60 (IQR:30-90) mg/day.

Pre-treatment echo showed a median LVEF of 45% and mean PAP of 66 ± 16 mmHg. A second echo at a median of 8 months follow-up showed a reduction of PAP to

60 ± 18 mmHg, p = 0.039, and a non-significant increase of TAPSE from 12.6 ± 0.9 to 14.6 ± 0.9, p = 0.06. However functional class did not improve significantly, 9 patients died and 8 were transplanted after a median follow-up of 17 months.

Conclusion: Treatment with sildenafil of patients with CHF and group II severe PH was associated with a reduction of PAP measured by echocardiography. However, functional class did not improve and mortality remained high in this high risk population. More studies are needed to confirm the efficacy and safety of the treatment with sildenafil for group II PH.

P486

Descriptive study of patients diagnosed with type 2 pulmonary hypertension receiving sildenafil in heart failure and pulmonary hypertension clinics

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Objectives: Type 2 pulmonary hypertension (HTP) has high mortality, whose fundamental treatment is the underlying cause. The aim of the study is describe treatment with sildenafil in this population. We describe epidemiological characteristics as well as clinical (NYHA) and hemodynamic parameters (echocardiography) improvement.

Methods: We studied patients with type 2 HTP (according to the classification by Dana Point) treated with sildenafil. Patients were seen in our specific clinics between January 2009 and December 2014. We included patients with mean pulmonary blood pressure (PAPm) ≥ 25 mmHg and capillary pressure ≥ 15mmHg.

Results: A total of 22 patients with type 2 HTP were in treatment with sildenafil. The mean age of the patients was 67.4 ± 9.4 years and 64% were women. The 55% corresponded to valvular etiology, 27% to systolic dysfunction and 18% to diastolic dysfunction. The diagnostic hemodynamic parameters assessed by right heart catheterization were PAPm of 52.35 ± 9.4 mmHg and PCP 28.29 ± 5.9mmHg. By echocardiography the mean systolic artery pressure was 72 ± 16.5mmHg. We found right ventricular dysfunction which was mild in 19%, moderate 19% and severe 14% of patients. The average duration of treatment was 27.05 ± 24.20 months with a mean dose of sildenafil 66.81 ± 19.36 mg/day. The improvement hemodynamic parameters evaluated by echocardiography were found in 53%. The readmission for fluid retention during follow-up occurred in 36% (8 patients). The death from any causes occurred in 18% (4 patients) of which 1 died of cardiogenic shock and the rest from non-cardiovascular causes. Drug discontinuation occurred in 14% (3 patients). The reasons were intolerance in 2 patients and 1 patient because lack of beneficial effect.

Conclusions: Treatment with sildenafil could apparently get a subjective improvement in functional class and hemodynamics in many patients. However treatment of the cause of type 2 HTP is essential. Further studies are needed to corroborate our findings.

P487

Clinical management of pulmonary arterial hypertension

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InParaguay the treatment for Pulmonary Arterial Hypertension is something emerging and there were no published data on the subject, which prompted us to conduct this study.

Objective: To evaluate the clinical response to medical treatment, by walk test 6 minutes in patients with pulmonary arterial hypertension.

Materials and Methods: Prospective cohort study where patients attending the consultation, from 01 January 2012 to 31 December 2014 was assessed Inclusion criteria: adults, both sexes, with pulmonary arterial hypertension (PAH) confirmed by right heart catheterization diagnosis, treatment compliance. 3 group of patients: Group A)Sildenafil, Group B)Sildenafil+Iloprost, Group C)Sildenafil+Bosentan. Clinical response was evaluated by walk test 6 minutes(6MWT) before starting treatment and at 6-weeks, 6MWT was considered poor prognosis <300 meters(m), indeterminate 300-400m and good prognosis>400m, taken as positive clinical response the ≥100m increase in 6MWT 6-weeks. Statistical analysis was performed with the data package SPSS Statistics 17.0, using descriptive statistics and t-test were considered significant p ≤ 0.05 (IC 95%).

Results: Of 328 patients who attended the consultation, diagnosis PAH was confirmed in 44 patients(13.4%), 42 met the inclusion criteria, leaving out the study 2 patients who did not complete the treatment.

Group A) Sildenafil (N = 19): female 18/19. Age: 51.8 ± 15.2 years. Pulmonary arterial pressure (mPAP): 40.1 ± 23.6mmHg. 6MWT-basal: 152.4 ± 80.8 vs 6MWT 6-weeks: 375.9 ± 126.7 (p < 0.001). Baseline 6MWT: <300m: 16/19 (84%), 300 to 400m: 3/19 (16%). 6MWT 6-weeks: <300: 4/19 (21%), 300 to 400m: 5/19 (26%), >400m: 10/19 (53%). They achieved an improvement ≥100m: 14/19 (74%).

Group B) Sildenafil+Iloprost (N = 12): female 10/12. Age: 41.4 ± 13.5 years. mPAP: 48.2 ± 12.1mmHg. 6MWT-basal: 118.1 ± 72.4 vs 6MWT 6-weeks: 301.5 ± 128.1 (p < 0.001). Baseline 6MWT: <300m: 12/12 (100%). 6MWT 6-weeks: <300: 6/12

(50%), 300 to 400m: 2/12 (17%), > 400m: 4/12 (33%). They achieved an improvement ≥ 100 m: 11/12 (92%).

Group C) Sildenafil+Bosentan (N = 11): Female 9/11. Age: 47.5 ± 13.7 years. m PAP: 45.4 ± 10.2 mmHg. 6MWT-basal: 119.0 ± 78.3 vs 6MWT 6-weeks: 218.5 ± 96.5 ($p < 0.05$). Baseline 6MWT: <300m: 10/11 (90%), 300 to 400m: 1/11 (10%). 6MWT 6-weeks: <300: 9/11 (82%), 300 to 400m: 2/11 (18%). Achieved an improvement ≥ 100 m: 7/11 (64%).

Conclusions: The clinical response to treatment was positive in a high percentage of patients. The group showed a better clinical response was the Group B.

P488

Reduced lung function in COPD and coincident heart failure is associated with increased left ventricular wall stress

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Background: COPD and heart failure exhibit a considerable coincidence. Beside well-known mechanisms of increased right heart load in COPD, dedicated changes of the left ventricle (LV) are ill-defined and the question remains, whether specific interactions exist beyond common shared risk factors.

Methods: LV wall stress was measured by cardiac magnetic resonance imaging in 28 patients with COPD (GOLD I to III) and heart failure (LVEF $42 \pm 19\%$) due to non-ischemic and ischemic cardiomyopathy.

Results: Reduced lung function was associated with LV dilatation. LV enddiastolic (by trend) and endsystolic volume ($p = 0.048$ for GOLD III vs I) increased from GOLD stage I through stage II to stage III. LVEF and LV mass were not different among GOLD stages. Reduced FEV1 was correlated with increased enddiastolic ($p = 0.0210$) and endsystolic LV volume ($p = 0.0413$) and with increased enddiastolic ($p = 0.0161$) and endsystolic LV wall stress ($p = 0.0315$), respectively. LV enddiastolic ($p = 0.048$) and endsystolic wall stress ($p = 0.034$) increased from GOLD I to III.

Conclusions: Reduced lung function was correlated with increased enddiastolic and endsystolic LV wall stress. It is suggested that respiration at a level of hyperinflation requires increased negative pleural pressure when compared with normal lung function, which is transmitted to the heart and increases transmural pressure gradients and thereby cardiac distending forces. Increased ventricular wall stress is known to exhibit a broad variety of unfavourable consequences, which could contribute substantially to a worse prognosis in COPD.

P489

Simple parameters predict significant pulmonary hypertension in patients with advanced heart failure

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Background: Pulmonary hypertension (PH) is a negative prognostic factor in patients (pts) with left heart failure (HF).

Aim: To determine simple predictors of significant PH (defined as mean pulmonary arterial pressure /mPAP/ ≥ 35 mmHg) in pts with advanced HF.

Patients and Methods: Two hundred and twenty six heart transplant candidates were retrospectively evaluated. Mean age was 48.1 ± 9.9 years, left ventricular ejection fraction $23.3 \pm 7.4\%$. Eighty-eight % of pts were in NYHA classes III or IV. Main etiologies of HF were dilated cardiomyopathy in 55% and coronary artery disease in 29% of pts. Right heart catheterization using Swan-Ganz catheter was performed after therapy optimization. Twenty simply available clinical and laboratory parameters were included in logistic regression analysis to determine independent predictors of significant PH.

Results: Significant pulmonary hypertension was present in 50% of pts. One-year mortality in these pts was 33.7% in comparison to 14.1% mortality in pts with mPAP <35 mmHg ($p < 0.005$). Coronary etiology of HF, right ventricular diameter >38 mm, and daily furosemide dosis >240 mg were identified as independent predictors of significant PH.

Conclusion: Coronary etiology of HF, right ventricular dilation, and high daily furosemide dosis are independent predictors of significant PH in pts with advanced HF. These pts should be referred to an HF center earlier.

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Effect of chronic carbon monoxide exposure on pulmonary artery pressure

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Background: Chronic exposure to moderate doses of carbon monoxide (CO) without poisoning is not rare. Several animal studies demonstrated that chronic CO

inhalation attenuated hypoxic pulmonary hypertension development and reversed established pulmonary hypertension however, there is no data about humans. We aimed to investigate the effect of chronic CO exposure on echocardiographic systolic pulmonary artery pressure which has not been studied previously.

Methods: Forty apparently healthy male indoor barbecue workers (age mean \pm SD; 33.0 ± 9.40) who were working in various restaurants for at least 3 years and 48 age-matched healthy men (age mean \pm SD; 34.3 ± 6.6) were included into the study. Demographic and laboratory characteristics were compared. Systolic pulmonary artery pressure was measured by adding estimated right atrial pressure to tricuspid regurgitation pressure gradient with transthoracic echocardiography.

Results: Average working time of the indoor barbecue workers in their jobs was 16.1 ± 7.3 years. Clinical characteristics of indoor barbecue workers and the control group were comparable in terms of body mass index, blood pressure, heart rate and lipid profile. However, carboxyhemoglobin concentration ($6.4 \pm 1.5\%$ vs. $2.1 \pm 1.3\%$, $p < 0.001$) and systolic pulmonary artery pressure (29.5 ± 6.6 mmHg vs. 18.6 ± 5.1 mmHg, $p < 0.001$) were higher in indoor barbecue workers than in the control group. In Pearson correlation analysis, there was significant correlation between carboxyhemoglobin concentration and systolic pulmonary artery pressure ($p: 0.01$, $r: 0.489$).

Conclusion: Contrary to the results of previous animal studies, we demonstrated that chronic CO exposure increased systolic pulmonary artery pressure in indoor barbecue workers. This is the first human study investigating and reporting an association between chronic CO exposure and pulmonary artery pressure. Although still in the normal range, increase in pulmonary artery pressure is noteworthy and warrants further research.

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Role of bnp and echo measurement for pulmonary hypertension recognition in patients with interstitial lung disease: an algorithm application model

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Purpose: This study evaluated the role of echocardiography and BNP in patients with interstitial lung disease (ILD), to identify those with PH and RV dysfunction. The aims of this study were: 1- to evaluate the accuracy of an algorithm including BNP, DLCO and echocardiographic measurements to identify PH and RV dysfunction; 2- to evaluate BNP and Echo values concordance in relation to right catheterization measurement.

Methods: We analyzed 113 patients with diagnosis of ILD. Echo examination included: Pulmonary systolic, diastolic and mean Arterial Pressure (PAPs, PAPd, PAP mean), End-Diastolic and End-Systolic right ventricle diameters, Inferior Caval Vein diameter, and Tricuspid Annular Plane Systolic Excursion (TAPSE). Patients revealing increased PAPs at echocardiography underwent to catheterization.

Results: Patients with PAPs >40 mmHg (37 patients), PAPmean ≥ 25 mmHg (23 patients) and PAPd ≥ 20 mmHg showed BNP increased (157 ± 96 vs 16 ± 14 pg/ml $p = 0.004$; 201 ± 120 vs 28 ± 17 pg/mL; 124 ± 88 vs 23 ± 18 pg/ml $p < 0.001$) as patients with TAPSE ≤ 16 mm (25 patients) (145 ± 104 vs 26 ± 21 pg/ml $p < 0.001$). In catheterized patients (37 patients) BNP was increased in patients with invasive PAPs > 40 mmHg (165 ± 112 vs 29 ± 14 pg/ml $p < 0.02$), as well as in patients with Wedge pressure >14 mmHg (199 ± 153 vs 54 ± 39 pg/mL; $p = 0.01$). ROC Curve analysis showed that elevated values of BNP, PAPs, PAP mean are able to assess PH. On the other hand, lower values of DLCO (<40%) and TAPSE (≤ 16 mm) detect PH. Logistic regression analysis of the previous parameters, confirmed their diagnostic role in PH detection.

Conclusions: In patients with ILD, an algorithm including BNP, DLCO and echocardiography could be useful for non invasive screening of PH

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Clinical profile and outcomes patients with pulmonary hypertension due to left heart disease: data from the Pan African Pulmonary hypertension Cohort study

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Background and Purpose: Little is known about pulmonary hypertension (PH) due to left heart disease (PHLHD) in Africa. We investigated the contemporary clinical profile and short term outcomes in sub-Saharan African (SSA) patients with PHLHD.

Methods: The Pan African Pulmonary hypertension Cohort (PAPUCO) is a multinational prospective observational registry involving 12 university centers across four SSA countries, namely Cameroon, Nigeria, Mozambique and South Africa. Cases with signs and symptoms of PH underwent echocardiographic assessment for cardiac disease and PH. PH was classified as mild (ie. right ventricular systolic pressure [RVSP]: 35-45 mmHg), moderate (RVSP: 46-60 mmHg) and severe (RVSP: >60 mmHg). Logistic regression models were used to determine the predictors of outcome (hospital admission and all-cause mortality) during follow-up.

Results: Of 209 patients diagnosed with any PH, 144 (mean age 53.3 ± 18.5 years, 40.4% men) had PHLHD. Mean RVSP was 60.4 ± 16.7 mmHg overall, and 41.6 ± 3.4 , 51.9 ± 4.4 , 78.1 ± 12.5 for mild ($n=47$), moderate ($n=32$) and severe PH ($n=62$) respectively. In multivariable analysis, left atrial diameter (OR = 0.55; 95%CI 0.28-0.82; $p < 0.001$) and TAPSE (OR = -0.99; 95%CI -1.51-0.47; $p < 0.001$) were predictors of RVSP. Heart failure with preserved ejection fraction was the most frequent (56%) cause of PH but valvular heart disease was associated with more severe PH ($p=0.009$). In all, 35 deaths and 41 hospital admissions were recorded after a median follow-up of 9.3 (25th-75th percentiles 6.8-15.2) months. There was a positive association between WHO-FC and mortality ($p=0.01$), RVSP and admissions ($p=0.03$) but not RVSP and mortality ($p=0.12$).

Conclusions: Among patients with PHLHD in SSA, left atrium size and TAPSE were significant predictors of RVSP. RVSP predicted admissions but not death after short term follow up. A long term follow-up of a larger sample is necessary to confirm these observations.

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Pulmonary hypertension in patients with myelofibrosis due to myeloproliferative syndromes: a mechanism unraveled

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Background: Pulmonary hypertension (PH) is a well-known complication of myeloproliferative syndromes (MPS) such as polycythemia vera (PV), essential thrombocythemia (ET) and agnogenic myelofibrosis (AM) in advanced stages. Although initially attributed to increased pulmonary vascular resistance (WHO group 1 PH), this entity was reclassified in 2009 in group 5 (unknown mechanism and miscellaneous PH). Our aim was to describe the prevalence and possible causes of PH in a series of patients MPS and myelofibrosis.

Methods: We studied patients with myelofibrosis secondary to MPS using echocardiogram, right heart catheterization and scintigraphy following intraarterial infusion of Tc99-labeled albumin macroaggregates.

Results: We included 11 patients with MPS and myelofibrosis (7 male, mean age 58 years, 4 with PV, 4 TE and 3 AM) during the period 2009-2014. All had JAK-2 gene mutations, bone marrow fibrosis and visceromegaly. Median NT-proBNP levels were 4597 pg/ml (range 175-5700). Echocardiograms showed pulmonary hypertension in most cases, with a mean pulmonary systolic pressure of 54 ± 17 mmHg (range 35-80). Right heart catheterization disclosed high cardiac output (HCO) in all patients. After ruling out other causes of HCO, a scintigraphy was performed after administrating Tc99-labeled albumin macroaggregates in the descending thoracic aorta. In every case, a percentage ($6.1 \pm 2.0\%$ of the radioactivity) of the labeled macroaggregates were plugged in the pulmonary capillary bed, which makes the diagnosis of microfistulas in the infradiaphragmatic territory.

Conclusion: Most patients with MPS and myelofibrosis show pulmonary hypertension associated with high cardiac output caused by microfistulas without a significant increase in pulmonary resistance. This finding has important clinical implications because pulmonary vasodilators (once recommended) should be contraindicated since they may worsen the clinical presentation.

HFpEF – HEART FAILURE WITH PRESERVED EJECTION FRACTION

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The relationship between biomarkers of cardiovascular stress, left ventricular remodeling and renal function in patients with ischemic chronic heart failure with preserved ejection fraction

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Purpose: Biomarkers of cardiovascular stress have been associated with incident cardiovascular outcomes. Their relationships with renal function, left ventricular remodeling, have not been well described. The aim of our study was to identify relationships between level of markers of cardiovascular stress (ST2, galectin-3), parameters left ventricular remodeling and renal function in patients with ischemic chronic heart failure with preserved ejection fraction (HFpEF).

Methods: The study involved 110 patients with CHF (92 men), mean age 60.1 ± 9.6 years with II-IV functional class (recommendations of the New York Heart Association) is due to ischemic heart disease. Serum levels of N-terminal pro-B-type natriuretic peptide (NT-proBNP), Cystatin C (CysC), Galectin-3 (Gal-3), ST2 were quantified by ELISA of 57 patients with HF and preserved ejection fraction (HFpEF) and 53 patients with HF and reduced EF (HFrEF). Echocardiography was performed using the General Electric Vivid 3 system. Nonparametric Mann-Whitney U-test for independent data and Spearman's rank correlation coefficient were calculated.

Results: With the purpose of verify the diagnosis of heart failure used determining the level of NT-proBNP, which is by 66.9 % ($p=0.0001$) was greater in patients with HFrEF. In patients with ischemic HFrEF showed the tendency to increase level of creatinine (4 %, $p=0.23$), cystatin C (13.1 %, $p=0.15$) and a lower glomerular filtration rate (6.5%, $p=0.09$). Reduction of LV ejection fraction was associated with increasing level galectin-3 (43.4%, $p=0.03$), ST2 (15.6%, $p=0.0002$), left atrial volume index (28.1%, $p=0.003$), systolic pulmonary artery pressure (28.7%, $p=0.0007$), and E/Eann (26.6%, $p=0.02$) - integral index end-diastolic pressure in the left ventricle. In patients with HFpEF established relationship between cystatin C and FC CHF ($r=0.33$; $p=0.03$), LAVi ($r=0.58$; $p=0.02$), IMMLV ($r=0.39$; $p=0.01$), LVEDV ($r=0.55$; $p=0.0001$), RVPs ($r=0.63$; $p=0.003$), NT-proBNP ($r=0.6$; $p=0.001$), GFR ($r=-0.37$; $p=0.02$) and level galectin-3 with NT-proBNP ($r=0.64$; $p=0.0004$). In our study no statistically significant relationship between the level of NT-proBNP and ST2.

Conclusions: In patients with ischemic chronic heart failure with preserved ejection fraction, against a lower markers of fibrosis and inflammation, established correlation between cystatin C and structural, functional parameters of cardiac remodeling and renal function. In patients with ischemic chronic heart failure no statistically significant relationship between NT-proBNP and ST2.

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Diagnostic performance of plethysmographic pulse amplitude ratio (PAR) in left ventricular dysfunction in patients with preserved and reduced left ventricular ejection fraction

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Purpose: PAR (pulse amplitude ratio) is now an admitted new marker in the diagnosis of diastolic left ventricular dysfunction. The question is if its value as an index of

Patients characteristics

Patient	1	2	3	4	5	6	7	8	9	10	11
Pulmonary Artery Pres. (S/D/Mean)	58/38/ 42	69/41/ 50	48/29/ 40	84/26/ 45	57/17/ 30	22/17 / 19	51/16 / 28	22/9 / 13	25/8 / 14	71/23 / 39	30/7 / 15
Pulmonary wedge pres.	28	37	27	13	9	7	13	7	8	12	6
Cardiac output (l/min)	12.5	8.0	11	7.1	8	7.3	8.7	6.7	7.45	6	7.8
Cardiac index (l/m/m ²)	5.5	4.0	6.6	3.6	5	4	4.8	4.0	4.5	3.9	5.1
Pulmonary vascular resistance (Wood U.)	1.2	1.4	1.2	4.5	2.6	3	1.7	0.9	0.8	4.5	1.1

acute heart failure (AHF) could be different between patients with preserved ejection fraction (pEF) and patients with reduced ejection fraction (rEF). The objective of this study is to compare the diagnostic performance of plethysmographic PAR between patients with pEF and patients with rEF.

Methods: In this prospective descriptive study conducted in the ED, we included patients admitted for acute dyspnea. We recorded proBNP level, PAR (obtained by calculating the minimal/maximal ratio of plethysmographic pulse) and echocardiographic parameters. A 511 patients were assessed and divided into two groups: acute heart failure group (AHF) and non acute heart failure group (Non AHF). The diagnosis of AHF was based on clinical data, proBNP level and echocardiography. Patients with AHF were divided into two subgroups: AHF with pEF (LVEF \geq 45%) and AHF with rEF (<45%).

Results: Patient's characteristics are shown in table 1. Diagnostic performance of PAR in AHF was assessed by the area under the ROC curve (AUC), it was significantly higher in HF group with rEF (0.81 vs. 0.45).

Conclusions: Plethysmographic PAR is unexpectedly more performant in the diagnosis of AHF in patient with rEF compared to those with pEF.

Table 1

	AHF n = 349 (69%)	Non AHF n = 162(31%)	
N = 511			
With pEF n = 59 (28%)	With rEF n = 254 (72%)		
Age, mean (SD)	67(12)	69(11)	60(16)* ...
Sex ratio (M/F)	1.36	1.05	2.28* ...
Diabetes, n(%)	33(55)	124(48)	50(30)* ...
Hypertension, n(%)	35(59)	166(65)	55(34)* ...
Coronary disease, n(%)	19(32)	46(18) [§]	17(10)* ...
COPD, n(%)	15(25)	39(15) [§]	66(40)* ...
proBNP, mean(SD)	4098(378)	6548(910) [§]	966(180)* ...
LVEF, mean%(SD)	64(6)	39(8) [§]	61(13)* ...
E/e' tissue doppler	10.72(6.5)	8.86(5.9)	6.93(3.9)
PAR, mean%(SD)	39(20)	56(21) [§]	29(18)* ...

Patient's characteristics. (*) ... p < 0.05 (Non AHF vs AHF with pEF and Non AHF vs AHF with rEF) (è) p < 0.05 (AHF with pEF vs AHF with rEF)

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Clinical features of heart failure with preserved ejection fraction in the arabian gulf region

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Aims: The prevalence, clinical features and outcomes of heart failure with preserved ejection fraction (HFpEF) vary across geographic regions. We sought to report the features of HFpEF in the Arabian Gulf Region.

Methods: We analyzed data of 4577 heart failure patients from the Gulf CARE registry. We compared HF patients with ejection fraction \geq 40% (HFpEF) and HF patients with EF <40% (HFrEF).

Results: 1550 patients (33.9%) had HFpEF and 3027 patients (66.1%) had HFrEF. Patients with HFpEF were older, more likely to be females, have atrial fibrillation, hypertension, sleep apnea but less likely to have coronary artery disease. HFpEF patients also had higher BMI, waist circumference, systolic blood pressure, and pulmonary artery pressure. HFpEF patients had significantly lower heart rate, a tendency to lower levels of NT Pro-BNP but higher estimated GFR. There was no significant difference in the duration of hospitalization or in survival at 12 months.

Conclusion: In the Arabian Gulf region, 33.9% of heart failure patients have preserved ejection fraction. Although the two types of HF patients have different clinical features, the duration of hospitalization as well as the survival was similar.

Features and outcome of HFpEF vs. HFrEF			
Variable	HFpEF (EF \geq 40)	HFrEF (EF<40)	P value
Age (years)	62.2 \pm 15.1	58.4 \pm 14.7	<0.001
Female Gender n(%)	880 (52.2%)	810 (29%)	<0.001
Atrial fibrillation n (%)	227 (14.6%)	332 (10.9%)	<0.001
Coronary artery disease n (%)	625 (40.3%)	1523 (50.3%)	<0.001
Hypertension n(%)	1001 (64.5%)	1782 (58.8%)	<0.001
Obstructive sleep apnea n(%)	53 (3.4%)	37 (1.2%)	<0.001
Body mass index (kg/m ²)	29.01 \pm 7.1	27.49 \pm 5.5	<0.001
Waist circumference (cm)	95.4 \pm 16.3	91.5 \pm 14.4	<0.001
Heart rate (beat/min)	93.9 \pm 24.4	98.9 \pm 21.9	<0.001
Systolic blood pressure (mmHg)	142.9 \pm 34.3	132.5 \pm 32.2	<0.001
N terminal Pro BNP (pg/ml)	5662 \pm 8914	6968 \pm 10565	0.06
Estimated GFR (ml/min/m ²)	70 \pm 39.39	67.4 \pm 32.4	0.018
Pulmonary artery pressure by echo(mmHg)	57.8 \pm 18.8	53.5 \pm 12.4	<0.001
Duration of hospitalization(days)	9.2 \pm 9.7	8 \pm 7.5	0.6
Survival at 12 months n(%)	1226 (79.09%)	2311 (76.3%)	0.1

GFR: glomerular filtration rate

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Galectin-3 in a sample of hospitalized heart failure patients with NYHA class iv symptoms:differences between HFREF and HFPEF

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Aims: Galectin-3 is a promising biomarker of myocardial fibrosis and remodeling in heart failure (HF), with established prognostic value.

Almost all existing data on galectin-3 have been derived from post-hoc analyses from randomized clinical trials. It has been suggested that galectin-3 is of particular value in patients with HF with preserved ejection fraction (HFPEF), who nowadays make up ~50% of all admitted HF patients. This study therefore, investigated a real-time population to determine the clinical and biochemical correlates of galectin-3 in patients with HF with reduced and preserved ejection fraction (HFREF and HFPEF), with severe symptoms (NYHA class IV), who were admitted for intensified pharmacological therapy.

Methods and Results: We included 53 HF patients, 47 with hypertension (90.4%) and 22 with ischemic heart disease (42.3%) as main etiology; all patients were Caucasian; their median age was 80 years (mean age 77 \pm 12); 18 males (34%), 35 females (66%); 29 were in sinus rhythm and 24 (45%) in atrial fibrillation; median BMI was 27.3, median creatinin 106 micromol/L, median urea 9.5 mmol/L, median galectin-3 27.8 ng/mL (interquartile range: 22.4 to 33.3); and median NT-proBNP 7013 pg/ml (interquartile range: 2471 to 13972).

Galectin-3 was elevated (>17.8 ng/mL) in 49 patients (93%), and positively correlated with creatinin (rs (Spearman Coefficient) 0.46; p < 0.001) and with urea (rs 0.37; p = 0.006).

Using echocardiography data, 35 patients (66%) had HFPEF (EF \geq 50%), while 18 (34%) had HFREF (EF < 50%); in HFPEF, median LVEDV and LVESV was 100 ml and 45 ml; while in HFREF median LVEDV and LVESV was 148ml and 86 ml (both: p < 0.01).

Galectin-3 median levels were more elevated in patients with HFPEF (29.8 ng/mL) than in HFREF (23.8 ng/mL, P = non-significant).

In HFPEF patients, galectin-3 levels were positively correlated with NTproBNP, urea, creatinin, and pulmonary arterial systolic pressure (PASP) (all P < 0.05). On the other hand, in HFREF, galectin-3 had no significant correlations with echocardiographic parameters, nor with biochemical parameters.

Conclusions: Galectin-3 levels were substantially elevated in admitted patients with NYHA class IV HF. Galectin-3 was (non-significantly) more elevated in patients with HFPEF, and correlated with various parameters of HF severity. In HFREF, galectin-3 had less clear relation to these parameters.

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Types of left ventricular remodeling in patients with coronary artery disease and preserved ejection fraction with and without hypertension (based on epidemiological studies)

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Objective: To evaluate the types of left ventricular remodeling in patients with coronary artery disease with and without hypertension with preserved ejection fraction.

Material and Methods: Primary screening held in 1295 men 20-59 years one of the mountainous regions of the Republic of Azerbaijan. In the first stage, all respondents conducted the following studies: filling cardiology questionnaire and a questionnaire to identify the degree of physical activity (PA), the presence of consumption habits of alcohol (A) and smoking (S), measurement of blood pressure (BP), anthropometry with the calculation of Kettle index (kg/m²), ECG-registration and determination of the mean concentrations of total cholesterol, triglycerides and high density lipoproteins cholesterol in the blood plasma. In the second stage all individuals with CHD held Doppler-echocardiography to determine hypertrophy, remodeling types and diastolic function of LV.

Results: Echocardiographic study of people with coronary heart disease found that 75.3% of respondents ejection fraction has been preserved, while 24.7% decreased. The study found that patients with coronary artery disease and the presence of hypertension remodeling types were distributed as follows: NM LV - 6.6%, CR LV - 16.1%, CH LV - 11.8%, EH LV - 10.8%. Respondents with verified coronary heart disease, but without the presence of hypertension picture was as follows: NM LV - 5.4%, CR LV - 5.4%, CH LV - 10.8%, EH LV - 8.6%.

Conclusions: Timely and adequate correction of hypertension in patients with coronary artery disease with preserved ejection fraction modern antihypertensive drugs to prevent further development of prognostically unfavorable types of left ventricular remodeling.

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Current state of heart failure with preserved ejection fraction in a secondary hospital

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Aims: The aims of this study were to describe the main features of hospitalized patients for HF PEF and to identify the prognostic factors related to mortality or readmission for HF.

Methods and Results: We prospectively evaluated 154 consecutive patients hospitalized for HF PEF (LVEF \geq 50%) in a secondary hospital between 2011 and 2012. All patients were followed for one year after discharge. Data related to HF rehospitalization and/or to all-cause mortality were collected during this period. Average patient age was 81 and 63% were women. Anaemia, hypertension and atrial fibrillation were the most prevalent comorbidities among these patients (Fig. 1). The mortality rate was 24%. In multivariable analysis, age over 80 years (OR 5.59; 1.60-22.48 CI 95%, $p=0.008$), plasma N-terminal brain natriuretic peptide (NT proBNP) higher than the median (OR 5.36; 1.84-15.65 CI 95%, $p=0.002$) and the need of chronic oxygen therapy (OR 4.19; 1.51-11.59 CI 95%, $p=0.006$) were associated with a higher risk of death. Out of the 82 patients without a prior history of HF, the Cox regression model identified plasma levels of NT proBNP higher than 1822.5ng/l (HR 3.67; 1.22-11.05 CI 95%, $p=0.021$) as the single most important independent predictor of readmission for HF.

Conclusions: HF PEF is common among octogenarians. Age, increased plasma levels of NT proBNP and long-term supplemental oxygen therapy are related to poor prognosis at follow up in these patients.

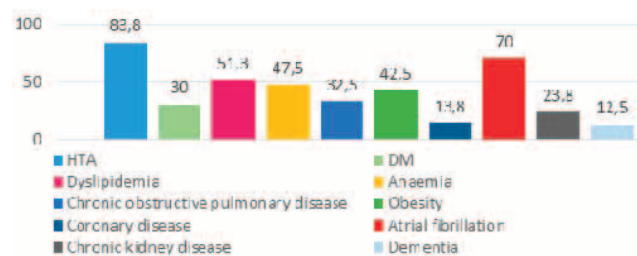


Fig 1. Comorbidity

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Aortic stiffness is a significant determinant of left ventricular diastolic dysfunction in metabolic syndrome patients

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Aim: The aim of this study was to evaluate the relationship of arterial stiffness and left ventricular diastolic dysfunction (LVDD) in metabolic syndrome (MetS) patients.

Methods: A cross-sectional study was carried among 1208 MetS subjects (aged 54 \pm 6, 65% women, 92% hypertensive, 94.8% having a body mass index (BMI) $>$ 25kg/m²) without overt atherosclerotic disease and systolic LV dysfunction. According to the 2D, conventional and tissue Doppler echocardiography findings, patients were divided into two groups: with LVDD (LVDD+, $n=406$ with relaxation abnormalities and $n=713$ with pseudonormalisation) and without LVDD (LVDD-, $n=89$). Arterial stiffness parameters (carotid to femoral pulse wave velocity (cfPWV) and aortic augmentation index (AIxHR75)) were assessed by applanation tonometry.

Results: In comparison to LVDD- patients, LVDD+ patients were older (55 ± 6 vs 51 ± 6) and had higher cfPWV (8.8 ± 1.6 vs 7.9 ± 1.34 m/s), AIxHR75 (24.7 ± 10.2 vs 19.7 ± 10), mean arterial pressure (108 ± 12.3 vs 101 ± 10 mmHg), heart rate (HR) (66 ± 10 vs 61 ± 9), left ventricular mass index (LVMI, 109 ± 24 vs 97.1 ± 22), BMI (32 ± 5 vs 30 ± 4 kg/m²), and insulin sensitivity index HOMA-IR (3.8 ± 3.4 vs 2.9 ± 1.4 , all $p < 0.05$).

We found significant correlations between arterial stiffness indices and diastolic function parameters, such as the ratio of early to late transmitral pulse Doppler velocities (E/A) (cfPWV = -0.19 , rAIxHR75 = -0.15 , $p < 0.05$), early diastolic mitral annular velocity (E') (cfPWV = -0.25 , rAIxHR75 = -0.18 , $p < 0.05$), and E/E' ratio (cfPWV = 0.17 , rAIxHR75 = 0.14 , $p < 0.05$). Also there was a significant correlation between E/E' ratio and LVMI ($r=0.324$), aortic pulse pressure (PP) ($r=0.265$), common carotid artery mean intima-media thickness (IMT) ($r=0.163$, $p < 0.05$).

Univariable analysis (Table 1) revealed the following significant predictors of LVDD: age $>$ 52.6, BMI $>$ 30, waist circumference \geq 107, cfPWV \geq 7.9, AIxHR75 \geq 21, aortic mean blood pressure \geq 105, aortic PP \geq 43, common carotid artery mean IMT \geq 593.5, HR \geq 64, LVMI \geq 87, HOMA index \geq 2.73 ($p < 0.05$). In order to identify predictors of LVDD a stepwise multiple logistic regression analysis with all significant variables was performed and several models have been obtained (Table 1, Model 1, Model 2). Age, gender and HR were placed in all regression models as covariate.

In models only age, HR, cfPWV and BMI (Model 1) or waist circumference (Model 2) remained significant predictors of the presence of LVDD ($p < 0.05$).

Conclusion: Carotid to femoral pulse wave velocity, an index of aortic stiffness, is a significant determinant of the LV diastolic dysfunction in subjects with metabolic syndrome.

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Heart failure with preserved ejection fraction: do different criteria define different groups of patients?

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Introduction: Heart failure with preserved ejection fraction (HFPEF) is a clinical syndrome that may account for over 50% of the patients admitted with acute decompensated heart failure. However, different criteria have been used in its definition and whether this means defining different groups of patients has not been addressed.

We aimed to analyse how different criteria used in the definition of HFPEF influence clinical characteristics, therapeutic approaches and outcomes of hospitalized patients with acute decompensated HFPEF, compared to those with heart failure with reduced ejection fraction (HFREF).

Methods: Retrospective analysis of hospitalized patients with new-onset or worsening pre-existing heart failure as the primary cause of admission in a Central Hospital, over a 6 month period, with follow-up after 10 months. Patients with HFPEF were analysed separately, according to three different definition criteria: group 1. ejection fraction (EF) $>$ 40%; group 2. EF $>$ 50%; group 3. EF $>$ 50% and left ventricle end-diastolic volume $<$ 97mL.

Results: 236 admissions were analysed. The prevalence of HFPEF in group 1 was 53.8%, 47.9% in group 2 and 18.6% in group 3.

According to the most used definition (group 2), compared to patients with HFREF, those with HFPEF were older, more often women, with hypertension and non-smokers; the etiology of the heart failure was non ischemic and an infection was the most prevalent factor precipitating decompensation. These patients were undermedicated, both in admission and at discharge. No significant differences were seen in length of stay, re-hospitalization or mortality.

Using either one of the definitions of HFPEF, compared with those with HFREF, patients were older, more frequently women and hypertensive ($p < 0.02$). Non

ischemic etiology was the most frequent in the three groups and infection the main decompensating factor. In the three groups of HFPEF, re-hospitalization and mortality were similar to those with HFREF (group 1: 19,7% vs 22,4%, $p=0,67$; group 2: 18,6% vs 21,1%, $p=0,65$; group 3: 15,9% vs 19,7%, $p=0,59$).

Conclusion: HFPEF is a frequent syndrome and affects mainly older people, women and hypertensive, independently of the definition used. Patients are undermedicated and remain with a poor prognosis, with event rates similar to the population with HFREF. The criteria used in its definition have an impact on its prevalence, but it is interesting to note that they don't influence clinical characteristics, etiology of HF, precipitating factor of decompensation or even prognosis.

ANIMAL MODELS AND EXPERIMENTATION

P502

Positive inotropic support in acute cardiac decompensation - haemodynamic and arrhythmogenic effects of levosimendan and catecholamines combined treatment in experimental heart failure

Granted by the Hungarian Scientific Research Fund (OTKA 10555)K V Nagy¹; EM Vegh¹; B Sax¹; A Kosztin¹; G Szucs¹; E Zima¹; N Turi-Kovats¹; V Kekesi¹; B Merkely¹

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Background: Ca²⁺-sensitizer levosimendan became first-line treatment in acute systolic dysfunction besides catecholamines (CAs). We aimed to evaluate haemodynamic and arrhythmogenic effects of levosimendan (LEV) administered together with catecholamines (dobutamine, DOB; dopamine, DA; norepinephrine, NE) in a canine heart failure (HF) model.

Methods: HF (n=12) was induced by chronic right ventricular tachy-pacing (240/min), continued until acute cardiac decompensation. Two experimental groups of anesthetized (ketamine-midazolam) animals were constituted: Group I. - continuous infusion of LEV (0.1 g/kg/min iv.) combined with 10-10 minutes infusion of different CA doses: DOB3-6-12, DA4-8-16 és NE0,04-0,08-0,16 ($\mu\text{g}/\text{kg}/\text{min}$, iv.); Group II. - CAs were given in same doses without LEV. Measured variables: blood pressure (BP), left ventricular end-diastolic pressure (LVEDP), contractility (dP/dt_{min}-max), duration of monophasic action potential at 50%, 90% of repolarisation (MAPD50, MAPD90). Number of ventricular premature beats (VES), ventricular tachycardias were also counted.

Results: In Group I. LEV alone did not alter mean BP (105 ± 13 mmHg) and LVEDP (28 ± 5 mmHg). However, dP/dt_{max}, dP/dt_{min} (1779 ± 313 and -1967 ± 322 mmHg/s) were increased by 56 ± 15, 49 ± 15 $\Delta\%$ ($p < 0,001$). There was further increase in dP/dt_{max} with combination of LEVO and CAs, maximal effect was observed with LEV+DA16 (+73 ± 19 $\Delta\%$, $p < 0,001$). LVEDP tended to decrease during LEV+DOB12 and to increase at LEV+NE0,16 (ns). In the CAs-only group (II.) basal haemodynamic parameters (BP, LVEDP, dP/dt_{max}, dP/dt_{min}) did not differ from Group I. Moreover, CAs without LEV exerted cardiovascular responses similar to those in LEV+CA group.

Malignant ventricular arrhythmias or increase in VES occurrence were not observed in both groups. During LEV infusion LV MAPD50 decreased significantly (214 ± 8 vs 242 ± 9 msec, $p < 0,01$), which was further shortened by LEV+NA0,16 (204 ± 20 msec, $p < 0,02$). Conclusion Co-administration of levosimendan and catecholamines elicited similar improvement in cardiac contractility to catecholamines given separately. This beneficial effect was not accompanied by malignant arrhythmias, despite of MAPD50 shortening during LEV infusion.

BASIC SCIENCE: ACUTE AND ADVANCED HEART FAILURE

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High rate right ventricular pacing causes global impairment of myocardial blood flow in an experimental model of heart failure

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Purpose: Prolonged right ventricular (RV) pacing at high heart rate (HR) induces dyssynchronous contraction and progressive left ventricle (LV) dysfunction in the experimental animal. The possible effects of pacing on regional or global myocardial blood flow (MBF) and on nitric oxide synthetases (NOS) gene expression are unknown. Aim of the study was to measure MBF and cardiac NOS expression in a group of minipigs undergoing prolonged high rate pacing.

Methods: Seven adult minipigs underwent RV apical pacing (220 beats/min) for 4 weeks. Positron emission tomography and 2D-echocardiography (ECHO) were performed at baseline (PRE) and soon after interruption of 4 weeks high rate pacing (POST). Regional myocardial blood flow (MBF) ([¹³N]ammonia as a flow tracer) was quantified in 17 LV segments from PET data. LV fractional shortening (FS) was

computed from ECHO. To evaluate the possible effects of dyssynchrony due to RV stimulation, all PRE and POST measurements were performed either during spontaneous rhythm and during PM induced rhythm (20 bpm over spontaneous HR to ensure capture). After the completion of the protocol, the hearts were excised for measurements of eNOS and stress induced iNOS gene expression in six myocardial regions corresponding to the mid LV segments in the PET 17 segments model.

Results: From PRE to POST, FS significantly decreased from 32.6 ± 3.4% to 15.8 ± 1.6% ($p < 0.001$) and MBF at spontaneous rhythm significantly decreased in all LV segments from 1.08 ± 0.25 to 0.88 ± 0.28 ml/min/g ($p < 0.001$). RV stimulated rhythm in normal hearts, induced an increase of MBF in the regions adjacent to the pacing site (septum and inferior walls) as compared with the opposite regions (1.39 ± 0.43 vs 1.15 ± 0.26 $P < 0.001$) but did not affect regional MBF distribution in the failing hearts (1,19 ± 0,46 vs 1,17 ± 0,40, ns). Regional eNOS expression was not significantly affected by prolonged RV pacing while the myocardial regions adjacent to the site of chronic stimulation had a higher expression of iNOS gene as compared to the opposite regions (1.50 ± 0.39 vs 0.78 ± 0.22, $P < 0.001$).

Conclusions: Prolonged high rate pacing in minipigs causes global reduction in LV function and a global decrease of MBF as observed in clinical dilated cardiomyopathy. LV dyssynchrony, caused by RV stimulation, is no more able to affect regional MBF distribution in the failing hearts despite increased myocardial stress in regions adjacent to stimulation. These results may have clinical implications for the timing of biventricular stimulation in patients with early or advanced LV dysfunction.

P505

Signature of circulating microRNAs in patients with acute heart failure

This study was supported by a Grant from the Dutch Heart Foundation:

Approaching Heart Failure By Translational Research Of RNA Mechanisms

(ARENA). The Ekaterina Ovchinnikova¹; D Schmitter²; E Vegter¹; C O' Connor³; D Bloomfield⁴; G Cotter⁵; A Mebazaa⁶; P Ponikowski⁷; A Voors¹; E Berezikov⁸

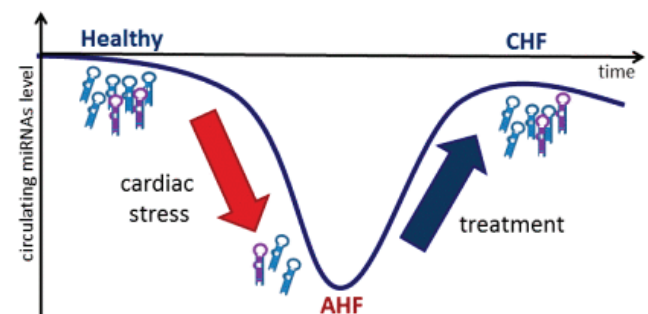
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Purpose: Circulating microRNAs (miRNAs) are promising markers of cardiovascular disease severity, progression and treatment response. The aim of the study was to identify circulating miRNAs associated with acute heart failure (AHF).

Methods: Plasma miRNA profiling included 128 patients with AHF from three different cohorts, 20 with chronic heart failure (CHF), 8 with acute exacerbation of chronic obstructive pulmonary disease (COPD) and 41 healthy controls. We measured plasma levels of miRNAs in discovery, validation, extended and COPD cohorts using quantitative reverse transcription-polymerase chain reaction (qRT-PCR).

Results: Plasma levels of miRNAs in patients with AHF were decreased compared to CHF or healthy controls. In sharp contrast to AHF, levels of circulating miRNAs were unaffected in COPD, another disease causing breathlessness, demonstrating that the effect was AHF-related. Panel of 7 miRNAs were confirmed to have decreased levels in the AHF patients of the discovery and validation cohorts. A further drop in miRNA levels within 48 hours after AHF admission was associated with an increased risk of 180 day mortality in a subset of the identified miRNAs.

Conclusions: Declining levels of circulating miRNAs were associated with increasing acuity of heart failure and mortality. The discovered miRNA panel may serve as a launch-pad for molecular pathway studies to identify new pharmacological targets and miRNA-based therapies.



Proposed model

P506

Transvenous stimulation of cardiac autonomic inputs improves subacute canine hemodynamics

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Despite advances in therapies for the management of heart failure, Acute Heart Failure Syndrome (AHFS) is a leading cause of mortality and morbidity. A catheter-based technology is being investigated to transvenously stimulate selective cardiac autonomic nerve inputs to modulate systemic hemodynamics for the treatment of AHFS.

This study's purpose was to investigate cardiac autonomic stimulation effects on canine hemodynamics. Four canines' autonomic nerve inputs were transvenously stimulated for 6 h. Hemodynamics were measured continuously during stimulation and compared to pre-stimulation values (stimulation off).

Cardiac output (CO) increased 114% (3.8 to 7.6 L/min) at 6 h. Stroke volume was the primary driver of CO augmentation increasing 93% (33 to 60 ml) at 6 h. Stroke volume improvements were driven initially by increases in left ventricular contractility (+10% at 1.5 h) followed by decreases in systemic vascular resistance (-53% at 6 h). These changes occurred with minimal increases in rate pressure product (RPP; +6% at 6 h), a marker for myocardial oxygen consumption.

The dramatic augmentation of system hemodynamics, in particular CO doubling with minor increases in RPP, suggests this technology is a potentially potent therapeutic tool to differentially augment CO without markedly increasing myocardial oxygen demand. This result was likely driven by the instantaneous increase in left ventricular contractility with small heart rate changes coupled with delayed onset vasodilation. Further potential likely exists to titrate therapy such that CO improvements are achieved in the presence of lowered RPP.

In conclusion, we believe this study represents promising progress towards providing clinicians with an effective and precise tool to improve clinical outcomes for AHFS patients.

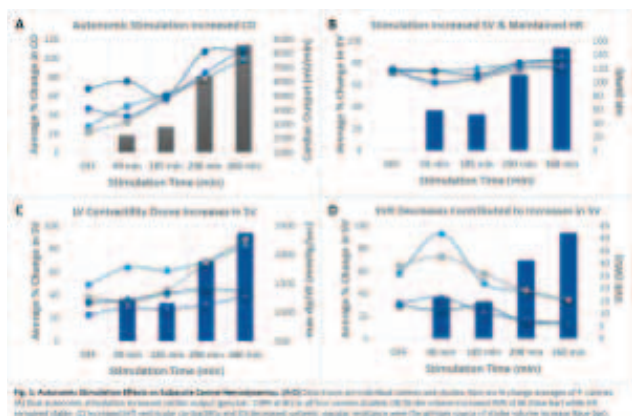


Figure #1: Autonomic Stimulation Effects

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Tramadol may induce cardiomyopathy

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Purpose: Tramadol is an opioid analgesic and norepinephrine releasing agent. There is increasing chronic use and abuse of tramadol, with recently reported tramadol related deaths. The toxic effect of tramadol on cardiac muscle would provide useful information in this context. To the best of our knowledge, the pathologic effect of tramadol on myocardium was not addressed in previous studies.

Methods: Eighteen adult male albino rats weighing 200-250 gm were randomly divided into tramadol group (12 rats) and control group (6 rats). Tramadol group received intraperitoneal (i.p.) tramadol hydrochloride in a single daily dose of 40 mg/kg, while control group received i.p. normal saline. After 14 days, animals were sacrificed. Left ventricles were examined by light and transmission electron microscopy.

Results: At the 7th and 9th days, 2 out of the tramadol treated rats died, while no deaths occurred in any of the control group. Light microscopic examination of the tramadol group revealed interstitial hemorrhage, widened interstitial space, and myocardial degeneration/contraction band necrosis. On semithin sections, myofiber lysis/disarrangement, perinuclear spacing, and mitochondrial clustering

were found. Electron microscopic examination of the tramadol group revealed nuclear abnormalities (chromatin clumping, loss of nucleoli, or perinuclear spacing), mitochondrial abnormalities (non uniform mitochondria, constrictions, clustering with loss of intermitochondrial contacts, fragmentation, or cavitation), myofibrillar lysis/disarrangement, and sarcolemmal thickening. Constellation of all of the above findings were found in the 2 dead animals. No abnormalities could be detected in the control group.

Conclusions: Tramadol may induce cardiomyopathy.

P508

Effects of hyperthermia and mild hypothermia on myocardial function in pigs: comparison to dobutamine

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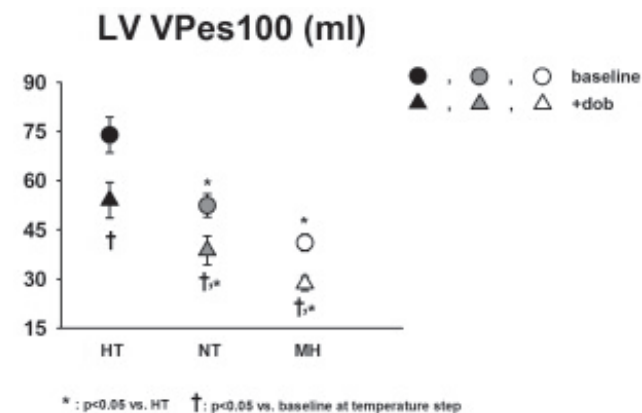
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Background: The optimal target temperature in resuscitated patients after cardiac arrest is unclear at present. We assessed the effect of hyperthermia (HT, 40.5°C), normothermia (NT, 38.0°C) and mild hypothermia (MH, 33.0°C) on systolic left ventricular (LV) function in healthy pigs and compared it to dobutamine infusion by pressure-volume analysis.

Methods: 9 anaesthetized, closed-chest pigs (67 ± 2 kg) were acutely instrumented for invasive pressure-volume analysis. Temperature was controlled by an intravascular device.

After baseline measurements at HT, intravenous dobutamine infusion was titrated to double LV dP/dtmax. Pigs were then cooled to NT and further down to MH and, at each temperature step, titrated dobutamine infusion was repeated. LV function was assessed by pressure-volume relationships derived from short aortic occlusions.



The calculated LV end-systolic volume at an end-systolic LV pressure of 100 mmHg (LVV-Pes100) was taken as a parameter of LV contractility (lower values indicate increased contractility).

Results: Heart rate and cardiac output decreased with cooling from HT to MH, while LV contractility increased (graph). The effect of cooling on LVV-Pes100 was of comparable effect size as dobutamine at a given temperature.

Conclusion: Cooling from HT to NT and from NT to MH increases LV contractility to a similar degree as a clinically relevant dose of dobutamine in the normal porcine heart. These data indicate that cooling can reduce the need for catecholamines during acute cardiac dysfunction and cardiogenic shock.

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Profound pressure unloading induced by a novel implantable counterpulsation assist device in a porcine model of acute heart failure

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Purpose: We have developed a novel implantable counterpulsation left ventricular (LV) assist device, the Pressure-Unloading Left Ventricular Assist Device (PULVAD), designed to provide LV pressure unloading and diastolic aortic augmentation. In the present study we aimed to investigate the effects of short-term PULVAD support on systemic hemodynamics in a large animal model of acute heart failure (AHF).

Methods: PULVAD comprises a pneumatically-driven polyurethane pumping chamber with a valveless opening, which is implanted in the thoracic cavity and is connected to the ascending aorta. The pump is synchronized on the basis of the ECG and operates through inflation of the device air space during diastole (injecting blood into the aorta), and deflation just prior and during systole (sucking blood from the aorta into the device blood sac).

6 farm pigs (84 ± 6 kgs) underwent induction of AHF by ligation of left anterior descending artery following median sternotomy. PULVAD was implanted in the thoracic cavity and connected to the ascending aorta using a vascular graft via partial clamping of the aorta (without extracorporeal circulation). PULVAD was driven by the Arrow Autocat 2 wave iabp system console and was synchronized on the basis of the ECG to provide pressure unloading of the LV along with aortic diastolic pressure augmentation. The animals were instrumented with a Millar pressure catheter for aortic pressure measurement. Systolic and end-diastolic aortic pressures (indices of LV afterload) were measured without LV support and after 30 seconds of PULVAD support.

Results: PULVAD support resulted in profound reduction of LV afterload, manifested as a significant decrease in systolic aortic pressure [SAP] (from 103.3 ± 15.4 to 87.4 ± 18 mmHg; $p < 0.001$) and in end-diastolic aortic pressure [EDAOP] (from 84.7 ± 13.8 to 58.6 ± 18.5 mmHg; $p < 0.001$). The magnitude of PULVAD-induced afterload reduction was evaluated at different levels of baseline (unassisted) SAP. The study measurements were divided into two groups based on median baseline (unassisted) SAP (Group A: $SAP < 106.5$ mmHg; Group B: $SAP > 106.5$ mmHg). The PULVAD-induced relative reduction of SAP (19.2 ± 11.6 vs $12.9 \pm 5\%$, $p = 0.03$) and EDAOP (37.7 ± 19 vs $26 \pm 11.9\%$, $p = 0.022$) was significantly greater in Group A vs Group B.

Conclusions: PULVAD, a novel implantable counterpulsation LVAD, provides efficient pressure unloading of LV in a large animal model of acute ischemic HF. Importantly from a clinical perspective, reduction of LV afterload is more profound across the range of arterial pressures typically observed in end-stage HF patients.

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Multi-species in vitro assays for shear-dependent total blood damage testing of ventricular assist devices

Technology Strategy Board for the Biomedical Catalyst Award (reference: 101462) CHRIS Chan¹; IL Pieper¹; KM Hawkins²; V Kanamarlapudi²; GD Foster¹; CA Thornton²

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Purpose: Ventricular assist devices (VADs) are an effective way to treat advanced heart failure in selected non-transplant eligible patients, both as temporary therapy (bridge-to-transplant) and permanent therapy (destination therapy). Although current VADs have benefited many patients, thrombosis and bleeding still remain common complications in heart failure patients with implanted VADs, and are linked to shear stress-induced damage to blood cells and proteins including erythrocytes, platelets and von Willebrand factor (vWF). The purpose of this study was to identify the species that is the most similar to humans and thus best suited for in vivo VAD testing by evaluating the species-specific response to mechanical shear stress in terms of haemolysis, complete blood counts, platelet activation and vWF size.

Methods: Human, bovine, ovine and porcine blood was subjected to different levels of shear rate using a rheometer. Haemolysis was measured by the Harboe assay and complete blood counts were determined by automated haematology analysis. Flow cytometry was used to monitor platelet activation, and the presence of high and low molecular weight (HMW & LMW) vWF multimers was detected through immunoblotting.

Results: Increasing shear rate in all tested species (human, bovine, ovine, and porcine) causes increased total blood trauma but there are species-specific differences. Haemolysis levels were most similar in human and ovine blood, whereas vWF damage and platelet activation were most closely correlated between human and porcine blood.

Conclusions: In summary, this study shows that there are species-specific blood damage differences to mechanical shear. In addition, this work also improves in vitro VAD evaluation and brings it a step closer to the assessment of total blood trauma. As VADs are increasingly used for the treatment of heart failure patients, it is important for device developers to gain a better understanding of the animal blood selection such that reliable comparisons can be made between devices and laboratories. These results lay the foundations for developing blood damage evaluation standards to enable the extrapolation of in vitro and in vivo animal data to predict safety and biocompatibility of blood-handling medical devices in humans.

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Relation between the evolution of soluble ST2 and coronary allograft vasculopathy in heart transplanted patients

This work was supported by the Instituto de Salud Carlos III through direct grants [Sara Borrell grant to N.S.F. and FIS PI12/02589] N Suarez¹; E Barge-Caballero¹;

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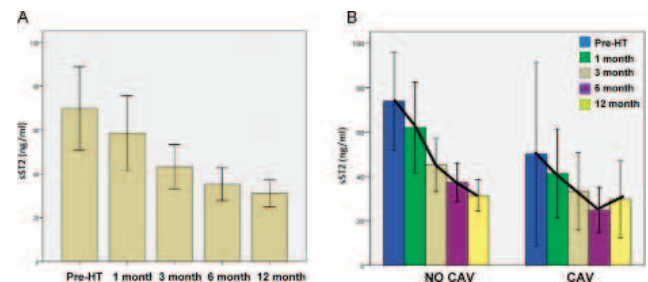
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Purpose: To evaluate the usefulness of soluble ST2 (sST2) levels as a new early marker of cardiac allograft vasculopathy (CAV) in heart transplanted (HT) patients.

Methods: Longitudinal study of 104 HT patients (52 ± 12 years, 76% men) who survived the acute phase post-HT. Serum samples were obtained pre-HT and during the first year post-HT (1, 3, 6 and 12 months post-HT) in order to measure the changes in sST2 by a commercial ELISA. The diagnosis of CAV was done by coronary angiography at 12 months post-HT. sST2 values were described as mean \pm SD. Linear regression was done to describe the changes of sST2/month follow up. The changes of sST2/month in patient with/without CAV were compared by Student's t-test. Logistic regression to predict CAV (adjusting by recipient age, sex, and the changes observed in sST2) was done.

Results: The incidence of CAV was 13/104 (12.5%) patients. sST2 values decreased after HT as follows: pre-HT 73.9 ± 59 ng/ml, 1 month 57.2 ± 44.4 ng/ml, 3 months 46.1 ± 30.9 ng/ml, 6 months 38.9 ± 25 ng/ml and 12 months post-HT 34.9 ± 20.5 ng/ml (Figure 1A). The change in the values of sST2/month post-HT was statistically significant (mean -3.0 ± 4.2 ; 95% CI $[-3.8; -2.2]$; $p < 0.001$) and was associated with the incidence of CAV post-HT ($p = 0.031$; Odds Ratio: 1.333). Moreover, sST2 values decreased more slowly post-HT in patients who developed CAV during the first year, with an increase of sST2 levels at the end of the follow up, comparing to the evolution of patients without CAV at 12 months (Figure 1B).

Conclusions: The exchange rate of sST2 along the first year post-HT was associated with the incidence of CAV, showing a slower decrease in sST2 values than patient without vascular disease. The probability to develop CAV was 33% higher/unit of increase of sST2.



P512

Setting up threshold value of iodine-123 metaiodobenzylguanidine imaging using medium energy collimators for prediction of cardiac events

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Purpose: The aim of our study was to assess the predictive value of cardiac iodine-123 metaiodobenzylguanidine (123I-MIBG) imaging and setup threshold value for prediction cardiac events in heart failure (HF) patients using optimal for 123I iodine medium energy collimators.

Materials and methods: We have prospectively investigated 87 patients with the New York Heart Association (NYHA) functional class II-IV HF, for whom conventional HF treatment algorithm is intended to apply. Cardiac 123I-MIBG planar imaging was performed in a supine position using medium energy collimators. Early and late heart-to-mediastinum (H/M) ratios, washout ratio (WR) were calculated. The data were collected from 2010 till 2014 year. After the cardiac 123I-MIBG imaging patients were observed clinical cardiologist form 13 up to 24 months. Adverse cardiac events and sudden cardiac death were calculated as cardiac events. Receiver Operating Characteristic (ROC) curve analysis under optimal sensitivity and specificity of the relationship, was determined the critical values of different parameters in predicting whether a patient will have cardiac events.

Results: Totally 11 (12,6%) patients died at the time of study. 57 (65,5%) patients were hospitalized because of for stabilization of heart failure clinical course and optimization of the treatment. ROC curves analysis obtained statistically significant results for cardiac adrenergic innervation: early H/M ratio - cutoff value of 2.26, area

under the curve (95 % CI) 0.672 (0.556; 0.788) with the sensitivity of 0.706 and specificity of 0.660 (p = 0.007); late H/M ratio - cutoff value of 1.95, area under the curve (95 % CI) 0.717 (0.610; 0.823) with the sensitivity of 0.735 and specificity of 0.604 (p = 0.001); and WR - cutoff value of 40.55 area under the curve (95 % CI) 0.658 (0.545; 0.771) with the sensitivity of 0.623 and specificity of 0.676 (p = 0.013), dividing patients to the groups of HF patients who will develop cardiac events and HF patients who will not develop cardiac events.

Conclusions: Cardiac 123I-MIBG imaging data acquired with medium energy collimators has statistically significant threshold values of early and late H/M ratio, and WR, separating patients to who will develop cardiac events and who not. Our study results are one of very few clinical results obtained using medium energy collimators for prediction of cardiac events.

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Ischemic mitral regurgitation as a preclinical model of heart failure: MRI characterization of chronic left ventricular and atrial remodeling

People Programme (Marie Curie Actions) of the European Union's Seventh Framework Programme (FP7/2007-2013) under REA grant agreement n° [608027] (FP7J Aguero¹; C Galan-Arriola¹; R Fernandez-Jimenez¹; J Sanchez-Gonzalez¹; J Solis¹; L Fernandez-Friera¹; GJ Lopez-Martin¹; D Sanz-Rosa¹; B Ibanez¹
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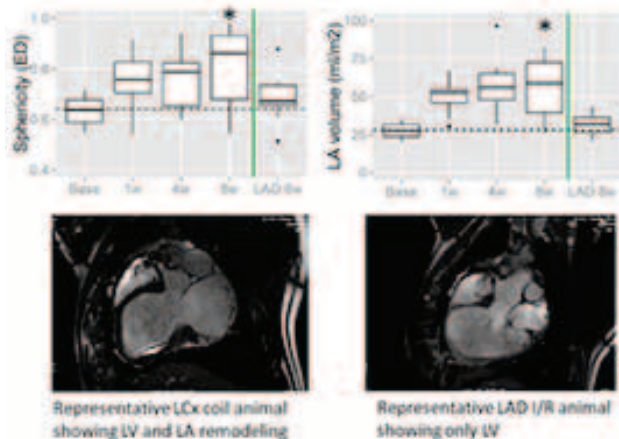
Background: In CHF, the left ventricle (LV) dilates as a consequence of scar formation replacing the myocardial tissue loss, along with a global shape distortion related to progressive remodeling in the remote myocardium.

Purpose: To create a large animal model of ischemic mitral regurgitation (MR) secondary to a chronic occlusion in the proximal left circumflex artery (LCx) in swine, in order to recapitulate key CHF features such as progressive LV and LA remodeling.

Methods: An embolization coil was percutaneously deployed to induce a chronic occlusion of the proximal LCx artery. Assessment of the LV, LA remodeling changes and ischemic MR was evaluated using serial cardiac MRI and 3D transesophageal echocardiography. A sham group and the standard myocardial infarction model of left descending anterior (LAD) ischemia/reperfusion (I/R) were used for comparisons.

Results: A significant degree of mitral regurgitation was found in most of the LCx group animals but not in LAD I/R. Both LAD and LCx models showed significant LV dilation as compared to control values. Despite a similar infarcted % of the LV myocardium, the LCx occlusion led to progressive LV volumes dilatation and abnormal chamber sphericity compared to LAD group. The LA chamber was markedly dilated in the LCx occlusion model, but similar to normal hearts in the LAD model (Figure).

Conclusions: 1- The LCx chronic occlusion model leads to a significant degree of secondary ischemic mitral regurgitation. 2- Compared to classic LAD ischemic/reperfusion model, a greater degree of LV remodeling and structural distortion is observed. 3- The swine model of ischemic MR is suitable for evaluating anti-remodeling therapies targeting LV or LA, as well as novel surgical or percutaneous mitral procedures.



LV sphericity and LA size by Groups

P514

ONO-4232, a lusitropic EP4 agonist, preserves PaO2 despite its vasodilating effect

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Background and Purpose: ONO-4232 is a selective agonist for EP4 subtype of prostaglandin E2 receptor. It has a unique LV-lusitropic action, in addition to its vasodilation effect, and is in clinical development for the treatment of acutely decompensated heart failure (ADHF). In general, vasodilators can improve pulmonary congestion, but there is a potential risk of worsening of gas exchange (i.e. reduction of PaO2) at excessive doses by intrapulmonary shunting, as cautioned for nitroglycerin. Of note, prostaglandin I2 (epoprostenol), a potent pulmonary vasodilator used for pulmonary hypertension, has been reported to increase intrapulmonary shunting. Therefore, we investigated the effect of ONO-4232 on PaO2 under a condition of hypoxic pulmonary vasoconstriction in dogs, in comparison with epoprostenol and various vasodilators commonly used for acute heart failure (AHF) in the clinic.

Methods and Results: The effects of intravenous infusion of ONO-4232 (3, 10, 30, and 100 ng/kg/min in dose ascending escalation, of 20 min each) and various vasodilators (i.e. nitroglycerin, carperitide, nicorandil, milirone, and epoprostenol) on PaO2 were investigated under partial pulmonary hypoxia induced by differential lung ventilation in dogs. The minimum dose of ONO-4232, 3 ng/kg/min, was selected because of the efficacy in a dog AHF model previously performed. Differential lung ventilation was carried out for 60 min by ventilating the posterior lobe of the left lung with a gas mixture of 95% N2 and 5% CO2, while other lobes ventilating with 95% O2 / 5% CO2. The PaO2 in the peripheral artery was reduced by 35.5 ± 2.2% at 60 min after the start of differential lung ventilation, suggesting that hypoxic pulmonary vasoconstriction was successfully induced in the isolated lung. ONO-4232 did not reduce PaO2 level despite of dose-dependent reduction of mean blood pressure (MBP) (% of predosing level at 30 ng/kg/min: 102.3 ± 15.9% for PaO2 and 72.7 ± 4.6% for MBP). Of note, all of other vasodilators examined, especially epoprostenol, demonstrated dose-dependent reduction in PaO2, in parallel with the reduction in MBP.

Conclusion: ONO-4232 did not reduce PaO2 under conditions of induced pulmonary hypoxia, in contrast to all other tested vasodilators, strongly suggesting that ONO-4232 did not increase intrapulmonary shunting. This beneficial effect of ONO-4232 would be highly desirable in the treatment of ADHF, especially patients with cardio-pulmonary congestions and symptoms of dyspnea.

P515

Characteristics of patients hospitalized for acute coronary syndrome complicated with acute heart failure in patients

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Purpose: The purpose of this study was to determine predictors of heart failure in patients hospitalized for acute coronary syndrome (ACS).

Methods: We studied all patients hospitalized for acute coronary syndrome over a period (15) fifteen month from (1 October 2010) to (31 December 2011). We compared baseline clinical characteristics and all interventions of patients who have experienced heart failure at admission or during hospitalization to the remaining patients.

Results: In this 15 months, 507 patients were admitted because of an ACS. Among those patients, 69 (13,6%) developed an acute heart failure at presentation or during hospitalization. In this group, patients were older (p = 0,007), more often male (p = 0,008), have more smoke habits (p = 0,008) and history of diabetes (p = 0,000). The acceleration of heart rate p = 0,05, anemia (p = 0,000), renal failure (p = 0,000) and stenosis of the anterior interventricular artery (p = 0,004) are also significantly associated with the occurrence of heart failure in patients hospitalized for ACS.

Conclusion: A better understanding of the characteristics and predictors of heart failure could help us to provide a better care for patients hospitalized for ACS.

P516

QSOX1 has a protective role in the myocardium face to acute stress

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Introduction: QSOX1 has been identified as a plasma biomarker of acute heart failure (AHF). As QSOX1 is a sulfhydryl oxidase, we hypothesized that QSOX1 has a role in the heart face to AHF.

Methods: Acute cardiac stress was induced by IP injections of Isoproterenol (ISO, 300 mg/kg/12h) for 2 days in mice (Balb-C or C57Bl/6 J) whereas control (C) received NaCl 9°. Mice were killed at day 3, after echocardiography. Some Balb-C mice received together with ISO antisense oligonucleotides (AOs) directed against

QSOX1. In parallel QSOX1^{-/-}(C57Bl/6 J) mice were generated using a QSOX1tm1a embryonic stem cell clone (KOMP). The KO construct contains a promoter-less lacZ gene under the control of the QSOX1 regulatory sequences. The mRNA levels were analyzed by RT-qPCR. The cellular level of oxidative stress was detected by using DHE.

Results: The ISO Balb-C mice exhibited a decreased shortening fraction (SF) (-7% vs control p<0.001, n=10/group) and increased lung weight/tibia length. Cardiac QSOX1 (x2, p<0.01) and BNP (x3, p<0.01) transcripts were induced in these mice. QSOX1 silencing by AOs enhanced signs of AHF after ISO (p<0.05 vs. WT+ISO). At baseline QSOX1^{-/-} adult mice did not display any cardiac or vascular phenotype. After ISO, lacZ expression dramatically increased in QSOX1^{-/-} hearts with the strongest β-galactosidase staining in the atria. In QSOX1^{-/-} mice receiving ISO, the SF decreased more than in WT (-10% ± % and -6%, respectively, p<0.05; n=14/group), pulmonary congestion was more severe (p<0.001 versus p<0.05 in WT); BNP and ANP levels increased (x2, p<0.001) in both WT and QSOX1^{-/-} groups. The severe cardiac dysfunction in QSOX1^{-/-} mice was associated with signs of enhanced inflammation (Galectin 3 and CD68) and of oxidative stress (increased DHE staining) (p<0.01 versus WT+Iso).

Conclusion: Taken together, the data indicated that QSOX1 protects the heart in response to acute stress.

P517

A novel myocardial bioprosthesis for cardiac regeneration

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Purpose: Cardiac tissue engineering, a novel therapeutical approach, combines the use of natural or synthetic supporting scaffolds with cardiomyogenic cells for myocardial damage restoration. In this context, we aimed to obtain a myocardial bioprosthesis based on decellularized myocardium refilled with adipose tissue-derived progenitor cells (ATDPCs).

Methods: Decellularized myocardial scaffolds were generated from porcine myocardium using two distinct decellularization protocols (DP): one protocol, DP1, was SDS-based, and the other, DP2, was trypsin based. Both protocols were followed by Triton X-100 treatment with some added modifications. Decellularization level was evaluated histologically and molecularly, the resulting scaffold structure was examined by scanning electron microscopy and matrix components were identified by immunohistochemistry. Obtained decellularized scaffolds were refilled with RAD16-I peptide hydrogel and porcine ATDPCs. After one week of recellularization, cellular viability was assessed using a commercial kit, cell density was determined by nuclei counting and expression of cardiac (GATA4, connexin43 and cardiac troponin T) and endothelial (Isolectin B4) markers was analyzed through immunohistochemistry.

Results: After both protocols were completed, decellularized scaffolds were free of cellular debris and nuclear material, preserved extracellular matrix three-dimensional architecture and its main components. One week following recellularization, ATDPCs were detected inside the decellularized scaffold and remained viable. However, in recellularized DP1 scaffolds the number of retained cells was significantly higher compared with recellularized DP2 scaffolds (236 ± 106 and 98 ± 56 cells/mm² for recellularized DP1 and DP2 scaffolds, respectively; P=0.04). Remarkably, in both recellularized scaffolds, ATDPCs expressed endothelial marker Isolectin B4, although only in recellularized DP1 scaffolds cells showed expression of cardiac markers GATA4, connexin43 and cardiac troponin T.

Conclusions: Acellular myocardial scaffolds, with preserved structure and matrix composition, were obtained with both decellularization protocols. However, the SDS-based protocol (DP1) produced myocardial scaffolds with better cell recolonization and promotes ATDPCs endothelial and cardiomyogenic differentiation.

P518

Is there an association between myocardial contractility disturbance and arterial system damage in patients with chronic heart failure?

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Purpose: to assess the relation between the association of large and small peripheral arteries changes and myocardial contractility disturbance in patients with chronic heart failure (CHF).

Methods: Patients (pts.) with chronic heart failure (CHF) (n=33; male:20; mean age:65 (61;72); MI n=25;80%) NYHA class II-III and 35 healthy controls (male:17; mean age:57 (51;63)) were enrolled. Digital photoplethysmography and nailfold computer videocapillaroscopy at baseline, during arterial,vinous occlusion were

performed. Endothelial function of small (occlusion index, IO) and large vessels (phase shear (PS, ms) were estimated. We evaluated remodeling of aorta (stiffness index (SI,m/s), arterioles (reflection index, RI%) and skin capillaries (capillary densities (CD,cap/mm²), maximal CD (CDmax). Contractility of left ventricle (LV) were determined by transthoracic echocardiography by ejection fraction of LV (LVEF,%).

Results: Endothelial dysfunction and remodeling of large and small vessels were found in CHF pts (IO,PS,SI,RI was significantly higher than in controls (p<0.05). However the measures of remodeling of large and small vessels did not correlate (SI,CD and CADmax (rs = 0,023,p<0,05). There was no association between PS and IO (rs = -0,27, p> 0,05). Individual assessment of associations of macro- and micro-circulation damage in pts. allowed to describe 4 types of arterial system changes: type 1- functional changes of large or small vessels; type 2-structural and functional changes of large vessels; type 3- structural and functional changes of small vessels, type 4-disturbance of both small and large vessels. We found that in CHF group was 12 % (n=4) pts. with type 1 and type 2. Type 3 had 9% (n=3) and 67 % (n=22) had type 4. In controls only 18% (n=6) had no changes. 3% (n=8) had type 1, type 2 had 17% (n=6), type 3 had 12% (n=4) and type 4 had 29% (n=10) participants. Myocardial contractility of LV was significantly lower in CHF pts. with disturbance of both small and large vessels (type 4) than in those who has types 1-3 of arterial changes (LVEF type1-3 - 49,7(49; 50) vs.LVEF type-4 - 42,8 (41;47), p=0,0004). CHF pts with type 4 has longer history of disease (CHF type1-3 - 4,1 (3;6) vs. type 4 -8,2 (5;11), p=0,03) and higher frequency of MI comparison with CHF pts with types 1-3 (OR- 4,5;95% CI. 1,08 to 3,7).

Conclusion: There are different combinations of large and small arteries changes in CHF patients. Those who had both large and small vessels damage had severer myocardial contractility disturbance, longer history of CHF. The level of arterial system damages might underlie CHF progression.

P519

Early changes in cardiac structure and function induced by a high caloric diet

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Purpose: Obesity cardiomyopathy is nowadays well characterized, however, the cardiac impact of a Western-type diet for a short period of time is still unknown. In this study we evaluated the cardiac structure and function of rats fed with a high-fat diet(HFD) for six weeks.

Methods: Wistar rats(100-150g) were randomly divided and fed with a regular diet(2.9kcal) or with a western-type diet enriched with carbohydrates, fat and salt(5.4kcal), resulting in 2 groups: RD and HFD. After 6weeks bi-ventricular function was assessed by echocardiography and invasive hemodynamic and samples obtained for morpho-histological, molecular and skinned cardiomyocyte functional evaluation.

Results (Fig): Administration of a HFD for 6weeks resulted in hyperglycaemia, resistance to insulin and glucose intolerance, without changes in body weight(RD 319 ± 9.3; HFD 342 ± 11.1). At the cardiac level, the HFD lead to heart hypertrophy as well as biventricular increased cardiomyocyte cross sectional area, higher deposition of fibrosis and collagen type II overexpression. Also, the echocardiography data showed in HDF group a decreased ventricular diameter and increased left ventricle(LV) wall thickness and right ventricle(RV) Tei index. These structural resulted in functional abnormalities such as LV increased passive tension, systolic pressure and RV impaired relaxation. *vs RD p<0.05

Conclusions: We have shown that HFD promotes biventricular hypertrophy and extracellular matrix changes and that the early structural alterations triggered by the HFD affect cardiac relaxation and diastolic function, specially in the RV. This study demonstrates that consumption of a Western-type diet for a short period of time has an early impact in cardiac structure and function even before body weight is significantly altered.

Structural data	RD	HFD	Functional data	RD	HFD
Heart/TL (g/cm)	2.3±0.01	2.5±0.06*	LVDS/BSA (mm/cm ²)	118±4.1	96±5.3*
LV Cardiom. CSA (µm ²)	381±4.92	440±7.67*	LVPWs/BSA (mm/cm ²)	72±3.2	89±1.2*
LV Fibrosis (%)	0.8±0.13	4.7±0.49*	LV Psystolic (mmHg)	108±3.9	113 ± 10.4
LV Collagen III (AU)	1.0±0.05	2.0±0.34*	LV Active tension (kN/m ²)	20±1.7	25±3.0
RV Cardiom. CSA (µm ²)	278±3.71	304±4.27*	LV Passive tension (kN/m ²)	3±0.13	7±1.2*
RV Fibrosis (%)	4.9±0.60	8.3±0.48*	RV Index TEI	0.26±0.01	0.33±0.01*
RV Collagen III (AU)	1.0±0.07	1.4±0.08*	RV Psystolic (mmHg)	22±1.0	27±1.1*
* vs RD p<0.05			RV τ g (ms ⁻¹)	4.4±0.81	18.5±2.90*

P520

Pacing induced cardiomyopathy is associated with reduced myocardial blood flow, hyperinsulinemia and enhanced myocardial glucose metabolism

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Purpose: Prolonged right ventricular (RV) pacing at high heart rate (HR) induces left ventricle (LV) dysfunction, endothelial dysfunction and nitric oxide deficiency in the experimental model. Purpose of this study was to assess whether this may translate into abnormalities of regional myocardial blood flow (MBF), systemic and myocardial metabolism as possible determinants of progressive heart failure.

Methods: Seven adult minipigs underwent RV apical pacing (220 beats/min) for 4 weeks. Positron emission tomography, 2D-echocardiography (ECHO) and venous blood sampling were performed at baseline (PRE) and soon after interruption of 4 weeks high rate pacing (POST). Regional myocardial blood flow (MBF) ([¹³N]ammonia as a flow tracer) and fasting glucose uptake (MGU) ([¹⁸F]fluorodeoxyglucose as a metabolic tracer) were quantitated in 17 LV segments from PET data. LV fractional shortening (FS) was computed from ECHO. Lipid and glucose profiles were measured from blood samples.

Results: From PRE to POST, FS significantly decreased from $32.6 \pm 3.4\%$ to $15.8 \pm 1.6\%$ ($p < 0.001$). Regional MBF significantly decreased from 1.08 ± 0.25 to 0.88 ± 0.28 ml/min/g ($p < 0.001$) while regional MGU increased from 2.0 ± 2.7 to 10.4 ± 7.7 mmol/min/100g ($P < 0.001$). Insulin levels increased from 1.29 ± 1.05 to 3.30 ± 1.51 U/mL ($P < 0.01$) and HDL cholesterol decreased from 29.0 ± 8.4 to 17.7 ± 10.4 mg/dL ($P < 0.05$) while all the other parameters remained unchanged. Regional MGU was inversely correlated with MBF ($P < 0.001$) and directly correlated with insulinemia ($P < 0.05$).

Conclusions: Prolonged high rate pacing in minipigs causes reduction in LV function, decrease in regional MBF and hyperinsulinemia as possible effects of endothelial dysfunction. These changes are mirrored by a compensatory increase in myocardial glucose metabolism which may exert a protective effect against progressive cardiac damage.

BASIC SCIENCE: BIOMARKER

P521

Association of circulating galectin-3 levels and Nt-pro-BNP with other measures of heart failure status

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Background: Because elevations in galectin-3 are thought to reflect a different pathophysiological axis (changes in extracellular matrix leading to ventricular remodeling) than the natriuretic peptides, there is substantial interest in the relationship between galectin-3 and natriuretic peptide measurements.

Purpose: To evaluate the association of circulating galectin-3 levels and NT-proBNP with other measures of heart failure status in patients with heart failure with preserved left ventricular ejection fraction (HFpEF).

Methods: Seventy six patients (41 males and 35 females; mean age 62.34 ± 9.2 years) with HFpEF of ischemic genesis were examined. The sGal3, Nt-proBNP, TNF-alpha and insulin were measured in serum by ELISA, according to manufacturer's instructions. HOMA index was calculated as a measure of IR at fasting state ($IR = \text{fasting glucose} \times \text{fasting insulin} / 22.5$). The echocardiographic parameters were measured with M- and B-mode echocardiography using Ultrasound's Vivid Three with a 2.5-MHz probe (Japan) and calculated following the American Guidelines of Echocardiography Society. For nonparametric Spearman's correlation analysis and Mann-Whitney U test were used. All statistical tests were 2-tailed, and $p < 0.05$ was considered statistically significant.

Results: The median NT-proBNP level was 140.16 pg/mL (interquartile range, $114.70 - 292.80$), the median galectin-3 level in this study cohort was 3.08 ng/mL (interquartile range, $2.64 - 3.51$). There was a no correlation between NTproBNP levels and galectin-3 levels ($r = -0.19$, $P = 0.092$). When evaluated by groupings examining above and below the median for each biomarker, NTproBNP and galectin-3 were discordant for 49 of 76 subjects (65.8%), divided approximately equally between low-NTproBNP high galectin-3 ($n = 25$) and high-NTproBNP low galectin-3 ($n = 25$). Compared with a group with low-NTproBNP and high galectin-3, there was significantly larger size left and right atriums, right ventricular, decreased in GFR and elevated creatinine levels in patients with high-NTproBNP low galectin-3. In contrast, high galectin-3 and low NTproBNP serum levels were associated with higher HOMA index scores, TNFa and insulin levels. Multiple linear regression analysis to identify clinical factors associated with elevated galectin-3, the strongest associations were for elevated TNFa ($F = 11.06$, $P = 0.001$) and elevated RBC ($F = 9.4$, $P = 0.0001$).

Conclusions: Our results suggested that sGal3 and NT-proBNP are biomarkers appeared to provide complementary diagnostic information when examined in isolation.

P522

Levels of N terminal pro brain natriuretic peptide in patients with chronic heart failure and anemia after different methods of treatments

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Purpose: Anemia in CHF is associated with a higher mortality. Of interest is studying the natriuretic peptide by CHF with anemia for diagnosis, evaluation, as well as a long-term forecast on the dynamics of the level of N terminal pro brain natriuretic peptide (NT pro BNP) can be judged on the effectiveness of the therapy. The aim of this investigation is to study the level of NT pro BNP in plasma in patients CHF with anemia while therapy with basic drugs, combinations basic drugs with erythropoietin (EPO) treatment, with intravenous iron treatment and combination therapy EPO with intravenous iron drugs.

Methods: In randomised clinical investigation were included 174 patients with CHF of NYHA I-IV class ischemic aetiology with anemia. Mean age of patients 60.6 ± 1.4 age. The Hb level of less 11g/dl by females and less 12g/dl males. All patients were divided into 4 groups. 27 patients (I group) received only basic drugs therapy CHF. 39 patients (II group) received therapy basic drugs + methoxipoli ethylene glycol epoietin- β (MEB) in dose 0.60 mg/kg . 44 patients (III group) received therapy basic drugs + (it included patients with iron deficiency) intravenous iron (Ferric (III) hydroxide saccharose complex) in dose 200 mg . 44 patients (IV group) received combination therapy comprising basic drugs, MEB and Ferric (III) hydroxide saccharose complex. Determine the levels of Hb, iron, ferritin, transferrin, EPO, NTproBNP before and after treatment.

Results: Thus, the results of our study that in patients with CHF with anemic syndrome while therapy basic drugs reduced levels of NT-pro BNP in plasma was not credible. Here comes that postulate in treating such patients should first be proper correction of anemia. The most significant reduction in level of NT pro BNP observed in IV group. Among patients in this group reduce NT pro BNP in plasma was -42.98% ($p < 0.01$). In patients with CHF triple combination in Ferric (III) hydroxide saccharose complex) with the MEB most reduces the level of NT pro BNP in plasma by -54.45% ($p < 0.001$). When comparing the results of the methods of treatment among patients with CHF with anemia was the smallest decrease of NT pro BNP in plasma in patients receiving therapy with MEB-at -29.01% ($p < 0.01$), and patients in this group had a greater reduction in NT pro BNP-to- 45% ($p < 0.01$). **Conclusion:** Thus, in patients with CHF and anemia triple combination intravenous iron with MEB the most reduces the level of NT pro BNP in plasma.

P523

A role for galectin-3 in myocardial remodelling in hypertensive rats

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Purpose: Arterial hypertension is associated with changes in cardiac structure and function, being consider as one of the main factors involved in heart failure (HF). In the last years, Galectin-3 (Gal-3) has emerged as a mediator of cardiac damage in different models of HF. The aim of this study was to investigate the effects of a Gal-3 activity inhibitor (MCP) on cardiac alterations in an experimental model of hypertension, as well as the possible mechanisms involved.

Methods: 4 groups of male rats were used: 1) Wistar-Kyoto (WKY), 2) spontaneously hypertensive rats (SHR), 3) WKY treated with MCP (100 mg/kg/day in drinking water, and 4) SHR treated with MCP for 6 weeks. Systolic blood pressure (SBP) was determined throughout the experimental period. Cardiac structure and function were evaluated by transthoracic echocardiography. Interstitial fibrosis was measured by picrosirius red staining and protein expression of fibrotic and inflammatory mediators (collagen I, TGF- β , CTGF, Gal-3, OPN and MCP-1) were measured by RT-PCR and western blot

Results: SHR group presented an increase in Gal-3 at cardiac level, as well as an increase in relative heart weight as compared to WKY group. Echocardiography data showed the presence of concentric hypertrophy in SHR group, accompanied by cardiomyocyte hypertrophy. No differences were found in systolic function in any of the animal groups studied. MCP treatment had no effect on cardiac function, histology or fibrotic and inflammation markers in WKY rats. In SHR rats, MCP treatment was not able to modify SBP, nor cardiac hypertrophy. However, Gal-3 inhibition was able to prevent the interstitial fibrosis observed in SHR group. Together with the decrease in total collagen levels, SHR rats treated with MCP presented lower cardiac collagen type I levels, as well as diminished TGF- β and CTGF expressions and inflammatory markers.

Conclusions: The increase of myocardial Gal-3 in hypertensive rats is accompanied by cardiac fibrosis, which could favour changes in cardiac structure and function. Gal-3 inhibition prevents cardiac fibrosis in hypertensive animals independently of blood pressure levels. Gal-3 emerges as a new therapeutic target in the fibrotic process associated to different pathologies.

P524

What we know about ACE2

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The Angiotensin converting enzyme 2 (ACE2) is part of the Renin Angiotensin System and catalyses the conversion of Angiotensin II to Angiotensin 1-7. The serum level of ACE2 was proven to be elevated during systolic heart failure and in the early stage of heart diseases (as in hypertension, etc), suggesting its role in their pathomechanisms. However, its serum level has not been investigated yet in patients with diastolic heart failure with preserved systolic function.

We compared the ACE2 activity of healthy volunteers (n = 45), patients with hypertension and preserved ejection fraction (n = 239), with systolic (n = 100) and with diastolic heart failures (n = 40). Activity of ACE2 was determined by fluorescent measurements. Systolic and diastolic heart functions were measured and documented by echocardiography.

We found a significant elevation of ACE2 activity in hypertensive patients compared to healthy volunteers (24.8 ± 0.9 vs 16.2 ± 0.8 UF/mL; $P < 0.001$). Moreover, the ACE2 activity was further elevated and significantly higher in patients with systolic heart failure compared to those with diastolic heart failure (42.5 ± 2.8 vs. 23.4 ± 1.7 ; $P < 0.001$). ACE2 levels positively correlated with the levels of the well-known biomarker, NT-proBNP ($r = 0.5$; $P < 0.01$). On the other hand, in groups with preserved systolic function (healthy, hypertensive and diastolic populations), the variability of the two parameters was independent of each other. ACE2 levels of patients with hypertension or systolic heart failure negatively correlated with the ejection fraction ($r = 0.46$; $P < 0.001$, $r = 0.2$; $P = 0.002$) however, there was no correlation in these parameters when comparing healthy and diastolic groups.

Our data suggest that ACE2 may have a role in the pathogenesis of systolic heart failures and hypertensive patients, however not in that of diastolic heart failure, making it suitable as a biomarker for differential diagnostic of heart failures.

P525

Circulating SDF1 α levels in heart failure: a matter of proper sampling

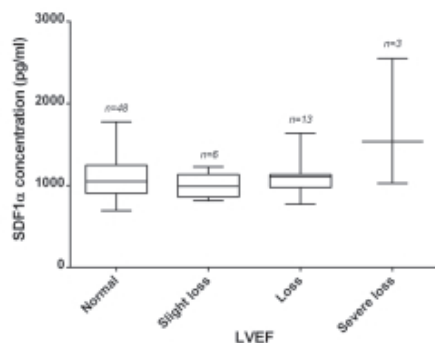
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Purpose: The chemokine Stromal cell-derived factor 1 α (SDF1 α , CXCL12) is currently under investigation as a biomarker for several cardiac diseases. The correct interpretation of SDF1 α levels is complicated by the occurrence of truncated forms that possess an altered biological activity for which until now the immunoreactivity is unknown. We studied the immunoreactivities of SDF1 α forms and evaluated the effect of adding a DPPIV inhibitor in sampling tubes on measured SDF1 α levels. Using optimized sampling, we measured DPPIV activity and SDF1 α levels in patients with varying degrees of heart failure.

Methods and Results: The immunoreactivities of SDF1 α and its degradation products were determined with three immunoassays. A one hour incubation of SDF1 α with DPPIV at 37 °C resulted in 2/3 loss of immunoreactivity. Incubation of SDF1 α with serum gave a similar result in each of the assays. The extent of ex vivo cleavage of endogenous SDF1 α under similar conditions was determined to be around 75%. Using appropriate sampling, SDF1 α levels were found to be significantly higher in those heart failure patients with a severe loss of left ventricular function (see Fig.). DPPIV activity in serum was not altered in the heart failure population.

Conclusions: We propose that all samples for SDF1 α analysis should be collected in the presence of at least a DPPIV inhibitor. In doing so, we found higher SDF1 α levels in subgroups of patients with heart failure. Our work supports the need for further research on the clinical relevance of SDF1 α levels in cardiac disease.



SDF1 α levels in HF patients

P526

Dynamics of laboratory endothelial dysfunction markers in patients with acute decompensated chronic heart failure, treated with anticoagulants

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Purpose: To assess the dynamics of laboratory endothelial dysfunction ED markers in patients with acute decompensated chronic heart failure (ADCHF) treated with anticoagulants

Materials and methods: The study included 60 ADCHF patients with sinus rhythm, mean age 68.6 ± 9.5 years, 35 women (58%), treated with prophylactic subcutaneous anticoagulants (heparin, enoxaparin or fondaparinux). The control group included 20 patients with compensated CHF (NYHA class I or II), mean age 68.4 ± 8.8 years, 11 (55%) women. Ejection fraction (EF) mean values in the two groups were $39.9 \pm 14.4\%$ and $54.8 \pm 10.3\%$, respectively ($p = 0.042$). Serum levels of ET-1, sICAM, sVCAM and VEGF-A were measured on admission and after anticoagulants had been discontinued. The study did not include patients with acute exacerbation of chronic diseases and active cancer.

Results: All ADCHF patients were identified with endothelial dysfunction. Baseline levels of most ED markers were significantly higher than in controls: ET-1 - 3.1 ± 0.5 vs. 1.1 ± 0.8 pg/ml ($p = 0.005$), sVCAM - 2004 ± 393 ng/ml vs 725 ± 174 ng/ml ($p = 0.017$), sICAM - 508 ± 77 ng/ml vs 204 ± 68 ng/ml ($p = 0.009$). No significant difference in baseline VEGF-A was found between the study and control groups.

After treatment ED markers decreased in all ADCHF patients, compared with baseline values, with ET-1 having fallen to 1.7 ± 1.3 pg/ml ($p = 0.004$), sICAM - to 390 ± 80 ng/ml ($p = 0.0006$) and sVCAM to 1661 ± 334 ng/ml ($p = 0.0004$), respectively. Inverse correlation between enoxaparin and sICAM values ($p = 0.006$, $\beta = -0.45$) and between fondaparinux and sVCAM values ($p = 0.002$, $\beta = -0.64$) was found in the studied ADCHF patients. Heparin effect on the dynamics in the studied markers was not significant.

Conclusion: All ADCHF patients had considerably increased baseline values of ED markers, which significantly decreased after treatment. At that, inverse correlation was found between enoxaparin and decreased sICAM, and between fondaparinux and decreased sVCAM values.

P527

Proteomic biomarker discovery workflow to identify left ventricular diastolic dysfunction in diabetic patients

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Heart failure has reached epidemic proportions affecting 10% of men and 8% of women aged 60 or above and is estimated to cost €10,000 per patient per hospitalisation. These figures are only exacerbated by the increasing prevalence of diabetes mellitus. Diabetes places patients at an increased risk for the development of cardiomyopathies, which are the major cause of death among this patient group. The best means of treatment for these patients is the prevention of the progression of the disease. However, individualising risk and detecting disease progression within this population is challenging and relies heavily on resource intensive cardiac imaging modalities such as Doppler-echocardiography. To help overcome practicality and cost issues for diagnosis and longitudinal monitoring of at risk diabetic patients we propose adopting a circulating biomarker approach. The aim of this ongoing study is to discover and validate candidate serum protein biomarkers that can be used to identify diabetic patients that have left ventricular diastolic dysfunction (LVDD). Candidate biomarkers will also be assessed for their ability to predict LVDD disease progression upon the completion of follow up data collection.

The biomarker discovery population consisted of 200 patients derived from within the STOP-HF cohort in Ireland. The cohort consisted of 4 sub-groups of 50 patients; Diabetes + LVDD; Diabetes + noLVDD; noDiabetes + LVDD; noDiabetes + noLVDD. All groups were age and gender matched, with LVDD being defined as left atrial volume index equal to or greater than 34 ml/m^2 and an $E' < 10 \text{ cm/sec}$.

Using mass spectrometry, the serum proteome of diabetic and non-diabetic patients, with and without LVDD was analysed. To enhance the depth of proteomic profiling, the 14 most abundant plasma proteins were depleted using affinity column chromatography. The protein peptide profile from these groups was then assessed and quantified using label-free LC MS/MS on a Thermo Scientific Q Exactive mass spectrometer with each sample run in triplicate. Statistical analysis is complete and we are currently in the process of selecting the top 50 proteins that show potential to differentiate LVDD in a diabetic and non-diabetic population. These proteins will be validated using multiple reaction monitoring mass spectrometry in a cohort of 1000 patients.

By identifying protein biomarkers that correctly identify diabetic patients with LVDD, we hope to improve the patients' quality of life enabling the potential for early intervention and reduce the socioeconomic burden that cardiovascular disease places on our health systems.

P528

Tetanectin, a potential novel biomarker of heart failure, is expressed within the myocardium and associates with cardiac fibrosis

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Purpose: Heart failure (HF) prevention strategies require biomarkers that predict disease manifestation. To address this we adopted a proteomic screening approach (2D-DIGE, mass spectrometry) to dissect the coronary sinus serum proteome of asymptomatic hypertensive patients with low and high risk for future HF development. Risk was based on B-type natriuretic peptide (BNP) levels. We identified several differentially expressed disease-associated serum proteins one of which was tetranectin (reduced 2.1-fold in high-risk patients) whose precise function is yet to be defined. The purpose of this study was to validate the proteomics discovery, quantify serum levels of tetranectin in a HF cohort, and assess the disease relevance of this novel protein in cardiac tissue.

Methods: Two patient cohorts were used. Firstly, peripheral serum was collected from a validation cohort of 60 asymptomatic hypertensive and 40 HF patients and samples were assayed for tetranectin by ELISA. Secondly, peripheral serum and atrial myocardial tissue was procured during cardiothoracic surgery from 32 patients and used to analyse circulating and cardiac tissue expression of tetranectin and compare it to fibrosis-related factors by ELISA, QPCR and histological tissue staining.

Results: In the validation cohort, tetranectin was found to be reduced in HF serum (by 50%, $p < 0.001$). Tetranectin showed higher diagnostic specificity and sensitivity for HF than BNP (AUC = 0.95 vs. 0.84) and highest performance characteristics were achieved by combining both (AUC = 0.98). In the second (tissue) cohort, low serum tetranectin correlated with high collagen turnover (PICP, PINP, both $r = -0.42$, $p = 0.016$). Myocardial tetranectin gene expression significantly correlated with collagen 1 and 3 (both $r = 0.46$, $p = 0.008$), MMP2 ($r = 0.46$, $p = 0.008$), and TIMP1 ($r = 0.55$, $p = 0.001$) genes. Novel expression of tetranectin protein was identified in patient myocardial tissue and localized and correlated with collagen protein (Picrosirius red staining) in interstitial and perivascular fibrotic regions. Finally, in vitro treatment of human cardiac fibroblast cells with TGF β significantly increased expression of the fibrotic genes collagen I and α SMA but inhibited tetranectin expression ($p < 0.001$).

Conclusions: Using a proteomics approach, we identified tetranectin as a promising novel HF biomarker. We also demonstrated for the first time tetranectin expression within human cardiac tissue and found correlations with the degree of tissue fibrosis observed. Further work to explore the functional role of tetranectin in the pathophysiology of cardiac fibrosis and HF should be undertaken.

BASIC SCIENCE: CARDIOMYOPATHY

P529

Effect of temperature on the relationship between cardiac power output and mixed venous oxygen saturation in healthy pigs: comparison to dobutamine

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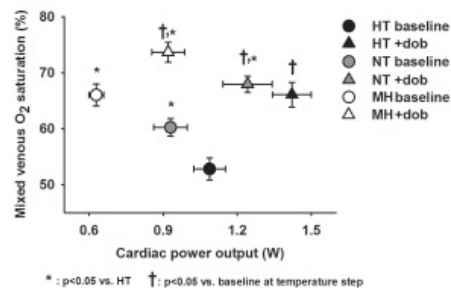
Background: A decrease of cardiac power output (CPO) is the strongest predictor of in-hospital mortality during cardiogenic shock. Experimental mild hypothermia (MH, 33.0°C) improves the systemic oxygen supply-demand balance during cardiac dysfunction in pigs, leading to an increase of mixed venous oxygen saturation (SvO₂) at a given CPO. We here tested the effect of hyperthermia (HT, 40.5°C) and MH on this relationship in healthy pigs, and compared it to dobutamine infusion.

Methods: 9 anaesthetized, closed-chest pigs (67 ± 2 kg) were acutely instrumented with Swan-Ganz and a left ventricular pressure-volume catheter. Temperature was controlled by an intravascular device.

After baseline measurements at HT, intravenous dobutamine infusion was titrated to double LV dP/dtmax. Pigs were then cooled to normothermia (NT, 38.0°C) and further down to MH, and at each temperature step, titrated dobutamine infusion was repeated. Mixed venous and arterial blood samples were taken for blood gas analysis.

Results: Cardiac output decreased with cooling from HT to NT and MH, and it increased with dobutamine infusion at each temperature. Whole body oxygen consumption decreased by 50% from HT to MH, while SvO₂ increased. At each temperature step, dobutamine infusion further increased SvO₂ (see graph).

Conclusion: The relationship between cardiac power output and mixed venous oxygen saturation is strongly temperature-dependent. Cooling improves the systemic oxygen supply-demand balance similarly to a clinically relevant dose of dobutamine at normothermia and HT, but at a lower CPO. These data imply that cooling is a therapeutic option in cardiogenic shock.



P530

I-1-deficiency leads to a reduced survival in a hypertrophic cardiomyopathy mouse model

Deutsche Forschungsgemeinschaft, German Heart Foundation/German Foundation of Heart Research Felix Friedrich¹; H Sotoud¹; B Geertz¹; F Flenner¹; S Reischmann¹; T Eschenhagen¹; L Carrier¹; A El-Armouche²

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Purpose: Hypertrophic cardiomyopathy (HCM) is a myocardial disease associated with left ventricular hypertrophy, diastolic dysfunction and interstitial fibrosis. Guideline-recommended treatment is based on beta-adrenoceptor and calcium channel blockers. Considering that mice deficient of protein phosphatase-1 inhibitor-1 (I-1), an amplifier in beta-adrenergic signalling, were protected from pathological adrenergic stimulation in vivo, we hypothesized that I-1 ablation could result in an improved outcome in a HCM mouse model.

Methods and Results: We crossed mice deficient of I-1 with homozygous myosin-binding protein C knock-out (Mybpc3 KO) mice exhibiting cardiac dilatation and reduced survival. Surprisingly, time of survival was shorter in double I-1/Mybpc3 KO than in single Mybpc3 KO mice. A longitudinal echocardiography study from 7 to 25 weeks of age showed lower fractional area shortening, higher diastolic left ventricular inner dimensions and end-diastolic volumes in Mybpc3 KO than in wild type control mice. As to single Mybpc3 KO, double I-1/Mybpc3 KO mice presented a higher left ventricular mass to body weight ratio and higher left ventricular end-diastolic volume with increasing differences over time. Phosphorylation levels of PKA-downstream targets and gene expression levels of hypertrophic gene program markers did not differ between I-1/Mybpc3 KO and single Mybpc3 KO mice, apart from a trend towards higher beta-myosin heavy chain levels in double I-1/Mybpc3 KO.

Conclusion: The data suggest that interference with beta-adrenergic signalling has no long-term benefit in severe MYBPC3-associated cardiomyopathy. Given the differences between mice and men, the data need to be interpreted with caution.

P531

Clinical significance of cysteine cathepsins in human dilated cardiomyopathy

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Background: Changes in the levels of proteases such as matrix metalloproteases, calpains and cathepsins family are associated with adverse cardiac remodeling an underlying mechanism responsible for progression of heart failure in several cardiomyopathies. Dilated cardiomyopathy or DCM is one such type of heart muscle disorder characterized by ventricular dilation and impaired systolic function. The critical role of both cathepsin L (CTSL) and cathepsin B (CTSB) in maintaining normal cardiac physiology has been observed in several studies. However no information was available on the status of these cysteine cathepsins in human peripheral blood mononuclear cells (PBMC's) of DCM patients.

Aim: The aim of the present study was to detect the activity of cysteine cathepsins (L and B) in DCM patients and to investigate whether levels of these cathepsins exhibit any correlations with the critical clinical parameters associated with DCM.

Methods: Peripheral blood mononuclear cells isolated from DCM patients (n=30) along with corresponding age matched healthy controls (n=30) were used to study the enzymatic activity of cathepsin L and B using spectrophotometry. Further a correlation analysis between the levels of these cathepsins with several clinical and echocardiographic parameters in small group of these DCM patients was carried out.

Results: The enzymatic activity of total cathepsins (L + B), cathepsin L and cathepsin B was found to be significantly higher (3 fold, 1.5 fold and 3.5 fold) respectively in DCM patients as compared to healthy controls. Area under the curve estimated by ROC analysis was found to be 0.84, 0.85 and 0.80 for CTSL+B, CTSL and CTSL respectively, which implicated their diagnostic utility. Moreover, when DCM patients were divided into two subgroups on the basis of calculated cut off values for CTSL+B, CTSL and CTSL enzyme activity based on ROC analysis, high levels of CTSL+B and CTSL were found to be significantly associated with poor left ventricular ejection fraction (LVEF) and dilation of both left ventricle end-diastolic and systolic dimensions in DCM patients.

Conclusion: This study for the first time demonstrates an association between elevation of CTSL+B and CTSL activity in DCM patients with severity of this disease. Therefore measurement of these cysteine cathepsins level in blood could prove useful in the management of Human Dilated Cardiomyopathy.

P532

Human umbilical cord blood derived mesenchymal stem cells improve cardiac function in cTnTR141W transgenic mouse model of dilated cardiomyopathy

The work was supported by grants from the Specialized Research Fund for the Doctoral Program of Higher Education in China(2012110611045). G Guogan Wang¹; X Gong¹

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Cell transplantation is a promising strategy in regenerative medicine, the beneficial effects of bone marrow mesenchymal stem cells (BM-MSCs) in the heart diseases are widely reported, however, MSCs in these studies are animal autogenous derived, data are still scarce on MSCs from human umbilical cord blood (UCB-MSCs). We investigated whether the intramyocardial xenogeneic administration of UCB-MSCs offers benefit in preserving heart function in cTnTR141W gene transgenic mouse model of dilated cardiomyopathy (DCM). Cultured UCB-MSCs, which were identified by morphology, differentiation and cell surface markers, were transplanted into cTnTR141W gene transgenic mouse to examine apoptosis, fibrosis, vasculogenesis and their associated Akt pathway. Moreover, we also determined levels of VEGF and IGF-1, growth factors required for their differentiation into cardiomyocytes, which also contributes in cardiac regeneration and improved heart function. One month after transplantation, MSCs significantly decreased chamber dilation and contractile dysfunction in cTnTR141W mouse. MSCs transplanted hearts showed a significant decrease in cardiac apoptosis and their regulation with Akt pathway. Cardiac fibrosis and cytoplasmic vacuolization in the MSCs group was significantly lower. Importantly, the levels of VEGF and IGF-1 were increased in MSCs transplanted hearts, suggesting endogenous cardiac regeneration. In vitro, the MSC-conditioned medium displayed anti-apoptotic activity in h9c2 cardiomyocytes subjected to hypoxia, further confirmed the paracrine effects of MSCs. In conclusion, UCB-MSCs preserve cardiac function after intramyocardial transplantation in a DCM mouse model, which may be associated with inhibition of cellular apoptosis, inflammatory, up-regulated expressions of Akt, VEGF, IGF-1 and enhanced angiogenesis.

P533

KATP is involved in cardioprotective effects of matrine against apoptosis in diabetic cardiomyopathy

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Objective: To explore the role of mitochondrial KATP in high glucose-induced apoptosis in cardiomyocytes.

Methods: Pretreatments of diazoxide (DZ) or 5-hydroxy-decanoic acid (5-HD) were administered to primary rat myocytes before high-glucose incubation. Mitochondrial activity was assessed by MTT method; mitochondrial membrane potential (MMP) and cell apoptosis were evaluated by flow cytometry; Western-Blot was applied to detect the expressions of cytochrome C and cleaved caspases-3.

Results: Compared with normal control and DZ pretreatment, high-glucose incubation significantly increased cell apoptotic percentage, at the same time, mitochondrial activity was inhibited, MMP decreased, expressions of cytochrome C and caspase-3 increased significantly (all P < 0.05). Compared with high-glucose incubation, pretreatment of 5-HD further increased apoptotic percentage, inhibited mitochondrial activity, decreased MMP and increased expressions of cytochrome C and caspase-3 increased significantly (all P < 0.05).

Conclusion: Under high-glucose environment, mitoKATP in myocytes affects mitochondrial activity and integrity by impacting MMP, then induces apoptosis via mitochondria-dependent pathway.

P534

Sepiapterin prevents left ventricular hypertrophy and dilatory remodeling induced by pressure overload in rats

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Background: Uncoupling of nitric oxide synthase (NOS) has been implicated in left ventricular hypertrophy (LVH) and remodeling induced by pressure overload (PO). We investigated whether sepiapterin administration after established LVH inhibits NOS uncoupling and prevents dilatory LV remodeling.

Methods and Results: PO was created by transverse aortic constriction (TAC) in rats. TAC was associated with a significant decrease in BH4 and a significant increase in BH2, giving rise to a marked decrease in BH4/BH2 ratio. Sepiapterin, a stable precursor of BH4, or a free radical scavenger N-2-mercapto-propionyl glycine (MPG) was given between 8 and 16 weeks after TAC. Sepiapterin or MPG inhibited nitrotyrosine formation, but only sepiapterin increased BH4/BH2 ratio and bioavailable NO in the heart after TAC. Sepiapterin but not MPG reversed cardiomyocyte hypertrophy induced by TAC. Expression of vascular endothelial growth factor (VEGF) and capillary density were attenuated between 8 and 16 weeks after TAC, but they remained increased by sepiapterin treatment. Sepiapterin prevented interstitial fibrosis and prevented dilatory LV remodeling which developed between 8 and 16 weeks after TAC. A NOS inhibitor, L-NAME abrogated the inhibitory effect of sepiapterin on cardiomyocyte hypertrophy, angiogenesis and dilatory LV remodeling.

Conclusions: Sepiapterin treatment after established LVH prevents dilatory remodeling induced by pressure overload. The beneficial effects of sepiapterin are mediated by increased bioavailability of NO but not decreased oxidative stress.

P535

Aging aggravates cardiac dysfunction in severe pressure overload

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Purpose: The prevalence of heart failure is increasing due to improved survival of cardiovascular disease in an aging population. Interestingly, the normal aging heart already shows a number of non-pathological structural and functional alterations which are reminiscent to the changes observed in the failing heart. These alterations may increase the vulnerability of the aging heart to develop heart failure. Consequently, we studied the effect of aging on left ventricular (LV) remodeling and dysfunction in response to mechanical overload.

Methods: Mice were subjected to severe pressure overload by transverse aortic constriction (TAC) at 3, 12 or 24 months of age. Eight weeks after TAC, LV geometry and function were measured. Subsequently, isometric force was studied in single permeabilized cardiomyocytes, and gene and protein expression levels were determined in LV tissue.

Results: In sham operated animals, aging resulted in increases in LV weight (25%), interstitial fibrosis (139%), and by decreases in LV dP/dt at 40 mmHg (dP/dtP40) (19%) and in dP/dtmin (27%) in 24 vs. 3 mo old mice (all p < 0.05). Passive myofilament force (Fpas) was increased during aging (44%), which, surprisingly, was accompanied with increased levels of the more compliant cardiac titin isoform N2BA (65%) (both p < 0.05), with unchanged phosphorylation of titin.

TAC produced LV hypertrophy, LV dilation, interstitial fibrosis, increased expression levels of hypertrophy marker genes and LV dysfunction in all age groups. Interestingly, the relative TAC-induced increase in LV weight was blunted from 89% at 3 mo to 59% at 24 mo compared to the age-matched shams. This was accompanied by 65% lower expression levels of α -skeletal actin (α -SKA) in 24 mo vs. 3 mo TAC mice (65%) (p < 0.05). The blunted hypertrophy response to TAC was associated with aggravated LV dysfunction, demonstrated by a further decrease in LV dP/dtP40 (33%) and dP/dtmin (32%) and increases in lung fluid (28%) and RV weight (28%) in the 24 vs. 3 mo old mice (all p < 0.05). LV dysfunction in 3 mo TAC mice was accompanied by increased cardiomyocyte maximal isometric myofilament force development (Fmax) (51%) and increased Fpas (157%) (both p < 0.05). The increased Fpas could not be explained by the increased N2BA:N2B ratio (49%), but could be explained by the 50% reduction of titin phosphorylation (both p < 0.05). Surprisingly, aging resulted in reductions of Fmax and Fpas to age-matched sham levels.

Conclusion: Aging blunted the hypertrophy and myofilament responses to severe pressure overload but aggravated global LV dysfunction.

P536

Development of experimental autoimmune myocarditis in the rat: assessing the kinetics of myocardial inflammation by nuclear imaging (PET)

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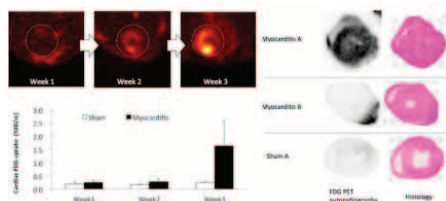
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Mortality of myocarditis is still high. Due to the invasive nature of endomyocardial biopsy, reliable non-invasive tools to diagnose inflammation are clinically needed. Here we established an experimental animal platform for the non-invasive monitoring of acute myocarditis including the kinetics of inflammation.

Methods: Autoimmune myocarditis (EAM) was induced by immunizing n=7 Lewis rats with porcine cardiac myosin in CFA or control-injected with adjuvant alone (n=5). 7, 14, and 21 days post-immunization the animals underwent nuclear imaging (micro-PET-system); after >10h fasting, static 10min chest FDG-PET-scans were obtained 60min after intraperitoneal FDG-application. In addition, 18F-FBnTP perfusion PET-imaging was performed, allowing to precisely localise cardiac FDG-signals before post-mortem histological analysis and autoradiography.

Results: Histologically, multiple focal cardiac inflammatory lesions with large numbers of infiltrating macrophages were observed in 5 out of 7 rat hearts. Concordantly, in these rats FDG PET-scans exhibited high focal tracer-signals (Fig. 1, A and B), whereas control hearts showed no relevant tracer-uptake (%ID/ml: 1.62 ± 0.93 vs. 0.25 ± 0.04 , $p < 0.001$; Fig. 1, Sham A). Serial FDG PET-images allowed to follow the time-course of tracer-accumulation (%ID/ml: 0.25 ± 0.10 , 0.28 ± 0.11 , and 1.62 ± 0.93 at days 7, 14, and 21, respectively; $p < 0.01$). Ex-vivo analysis confirmed co-localization of areas with FDG-uptake and those with inflammatory infiltrates.

Conclusions: PET-imaging appears well-suited for the non-invasive serial monitoring of cardiac inflammation in a rat-model of acute EAM; thus, our experimental platform might also represent a useful tool to evaluate novel imaging modalities and/or therapeutic strategies in human myocarditis.



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Contractility of left ventricular myocardium in patients with ischemic cardiomyopathy: morphological substrate

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Objective: To assess condition of the left ventricular (LV) myocardium in zones with altered local contractility of different degree in patients with ischemic cardiomyopathy (ICMP).

Methods: The objects of the study were myocardium biopsy samples from 36 patients with ICMP (mean age = 56.2 ± 7.8 years) and with the apical anterior aneurysm. During the operation of surgical ventricular reconstruction myocardial biopsy samples were harvested from anterior, posterior and lateral walls of LV and from ventricular septum at the LV site from all the patients. The zones from which the samples were taken were correlated with their contractility (normokinesis, hypo-, a- and dyskinesis). The biopsy material was processed and the slices were stained with hematoxyline-eosin and pikrofuksin. Morphometry and statistical analysis of numeric data were performed. Impaired local contractility of LV myocardium was evaluated by EchoCG study on the Acuson 128 XP/10 according to the recommendations of the International Society of Echocardiography.

Results: Normokinetic zones of LV myocardium were characterized by polymorphism and increased size of cardiac myocyte (CMC) nuclei, by the presence of areas with hyperextension of "myocardial fibers", and small amount of connective tissue. In the hypokinetic zones one can notice perinuclear edema in CMCs; their cytoplasm is stained unevenly; the layers of pericellular and perivascular connective tissue get thicker; endocardium is thickened insignificantly.

Akinetic zones are characterized with diffuse fibrosis, formation of "lacunes" and lowered total count of CMCs. The remaining CMCs sometimes look normal, sometimes take stellate shape and form branching of "myocardial fibers". Proliferation of smooth muscle cells of arteriola walls is registered in akinetic and dyskinetic zones.

In dyskinetic zones of LV myocardium one can see acute fibrosis, vacuolated CMCs with unevenly stained cytoplasm as well as fragmentation and "splitting" of myofibrils. Capillaries and larger vessels often appear in the endocardium of such zones; inflammatory infiltrate is often revealed.

We found statistically significant correlations of myocardial segmental kinesis (normokinesis-hypokinesis-akinesis-dyskinesis) with specific volume (SV) of parenchyma ($r = -0.205$, $p = 0.02$), SV of stroma ($r = 0.310$, $p < 0.001$) and SV of perinuclear edema ($r = -0.216$, $p = 0.02$).

Conclusions: the structure of LV myocardium in patients with ICMP with apical anterior aneurysm is heterogeneous, presented as a combination of diffuse and focal changes and related to its functional condition.

Young Investigator Award: Basic Science

Sunday 24 May 2015 08:30–10:00

Location: Agora

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Titin phosphorylation by pkg as a mechanism of acute adaptation to myocardial stretch

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Introduction: Acute myocardial stretch leads to an increase in contractility and a progressive decrease in myocardial stiffness. Titin is the main determinant of passive tension at physiological sarcomere lengths and its distensibility is increased via phosphorylation of its spring elements by cGMP-dependent protein kinase (PKG). PKG can be activated by nitric oxide (NO) and natriuretic peptides (NPs), which are mediators released upon acute stretch.

Methods: Myocardial strips dissected from left ventricle (n = 10) and right atrium (n = 14) of patients subjected to cardiac surgery and isolated papillary muscles from rabbit right ventricle (0,2 Hz; 30 °C) were subjected to acute myocardial stretch from 92 to 100% of Lmax (the length associated with maximal active tension). Different groups of rabbit muscles were incubated with Rp-8-Br-PET-cGMPs (PKG inhibitor, 10-6 M, n = 7), LNA (NO synthase inhibitor, 10-5 M, n = 8), hydroxocobalamin (NO scavenger, 10-3 M, n = 8), A-71915 (natriuretic peptide receptor A (NPR-A) antagonist, 10-6 M, n = 9), and the three latter drugs simultaneously (n = 10). All-total titin phosphorylation was stained with Pro-Q Diamond (phospho-protein) and indexed to total-protein signals using Sypro Ruby;. Values are given as mean±SEM and statistical significance was set to p < 0.05.

Results: After acute overload, there was a progressive decrease in passive tension over 15 minutes of stretch: 27 ± 8% and 27 ± 6% in human atrium and ventricular muscles respectively, and 43 ± 2% in rabbit papillary muscles. This decrease in myocardial stiffness was attenuated by 40% after PKG inhibition. Isolated NO synthase inhibition, NO scavenging and NPR-A antagonism did not modify the adaptive diastolic response to stretch. However, a significant (29%) blunting of the effect was observed when the three interventions were exerted simultaneously. Titin phosphorylation increased significantly over the 15 minutes following myocardial stretch in both human (11 ± 1% vs 41 ± 8% in atrium and 27 ± 8% vs 71 ± 21% in ventricle muscles) and rabbit (13 ± 2% vs 23 ± 3%) muscles.

Discussion: The progressive decrease in myocardial stiffness after acute haemodynamic overload seems to depend on PKG activity, which represents potential therapeutic target in patients with pathologically rigid myocardium. Moreover, blocking the NO and NPs systems, which converge on PKG activation, seems to attenuate this adaptive diastolic response. Titin phosphorylation, which is known to increase myocardial distensibility, is probably involved in this new myocardial response to stretch in both animals and humans.

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Integration of deep sequencing data reveals global regulation of gene expression in human cardiac hypertrophy and heart failure by differential methylation, hydroxymethylation and microRNA expression

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Purpose: Many pathways and genes involved in hypertrophy and heart failure have been described in animal models, but how the transition from compensatory hypertrophy to heart failure is initiated in humans remains unclear. This study aims to identify global mechanisms of gene regulation in the human heart in response to biomechanical stress (pressure overload) by analyzing the transcriptomes and

comparing the contribution of methylation, hydroxymethylation and ncRNAs in aortic stenosis patients with two disease conditions: compensatory hypertrophy (normal ejection fraction) and heart failure (reduced ejection fraction).

Methods: DNA and RNA were extracted from snap frozen human myocardial biopsy samples and RNA-sequencing (RNA-seq), methylated DNA immunoprecipitation-sequencing (MeDIP-seq), hydroxymethylated DNA immunoprecipitation-sequencing (hMeDIP-seq) and smallRNA-sequencing (smallRNA-seq) was carried out using deep HiSeq high throughput sequencing. By comparing the patients' data to control samples without heart disease using five replicates for each group and experiment, differentially expressed genes, differentially methylated regions, hydroxymethylated regions and differentially expressed microRNAs were identified.

Results: As expected, the transcriptomes show a high degree of deregulation. Transcriptionfactor (TF) network analysis suggests that approximately 20% of condition specific differential expression might be a result of TF regulation. While the methylome is slightly changed in both conditions, the hydroxymethylome is massively changed in heart failure suggesting a regulatory contribution to the failing hypertrophic phenotype. Furthermore, differential expression of microRNAs is increased in heart failure and network and target analysis suggests that almost all candidates are involved in the regulation of differentially expressed genes in both, the compensatory hypertrophy group and heart failure group.

Conclusion: The data presented here suggest a regulatory contribution of hydroxymethylation and the regulation by microRNAs during the transition of human compensatory hypertrophy to heart failure.

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Perinatal titin isoform switch is associated with decreased sensitivity for oxidative passive force modulation in rat left ventricular cardiomyocytes

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Purpose: This study evaluated the hypothetical involvement of titin oxidation in the molecular mechanism of perinatal diastolic dysfunction. Perinatal adaptation to extrauterine life involves a titin isoform switch resulting in a gradual increase in the expression of the less compliant N2B isoform in expense on a gradual decline in the expression of the more compliant N2BA isoform leading to an increase in Ca²⁺-independent passive force (F_{passive}) in cardiomyocytes with age. Here we attempted to reveal how titin isoform composition and oxidative insults influence F_{passive} of left ventricular (LV) cardiomyocytes in juvenile rats following birth.

Methods: Mechanical and biochemical studies were performed at different stages of postnatal development (i.e. at 0, 7 and 21 days) of control Wistar rats. F_{passive} was measured in single, mechanically isolated and permeabilized LV cardiomyocytes. The effects of protein oxidation on F_{passive} was evaluated following in vitro exposures to an oxidative agent, 2,2'-dithiodipyridine (DTDP, 10 mM) in cardiomyocytes followed by the application of the antioxidant dithiothreitol (DTT, 10 mM). Titin isoform composition was analyzed by SDS-gel electrophoresis and Coomassie protein staining.

Results: F_{passive} was significantly increased with age in a range of sarcomere lengths (SL, between 1.9 and 2.5 μm) following birth in rats. F_{passive} was significantly lower in the 0- and 7-day-old groups than in the 21-day-old animals (0.11 ± 0.01 kN/m² vs. 0.26 ± 0.02 kN/m² vs. 0.56 ± 0.02 kN/m², respectively, SL: 2.3 μm, P < 0.05, n = 10-13). The N2BA/N2B ratio of titin isoforms showed age-dependent characteristics (80 ± 1%/20 ± 1%, 41 ± 1%/59 ± 1% and 10 ± 1%/90 ± 1% in 0, 7 and 21 day-old rats, respectively, n = 5-7). DTDP significantly increased F_{passive} in 0- and 7-day-old rats, but to a lesser extent in 21-day-old animals (ΔF_{passive} normalized to the baseline values in the three age groups: 99 ± 26%, 65 ± 23%, 39 ± 21%, respectively, P < 0.05 0-day-old group vs. 21-day-old group, SL: 2.3 μm, n = 7-8). The effects of DTDP were completely reverted by the application of DTT in 0-, 7- and 21-day-old animals (0.10 ± 0.01 kN/m², 0.21 ± 0.02 kN/m², 0.51 ± 0.08 kN/m², respectively, SL: 2.3 μm, n = 7-8).

Conclusion: Cardiomyocyte maturation following birth is accompanied by a gradual decline in the oxidation evoked increases in F_{passive}, presumably because the compliant N2BA titin isoform is more sensitive to oxidative insults than the N2B titin isoform.

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GATA2-mediated miRNA regulation in endothelial cells

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Introduction: The transcription factor GATA2 plays a role in vascular biology by regulating complex transcriptional networks. During cardiovascular disease, the normal expression pattern of microRNAs (miRNAs) changes significantly, which leads to altered signalling cascades. The expression of miRNAs can be regulated by transcription factors, including GATA2. However, GATA2 downstream-regulated miRNAs in endothelial cells have not been characterized. Due to the important role of GATA2 for vascular system control, the investigation of downstream-regulated miRNAs as well as their target genes is of great interest to understand endothelial cell function and related paracrine signalling.

Methods and Results: To identify GATA2-regulated miRNAs in endothelial cells, we modulated GATA2 expression level in human umbilical vein endothelial cells (HUVECs) via siRNA-mediated silencing of GATA2 or transduction of a GATA2 overexpression construct. Upon siRNA-mediated GATA2 knockdown, qRT-PCR-dependent global miRNome-screening and subsequent validation experiments identified GATA2-regulated miR-126 and miR-221. MiRNA promoter analysis revealed that pro-angiogenic miR-126 is regulated by GATA2 on transcriptional level which is accompanied by altered expression of miR-126 host gene EGFL7 and pri-miR-126. Anti-angiogenic SPRED1 and FOXO3a are confirmed as miR-126 target genes potentially contributing to the defective GATA2 phenotype inhibiting formation of normal vascular structures. In contrast to GATA2 deficiency, supplementation with miR-126 normalized the expression profile of decisive endothelial cytokines and thus implicates pro-angiogenic paracrine effects. Intrinsic regulation of anti-angiogenic miR-221 is dependent on GATA2 via demethylation of a putative CpG island in the miR-221 promoter. Mechanistically, a reverted GATA2 phenotype by endogenous suppression of miR-221 is at least in part mediated through direct pro-angiogenic miR-221 target genes ICAM1 and ETS1. In a mouse model of carotid injury, systemic supplementation of miR-126 nanoparticles improved reendothelialization behaviour of injured carotid artery and thus suggests a new therapeutic concept of endothelial lesions.

Conclusion: In conclusion, we highlight GATA2-dependent regulation of miR-126 and miR-221 which has an important function on endothelial biology and angiogenesis. Endothelial dysfunctions with severe angiogenic defects developed from silencing of endothelial specific genes can be reverted by supplementation of miRNAs sustaining endothelial repair capability.

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Lysyl oxidase overexpression impacts cardiovascular remodelling

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Purpose: The disturbance of extracellular matrix (ECM) composition and structure plays an important role in cardiovascular remodelling and in the progression of heart failure. Lysyl oxidase (LOX) is a key enzyme in ECM remodelling. Because LOX deficiency is lethal, we have developed a transgenic mouse model to study the impact of LOX overexpression on cardiovascular remodelling.

Methods and Results: A new mouse model that over-expresses human LOX was generated by conventional methods. Transgene expression was determined by real time PCR in 8 different tissues including aorta, heart, kidney, white adipose tissue (WAT), brown adipose tissue, lung, liver and skeletal muscle. The maximum expression of human LOX was found in aorta followed by heart and WAT. Neither the expression of endogenous LOX nor the expression of other LOX-Like (LOXL) isoenzymes was modified by transgene expression in aorta, heart or WAT.

We tested the impact of LOX over-expression on cardiovascular remodeling in TgLOX mice and their wild-type (WT) littermates mice after chronic infusion with Ang II (1.4 µg/kg/min) or saline by using osmotic minipumps (n = 10 per group). Ang II-induced aortic diameter dilation studied by echography was similar in TgLOX and WT mice after Ang II infusion. However, the mortality rate due to aortic rupture was higher in WT mice (20%) compared to TgLOX mice (0%). Cardiac function was evaluated by echocardiography. We observed that Ang II infusion decreased ejection fraction (EF) and fractional shortening (FS) in TgLOX mice, while they were augmented in WT mice. A stronger hypertrophic response induced by Ang II was observed in TgLOX mice as evidenced the increased LV mass and left ventricle posterior wall (LVPW) thickness in diastole and systole and the higher HW/BW ratio compared with WT mice. Accordingly, the left ventricular inner diameter (LVID) in systole and diastole was significantly lowered in TgLOX mice compared with WT animals. However, Ang II similarly increased the mRNA levels of hypertrophic markers such as ANP and β -HMC in both transgenic and WT mice. The values of cardiac output and stroke volume remained similar in both groups. Finally, LOX overexpression increased the Ang II-induced expression of pro-inflammatory (Emr-1, IL6, Mmp-9) and fibrosis-related (Serpin-1, Col-1a1) markers in cardiac tissue compared with WT mice.

Conclusions: We have developed a valuable model to improve our knowledge about LOX biology in the cardiovascular system. Our data evidence that LOX over-expression impairs cardiac function under hypertensive conditions.

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Increased myofilament calcium sensitivity triggers mitochondrial emission of reactive oxygen species in hypertrophic cardiomyopathy and contributes to arrhythmias

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The most common causes of hypertrophic cardiomyopathy (HCM) are mutations of genes encoding sarcomeric proteins, such as myosin-binding protein C (MYBPC3) or troponin T (TnT). Many mutations increase myofilament calcium (Ca) sensitivity, implying that more contractile work is generated at any given cytosolic Ca ([Ca]_c). Increased work generates ADP which accelerates mitochondrial respiration, oxidizing NADH to NAD⁺. The Krebs cycle regenerates NAD⁺ to NADH and is activated by mitochondrial Ca ([Ca]_m). Since the Krebs cycle also controls NADPH that is required by anti-oxidative enzymes for H₂O₂ elimination, we speculated that in HCM, increased myofilament Ca sensitivity provokes a pro-oxidative shift in the NAD(P)H redox states and thus, mitochondrial H₂O₂ emission, possibly contributing to arrhythmias. In cardiomyocytes, the Ca-sensitizer EMD 57033 (3 µM) reduced diastolic sarcomere length by 2% and increased systolic shortening 2.5-fold without elevating Ca. This oxidized NAD(P)H by 20%. When increasing myocyte workload by elevating stimulation frequency from 0.5 to 5 Hz combined with b-adrenergic stimulation (ISO; 30 nM), EMD provoked NAD(P)H oxidation and mitochondrial H₂O₂ overflow, which could be prevented by increasing [Ca]_m with CGP-37157 (CGP), an inhibitor of the mitochondrial Na/Ca exchanger. In cardiomyocytes from HCM Mybpc3-targeted knock-in mice (KI) carrying a Ca-sensitizing point mutation, diastolic sarcomere length was shorter and systolic shortening stronger after ISO/5Hz than in wild-type (WT) myocytes (p < 0.0001) without differences in [Ca]_c or [Ca]_m. NAD(P)H redox state was slightly more oxidized at baseline in KI vs. WT myocytes, which was aggravated after ISO/5Hz (p < 0.05). Despite similar mitochondrial O₂-formation, H₂O₂ emission increased in KI vs. WT myocytes during redox state oxidations in response to ISO/5Hz (p < 0.05), both sensitive to CGP. In mitochondria, no differences in respiration, O₂- production or H₂O₂ emission (±ADP) were detected between genotypes. In a second HCM mouse model expressing the I79N Tnn2 mutation, NAD(P)H was more oxidized in isolated myocytes, which was antagonized by CGP. In Langendorff-perfused hearts, rapid pacing provoked NAD(P)H oxidation (by 8%) and arrhythmias (50%) in I79N hearts, while WT hearts remained stable. Both NAD(P)H oxidation and arrhythmias were completely prevented by CGP. We conclude that increased myofilament Ca sensitivity in HCM induces mitochondrial ROS emission by a mismatch between ADP-induced oxidation and [Ca]_m-induced regeneration of the NAD(P)H redox state. This novel mechanism may contribute to arrhythmias in HCM.

Moderated Poster Session 3 – Established and emerging approaches in cardiomyopathies

Sunday 24 May 2015 10:00–11:00

Location: Poster Area

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Retrospective assessment of immunosuppressive agents in virus-negative inflammatory cardiomyopathy

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Purpose: Virus-negative inflammatory cardiomyopathy (CMP) is defined according to the WHO, including CMP with ≥ 14 infiltrating inflammatory cells per mm^2 without viral presence in endomyocardial biopsy (EMB). To date, no studies evaluated the efficacy of immunosuppression on patients who fulfilled this WHO definition. The purpose of this study is to assess the efficacy of immunosuppressive agents in virus-negative inflammatory CMP.

Methods: Within the local cardiomyopathy registry, a total of 487 DCM patients underwent EMB between 2008 and 2014, of whom 93 fulfilled the WHO criteria for virus-negative inflammatory CMP. Sixty-eight patients did not and 25 did receive immunosuppressive therapy. To correct for (possible) selection bias, 2:1 propensity score matching using age, gender, duration of symptoms, NYHA class, was performed, resulting in 50 untreated and 25 treated patients. Primary outcome was assessed using left ventricular ejection fraction (LVEF) after one year follow up.

Results: No significant difference with baseline characteristics was observed, including optimal standard heart failure medical treatment. Although both groups demonstrated a significant increase in LVEF ($p < 0.001$) after one year, a significant higher increase of LVEF was revealed in treated as compared to untreated patients after 1 year follow-up ($P = 0.041$; figure 1). Long-term follow-up (median follow-up was 35 months [21-48]) demonstrated 5 patients died in the untreated as compared to 1 in the treated group.

Conclusion: This retrospective study shows that immunosuppression leads to a higher increase of left ventricular function in patients with virus-negative inflammatory cardiomyopathy. This conclusion triggers further prospective trials.

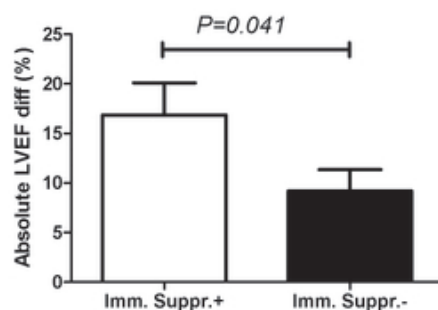


Figure 1: One year LVEF increase.

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Estimation of right ventricular function by 2D longitudinal strain more accurately predicts prognosis in chronic heart failure patients

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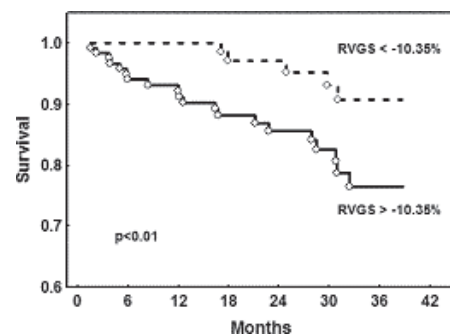
The aim of this study was to evaluate the role of two-dimensional (2-D) speckle tracking measures of right ventricular systolic function in predicting the mortality of patients affected by chronic heart failure (CHF).

We enrolled 274 outpatients (77% males, 64 ± 14 years, NYHA class 2.2 ± 0.7 , left ventricular ejection fraction, LVEF, $34 \pm 9\%$) with CHF (ESC criteria), in stable clinical conditions (> 1 month) and in conventional therapy (91% ACE-inhibitors and/or ARBs, 94% betablockers). At echocardiogram, 4-chamber view (frame rate 50-70/sec) was obtained in order to evaluate by 2-D speckle tracking (Echo-PAC, GE) analysis the global strain of right ventricle (RVGS). Tricuspid annulus systolic excursion peak (TAPSE) was also calculated.

During follow-up (21 ± 12 months), 26 patients died (19 for cardiovascular causes and 7 for non cardiovascular causes). Seven patients underwent heart transplantation. RVGS was associated to mortality at univariate (HR: 1.16; 95%CI: 1.068-1.26; $p < 0.001$; C-index: 0.69) as well as at multivariate analysis (HR: 1.11; 95%CI: 1.012-1.217; $p < 0.01$; C-index: 0.82) in a model including age, NYHA class, LVEF. On the other hand, TAPSE was not associated to mortality.

Figure shows Kaplan-Meier curves for survival of patients dichotomized according to RVGS median value.

In conclusion, our findings demonstrate the independent role of 2D strain in the assessment of right ventricular function in predicting mortality as well as its superiority in comparison to traditional monodimensional parameter. These data strengthen the clinical usefulness of this echocardiographic approach in daily management of CHF outpatients.



Figure

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Prediction of response to cardiac resynchronization therapy by the imbalance in regional left ventricular myocardial work

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Patients with left ventricular (LV) dyssynchrony have a marked imbalance in LV myocardial work distribution with wasted work in the septum and increased work in the lateral wall. We hypothesized that a low septum to lateral wall (SL) myocardial work ratio at baseline predicts LV pump function improvement during Cardiac Resynchronization Therapy (CRT).

Methods: Twenty patients (age 65 ± 10 years, 15 men) underwent CMR tagging for regional LV circumferential strain assessment, and invasive pressure-volume loop assessment using a conductance catheter at baseline and during biventricular pacing. Segmental work at baseline was calculated from regional strain rate and LV pressure. Subsequently, the SL work ratio was calculated by dividing the net result of useful work and wasted work of the septum by the net result of useful work and

wasted work of the lateral wall. This measure of imbalance of myocardial work was related to acute pump function (SW) improvement during CRT.

Results: During biventricular pacing, SW increased by +33% ($P < 0.001$). SW improvement by CRT was found to be significantly related to the SL work ratio at baseline ($R = -0.54$; $P = 0.015$). Moreover, the SL work ratio was demonstrated to be a stronger predictor of response to CRT than QRS duration and other measures of dyssynchrony or discoordination (Figure 1). Assuming a SW improvement cut-off value of 20%, 13 patients were classified as responder. They showed a significantly lower SL work ratio compared with 7 non-responders (-0.07 ± 0.24 vs. 0.62 ± 0.49 ; $P < 0.001$).

Conclusion: The contribution of the septum to LV work varies widely in CRT candidates with LBBB. The lower the septal contribution to myocardial work (or the higher the septal waste) at baseline, the higher the pump function improvement that can be achieved during CRT.

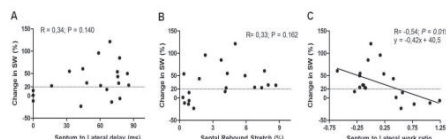


Figure 1

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Early arrhythmic events in idiopathic dilated cardiomyopathy

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Purpose: The aims of the study were to provide an insight into the prevalence and characterization of patients with early sudden cardiac death/major ventricular arrhythmias (SCD/MVAs) and to identify possible reliable indicators of early SCD/MVAs in a large cohort of dilated cardiomyopathy (DCM).

Methods and Results. From 1988 to 2014, 952 patients with DCM were consecutively included in the Heart Muscle Disease Registry of Trieste. Globally, 20 patients (2.1% of the overall population) experienced SCD/MVAs within the first 6 months after enrollment (primary end-point). At baseline, they showed a worse functional class (NYHA III-IV 42% vs 22%, $p = 0.038$), a longer QRS duration (127 ± 41 msec vs 108 ± 33 msec, $p = 0.013$) and a more dilated left ventricle (indexed left ventricular end systolic volume (LVESVI) 82 ± 49 ml/m² vs 67 ± 34 ml/m², $p = 0.049$). The rate of betablockers administration was significantly lower compared to patients without early SCD/MVAs (59% vs 83%, $p = 0.008$), mostly due to hemodynamic intolerance. At multivariate analysis, LVESVI (OR 1.012, 95% CI 1.000-1.024, $p = 0.043$) and QRS duration (OR 1.017, 95% CI 1.003-1.030, $p = 0.015$) were significantly associated with the primary end-point, whereas betablockers demonstrated a protective effect (OR 0.169, CI 0.048-0.593, $p = 0.006$).

Conclusions: In patients with DCM, the risk of major arrhythmic events in the first phase of the disease is not-negligible. Baseline LVESVI, QRS duration and intolerance to betablockers therapy might be useful tools in the arrhythmic early risk assessment of DCM patients.

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Cardiac magnetic resonance assessment of dilated cardiomyopathy by comparison to histology in patients with disease duration more than 6 months

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Purpose: The purpose of this study was to evaluate the possibilities of cardiac magnetic resonance (CMR) in patients with dilated cardiomyopathy (DCM) with disease duration more than 6 months and compare the results with endomyocardial biopsy (EMB) and biomarkers.

Methods: CMR was performed in 51 patients with DCM (36 men and 15 women, mean age \pm SD) of 43 ± 11 years, mean duration of chronic heart failure (CHF) of $4, 1 \pm 3, 4$ years). CMR assessment of myocardial inflammation used the following parameters as recommended the «Lake Louise Criteria»: myocardial edema, global relative enhancement (GRE), and late gadolinium enhancement (LGE). CMR imaging was performed by using a 1.5-T Tomograph. The CMR protocol included the following sequences: cine MR images (True FISP); T2-weighted images (Turbo Spin Echo); T1-weighted images (Spin Echo) before and over 4-5 min after intravenous administration of 0, 15 mmol Gd-DTPA/kg body weight; two sequences were performed (True FISP; Turbo FLASH) in delayed enhancement phase after

Gd-DTPA injection (over 10-15 min). Twenty-five patients underwent EMB. The levels of N-terminal natriuretic peptide type B (NT-proBNP), of high-sensitivity cardiac troponin T (hs-cTnT) and high-sensitivity C reactive protein (hs-CRP) were estimated of all patients.

Results: Myocardial edema and GRE have not been reported in any cases. LGE was found in 20 patients (39%). LGE were mainly seen in the infero-lateral segments of LV (65%). Among the 20 LGE-positive patients mainly location was subepicardial and intramyocardial in 47% and 30% of cases, respectively. The levels of NT-proBNP and hs-cTnT ($P < 0.05$) were significantly higher in the group patients with LGE ($n = 20$) than in the group without LGE ($n = 31$). Median levels of hs-CRP in the blood plasma of patients in both groups did not differ significantly. NT-pro-BNP levels correlated significantly with LGE volume ($r = 0.20, p < 0, 05$). There was no correlation between volume of LGE and levels of hs-cTnT and hs-CRP. Myocardial inflammation was confirmed by immunogistology in 14 patients (56%). Chronic myocarditis was found in 9 patients with LGE (90%) and only 5 patients without LGE (33%), it was statistically significantly ($p = 0, 01$).

Conclusions: The presence only of LGE in patients with DCM with disease duration more than 6 months is suggestive of the presence of ongoing inflammation, despite the absence myocardial edema and GRE by CMR.

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Adverse events in continuous-flow LVAD recipients: gastrointestinal bleeding is still notable?

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Purpose: The incidence of gastrointestinal bleeding (GIB) is high in patients receiving continuous flow left ventricular assist device (CF-LVAD) support. Patient populations, etiology and risk factors are still poorly understood. Diagnostic and treatment pathways are various, without unique algorithm. The aim of this study was to evaluate and identify risk factors that make these patients prone to GIB.

Methods: We reviewed the data of 71 consecutive patients who had CF-LVADs implanted between May 2012 and June 2014. Patients' demographics, presentation and treatment strategies were evaluated.

Results: Sixty-five men, 6 women (mean age of 55 ± 12 years) underwent implantation LVADs (42 BTT, 29 DT). Overall, 23.9% of patients (17/71) had at least one GIB. GIB was confirmed by endoscopy in 13 pts. with arteriovenous malformation identified as a major source of bleeding in 8/13 (61%). Multiple bleeding episodes were registered in 3 patients (median number of GIB episodes is 4). All patients with GIB were men, mostly with LVAD as bridge-to- transplant therapy ($p = 0.026$). There was no significant difference in incidence of GIB in regard to device type: HVAD (29%) vs. HMII (22%), $p = 0.556$, in INTERMACS score ($p = 0.231$) and blood type ($p = 0.877$). Aortic valve was confirmed to be open by echocardiography in 58% of GIB patients with HMII. On the regression analysis only significant risk factor for GIB was presence of chronic kidney disease (OR = 4.34, 95% CI = 1.26-14.94, $p = 0.02$). At the time of first bleeding we identified 7 pts who were hemodynamically stable (MAP > 70 mmHg, Hb ≥ 7.0 g/dl and INR < 3.5 IU) when presenting at hospital and who did not required admission. At discharge for first GIB, 92% of patients were restarted on both aspirin and warfarin.

Conclusion: In CF-LVAD patients there is still high incidence of GIB. Fortunately, it is mainly single event. Most initial GIB occurred within first month after surgery, thus prevention strategies should be focused at this vulnerable post-implantation period. Patients experiencing GIB and are hemodynamically stable may medically be treated in outpatient setting, but this should be confirmed prospectively in the future studies.

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Use of short-term mechanical circulatory support and predictors of outcome in patients with cardiogenic shock secondary to fulminant myocarditis

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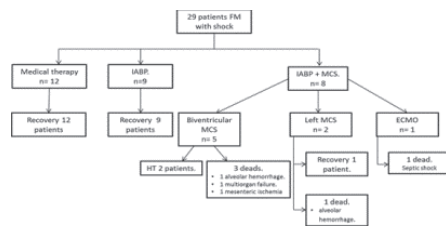
Introduction: Fulminant myocarditis (FM) is a rare form of myocarditis that rapidly progresses to cardiogenic shock and death if not treated. The aim of this study was to evaluate the need for mechanical circulatory support (MCS) and predictors of outcomes in patients with FM.

Methods: Study of patients with acute myocarditis complicated with cardiogenic shock admitted from 2006 to 2014. Myocarditis was diagnosed either with endomyocardial biopsy (EMB) (Dallas criteria) or by cardiac magnetic resonance (CMR).

Characteristics of patients who died or were transplanted and patients discharged alive were compared by the chi-square and t-Student tests.

Results: 29 patients (48.3% male, median age 43.1 years) were studied. Mean follow-up was 2.15 years. Diagnosis of FM was done by EMB in 24 patients. The most common finding was lymphocytic infiltrate (87.5%). 13.8% of patients had autoimmune disease and 6.9% HIV infection. Median left ventricular ejection fraction (LVEF) was 25%. Intravenous methylprednisolone was given in 86.2% of patients and 79.3% received inotropes. 58.6% needed an intraaortic balloon pump (IABP) and 8 patients (27.6%) MCS. Outcomes are in figure. Patients who died or underwent HT had a shorter prodromal phase (1 vs 7 days), lower systolic blood pressure (80 vs 99 mmHg), cardiac index (1.4 vs 2.08 l/min/m²) and LVEF (16.5% vs 31.6%) than survivors without HT ($p=0.047$, $p=0.006$, $p=0.028$ and $p=0.009$ respectively). Patients with IABP, mechanical ventilation or MCS had a higher mortality ($p=0.014$, $p=0.001$ and $p=0.001$ for each). Median LVEF at discharge was 50.6%.

Conclusion: FM requires an early and aggressive treatment. Sicker patients required MCS and had higher mortality. In survivors recovery of cardiac function occurred in the first month. Long term prognosis is excellent.



Outcomes in fulminant myocarditis

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Atrial fibrillation and hyper-response to cardiac resynchronization therapy

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Purpose: Hyper-responder rate to cardiac resynchronization therapy (CRT) is estimated around 5-10%. Although CRT indication is not questioned for patients with atrial fibrillation (AF), there are not many data concerning the percentage of hyper-responders in this group of patients.

Methods: Results from a multicenter retrospective observational study performed at 15 Spanish centres. Each centre included consecutive patients subjected to implantable cardioverter-defibrillators (ICD) implantations for a primary prevention (from January 2010 until December 730). We analysed the hyper-response rate among patients with permanent AF at the moment of an ICD-CRT implantation. A hyper-response was defined as ejection fraction >50% and a NYHA class I after 6 months.

Results: From a total of 1174 ICD implantations, an ICD-CRT was implanted in 495 patients. Among the ICD-CRT patients, there were 211 patients (42.6%) with permanent AF. Morbidity was higher in patients with permanent AF than in those with sinus rhythm (SR) (table 1). There were a 9.7% of hyper-responders among the total of CRT patients. Despite that the patients with AF showed a worse clinical profile, there were not any differences statistically significant regarding the hyper-responders (10.2% SR vs 9% AF, $p=0.7$). There were a higher percentage of patients with AF who died: more total deaths in monitoring (8.8% of patients with SR vs 18.7% of patients with AF, $p<0.01$) and more cardiovascular deaths (5.6% of patients with SR vs 13.9% of patients with AF, $p<0.01$).

Conclusions: In our series, despite that AF patients had a worse clinical profile and mortality was higher, there were not any differences statistically relevant regarding the hyper-response to CRT rate.

CRT Group Comorbidity: SR vs AF

	SR	AF	p
Renal Failure (MDRD<60ml/min)	86 (33.1%)	86 (46%)	<0.01
NYHA III-IV	174 (61.3%)	153 (72.5%)	<0.01
Age≥70 years old	94 (33.1%)	98 /46.4%	<0.01
Blood Urea nitrogen > 26 mg/dl	87 (34.8%)	90 (50%)	<0.01
Left Bundle Branch Block	241 (84.9%)	154 (73%)	<0.01
Previous Hospitalization for Heart Failure	76 (26.8%)	94 (44.5%)	<0.01
Previous treatment with digoxin	26 (9.2%)	62 (29.4%)	<0.01
Heart Failure Hospitalization during follow-up	47 (16.7%)	75 (35.7%)	<0.01

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Determinants of beta-blocker underprescription in a population-based cohort study of outpatients across different heart failure phenotypes

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Background: Although beta-blockers are the recommended therapy for heart failure (HF) patients, their tailored prescription is still suboptimal. The relative impact of predictors of underprescription of beta-blockers across different HF phenotypes is not clearly known.

Purpose: Aim of the study was to identify the factors determining underprescription of beta-blockers in a large population-based cohort of outpatients across different HF phenotypes (LVEF≤40% - HF_rEF, LVEF 41-49% - HF_{pe}EF, LVEF ≥50% - HF_pEF).

Methods: From November 2009 to October 2013, all consecutive HF outpatients with available LVEF were considered. Clinical variables of study population were derived from the E-data chart for Outpatient Clinic collected in a regional Data Warehouse.

Results: 2424 patients (57% males, mean age 78±9 years, NYHA III-IV 18%) were analyzed. HF_rEF, HF_{pe}EF and HF_pEF patients were respectively 597 (25%), 1457 (60%) and 358 (15%) patients. The overall high mean age and non cardiac comorbidities (mean 3.2±2.5; 63% patients presenting ≥ 3 non cardiac comorbidities) ran similarly across HF phenotypes. In 1168 (49%) patients beta-blockers were not prescribed (45% in HF_rEF, 52% in HF_{pe}EF and 42% in HF_pEF; $p<0.001$). Among patients on beta-blockers, those treated with <50% of target doses were 57%. Heart rate was ≥70 bpm in 47% (73% in sinus rhythm) of patients with beta-blockers, whereas it was ≥70 bpm in 41% of patients without (80% in sinus rhythm) ($p=0.008$). Compared to patients on beta-blockers, those not treated were older, more frequently female, in NYHA class III-IV and affected by COPD, but less likely to have a history of hypertension. Considering the target dose, there were 62%, 51%, and 57% patients treated with <50% of target doses in HF_rEF, HF_{pe}EF and HF_pEF, respectively ($p<0.001$). No significant difference in heart rate among HF phenotypes emerged. At multivariable model for non-prescription of beta-blockers in overall population, age, NYHA class III-IV, HF_{pe}EF phenotype, COPD, hypertension and valvular disease were independent predictors. Age, advanced NYHA class and COPD were confirmed as independent predictors across all HF phenotypes.

Conclusion: In our study cohort characterized by older age and frequent non cardiac comorbidities, there was a beta-blockers under prescription in all HF phenotypes. Moreover, age, symptoms and COPD emerged as independent predictors of non-prescription across all HF phenotypes.

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Prognostic value of peak treadmill exercise echocardiography in heart transplant recipients with coronary atherosclerosis and preserved resting left ventricular ejection fraction

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Purpose: In heart transplant (HT) recipients with coronary artery disease (CAD), the efficacy of an invasive strategy remains controversial, especially among those with a preserved left ventricular ejection fraction (LVEF) and no or mild symptoms. Our hypothesis is that in these cases exercise echocardiography (EE) might provide relevant information to guide therapy.

Methods: We conducted a retrospective analysis of 42 oligosymptomatic HT recipients with a previous angiographic diagnosis of CAD and resting LVEF>40% who

underwent peak treadmill EE. CAD was defined as any angiographic stenosis >50% of the luminal diameter of ≥ 1 epicardial vessel. Both donor-transmitted and de novo coronary lesions were considered as CAD. Patients were followed up to a maximum of 10 years after EE. The Kaplan-Meier method was used to compare patients with negative vs. positive EE with regard to the occurrence of cardiac events death, retransplantation, heart failure (HF) admission, acute coronary syndrome (ACS) or late coronary revascularization (>90 days after EE). EE was considered as negative if no symptoms, no ST-segment changes and no echocardiographic evidence of ischemia were noticed.

Results: Mean age of HT recipients was 60 ± 13 years. Mean time elapsed since HT was 7.7 ± 5.7 years. 33 (79%) patients were men and 10 (24%) patients had donor-transmitted CAD. 4 (8%) patients referred atypical angina, 1 (2%) patient had exertional dyspnoea and 37 (88%) were asymptomatic. 30 (75%) patients received

m-TOR inhibitors. 20 (48%) patients had a negative EE. 8 patients (19%) developed ECG changes, and 20 (48%) patients had echocardiographic evidence of ischemia. No patient developed symptoms. Early after EE (<90 days), 6 patients with a positive EE underwent PCI and 1 underwent CABG. Over a mean follow-up of 3.8 ± 2.6 years, 6 (14%) patients died, 13 (31%) were hospitalized for HF, 5 (12%) presented an ACS, 5 (12%) underwent late PCI and 3 (7%) underwent retransplantation. Kaplan-Meier analysis showed a significantly lower incidence of cardiac events in patients with a negative EE than in those with a positive EE (log rank $p = 0.011$). Among 20 patients with a negative EE, only 1 (5%) died and no one was retransplanted.

Conclusions: EE provides significant prognostic information in oligosymptomatic HT recipients with angiographic CAD and preserved resting LVEF. Long-term outcome of patients with a negative EE is good, even when managed with a conservative strategy.

Clinical Case Corner 2 – When drugs are not enough

Sunday 24 May 2015 10:00–11:00

Location: Poster Area

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Dual-site left ventricular pacing-a new option for non-responders to cardiac resynchronization therapy?

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Cardiac resynchronization therapy is a novel pacing therapy for severely symptomatic congestive heart failure (CHF) patients with ventricular conduction delay and preserved sinus rhythm. Few data are available concerning the benefit of CRT in CHF patients with chronic atrial fibrillation (AF) and complete heart block. We report here the problems and benefits associated with CRT and then dual-site left ventricular pacing in a patient with a permanent pacemaker implantation (PPI) for sick sinus syndrome, who developed chronic AF with uncontrolled tachycardia, AV node ablation and CHF during follow-up.

A 62 years-old female patient underwent PPI (DDD) at the age of 45 for sick sinus syndrome with paroxysmal AF. Seven years following the PPI, the patient developed symptoms of CHF and chronic AF. The rhythm control of AF was ineffective and AV node ablation was performed eight years after the initial PPI. When the PG showed battery depletion after 8 years of PPI, CRT was selected. The LV lead was positioned in the posterior vein of CS. After the procedure symptoms of CHF slightly improved and the medical therapy was continued. The patient was admitted in cardiosurgical department of our hospital 15.04.2013 with the worsened symptoms of heart failure (NYHA IV). Echocardiographic examination showed dilated cardiac chambers, the ejection fraction of 19 %, severe mitral regurgitation, the lateral wall contraction delay. Chest X-Ray showed approximately parallel RV and LV leads, so we made a conclusion that LV lead could be dislodged and resynchronization therapy was ineffective. A revision procedure was performed after 5 days of intravenous diuretics. We found the LV lead located in the posterior heart vein with normal parameters of sensing and pacing and QRS duration of 228 ms. We implanted another LV lead in the lateral branch of CS. The lead had a satisfactory LV capture threshold (1.5 V at 0,5 ms pulse duration) and without phrenic nerve stimulation. LV lead was then connected to the atrial port, while the RV lead and previously implanted LV lead were connected to the ventricular port of the 2-chamber pacemaker through the Y-connector. The PG was programmed with interventricular delay of 30 ms, thus initiating CRT. The ECG with new LV lead showed AF with a QRS duration of 130 ms. The patient had significant improvement in her symptoms of heart failure following the procedure (Tab.1) and she was discharged from our hospital with optimal medical treatment adjusted (b-blockers, diuretics, aldosterone antagonists, dabigatran, ACE-inhibitor).

Conclusion: We performed left ventricular bifocal pacing in only one case. The second LV lead implantation was technically possible because of wide CS ostium and an appropriate target vein (lateral branch of CS). This method of pacing brought to decrease of intraventricular conduction delay and improving the symptoms of HF in short-and long-term follow-up. We suggest this method to be useful in patients with chronic AF, who are non-responders to conventional CRT due to intraventricular conduction delay and we need more patients to prove it.

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Recurrent postinfarction ventricular septal rupture

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Introduction and case report description: A 50-year-old man presented with inferior acute STEMI. Primary PCI was performed successfully. He was admitted to the coronary care unit in Killip class II, and a harsh systolic murmur prompted transthoracic echocardiography (TTE), which demonstrated mild left ventricular systolic dysfunction (LVSD) and a 40mm posterior ventricular septal defect (VSD) generating a wide left-to-right shunt. The patient underwent emergent surgical repair and VSD closure with a dacron patch. Two weeks after he was discharged with mild LVSD, severe right ventricular systolic dysfunction (RVSD), moderate mitral regurgitation (MR) and mild residual VSD. The patient was readmitted 24h later on severe acute heart failure, requiring vasodilators, inotropic therapy and high dose diuretics. Subsequent TTE revealed tearing of the patch with widening of the recurrent septal defect (30 mm), severe ischaemic MR, mild LVSD and severe RVSD. Given these findings reintervention was indicated, with suturing closure of the VSD and prosthetic mitral valve replacement (MVR). The patient's postoperative course was prolonged and complicated due to severe cardiogenic shock. He was finally discharged after 72 days of admission. TTE revealed biventricular systolic dysfunction. He is currently being considered for heart transplant.

Questions, problems or possible differential diagnosis: Postinfarction VSD is a rare (1-2%) but life-threatening complication with poor prognosis. Perioperative mortality predictors are cardiogenic shock, RVSD, emergency surgery, posterior VSD, renal impairment and complex VSD. Operative timing, perioperative management, type of repair and need for concomitant coronary artery bypass grafting (CABG) or MVR remain controversial.

Answers and discussion: Whereas current guidelines recommend emergent or early surgical repair, improved outcomes have been recently showed with delayed repair allowing consolidation of the infarct scar and haemodynamic stability. Perioperative management should be directed toward reduction of left ventricular afterload using vasodilators and intra-aortic balloon pump (IABP) when needed. Ventricular assist devices and extracorporeal membrane oxygenation have only been proved helpful in short series. Transcatheter closure has a role in selected patients with simple defects (<15 mm). Need for concomitant CABG or MVR in patients with at least moderate MR still remains uncertain.

Conclusions and implications for clinical practice:

The reported case illustrates complexity in VSD management. Could a deferred surgery, perioperative usage of IABP or initial MVR have improved outcomes in a patient with two predictors of mortality (posterior VSD, RVSD)? Should heart transplantation be considered as first alternative in such patients?

Improving in HF symptoms

	Before the procedure	6 days after	4 months after	8 months after
6-min walk test, m	0	450	400	550
NYHA	IV	II	II	0

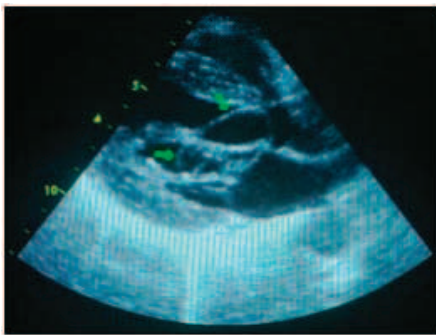
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Giant blood cyst of the mitral valve with the obstruction of the left ventricular outflow tract

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Intracardiac blood cyst is a rare congenital abnormality, occurring mainly at autopsy of fetuses or children under the age of 6 months. Most cysts are often located on the valve apparatus and are a soft round cardiovascular tumor with thin smooth walls and liquid hemorrhagic content. As a rule, they are small and spontaneously disappear in childhood, but in adults they may reach large sizes and depending on their localization, can be accompanied by valve dysfunction symptoms or left ventricular (LV) outflow tract obstruction. A female, 28-year-old, was admitted to the clinic with complaints of exertional dyspnea, dizziness. Auscultatory there is systolic murmur in all points, the rest - within normal. Transthoracic echocardiography: There are 3 round floating thin masses with some echonegative content in the LV cavity, that are attached to the ventricular surface of the anterior mitral valve cusp, one sized 19x19 mm and another two masses sized 8x8 mm. In systole the larger sized mass prolapses into the LV outflow tract, creating an obstruction of blood flow with the maximum pressure gradient of 144 mm Hg at rest. Moderate hypertrophy of the left ventricular myocardium. Magnetic resonance imaging confirmed the existence of cysts. Taking into account the existence of intracardiac mass that creates significant obstruction of the left ventricular outflow tract, the patient was operated - removal of the mass and mitral valve replacement. Intraoperative: There is some liquid mass lesion: one sized 20x30 mm and another two sized 10x10 mm each visualized on the ventricular side of the anterior mitral valve cusp at the place chord attachment in the segment A2. All masses have a common cavity filled with liquid, similar to the hemolyzed blood. Excision of cysts formed a large defect of the anterior cusp resulting in valve replacement. Histological examination confirmed the true (congenital) cyst. The postoperative period was uneventful. Since intracardiac cyst is a very rare pathology, there is currently no common opinion on the optimal management of patients. Probably it is justified to manage conservatively asymptomatic patients with small cysts before symptoms appear. At the same time, it is impossible to predict the scenario of blood cyst progression. Therefore, to prevent the development of serious complications, the resection of the cyst followed by grafting or valve replacement is performed in most cases. In the case of our patient, the cyst was innate and led to the obstruction of the left ventricular outflow tract. Taking into account the size of the cyst and relative complications, in our case, the tactics choice is obvious.



Blood cyst

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Incidental finding of short QT syndrome in a young patient with Carvajal Syndrome presenting with acute heart failure and a right ventricular mass.

A case report

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Introduction: Carvajal Syndrome is a variant of arrhythmogenic right ventricular cardiomyopathy (ARVC) characterized by left ventricular involvement. Patients (pts) may remain asymptomatic for long, and diagnosis is usually achieved when RV failure occurs. Short QT syndrome (SQTS) is a rare arrhythmogenic disease with a wide spectrum of clinical manifestations, ranging from asymptomatic carriers of mutated genes to pts experiencing sudden cardiac death. Case report: A healthy and sporty 30-year-old woman with an unremarkable medical history went to the ER complaining dyspnoea on minimal exertion, ascites, genital and peripheral oedema in the last 2 weeks. An ovarian disease was suspected first, but instrumental tests performed were all negative. Chest radiography revealed

significant pleural effusion with cardiac shadow enlargement. On ECG diffuse low voltages with scanty progression of the R wave and diffuse T wave alterations were present. Echocardiography revealed biventricular dilation and diffuse hypokinesia, with severely reduced ejection fraction (EF, 15%), moderate amount of pericardial effusion and the presence of an oval mass of about 2x2.5cm in the apex of the RV. This was highly suspicious for either an intra-cardiac tumour or a thrombus. She was transferred to the cardiac intensive care unit where therapy was started (intravenous diuretics and heparin, ACE-inhibitors and beta-blockers). Constant ECG monitoring revealed several symptomatic episodes of polymorphic non-sustained ventricular tachycardia, further complicating the clinical course as well as hypotensive episodes related to attempts of therapy up-titration. On cardiac magnetic resonance imaging (cMRI), the gold standard technique for diagnosis of ARVC, the RV appeared highly trabeculated with mild subepicardic delayed enhancement in the intra-ventricular septum and apex, extending to the lateral wall of the left ventricle. Thus, diagnosis of ARVC with left ventricular involvement was achieved (Carvajal Syndrome). Also, tissue characterization of the RV mass identified it as a thrombus. Ivabradine was added for better heart rate control, since beta-blockers up-titration was difficult because of hypotension. Contrast enhanced chest CT revealed multiple sites of micro-pulmonary embolization of the RV thrombus in the pulmonary circulation. The thrombus resolved completely 17 days after initiation of intravenous heparin. Before home discharge in good clinical conditions with the maximum tolerated therapy, the pt was implanted an ICD for primary prevention. During ambulatory follow up therapy up-titration proceeded, and periodic echocardiography evaluations showed constant improvement of EF up to 44% one year after the index event. Also, cardiopulmonary exercise test revealed significant improvement in VO₂ (from 6.2 ml/Kg/min to 16 ml/Kg/min) and normal VE/VCO₂ slope, with an overall risk score reduced from high to medium. Genetic testing was performed in the patient and her relatives during follow up. None of the known mutations responsible for ARVC were found. However, a mutation of the gene KCNH2 correlated to short QT syndrome (SQTS), was evident, although the main electrocardiographic features of the disease were not present. Discussion: Only in 30-50% of pts with ARVC the underlying genetic alteration is identified with genetic testing, since many mutations responsible for this cardiomyopathy have not yet been identified. Also, genetic diagnosis of SQTS per se may not be significant if clinical and electrocardiographic features of the syndrome lack. Apart from the rarity of this condition, our case suggests that an aggressive treatment of acute heart failure due to ARVC can almost completely restore cardiac function.

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Mitral valve chord rupture after resynchronisation for ischaemic cardiomyopathy, treated by urgent MitraClip repair, with late repair failure and pulmonary valve tear from displaced defibrillator lead

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Introduction: We present a 74 year-old man with known ischaemic cardiomyopathy and mild mitral regurgitation due to restricted mitral valve posterior leaflet (PMVL). A week following resynchronisation therapy, he developed a rare complication, presenting with sudden acute pulmonary oedema from PMVL chord rupture. His condition was stabilised with urgent percutaneous mitral valve repair. Later he developed severe right heart failure from a second rare event, caused by displacement of the right ventricular defibrillator lead, resulting in trauma to the pulmonary valve and severe pulmonary regurgitation.

Case History: Our patient had a history of breathlessness and echocardiography showed a significantly impaired left ventricular function with hypokinetic inferior and inferolateral walls, and mild mitral regurgitation due to a restricted posterior leaflet. Angiography showed an occluded right coronary artery, and diffuse circumflex artery disease. Cardiac MRI confirmed partial thickness inferior and inferolateral infarction, without reversible ischaemia. He remained breathless despite optimal medical therapy, therefore underwent implantation of a cardiac resynchronisation defibrillator with symptomatic improvement. A week later, on a cruise, he decompensated with sudden breathlessness, and required resuscitation and intubation for acute pulmonary oedema. Transoesophageal echocardiography revealed torrential mitral regurgitation due to a flail posterior leaflet (P3), without evidence for a new infarct. The patient was deemed too high risk for surgery, and instead had urgent percutaneous mitral valve repair with two MitraClips, reducing the regurgitation to moderate. His defibrillator lead had also displaced into the pulmonary artery. After lead re-positioning, a pulmonary valve anterior leaflet tear and prolapse, with severe pulmonary regurgitation, was found. He improved initially over a month, but gradually worsened again with pulmonary and peripheral oedema. Repeat investigations revealed worsening mitral regurgitation and dislodgement of one of the MitraClips. He eventually underwent successful mitral and pulmonary valve surgery.

Discussion, Conclusions, and Clinical Implications: Although mitral regurgitation can rarely worsen following resynchronisation, sudden decompensation from spontaneous mitral valve rupture has not been described. We postulate that this may

be due to changes in the left ventricular contraction pattern or pressure, causing further chord tension. Our case demonstrates that emergency percutaneous mitral valve repair is an excellent alternative to the prohibitive risks of conventional surgery, although in our patient, it had limited durability. We separately describe gross displacement of the defibrillator lead causing severe disruption to the pulmonary valve. It should be recognised that such an event can occur following device implantation.

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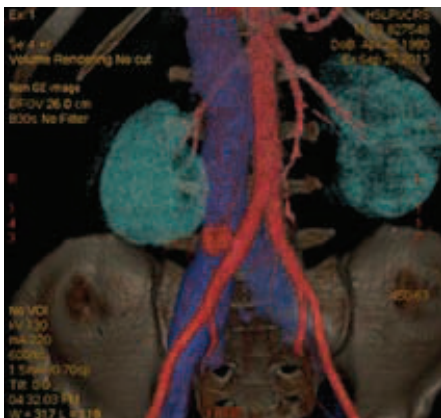
High output heart failure due to arteriovenous fistula after an orthopedic surgery

L Lucas Celia Petersen¹; M Salame¹; MA Goldani¹; SVG Wanderley¹; TR Reichert¹; CVE Drebes¹; M Crencenzio¹; JS Jardim¹; JCVG Guaragna¹; JCVG Danzmann¹

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Introduction: Heart failure is usually associated with a low cardiac output. A few conditions may cause a high output state which can lead to high output heart failure. A preserved ejection fraction and warm extremities may lead to the diagnosis and a correctable aetiology should be sought. Case report: A 34 years-old male comes to the emergency department with progressive symptoms of dyspnea, abdominal distension with discomfort and peripheral edema with marked limitation to ordinary tasks. He had a previous history of surgical treatment of a lumbar herniated disc, nephrolithiasis, gastritis and palpitations. He was taken sotolol, furosemide and pantoprazole. Previous exams showed: Normal electrocardiogram and minimal ectopies on holter test. Treadmill test with good functional class, occasional ectopies and no evidence of ischaemia. Myocardium Magnetic Resonance Imaging identified a mild biventricular dilatation, no perfusion deficit and a small mesocardial fibrosis in the inferior wall of left ventricle. Vital signs were normal. On physical exam there was bilateral basal crackles, B3, jugular venous distention, hepatomegaly, systolic-diastolic murmur on the lower right abdomen and +4/4 pitting leg edema. Intravenous furosemide was given with progressive clinical improvement and exams ordered. Laboratory exams were normal with exception of elevated creatinine. Chest radiography showed mild congestion and an echocardiogram revealed a normal ejection fraction (57%) with biatrial dilatation and important pulmonary hypertension. Abdominal ultrasound showed free-fluid, enlarged liver and inferior vena cava / hepatic veins. A Computed Tomography Angiography identified a 0,7 cm iliac arteriovenous fistula. The diagnosis of high output heart failure due to iliac arteriovenous fistula was made. Surgical correction with endoprosthesis was made with a good outcome. The patient became gradually better, almost asymptomatic when discharged 15 days later with aspirin, atenolol and pantoprazole. Description of the problem: A detailed physical exam is often forgotten, especially the abdomen, which can give information on degree of congestion (ascites, hepatomegaly and jugular venous distension on liver palpation) and vascular flow (murmurs on aorta, renal and iliac arteries). Possible differential diagnosis: Abdominal murmurs could represent turbulence through stenosis or dissection or an arteriovenous fistula. Discussion: Aortocaval and iliac arteriovenous fistula are a rare condition which results of a pre-existing aneurism erosion, herniated disc repair or trauma. Clinical findings may be local, arterial, venous and cardiac.

Conclusion: The importance to investigate the aetiology of heart failure applied to a critical history taken and physical exam to direct treatment and possible cure of a reversible cause. High output heart failure should be reversible when the underlying cause is corrected.



CT-Angiography

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The fatal heart failure - a natural course of cor triatriatum sinister

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Introduction: Cor triatriatum sinister (CTS) is a rare cardiac anomaly with an incidence of 0.1-0.4% of all congenital heart defects. Clinical course and management of this pathology influenced by the degree of obstruction between the two left atrial chambers.

Case report description: 20 years ago a 39 year-old man was consulted by the cardiologist because of 1 month history of palpitations, dyspnea and reduced exercise tolerance. He was followed by general practitioner from the age of 16 due to rheumatic heart disease. Physical examination revealed normal arterial blood pressure, irregular heart rate of about 110 bpm, and the diastolic heart murmur at the apex was heard, liver enlargement and mild peripheral edema. An electrocardiogram showed atrial fibrillation (AF) with a rate of 118 bpm and the signs of left ventricular hypertrophy. Transthoracic echocardiography (TTE) revealed moderate mitral and mild tricuspid regurgitation, moderate pulmonary hypertension and big left atrium (LA) which was subdivided by additional membrane into two chambers (Fig. 1.A). The membrane had fenestration and the maximum pressure difference across the membrane was 13 mmHg (Fig. 2 and Fig.3). The diagnosis of cor triatriatum sinister was made. After discussion with cardiac surgeon, it was decided to perform surgical resection of the membrane. The patient refused to undergo surgery and was treated conservatively. Patient was seen by cardiologist on irregular basis due to patient noncompliance and routine follow-up was performed one or two times per two year. This time TTE revealed very big LA (11,3 x 7,5 cm), the membrane defect (3,5 x 1 cm) with almost unchanged maximal gradient across the membrane, right heart failure, pulmonary hypertension and severe mitral and moderate tricuspid regurgitation (Fig. 1. A-C). On the chest X-ray pulmonary venous congestion, pleural effusion, marked cardiomegaly and liver enlargement was presented (Fig. 4). The condition of the patient critically deteriorated at the age of 59 years after viral infection. He was admitted to the intensive care unit with severe shortness of breath, pulmonary and peripheral edema. Despite severe condition the patient refused to undergo surgical treatment and died.

Discussion: The rarity of this congenital anomaly and symptoms variability may explain the late diagnosis of cor triatriatum. Patients with this anomaly typically present in infancy due to the obstructive nature of the left atrial membrane, with the creation of a pressure gradient with resultant elevation in pulmonary venous and arterial pressures. However, some cases may present in adulthood. Differential diagnosis should consist of congenital obstructions of the left ventricle inflow: cor triatriatum sinister, congenital mitral stenosis, pulmonary venous obstruction and supramitral ring. TTE is perceived to be the imaging test of choice. The problem in this situation was late diagnosis of cor triatriatum and patient's refusal to undergo surgical treatment. Surgery should be considered in all patients presenting with signs and symptoms of left ventricle inflow obstruction, pulmonary hypertension and right heart failure.

Conclusions and implications for clinical practice: In conclusion, this case report demonstrates the delayed diagnosis and natural course of exceptionally rare cardiac anomaly - cor triatriatum sinister. The early diagnosis and surgical treatment of this anomaly is essential in order to avoid the severe complications and death. The doctor and patient compliance should take important role in daily practice. Our case adds further to the published literature on this rare congenital anomaly.

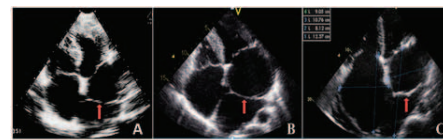


Fig.1. Transthoracic echocardiography apical 4-chamber views revealing a membrane (arrow) subdividing the left atrium into two chambers. The dynamic of heart changes throw the years 1995 (A), 2007 (B), 2014 (C).

The natural course of cor triatriatum

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Single ventricle heart failure after long-term survival of a modified Blalock-Taussig shunt

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¹Hospital Luz, Lisbon, Portugal

Medical evolution has allowed improving the survival of patients with congenital heart disease giving rise to an increasing number of patients who reach adulthood. Today, the number of adult congenital heart disease (ACHD) cases already exceeds the number of pediatric counterparts. Taking into account the growing complexity of ACHD and their age-dependent comorbidities, the management of these patients

became a unique challenge as recommendations on how to manage acute heart failure (AHF) on these patients are lacking. The authors present the case of a previously NYHA class II, 44 years old patient with ACHD, admitted with acute decompensated heart failure. He had a single ventricle with pulmonary atresia, previously submitted to three modified Blalock-Taussig shunts (BTs) at age 2, 12 and 19 years old. A transthoracic echocardiogram (TTE) performed at admission documented a severe ventricular systolic dysfunction, not present in previous examinations. A thoracic CT angiography confirmed shunt patency. Conventional treatment was initiated but without success. Levosimendan was added to ongoing therapeutics, and under beta-blockade at 0.05 mcg/kg/min perfusion, without loading dose, for 24 hours. There was a favorable clinical improvement with an appropriate decongestion. An episode of rapid atrial fibrillation was observed (24 hour after levosimendan) probably hypomagnesemia related. Optimization of HF with BB, ACEi, ARM and ivabradine was well tolerated. A TTE 120h after levosimendan showed qualitative improvement in ventricular systolic function. Right heart catheterization showed a moderate increase in pulmonary artery pressure (PAP) (right PAP 44/31 (38) mmHg; left PAP 48/30 (42) mmHg), and moderately elevated pulmonary vascular resistance (PVR) 3,4 Wood units (mmHg.min/L). The patient was discharged in NYHA class III referred for heart transplantation. From the authors' knowledge, this is the first report of a successful levosimendan use in an AHF of a BTs long-term survivor.

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Surgical treatment of hypertrophic obstructive cardiomyopathy in a patient with severe hypertrophy, ventricular tachycardia and septal myocardial fibrosis

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Inpatients with hypertrophic cardiomyopathy myocardial fibrosis is an independent predictor of adverse outcome. The mechanism of sudden death in HOCM is

ventricular tachycardia/fibrillation emanating from areas of fibrosis. In the absence of generally accepted standards for surgical treatment of HOCM in patients with severe hypertrophy and septal myocardial fibrosis a new technique of HOCM surgical correction was proposed. This approach avoids mechanical damage to the heart conduction system and for the surgeon it improves visual inspection of the area to be resected. We present a case-report of a 33-year-old female patient with biventricular obstruction, extreme hypertrophy (interventricular septum thickness 35 mm), septal myocardial fibrosis and episodes of ventricular tachycardia who underwent surgical correction according to this novel procedure. The areas of septal myocardial fibrosis as identified by delayed enhancement imaging were excised under direct visual inspection in the middle part of the right side of the interventricular septum and in upper third part. After surgical correction of HOCM and precise removal of septal myocardial fibrosis the patient had no ventricular tachycardia and no syncopal or presyncopal episodes. The advantage of the approach is an effective surgical treatment of hypertrophic obstructive cardiomyopathy (HOCM) in patients with severe hypertrophy and septal myocardial fibrosis who can not be treated with the current techniques.

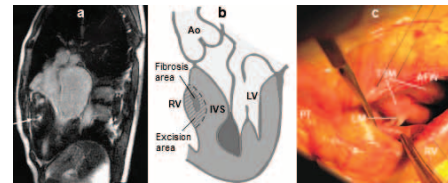


Figure 1: (a) Delayed hyperenhancement ma

Nursing Investigator Award

Sunday 24 May 2015 11:00–12:30

Location: Agora

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Patients perceptions of illness severity in advanced heart failure

National Institute of Nursing Research of the National Institutes of Health under award number 1R01NR013419L Lisa Kitko¹; J Hupcey¹

¹The Pennsylvania State University, College of Nursing, University Park, United States of America

Purpose: Advanced heart failure (HF) impacts over 5 million Americans, with this number doubling by 2030. Across the globe, the rate of heart failure is also on the rise, with estimates of 22 million worldwide, such that the World Health Organization has begun to evaluate heart disease data more systematically. The future global impact of heart failure has been called an "emerging pandemic" that must be addressed. Further complicating the high incidence of HF, is a five year mortality rate that approaches 50% and an unpredictable heart failure trajectory. End-of-life (EOL) treatments for HF, including EOL discussions and referral to appropriate services, such as palliative care and hospice, have been recommended to meet the needs of HF patients, but are not widely used by the HF population. To help determine why EOL services may not be utilized, this study investigated the perceptions of illness severity in advanced HF patients.

Methods: As part of a longitudinal study of investigating the EOL trajectory of patients with HF, 100 adult patients with a predicted survival of <1-year versus (n=40) <2-year (n=60) were interviewed. Predicted survival was determined by Seattle Heart Failure Model at time of enrollment. During the initial interview, patients were asked to describe their disease and where they see themselves in one-year. Qualitative content analyses of the interviews were done by two analytic teams blinded to patients' predicted survival. Research team members then came together to participate in group comparative analysis.

Results: The majority of patients in both groups (80% in <1year and 87% in <2 year) did not understand the severity or the terminality of their HF. Out of the 54 patients who have died, only 13% perceived HF as a terminal disease. Many patients described their health deterioration as part of the aging process. Regardless of predicted or actual survival, EOL discussions rarely occurred and few patients were offered EOL services.

Conclusions: The majority of patients did not view HF as a terminal disease even with a limited predicted survival. Lack of perception of terminal course of HF may impact patients' acceptance of EOL discussions and planning and EOL services. As the global incidence of HF approaches epidemic levels, innovative delivery services will be required to address EOL issues in this population even without patient acceptance of disease terminality.

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Changes in perceived health of heart failure patients after CRT implantation

HFANurse Training Fellowship;MedtronicAB, StJude Medical, Sweden; Icel Nurses' Ass and Landspítali Univ Hosp Science Funds, IcelandB Ingadottir¹; I Thylen²; T Jaarsma¹

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Purpose: The number of patients with heart failure who receive cardiac resynchronization therapy (CRT) is increasing and little is known about the effects on their health or on their short term recovery. The purpose of this study was to describe the health complaints that patients have before the CRT implantation, and 2 weeks after receiving the device and to assess factors related to those changes.

Methods: Data were collected in a prospective multicenter survey study from 104 adult patients undergoing elective, first time device implant (mean age 69±9, 78% men, 71% received CRT-D) from Sweden and Iceland.

Patients completed the Adjusted Postoperative Recovery Profile, a 19 item instrument with score ranging from 1 to 4 (1=severe complaint, 4=no complaint) and possible scores 19-76, before and after the implantation. Seven CRT specific questions were added after the implantation and analysed separately.

Results: There was a statistically significant improvement in perceived health 2 weeks after CRT implantation. The mean scores of the Adjusted Postoperative Recovery Profile increased from 63±9 to 67±7 t=-5.2 p<0.001). In total 12 out of 19 health complaints improved. Largest changes were found in fatigue, gastrointestinal function, anxiety and worry, social activities and reestablishment of everyday life (p<0.001). Other health complaints that improved included mobilisation, muscle weakness, and concentration (p<0.005) and sleeping problems, sexual function, feeling down and being dependent on others (p<0.05).

Patients in higher NYHA functional class reported more improvement than patients in lower class (F 4.78 p<0.005) and patients with work experience within health/social care reported less improvement than others (t=2.65 p<0.01). No other background factors were significantly related to improvement. With regard to CRT specific questions we found that after 2 weeks the majority of the patients were bothered by stiffness in the shoulder (60%) and the device sticking out (59%). Less patients experienced problem with pulsation around the device (28%), tachycardia (23%), how the scar looks (17%), hiccups (7%) and wound healing (6%).

Conclusions: At short term follow-up after CRT implantation heart failure patients reported significant improvements in physical and psychosocial health. Stiffness in the shoulder and the feeling that the device is sticking out were the most common procedure-related complaints.

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Comparative validity of depression assessment scales for screening depression in heart failure

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Purpose: To evaluate the performance of common depression tools in HF patients in both acute or outpatient setting.

Methods: At hospital admission and 6-month later, N=118 (99% male, 68.9±10 years) were evaluated for clinical depression. Both times, 3 screening tools (Beck Depression Inventory [BCI], Patient Health Questionnaire [PHQ]-2, and PHQ-9) were completed. Clinical depression was measured by the Diagnostic Interview Structured Hamilton (DISH). Tool performance was evaluated with receiver operating characteristics (ROC) analysis and calculation of sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV).

Results: In-hospital and 6 months post-hospitalization, 24 (20.3%) and 14 (14.6%) exhibited clinical depression, respectively. For all 3 tools, the areas under the curve (AUC) were significant (Table). At hospitalization, cut-off scores above normally suggested provided superior sensitivity, specificity, PPV and NPV. For screening with high cut-offs, the BDI yield acceptable sensitivity. For case-finding, the BDI exhibited excellent specificity and NPV at a high cut-off. At 6 months, the PHQ-2 yielding a stronger specificity and NPV than the BDI or PHQ-9.

Conclusion: While all 3 tools were useful for depression screening and case-finding, timing relative to hospital admission influences performance.

Sensitivity & Specificity of Instruments

Instrument	AUC (95% CI)	Score	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Hospital Admission						
BDI	.90*(.82-.98)	10	91.7	61.1	37.3	96.7
16	.80	90.5	69	94.5		
PHQ-2	.80*(.70-.89)	3	45.8	82.1	39.3	94.9
4	.33.3	93.6	57.1	90.8		
PHQ-9	.83(.73-.92)	5**	91.7	48.9	31.4	96.7
12	.54.2	87.2	52	90.7		
6-month						
BDI	.88*.80-.96	10	92.9	73.1	37.1	98.4
16	.64.2	89.0	56.3	93.8		
PHQ-2	.87*.74-.99	3	71.4	92.6	62.5	94.9
4	.42.8	97.5	75	90.8		
PHQ-9	.83*.69-.96	5**	84.6	72	32.4	96.7

LEGEND: *p < .001; **cut-off for mild depression;

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IV diuretics in the community: the experience of heart failure patients and carers

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²East Sussex Healthcare NHS Trust, Hastings, UK., United Kingdom

We report heart failure patients and their carers' experience of receiving intravenous (IV) diuretics in a community setting in 10 NHS organisations in the UK. It is usual practice to admit patients to hospital for IV administration when they fail to respond to an increase in oral diuretics. UK health policies emphasise the importance of developing services which are responsive to patients' needs and delivered closer to home. This 2 year study aimed to discover if patient/carer satisfaction was increased by receiving home-based care and to establish feedback about the difference it made to their experience, when compared to hospital-based care.

Methods: Case study methodology was used. Patients who had failed to respond to oral diuretics were recruited from existing community heart failure nurse case-loads. Bolus doses of IV diuretics were given according to the study protocol either in the patient's own home or close to home with patients returning home each day. A survey questionnaire was administered to a purposeful sample of patients and carers shortly after completion of treatment. Face validity of the instrument was established via a panel of experts.

Results: 55 patients and 45 carers responded. All patients (100%) and 93% of carers, who completed the survey found home-based treatment preferable to hospital admission, often because it avoided a wide range of challenges associated with hospital stays. 53 patients (96%) indicated they were satisfied (15%) or very satisfied (82%) with the service over-all. Both patients and carers indicated that they got a wide range of personal benefits from staying at home, particularly those who knew they were approaching the end of life. The continuity of care provided by the same nurses was highly rated as was the lack of disruption for patients and family when compared to hospital admission. Some carers find the worry and responsibility of having the patient at home during a complex treatment a challenge, but only a small number would prefer hospital admission.

Conclusion: A home-based IV diuretic service is strongly preferred to hospital admission by the majority of patients and carers surveyed in this study and their overall experience of care is improved. Although not a representative sample, the study suggests that providers of care for patients with chronic heart failure should consider offering home-based IV diuretics as a treatment choice, provided that support for the carer is available.

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Subgroups of heart failure patients based on symptom occurrence-a latent class analysis

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Purpose: Heart failure (HF) is a progressive, symptomatic disorder. Recognizing and responding to symptoms is essential for patients to get timely treatments. Previous studies reported that patients with HF would experience 5 to 15 symptoms concurrently, and the patterns of symptoms were quite different, which might make

patients difficult to recognize the deterioration of HF. The aims of this study were to describe symptoms happened on HF patients before hospitalization, identify subgroups of patients with different patterns of symptoms, and compare differences in patients' characteristics among subgroups.

Methods: From March to September 2014, HF patients from one cardiovascular disease hospital were recruited in the study using the convenient sampling method. Symptoms happened in the week before hospitalization were collected with the Chinese version of Memorial Symptom Assessment Scale-Heart Failure (MSAS-HF). Patients were also asked to report the occurrence of bendopnea, which was a newly confirmed HF symptom. Latent class analysis (LCA) was conducted based on the symptoms, of which the incidence rate was above 30%, to identify subgroups among HF patients. Analysis of variance or χ^2 test was used to compare differences among subgroups.

Results: 145 patients (mean age 51.80 ± 16.11 yrs; 77.2% male; 88.6% NYHA III/IV) participated in the study. The most prevalent symptoms were shortness of breath (83.4%), lack of energy (73.8%), sweats (71.0%), difficulty breathing when lying flat (64.1%) and lack of appetite (62.8%). Four different subgroups were identified using LCA: the multiple typical symptom group (Group 1, 24.29%), the moderate typical symptom group (Group 2, 55.92%), the atypical symptom group (Group 3, 9.42%), and the short of breathing group (Group 4, 10.16%). Patients in the Group 3 were more likely to be younger (38.08 ± 16.22 yrs) and still at work (76.9%) comparing with the Group 1 and the Group 2 ($P \leq .05$). There was no significant difference in NYHA classes and NT-proBNP levels between patients in the Group 3 and other groups. Patients in the Group 4 mostly had lower NYHA classes and NT-proBNP levels (≤ 1000) than those in the Group 1 and the Group 2 ($P \leq .05$).

Conclusion: HF patients always fail to recognize and respond to symptoms, and thus delay for seeking care. This study identified four subgroups of patients with different patterns of symptoms before hospitalization. Patients who had atypical symptoms may need more concerns and education on self-management. Future studies to examine the stability of the subgroups and impact factors are warranted.

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Hospital to home, heart failure across the divide

P Paula Candlish¹

¹Central Coast Local Health District, Heart Failure Service, Gosford, Australia

Aims: To improve the quality of life of heart failure patients by enhancing patient care through the provision of a multidisciplinary management model to ensure optimal treatment, education and support for patients, carers and significant others.

Objectives: To increase patient/family and significant others' knowledge and management of heart failure.

To ensure patients are on optimal treatment including ACE Inhibitors, Beta-Blockers and Spironolactone (where appropriate).

Facilitate a pre-discharge review of all patients with heart failure, with a continuum of care into the community.

Increase health professional's knowledge of the current treatments and management for heart failure.

Inpatient: The patient on referral are seen prior to their discharge and informed about the service, and given education and information

Phone Follow-up: After discharge the patient has a phone follow-up by the heart failure nurse. This call is conducted within 5-7 days of discharge to achieve the best outcome.

Home Visit: A home visit is conducted for those patients not seen in hospital prior to discharge or referred from the community (either by their GP or Specialist), and those who are not coping well at home. This visit has a similar structure to that of the in-patient visit.

Group rehabilitation: All patients are offered the chance to attend a center based rehabilitation program tailored to suit patients with heart failure.

Outpatient Clinic: Patients are able to attend an outpatient clinic staffed by a staff specialist/advanced trainee and a nurse practitioner.

3000+ patients registered with the service from June 2003 and January 2015.

Average age 77 (range 24 – 115)

67% Male

Mortality: only 31% of the cohort have deceased over the 12 years of the program.

75% Optimal medication

23% increase in 6 minute walk test

25% increase in Patient knowledge

All had an admission (all causes)

20% have had a readmission for a cardiac condition in 12 years.

8% annual readmission rate

0.01% had a readmission within 28 days

Low percentage of patients are non- English speaking or Aboriginal/Torres Strait Islander.

The Heart Failure Service commenced on 31st January 2003. It cares for patients across the continuum from acute to community. It has enrolled over 3000 patients, and continues to manage over 500 requiring some form of active intervention. It has been shown to reduce readmissions, increase patient knowledge and exercise tolerance, using experienced system navigators such as a clinical nurse specialist and a nurse practitioner.

Young Investigator Award: Clinical

Sunday 24 May 2015 14:15–15:45

Location: Agora

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Lysyl oxidase-like-2 inhibition decreases cardiac fibrosis and improves diastolic dysfunction in experimental and clinical heart failure with preserved ejection fractionK Savvatis¹; J Yang²; M Kasner³; S Van Linthout¹; P Fan⁴; J Diez⁵; L Yao⁴; CP Chang²; C Tschoepe⁶¹Berlin-Brandenburg Center for Regenerative Therapies, Berlin, Germany; ²Indiana University School of Medicine, Krannert Institute of Cardiology and Division of Cardiology, Department of Medicine, Indianapolis, United States of America; ³Charite - Campus Benjamin Franklin, Cardiology & Pneumology, Centrum 11 (Cardiovascular Medicine), Berlin, Germany; ⁴Gilead Sciences Inc., Foster City, United States of America; ⁵University Clinic of Navarra, Centre for Applied Medical Research, Navarra, Spain; ⁶Charite - Campus Virchow-Klinikum (CVK), Department of Cardiology, Berlin, Germany**Purpose:** Lysyl oxidase-like-2 (LOXL2) promotes cross-linking of fibrillar collagen I and fibrosis. Heart failure with preserved ejection fraction (HFPEF) is characterised by increased myocardial stiffness due to several mechanisms, among others due to increased collagen deposition and cross-linking of collagen fibers in the myocardium. We sought to examine the role of LOXL2 and its inhibition in HFPEF in patients and in an experimental model of cardiac hypertrophy.**Methods:** We investigated 41 HFPEF and control patients. Assessment of diastolic function was performed invasively and by echocardiography. The amount of collagen, collagen cross-linking and LOXL2 were studied in endomyocardial biopsies. Transaortic constriction (TAC) was performed in mice and an anti-LOXL2 antibody was administered 2 weeks after TAC. The amount of fibrosis, collagen cross-linking, LOXL2 and hemodynamic function were studied after 10 weeks. Furthermore, the effects of LOXL2 inhibition by knockdown of the LOXL2 gene were studied on isolated murine cardiac fibroblasts stimulated with TGF- β .**Results:** Patients with HFPEF showed a significantly higher amount of collagen I and total collagen compared to healthy controls. LOXL2-expression was 2.5 times higher in HFPEF patients and was correlated with significantly higher collagen amount and collagen cross-linking compared to controls. Higher LOXL2 levels, total collagen and collagen cross-linking were associated with higher filling pressures and increased left ventricular stiffness.

Mice showed a significant cardiac hypertrophy, increased interstitial fibrosis, collagen cross-linking and LOXL2 amount, as well as progressive diastolic and systolic dysfunction 10 weeks after TAC. Administration of an anti-LOXL2 antibody decreased the degree of cardiac fibrosis and significantly improved hemodynamic function.

Isolated cardiac fibroblasts showed an increased migratory capacity after TGF- β stimulation, which was reduced after LOXL2-knockdown. Furthermore, LOXL2-knockdown significantly inhibited intracellular TGF- β signaling by decreasing downstream mediators of TGF- β .**Conclusions:** Myocardial LOXL2 is increased in clinical and experimental HFPEF and leads to higher myocardial fibrosis, collagen cross-linking and LV-stiffness. Inhibition of LOXL2 ameliorated myocardial fibrosis and LV stiffness by decreasing total collagen amount, collagen cross-linking and activation of cardiac fibroblasts. Inhibition of LOXL2 might be a novel therapeutic target in patients with HFPEF and progressive myocardial fibrosis.

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Proteomic profiling and the risk of heart failureSwedish research council, Swedish heart and lung foundation, Marianne & Marcus Wallenberg foundation M Markus Stenemo¹; T Fall¹; E Ingelsson¹; J Sundstrom¹; L Lind¹; J Arnlov¹¹Uppsala University, Department of Medical Sciences, Uppsala, Sweden**Purpose:** Emerging technologies have made it possible to simultaneously measure a large number of circulating proteins. The utility of this approach to identify novel heart failure biomarkers has not been reported.**Methods:** We explored and validated associations between 92 plasma proteins, assessed by a proximity extension assay (Proseek Multiplex CVD, OLINK Bioscience), and the risk of heart failure in two independent community based cohorts; Uppsala Longitudinal Study of Adult Men (ULSAM; n = 726; median age 78 years; 98 heart failure events during 8 years follow-up), and Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS; women 50%, n = 963; median age, 70 years; 98 heart failure events during 10 years follow-up).**Results:** In ULSAM, 18 proteins were significantly associated with heart failure incidence in age-adjusted cox proportional hazard models after taking into account the multiple testing using a false discovery rate of 5%. The association between 10 of these proteins and heart failure incidence were replicated in PIVUS at nominal p-values (Table). All, but one protein (CCL20) remained independently associated with heart failure, even after adjustment for established heart failure risk factors (p < 0.05 for all).**Conclusion:** Using a state-of-the-art proteomics chip, several novel independent heart failure risk markers were discovered and replicated in 2 independent cohorts. Our data suggest that large scale proteomic analyses is a promising way of discovering new and relevant heart failure risk markers.

Table. Proteins and heart failure risk.

Protein	Protein Full Name	ULSAM Hazard Ratio (95% CI)	PIVUS Hazard Ratio (95% CI)
NTproBNP	N-terminal pro-B-type natriuretic peptide	2.01 (1.59, 2.56)‡	2.35 (1.88, 2.94)‡
GDF-15	Growth/differentiation factor 15	1.51 (1.25, 1.83)‡	1.69 (1.35, 2.1)‡
AM	Adrenomedullin	1.51 (1.22, 1.86)‡	1.51 (1.19, 1.93)‡
FGF-23	Fibroblast growth factor 23	1.5 (1.25, 1.79)‡	1.44 (1.21, 1.72)‡
TIM-1	T cell Ig and mucin 1	1.48 (1.24, 1.75)‡	1.66 (1.32, 2.07)‡
MMP-12	Matrix metalloproteinase-12	1.43 (1.17, 1.74)‡	1.62 (1.31, 2)‡
CCL20	C-C motif chemokine 20	1.34 (1.14, 1.57)‡	1.24 (1.03, 1.5)*
AGRP	Agouti-related protein	1.34 (1.1, 1.63)†	1.4 (1.12, 1.76)†
TRAIL-R2	TNF-related apoptosis-inducing ligand receptor 2	1.33 (1.09, 1.63)†	1.24 (1.14, 1.35)‡
SPON1	Spondin-1	1.33 (1.09, 1.63)†	1.49 (1.17, 1.89)†

‡, p-value < 0.001; †, p-value < 0.01; *, p-value < 0.05

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Impact of non-cardiac comorbidity on mortality and morbidity in a predominantly elderly heart failure population among different heart failure phenotypesA Iorio¹; M Senni²; S Poli³; E Zamboni³; G Barbati¹; G Faganello¹; G Sinagra³; L Tarantini⁴; G Cioffi⁵; A Andrea Di Lenarda¹¹A.S.S. n 1, Cardiovascular Center, Trieste, Italy; ²Ospedale Papa Giovanni XXIII, Cardiovascular Department, Bergamo, Italy; ³Ospedali Riuniti and University of Trieste, Cardiovascular Department, Trieste, Italy; ⁴San Martino Hospital, Belluno, Italy; ⁵Villa Bianca Hospital, Trento, Italy**Background:** Information on comparative prognostic impact of comorbidity across different heart failure (HF) phenotypes has not been widely known.

Objectives: The object of our study was to compare the prevalence and relative impact of a wide range of noncardiac comorbidities and multiparametric risk score (3CHF score) across different HF phenotypes (LVEF \leq 40% - HFpEF, LVEF 41-49% - HFbEF, LVEF \geq 50% - HFpEF).

Methods: From October 2009 to December 2013 we studied all consecutive ambulatory patients with HF whose ejection fraction had been assessed. Clinical variables were derived from the E-data chart for Outpatient Clinic collected in a regional Data Warehouse.

Results: A total of 2424 patients (mean age 78 \pm 8, 57% men) were included. Of these 1457 (60%) had HFpEF, 358 (15%) HFbEF, 597 (25%) HFrEF. The high mean age and comorbidity rates (mean 3.2 \pm 2.5; 54% patients with \geq 3 non cardiac comorbidities) ran similarly across different HF phenotype, except for renal disease, which was more frequent in HFrEF group, and obesity which was more frequent in HFpEF group. At a follow-up of 28 \pm 14 months, 502 (21%) patients died. Of these 168 (28%) had HFrEF, 60 (17%) had HFbEF, and 273 (19%) had HFpEF ($p < 0.001$). The increasing number of noncardiac comorbidities per patient was associated with higher rates of mortality (HR 1.4 [IC 1.2-1.5]; $p = 0.001$), HF hospitalization (HR 1.5 [IC 1.3-1.7]; $p < 0.001$) and all-cause hospitalization (HR 1.5 [IC 1.3-1.6]; $p < 0.001$). Univariable Cox analysis, including interaction with HF phenotype, revealed a similar impact of noncardiac comorbidities on mortality across HF phenotypes, except for diabetes mellitus which contributed to a higher hazard of mortality in HFrEF vs HFpEF (HR 1.8 [IC 1.2-3.3]; $p = 0.05$ for interaction). In addition to this, at ROC curve, multiparametric 3 C-HF score showed similar prognostic accuracy for one year mortality among different HF phenotype (AUC 0.73-HFrEF, AUC 0.76-HFbEF, AUC 0.72-HFpEF; $p = 0.06$).

Conclusion: In an elderly real-world HF population there was a high comorbidity burden that contributed significantly to high rates of mortality and morbidity. However, individually, most comorbidities had similar prognostic impact on mortality across all HF phenotypes. Multiparametric 3 CHF score showed high prognostic accuracy, similar in all HF phenotypes. These observations may suggest that, in the setting of elderly HF patients, the management of comorbidities could have a crucial role on prognosis irrespective of HF phenotype.

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Prognostic relevance of gene-environment interactions in dilated cardiomyopathy patients: applying the MOGES classification

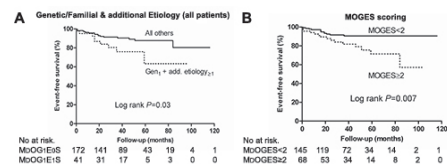
M R Mark Hazebroek¹; S Moors¹; R Dennert¹; A Van Den Wijngaard²; I Krapels²; M Hoos¹; J J Merken¹; H Crijns¹; H P Brunner-La Rocca¹; S Heymans¹
¹Maastricht University Medical Center, Department of Cardiology, Maastricht, Netherlands; ²Maastricht University Medical Centre (MUMC), Clinical Genetics, Maastricht, Netherlands

Purpose: To investigate the applicability and prognostic relevance of the newly proposed MOGES classification - (M)orphofunctional; (O)rgan involvement; (G)enetic or familial; (E)tiology; (S)tage - in dilated cardiomyopathy (DCM) patients. **Methods:** DCM patients were enrolled within the Maastricht Cardiomyopathy Registry. We excluded patients with ischemic, valvular, hypertensive and congenital heart disease. All patients underwent complete diagnostic work-up, including genetic evaluation and endomyocardial biopsy. Long-term outcome used a combined endpoint of life-threatening arrhythmia, heart transplantation, and death. Left ventricular reversed remodeling (LVRR) at 12 months was assessed.

Results: 213 consecutive DCM patients were included, with organ involvement in 35 (16%) and genetic/familial DCM in 70 (33%) patients, including 16 (8%) with a pathogenic mutation. At least 1 etiology was found in 155 (73%) patients, of whom 48 (23%) had more than 1 possible etiology. LVRR was more common in non-genetic/familial than with genetic/familial DCM (40% vs 25%; $p = 0.04$). After a median follow-up of 47 [30-67] months, organ involvement and higher NYHA-class were independent predictors of adverse outcome ($P = 0.010$ and $P = 0.044$, resp). Genetic/familial DCM per se was of no prognostic significance, but when accompanied with additional etiological-environmental factor(s) i.e. significant viral load, immune-mediated, rhythm disturbances and/or toxic triggers, worse outcome was

revealed ($P = 0.010$; Figure 1A). Higher presence of MOGES attributes showed an adverse outcome ($P = 0.007$; Figure 1B).

Conclusion: All attributes in the MOGES - organ involvement, genetic/familial, etiology, stage - have independent prognostic value, whereas presence of ≥ 2 attributes was the strongest predictor of adverse outcome.



Event-free survival curves for DCM pts

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Biomarkers activity and the effect of NT-proBNP guided therapy in high risk patients with chronic heart failure after acute decompensation

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¹Russian Cardiology Research and Production Complex, Moscow, Russian Federation

Purpose: to evaluate the change of the biomarkers concentration in the group of heart failure (HF) therapy guided by NT-proBNP vs standard treatment of CHF patients (pts) at high risk after acute decompensation.

Methods: In the prospective single-center trial we included 105 hospitalized pts with ADHF III-IV FC NYHA and LV systolic dysfunction due to coronary artery disease and dilated cardiomyopathy. 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 (group 1) and standard HF therapy (group 2). Pts in both groups didn't differ by the main clinical characteristics. At discharge, NT-proBNP concentration was 3651 (2191,5; 6613,0) pg/ml in group 1 and 2862,0 (2015,0;4761,50) pg/ml in group 2, $p = 0,488$. Blood sampling to determine the biomarkers concentrations (NT-proBNP, sST2, copeptin, galektin-3, hs Troponin T) were collected at discharge from the hospital, and 3 and 6 months after. Filling pressure was assessed by E/E'.

Results: At the end of the study all pts in groups 1 and 2 have been treated by recommended combination of iACE/ARB+beta-blocker+MRA (100%), but the mean doses at the 6 months of treatment were significantly higher in NT-proBNP-guided group, $p < 0.05$. After 6 months of follow-up, in group 1 median NT-proBNP concentration significantly decreased to 1585,5 (976,5;2612,5) pg/ml ($\Delta\% = -53,1\%$), whereas in group 2 to 2450,0 (2028,0; 3328,0)pg/ml ($\Delta\% = -11,1\%$), $p = 0.024$. Median sST2 concentration significantly decreased from 38,4 (23,4;60,6) ng/ml to 22,9 (12,7;30,4) ng/ml in group 1 ($\Delta\% = -37,1\%$) and from 39,7 (24,9; 50,9) ng/ml to 30,9 (30,2;47,3) ng/ml in group 2 ($\Delta\% = -10,4\%$), $p = 0,0001$. Median copeptin concentration reduced from 34,6 (18,9; 28,4) pmol/l to 23,5 (17,2; 28,4) pmol/l in group 1 ($\Delta\% = -29,9\%$) and from 34,3 (23,9; 42,4) pmol/l to 32,1 (24,8; 38,9) pmol/l in group 2 ($\Delta\% = -3,4\%$), $p < 0,001$. Concentration of Gal-3 significantly decreased only in group 1 ($\Delta\% = -29,9\%$), $p = 0,0001$; in group 2 it was non significantly ($\Delta\% = -4,6\%$), $p = 0,099$. Furthermore, a significant decrease of hs Troponin T revealed only in group 1 ($\Delta\% = -26,5\%$, $p = 0,003$). In group 2 $\Delta\%$ hs Troponin T = $-0,4\%$, $p = 0,959$. $\Delta\%$ NT-proBNP, $\Delta\%$ sST2 and $\Delta\%$ copeptin closely and significantly correlated with $\Delta\%$ E/E' (relatively $r = 0,67$; $r = 0,63$ and $r = 0,7$, $p < 0.01$ for all).

Conclusion: In NT-proBNP-guided therapy group found more significant reduction of concentrations of biomarkers, especially sST2 and copeptin compared with standard HF therapy and change of these biomarkers were closely associated with the filling pressure decrease.

Moderated Poster Session 4 – Clinical management of chronic heart failure

Sunday 24 May 2015 15:45–16:30

Location: Poster Area

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Effect of the angiotensin receptor neprilysin inhibitor LCZ696 compared with enalapril according to age in PARADIGM-HF

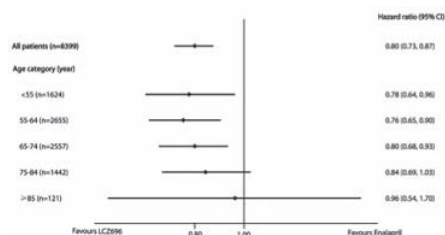
Novartis Pharmaceuticals J V McMurray¹; P S Jhund¹; M Fu²; T Katova³; J L Rouleau⁴; SD Solomon⁵; K Swedberg⁶; M Zile⁷; M Salko⁸; M Packer⁹
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Background: The average age of heart failure (HF) patients in international clinical trials is usually younger than in Western Europe/North America because patients in other geographical regions develop HF at an earlier age. Trial exclusion criteria based on co-morbidity and other factors also lead to inclusion of fewer elderly patients. Older patients may also be more intolerant of drugs used to treat HF. It is therefore important to understand the effect of new therapies across the spectrum of age.

Methods: Patients in NYHA class II-IV, LVEF $\leq 40\%$ and a mildly elevated BNP/NT proBNP concentration were enrolled in a run-in period of treatment with enalapril 10 mg bid followed by LCZ696 100 mg bid, increasing to 200 mg bid. Consenting patients tolerating both treatments and fulfilling pre-specified safety criteria (systolic BP ≥ 95 mmHg, eGFR ≥ 30 ml/min/1.73m² and no decrease $>35\%$ from baseline, serum potassium <5.5 mmol/l) were randomized to enalapril 10 mg bid or LCZ696 200 mg bid. We examined the effect of study-therapy according to age category at randomization.

Results: 8399 patients aged 18-96 yrs were randomized. The effect of LCZ696, compared with enalapril, on the primary outcome of cardiovascular (CV) death or HF hospitalization (HFH) is shown in the Figure. Overall, LCZ696 reduced the primary composite by 20% (HR 0.80, 95% CI 0.73-0.87; $p=0.0000004$) and this benefit over enalapril was consistent across the age-range studied (treatment \times age interaction $p=0.94$). Similar findings were seen for the components of the composite and all-cause mortality. Adverse events increased with both study drugs as age increased but were not common and rarely led to study-drug discontinuation.

Conclusion: LCZ696 had a favourable benefit/risk profile compared with enalapril over a wide age-spectrum.



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Prognostic role of a combined strategy BNP-six-minute walking test in risk stratification of patients with chronic heart failure: preliminary data from an italian policentric study

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A reliable risk assessment in patients (pts) with chronic heart failure (CHF) is a difficult task. Daily practice is mainly based on clinical evaluation but this strategy is often misleading and does not allow accurate prognostic stratification. On the other hand the combination of simple instrumental and laboratory parameters, widely available and low-cost, could sharpen the simplistic clinical examination and guide on the right path the follow-up.

Aims: We sought to evaluate the prognostic ability of a strategy which, on top of routine laboratory test and echocardiography, involves the association of the BNP to the six-minute - walking test (6MWT).

Patients and Methods: We prospectively followed-up 616 stable CHF outpatients with both preserved and reduced left ventricular ejection fraction (EF) by using a thorough clinical, laboratory and instrumental evaluation, including the 6MWT and the BNP. The primary end-point was death from any cause.

Results: Mean age was 70 \pm 11 years (76% aged > 65), 33% were females, 35% had ischemic heart disease, 18% were in NYHA class III, and 70% were on beta-blockers. Median EF was 45 \pm 11% (37% with EF $>50\%$), median BNP was 90 pg/ml, (interquartile range 25-130), and the mean distance covered during the 6MWT (m) was 314 \pm 102 m. During a 60 months follow - up 76 pts died (12% of the population). Prognosis was independent from EF. Accurate risk stratification was possible by BNP cut off values and by m covered at 6MWT extrapolated by ROC curves (330 pg/ml and 323 m, respectively) and by means of survival Kaplan-Meier curves. 6MWT divided survivors in two groups: 64% in the group who walked <323 m and 87% in that who performed >323 m (Chi-square log rank 24.4, $p < 0.0001$). By combining BNP and 6MWT survivors were divided into four groups: 31% BNP >330 pg/ml and <323 m, 68% in BNP >330 pg/ml and >323 m, 82% BNP <330 pg/ml and <323 m, 92% BNP <330 pg/ml and >323 m (Chi-square log rank 113, $p < 0.0001$).

Conclusions: High BNP levels (>330 pg/ml) linked to a reduced exercise capacity during 6MWT (<323 m) depicted a high risk CHF population. The combined strategy BNP- 6MWT is feasible, reliable and low-cost, outstanding features in our updated society. Moreover, as mortality predictor, it retains a higher value compared to clinical evaluation alone, independent from EF.

Our results highlight the opinion that the 6MWT is a first - line test and an excellent and tool for ongoing monitoring risk stratification of a population of elderly CHF pts.

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General practitioners' judgment of chronic heart failure in the oldest old. Insights from the BELFRAIL study

theBELFRAIL study was supported by an unconditional grant of the Fondation Louvain. GVP is a fellow of the research foundation flanders (FWO). M Smeets¹; J Degryse²; B Aertgeerts¹; S Janssens³; W Adriaensen¹; C Mathei¹; G Van Pottelbergh¹; P Wallemacq⁴; JL Van Overschelde⁵; B Vaes¹

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Purpose: To investigate the relationship between general practitioners' (GPs) judgment of chronic heart failure (CHF) and objective cardiac abnormalities and to study their respective prognostic value for 5-year mortality in patients aged 80 and older.

Methods and Results: This research protocol was embedded within the prospective, population-based BELFRAIL study in Belgium. At baseline, 525 patients (mean age 85 ± 3.7 years, 37% men) were clinically assessed by their GPs, had NT-proBNP levels determined and received a detailed echocardiography at home. GPs were asked to judge the presence of CHF and to list their arguments pro or contra. Cause-specific mortality was collected until 5.2 ± 0.25 years after baseline. GPs suspected CHF in 154 patients (29%). Little overlap was found between registered signs and symptoms, and the actual arguments used pro or contra CHF. The prevalence of objective cardiac abnormalities was 35% ($n = 183$). GPs' judgment predicted objective cardiac abnormalities inaccurately (sensitivity 45% (95% CI 38-53), specificity 79% (95% CI 75-83)). Both objective cardiac abnormalities and GPs' diagnoses of CHF were good predictors of 5-year mortality (HR 2.1 (95% CI 1.6-2.7) vs 1.7 (95% CI 1.3-2.3), respectively). The net reclassification improvement (NRI) for cardiovascular mortality showed a positive trend for objective cardiac abnormalities with respect to GPs' judgment (10% (95% CI 8-13%), P value 0.13).

Conclusions: GPs' judgment and objective cardiac abnormalities correlated poorly. Nevertheless, both were successful in identifying patients at high risk of death. Furthermore, objective cardiac abnormalities showed an improvement of 10% for cardiovascular mortality risk classification with respect to GPs' judgment.

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Sleep-disordered breathing are associated with impaired cardiac sympathetic innervation and incrementally predict prognosis in heart failure patients

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Background: Unfavorable effects of sleep-disordered breathing (SDB) in heart failure (HF) are mediated by impaired sympathetic activity. However, few data are available on SDB and cardiac adrenergic impairment.

Objectives: to assess the relationship between SDB, cardiac sympathetic innervation and prognosis in HF patients.

Methods: Ninety-four patients (66.1 ± 9.8 years) with systolic HF (median left ventricular ejection fraction $32 \pm 7\%$) underwent nocturnal cardiorespiratory monitoring to assess presence and type of SDB by Apnea/Hypopnea Index (AHI), and 123I-MIBG myocardial scintigraphy to calculate heart-to-mediastinum (H/M) ratios and 123I-MIBG washout rate. Patients were prospectively followed for 29 ± 18 months for the combined endpoint of cardiovascular death and HF hospitalization.

Results: Of 94 patients, 72 (77%) showed SDB and, compared to non-SDB, significantly reduced early (1.67 ± 0.22 vs 1.77 ± 0.13 ; $p = 0.019$) and late H/M ratio (1.50 ± 0.22 vs 1.61 ± 0.23 ; $p = 0.038$). At multiple linear regression analysis, early and late H/M remained independent predictors of AHI ($\beta = -0.749$; $p < 0.001$; $\beta = -0.830$; $p = 0.001$, respectively). Similarly, AHI was the only predictor of early ($\beta = -0.643$; $p < 0.001$) and late ($\beta = -0.453$; $p < 0.002$) H/M ratio. Patients with AHI above the median showed significantly higher event rates and worse survival compared to patients with AHI below the median (35% vs 9%, respectively; $p = 0.003$). Similarly, patients with moderate-severe disorder showed significantly increased incidence of the combined endpoint and worse survival compared to patients with mild or no disorder (35% vs 11.7%; $p = 0.007$). Adding SDB variables to the already known prognostic role of 123I-MIBG imaging, we observed an incremental prognostic discrimination with the worst survival in patients with both SDB and H/M impairment.

Conclusions: Patients with systolic HF and SDB show more impaired cardiac adrenergic innervation and more adverse prognosis compared to HF patients without SDB.

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Initial clinical results of the REDUCE LAP-HF TRIAL (REDUCE elevated left atrial pressure in patients with heart failure trial)

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Introduction: Therapeutic options for Heart Failure with preserved ejection fraction (HFpEF) are limited. Increased left atrial pressure (LAP) is a key contributor to the symptoms, in particular during physical activity. A novel shunt device intended to lower LAP is being evaluated. Patient demographics and initial results will be presented.

Objective: Evaluation of the safety and performance of the Inter Atrial Shunt Device System II, designed to directly reduce elevated LAP in patients with HFpEF.

Methods: The REDUCE LAP-HF Trial is a prospective, non-randomized, open label trial to evaluate a novel device that creates a small permanent shunt at the level of the atria. Up to 100 patients with ejection fraction (EF) $\geq 40\%$ and New York Heart Association (NYHA) class III or IV HF with a pulmonary capillary wedge pressure (PCWP) ≥ 15 mmHg (rest) or ≥ 25 mmHg (during supine bike exercise), resting CVP < 14 mmHg, and PVR < 4 Woods Units will be enrolled and implanted with an IASD System II. Primary outcome measures for safety are: peri-procedural and 6 months major adverse cardiac and cerebrovascular events (MACCE) and systemic embolic events. Primary outcome measures for device performance include: success of device implantation, reduction of PCWP at rest and during exercise, and demonstration of left to right flow through the device. Key secondary endpoints include exercise tolerance, quality of life, and the incidence of heart failure hospitalization.

Results: Patient demographics, and initial clinical results of the first 50 patients implanted will be reported.

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Monitoring of pulmonary congestion in chronic heart failure patients with multiple re-hospitalizations for acute decompensation

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Prediction and prevention of re-hospitalizations for acute heart failure (AHF) in patients with congestive heart failure (CHF) is an unmet need. In this study we used a new type of impedance technique based on calculated lung impedance (LI) rather than on the traditionally measured transthoracic impedance for monitoring and prediction of re-hospitalization for AHF.

Aim: To determine the dynamics of pulmonary congestion at admission for AHF during long-term follow-up in CHF patients.

Method and Results: Since the new technique is 25 times more sensitive than the traditional one it enables the measurement of small amounts of lung fluid at the early asymptomatic stage of interstitial edema. Decreasing LI reflects increasing lung fluid. Signs, LI and ratio of the instantaneous LI to the calculated baseline LI (Δ LIR) were monitored monthly in the outpatient clinic in 250 CHF patients (68 ± 11 years-old, male- 80%, LVEF- $28 \pm 7\%$) at NYHA II/III/IV (107/100/43). Initial NT-proBNP level was 3594 ± 5114 pg/ml. Duration of follow up was 36 ± 22 months (6940 visits). Of 222 study patients, 179 were admitted for AHF, 31 for non-AHF causes only and 40 were not hospitalized at all during the follow up period. Of the 179 CHF patients who were admitted 548 times for AHF, 79 were followed for more than 4 years, with at least one admission each year of follow up (overall 405 re-hospitalizations). Mean Δ LIR values at admission for AHF during the first to fourth year of follow up were $-32.74 \pm 5.7\%$, $-38.3 \pm 6.2\%$, $-43.6 \pm 5.8\%$ and $-48.1 \pm 6.3\%$, respectively ($p < 0.001$).

Conclusion: our findings support the notion that as heart failure persists and follow up increases, patients adapt better to higher degrees of pulmonary congestion and only a pronounced exacerbation of lung fluid accumulation and congestion will prompt hospitalization for AHF.

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Are there any differences between diabetics and non diabetics in chronic heart failure?

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Objective: The objectives of our study are to show prevalence of diabetics in heart failure population and to compare epidemiological profiles of diabetics and non diabetics.

Material and Methods: We included 1613 patients, diabetics and non diabetics, admitted in united of heart failure in our center of Cardiology from May 2006 to September 2014. All patients were evaluated clinically with monitoring of blood pressure (BP), 6 min walk test and electrocardiogram. Two-dimensional echocardiography and laboratory tests were performed in all patients. Coronarography was realised at 298 patients.

The data are presented as numbers, percentages, and medians with interquartile range. The distribution of variables was compared between diabetics and non diabetics by chi2 test with confidence intervals.

Results: 1613 patients were studied, the median age was 65 years (42- 94 years) and 63% were men. 519 (32%) had diabetes. Diabetics patients were younger than non diabetics (56 years and 66 years). Stroke (23% and 18%) and myocardial infarction (37% and 27%) were more frequent and renal function was more affected in diabetics group. Atrial fibrillation was lower in diabetics group (7% and 17%). Ejection fraction of left ventricle was higher (48,5% and 35%) in diabetics group, but 51% of them had diastolic dysfunction with higher filling pressures. There weren't differences in coronarography. Concerning treatment, 34% of diabetics arrive at maximal

beta-blockers treatment (more than non diabetics 16%). Frequency of decompensation was more important in diabetics group.

Conclusions: So, frequency of diabetes in Moroccan heart failure population is higher. Significant differences exists in comorbidities, ventricular function, maximal beta-blockers treatment and frequency of decompensation between diabetics and non diabetics with chronic heart failure. These findings emphasize the importance of individualised management and need for more comprehensive recruitment of diabetics in clinical trials.

Clinical Case Corner 3 – Strategies in end-stage heart failure

Sunday 24 May 2015 15:45–16:30

Location: Poster Area

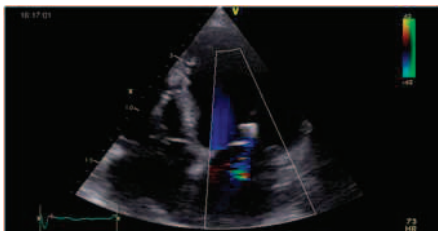
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MitraClip and cardiac resynchronization therapy: an advantageous combination to reduce mitral regurgitation in patients with decompensated heart failure

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Introduction: Moderate to severe functional mitral regurgitation (FMR) is common in heart failure (HF) patients and there is evidence that cardiac resynchronization therapy (CRT) not only decreases it but contributes to reverse left ventricular remodelling with improvement of systolic and diastolic function. However, FMR has been reported to persist in about 20% to 25% of CRT patients. Treatment with MitraClip has been proposed as an additional therapeutic option in selected patients with FMR. We report the case of a 76-year-old man, affected by refractory congestive HF and non responder to the lonely CRT, who underwent a combined treatment with MitraClip and CRT upgrading. Description of the problem: A 76-year-old man, who had had, 14 years before, an acute coronary syndrome with left bundle branch block and preserved left ventricular function treated with coronary artery bypass graft, was admitted for recurrent, refractory congestive HF. Echocardiography showed a left ventricle dilation with an Ejection Fraction (EF) of 30% and a moderate FMR. Cardiac catheterization demonstrated a good function of coronary artery bypass grafts. Patient underwent to CRT and Implantable Cardioverter-Defibrillator (ICD) implantation. Despite optimal pharmacological and device therapy, during the consecutive year, patient remained highly symptomatic (NYHA class IV) with several episodes of decompensated acute HF. Echocardiography showed a progressive remodeling and worsening of FMR that became severe. Since Euroscore II was 20%, it was decided to proceed with transcatheter implantation of the MitraClip system, getting a reduction of the FMR from severe to mild, an increase of EF to 40% and a significant functional improvement up to NYHA class II. At 3 months follow-up, the echo showed again a worsening of FMR from mild to moderate, so a new upgrading of CRT was made, setting the interventricular (VV) delay between left and right ventricular activation on -50 milliseconds (ms; Figure 1). At 1, 6 and 12 months follow-up, FMR was stable on mild degree and patient didn't present further episodes of decompensated acute HF. Problems and discussion: In patients with HF, FMR is consequence of the mitral annulus dilation, the increased distance between the papillary muscles and their dyssynchrony with the adjacent myocardium. In our case the association of MitraClip, that favours reverse remodelling, and CRT, with an opportune synchronization between lateral and septal walls of the left ventricular chamber, can lead to a substantial reduction of FMR severity. **Conclusions:** Our case demonstrates that a combined, echo-guided treatment with MitraClip and CRT with an appropriate timing and upgrading can improve FMR, EF and functional class in patients with clinically significant FMR who are non responders to the lonely CRT.



FMR during pacing at VV delay -50 ms

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GTN to increase pulsatility in a patient with VA ECMO for refractory cardiogenic shock

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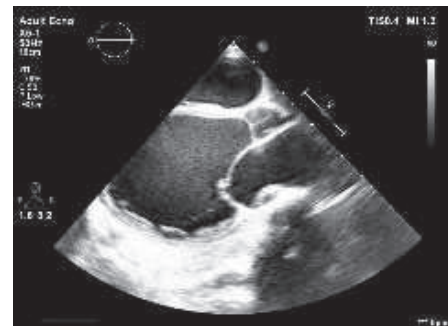
We present a case of a 22 years old man who was admitted to our tertiary referral centre for consideration of Biventricular Ventricular Assist Device (BIVAD) insertion vs. transplant assessment.

He had no significant medical history, and was initially admitted in August with signs and symptoms of congestive heart failure. A DCM (dilated cardiomyopathy) of uncertain cause was diagnosed. Cardiac MRI (Magnetic Resonance Imaging) did not show any late gadolinium enhancement; left ventricular ejection fraction (LV EF) 12%. He was stabilised with optimal medical therapy, and discharged home weeks later.

The patient was readmitted 3 weeks later with worsening heart failure, acute kidney injury, and presumed-hypoxic hepatitis. Despite maximal medical therapy and IABP (Intra Aortic Balloon Pump) the patient remained in profound cardiogenic shock. Peripheral VA ECMO (Veno Arterial Extracorporeal Membrane Oxygenation) was inserted and the patient was transferred to our centre.

Soon after arrival patient lost pulsatility, had a drop in ETCO₂ (End Tidal CO₂) and a rising CVP (Central Venous Pressure). Bedside transthoracic echocardiography TTE (see images) confirmed absence of LV ejection and the aortic valve was closed. LV dilatation had increased, was ballooning and filled with spontaneous echocontrast. Patient who lost pulsatility and responded initially to inotropic support, lost pulsatility again. Because it was thought that a reduction in afterload could facilitate LV ejection, we decided to bolus GTN. This had an immediate response of increased MAP (Mean Arterial Pressure), reduced CVP, increased ETCO₂, and evidence of restoration of LV ejection.

This case reflects the complexity of the hemodynamic management of patients undergoing peripheral ECMO. In some cases reducing the afterload would be the best strategy to achieve LV ejection.



Parasternal long axis. AV closed.

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Ventricular remodeling after cardiac resynchronization therapy in a heart transplant recipient

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We report the successful ventricular remodelling following cardiac resynchronization therapy (CRT) in a 70-year-old woman, 6 years after heart transplantation (HT) for dilated cardiomyopathy.

The patient developed complete atrioventricular block in the post-operative period, not recovered after 4 weeks of epicardial pacing, so a single chamber ventricular pacemaker was implanted (VVI mode).

The initial clinical course was favourable, with no rejection episodes. The coronariography performed one year after HT showed a significant stenosis due to cardiac allograft vasculopathy (CAV) in the left anterior descending artery, so a drug eluting stent was implanted. Left ventricular ejection fraction (LVEF) was normal.

Six years later, the patient was admitted with heart failure signs and symptoms, with severely reduced LVEF. She was in ventricular pacemaker rhythm (QRS 180 msec). Left and right catheterizations were performed showing adequate stent patency, with no CAV progression, and elevated cardiac pressures and low cardiac output. Also, an endomyocardial biopsy was performed, and both cellular and humoral rejections were discarded.

The situation did not improve despite optimal heart failure therapy, and considering long right ventricular pacing ventricular dysfunction, an upgrade to CRT was performed.

The patient could be discharged and a significant improvement in functional status was confirmed on follow-up (NYHA I). QRS duration was shortened by 40 msec. An echocardiography performed three months later showed reduction in left ventricular telediastolic diameter (from 58 mm to 51 mm after CRT) as well as recovery of LVEF (from 28% to 50% after CRT).

This case emphasizes the possible role for CRT in heart transplant patients with LVEF dysfunction and heart failure due to long right ventricular pacing. In our patient, biventricular pacing contributed to improve left ventricular diameters and ejection fraction, thus contributing to improvement in functional class. Consequently, CRT should be considered in case of heart transplant recipients with accepted indications for this therapy.

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Escalation of extracorporeal life support as a bridge to lung transplantation in end-stage lung disease

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A 45 years old man with end-stage lung disease related to cystic fibrosis deteriorating over a year was assessed and placed on waiting list for LTx. Due to continuous deterioration and poor gas exchange, he was started with non-invasive ventilation but in view of type 2 respiratory failure, VV ECMO was introduced with bicaval dual lumen catheter inserted via right internal jugular vein.

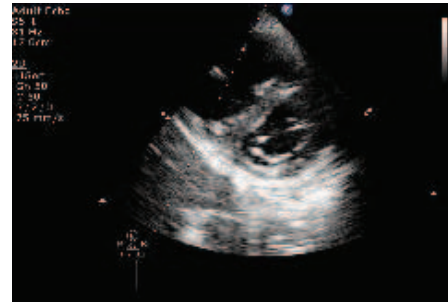
The VV ECMO improved the gas exchange and the arterial oxygen saturation was maintained around 90%. However, due to multiple episodes of desaturation a second oxygenator was introduced in parallel into the VV circuit on 10th day which improved the blood saturation.

On 13th day due to deterioration in gas exchange on VV ECMO and continuous non-invasive ventilation, patient was intubated and started on invasive ventilation. Moreover, next day systemic pressure started falling despite of high vasopressor support and trans-oesophageal echocardiography showed severely dilated right ventricle in conjunction with poor gas exchange and increasing metabolic acidosis. With the diagnosis of worsening cor pulmonale, the VV ECMO was converted to VVA configuration to off-load right ventricle, improve systemic pressure and saturation. It was achieved by inserting a 19F arterial cannula into the left common femoral artery and dividing the outflow pipe into this femoral arterial cannula and outflow arm of cannula. A 12F cannula was introduced into the left femoral artery for distal limb perfusion and received blood from an offshoot of the pipe leading to the main femoral artery cannula.

The right ventricle was normalized immediately on TOE, the systemic pressures and saturation were improved and the acidosis was cleared over 24 hours. While waiting for a suitable donor, he was stabilized on VVA ECMO.

On 21st day of admission, as suitable donor was found and bilateral lung transplantation was performed. The post-operative course was smooth, however requiring tracheostomy and slow respiratory wean. He also suffered ischemia of left foot due to ECMO cannula related thrombosis in the femoral artery, but did not require amputation.

Patient made good recovery and was discharged home in a month's time.



IVS flattening and RV dilatation

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Direct left atrial pressure monitoring in patient with total artificial heart

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Introduction: The Millar Mikro-Cath Pressure Catheter is a device for direct left atrial pressure (LAP) monitoring. Syncardia total artificial heart (TAH) as bridge-to-transplant therapy offers benefits to patients with biventricular failure as it avoids complications (i.e., right ventricular failure, arrhythmias, regurgitations, low blood flows). We present the unique case of direct LAP monitoring in patient that underwent TAH placement in order to better optimize patients' early hemodynamics and device operating parameters. Case report description: The patient is 65 years old man, presented at our facility with refractory cardiogenic shock and intra-aortic balloon pump placed due to post-myocardial infarction ventricular septal defect (VSD). At first percutaneous ventricular device was inserted for percutaneous VSD closure that failed. Then, for severe biventricular failure (INTERMACS profile 1) he underwent urgent Syncardia TAH implantation. During the same procedure the Millar Mikro-Cath was inserted into the left atrium for postoperative optimization of the left artificial ventricle. The central venous catheter was used to optimize right artificial ventricle operating parameters and patient's hemodynamics. Problems: Optimal intracardiac flows early after TAH placement decrease risks for acute kidney injuries, liver injury and pulmonary congestion. In patients with TAH left atrial pressure can't be assessed by pulmonary capillary wedge pressure.

Answers and discussion: The Millar catheter was left in place for monitoring for 3 days. The LAP ranged from 23 mmHg to 17 mmHg. Hemodynamics of the patient before and after optimizing of TAH operating parameters (POD1) is shown in Table 1. The patient had improvement in renal function and was extubated on postoperative day 2. We observed no complications (thrombosis, bleeding) associated with use of LA catheter and was removed safely with PTT between 50-60 seconds. During their early post-operative stay in ICU due to elevated right and left sided cardiac pressures, left and right sided vacuum (TAH operating parameters) were changed with decrease in left atrial and right heart filling pressures.

Conclusion: Immediate postoperative direct LAP monitoring with the Millar Mikro-Cath device in patient with TAH appears safe and reliable in optimizing patient's early hemodynamics.

LV flow rate (ml/beat)	51	57
RV flow rate (ml/beat)	46	53
LAP (mmHg)	23	17
CVP (mmHg)	17	13
Left drive pressure (mmHg)	200	200
Right drive pressure (mmHg)	90	90
HR (bpm)	138	138
Vacuum	8/10	12/12
MAP (mmHg)	69	73

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Resuscitated sudden death followed by heart transplantation in a young patient due to anomalous origin of left coronary artery

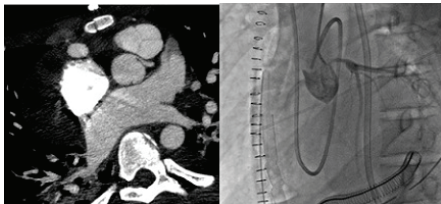
I Toranzo Nieto¹; C Sorto Sanchez¹; L Ruiz Guerrero¹; V Burgos Palacios¹; M Cobo Belaustegui¹; V Exposito Garcia¹; C Castrillo Bustamante¹; M Ruiz Lera¹; A Canteli Alvarez¹; J Zueco Gil¹

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Introduction: Coronary anomalies are an uncommon cause of sudden cardiac death (SCD) and its diagnosis is challenging.

Case report: A 15-year-old male was admitted after out-of-hospital cardiac arrest and cardiopulmonary resuscitation at the end of a soccer match. The patient had a previous history of presyncope after exercise, suggesting neurally mediated origin (normal TTE, EKG and Treadmill Test; Tilt-test positive). At the end of the match he felt dizzy and collapsed. The first cardiac rhythm was extreme bradycardia. Carotid pulse was weak and the patient remind unconscious, thus orotracheal intubation and mechanical ventilation were started. Spontaneous circulation was then achieved. On admission the EKG showed sinus tachycardia, and a TTE showed biventricular dysfunction. Once in the Cardiac Care Unit he developed hypotension unresponsive to inotropes leading to pulseless electrical activity. ACLS maneuvers were initiated unsuccessfully so an intra-aortic balloon pump (IABP) and a peripheral veno-arterial ECMO system were implanted leading to recovery of the spontaneous circulation. In the next hours the support was found to be insufficient so short-term LVAD was implanted. Serial echocardiograms showed not left ventricular recovery and weaning trials were not tolerated due to anterior wall akinesis. Myocardial biopsy showed no evidence of myocarditis. The EKG showed ischemic changes and there was a suspicious image in the short axis view of the aortic valve in the transesophageal echocardiography concerning the origin of the left main artery (LMA). The coronariography showed no lesion but a narrowed LMA origin. Cardiac CT confirmed the existence of an anomalous LMA origin from the right sinus with an interarterial course between the aortic and pulmonary arteries. Finally he was listed to urgent cardiac transplant. After 51 days on support, he underwent orthotopic heart transplantation, but he developed primary graft failure requiring V-A ECMO. After nine days it was possible to withdraw of the ECMO and he was discharged with normal graft function. Pathological anatomy of the explanted heart showed anterior wall myocardial infarction and an anomalous origin of the LMA from the right sinus with an interarterial course.

Discussion: This case emphasizes the importance to consider coronary anomalies in the differential diagnosis of SCD. Not every CAA has the same potential risk to cause SCD. Systematic TTE looking for the coronary arteries origin should be performed. Further studies, should be carried out to assess its origin and course owing to its important prognostic role.



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Successful treatment of a recurrent LVAD-thrombosis using systemic thrombolysis

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¹University of Duisburg-Essen, West German Heart Center, Cardiology, Essen, Germany

Introduction: A 50-year-old male with a history of advanced non-ischemic heart failure was urgently admitted to our hospital due to acute clinical deterioration and symptoms of a low cardiac output state. An intracorporeal continuous-flow left ventricular assist device (LVAD) was implanted as a bridge to transplantation 8 months ago.

Description of the problem, procedures, techniques and equipment used: Mental status and neurological examination on admission were normal and there were no manifestations of respiratory distress. However, the patient exhibited signs of peripheral hypoperfusion. His blood pressure was not measurable, his pulse not palpable and he had cool extremities. There was no dehydration or other identifiable causes of hypovolemia and his skin turgor was normal. The drive-line exit site was free of infection. The ECG revealed a mild sinus tachycardia. The laboratory work-up showed an INR of 1,08, indices of hemolysis, but no markers of infection. The LVAD system controller displayed a critical alarm signal. A subsequent analysis of the device data uncovered abnormally high power (7,3 W) and relatively low flow values, when compared to the patient's baseline values. A bedside echocardiogram was not suggestive of a low-preload condition and revealed no further acute abnormalities.

Questions, problems or possible differential diagnosis: What is the diagnosis/differential diagnosis? Which is the preferred treatment strategy? Which safety issues are we confronted with?

Answers and discussion: The differential diagnosis includes low-preload conditions, e.g., bleeding and severe fluid depletion, sepsis, right ventricular failure and device-thrombosis. In the context of subtherapeutic anticoagulation, mild hemolysis, normovolemia and an abnormally high power reading of the device, an LVAD-thrombosis seemed to be the most likely diagnosis. After initiation of unfractionated heparin infusion, a systemic thrombolysis with alteplase was administered via a peripheral venous catheter. A rapid clinical improvement with decrease of the device parameters (power decreased from 7,3 W to 4,6 W) was observed within hours. There were no neurological adverse events or bleeding complications in the postlytic period. The patient was diagnosed with a recurrent pump-thrombosis 8 days later and underwent a second course of successful uncomplicated thrombolytic treatment with alteplase. He remains free of complications in follow up. Currently, there is no consensus recommendation regarding the management of LVAD-thrombosis. Treatment options include surgical device exchange, urgent transplantation or medical therapy consisting of heparin or other anticoagulants, GP IIb/IIIa inhibitors and fibrinolytics, used alone or in combination. Stroke and intracranial or systemic bleeding are the most feared complications of systemic thrombolysis for LVAD thrombosis. Furthermore, a subsequent surgical device exchange after failure to respond to thrombolytic treatment is accompanied with an increased perioperative risk.

Conclusion/Implications to clinical practice: Strict control of anticoagulation and compliance to therapy is imperative. LVAD-thrombosis constitutes a life-threatening complication which requires immediate treatment. Current management is individualised. A thrombolytic therapy, in the absence of contraindications, seems to provide a safe alternative to invasive procedures. Future studies are needed to identify the patients who would benefit from a medical therapy and the preferred regimen, dosage and duration of administration.

Clinical Case 3 – The great fire: when inflammation hits the heart

Sunday 24 May 2015 16:30–18:00

Location: Agora

730

Tuberculosis myocarditis as an unusual case of acute heart failure

C I Clara Ines Saldarriaga¹; JC Catano¹; G Roncancio¹;

¹Cardiovascular Clinic Santa Maria, University of Antioquia cardiology department, Medellin, Colombia; **Introduction:** Myocardial affectionation by tuberculosis infection is unusual and can be found in 0,2 % of the patients. Most of the cases are diagnosed post - mortem. We present the clinical case of a young woman with pleural tuberculosis who developed and acute heart failure that was caused by tuberculosis myocarditis. Twelve months after treatment, the systolic function has fully recovered.

Case Report: A 34 years old woman was admitted to the hospital because of 3 months of fever, pleuritic chest pain and weight loss. The clinical examination revealed signs of a right pleural effusion that was confirmed by chest X ray (FIGURE 1), the EKG showed a sinus tachycardia (FIGURE 2) . A diagnostic thoracentesis was performed showing a lymphocytic complicated exudate, for this reason a thoracotomy and a pleural biopsy was performed. The histopathology reported findings of pleural tuberculosis. Anti- tuberculosis treatment was started with Isoniazid, rifampicin, Streptomycin and ethambutol (HRZE) but the patient was not compliant with the medications and 6 weeks after she was admitted to the hospital with diagnosis of acute heart failure. The echocardiogram reported a global decrease in contractility, the ejection fraction was 15%, the left ventricle was dilated, with increased left ventricular end-diastolic and end-systolic diameters (FIGURE 3) . An endomyocardial biopsy was performed, the PCR (Nucleic acid amplification technique) for M. tuberculosis confirmed the diagnosis of tuberculosis myocarditis. Resistance to tuberculosis treatment was rule out and the patient was started again on HRSE plus heart failure medications that included beta blockers, ACE inhibitors, spironolactone and diuretics. Twelve months after the treatment was started, the left ventricular function fully recover, the new echocardiogram showed an ejection fraction of 60% with normal diameters (FIGURE 4) and the functional class improved to NYHA I.

description of the Problem: A wide variety of systemic diseases like tuberculosis or sepsis may affect the heart by a number of different mechanisms, including increasing demands on the heart, , affecting the or promoting cardiovascular disease. To identify the cause of the acute heart failure in this patient was an important issue because it will determine the need of an etiological treatment

Questions, Problems and Differential Diagnosis: The differential diagnosis in this patient was a septic cardiomyopathy, a viral myocarditis or a chronic heart failure that was decompensated by a pulmonary infection. In this case the endomyocardial biopsy helps us a lot in the process of ruling out another causes of heart failure.

Answers and Discussion: Tuberculosis myocarditis is a potential reversible cause of acute heart failure. It is unusual but the it can be diagnosed by performing an endomyocardial biopsy or a cardiac MRI, there are few reports of this disease in literature, most of them were diagnosed post mortem. A successful treatment must include the combination of heart failure and anti- tuberculosis medications. **CONCLUSIONS** Tuberculosis myocarditis is and unusual case of acute heart failure that can be fully reversible if the patient gets the right treatment . The diagnosis of this disease represents a clinical challenge but this case illustrates the importance of the endomyocardial biopsy and the use of the Nucleic acid amplification technique for M. tuberculosis in the diagnosis.

731

Diagnostic role of CMR in an unusual case of left ventricular hypertrophy

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¹St Richard's Hospital, Chichester, United Kingdom

We present an unusual cause of severe Left Ventricular Hypertrophy (LVH) and describe the diagnostic importance of Cardiac Magnetic Resonance (CMR).

A 46-year-old lady presented with a 2-day history of exertional central chest pain. This developed into intermittent rest pain associated with dyspnoea, nausea, and diaphoresis. She had no significant past medical history. Cardio-respiratory examination and initial ECG were unremarkable. Subsequent ECGs confirmed dynamic change with T wave inversion in leads II, III, aVF, and V3-V6. Troponin I was elevated at 6.22µg/L (<0.04µg/L) peaking at 11.07µg/L. Chest x-ray was normal.

What is the main differential diagnosis and how would you investigate further?

She was treated with dual antiplatelet therapy and fondaparinux for a presumed acute coronary syndrome. Transthoracic echocardiography revealed severe concentric left ventricular hypertrophy (LVH) with severely impaired systolic function (LVEF <35%). The valves were normal. There was a small pericardial effusion.

At this stage the differential diagnosis included, acute coronary syndrome (with bystander LVH), hypertrophic cardiomyopathy (HCM), acute myocarditis, Anderson-Fabry's disease, and cardiac amyloidosis.

What would be the next diagnostic steps?

Coronary angiography demonstrated normal arteries. To examine the myocardial architecture in more detail CMR (1.5T) was undertaken. This confirmed severe global LVH with maximal septal wall thickness of 21mm, and poor LV function. There was a widespread increase in myocardial T2 signal consistent with oedema. On late Gadolinium imaging there were extensive areas of myocardial enhancement with relative sparing of the basal-mid lateral wall [figure 1]. Over the next few days her symptoms subsided in concert with falling inflammatory markers and troponin. The patient was discharged on a beta-blocker and ACE inhibitor.

What is the diagnosis?

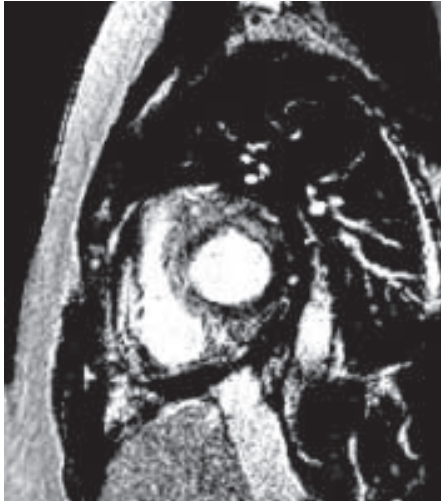
At four months the patient reported minimal exertional breathlessness. This was reflected in her imaging. CMR confirmed a marked improvement in left ventricular function (EF 55%) and complete resolution of LVH (septum 10mm). However, there was evidence of residual myocardial fibrosis with sub-epicardial enhancement involving septal, inferior and apical-anterior walls.

Thus, serial CMR confirmed an acute inflammatory stage with myocardial injury and oedema with subsequent resolution of the inflammation and associated LVH. Good (but incomplete) recovery of LV function was noted with evidence of patchy myocardial scar. The combined clinical and serial CMR findings therefore supported a diagnosis of acute (presumed viral) myocarditis.

Discussion: Acute myocarditis may present in a number of ways but commonly mimics an acute coronary syndrome. Although an uncommon finding, in this case a florid inflammatory response resulted in the appearance of LVH on echocardiography. At this stage a differential diagnosis included infiltrative conditions such as amyloidosis and HCM. CMR was enlightening, demonstrating typical appearances of acute and convalescent myocarditis.

Conclusions and implications for clinical practice

1. Acute myocarditis should be considered in patients presenting with symptoms and evidence of myocardial necrosis in the absence of coronary disease
2. Severe left ventricular hypertrophy is an uncommon but recognised manifestation of acute severe myocarditis
3. CMR is a powerful tool in the differentiation of a variety of conditions that can result in left ventricular hypertrophy.



732

Left ventricular dysfunction associated with ulcerative colitis treated with mesalazine: a case report

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Mesalazine is a common treatment for active ulcerative colitis and hypersensitive reactions to this product have been reported. The exact mechanism by which mesalazine might prompt myocardial inflammation is not known. We describe a case of mesalazine induced left ventricular dysfunction in ulcerative colitis.

We present the case of a 67 year-old female with ulcerative colitis treated with mesalazine, who presented exertional chest pain and dyspnea. Evaluation revealed a global hypokinesia with a severe left ventricular dysfunction. The patient had a medical history of hypertension with an echocardiogram made two years before with normal left ventricle. As an adverse reaction associated to treatment with mesalazine was suspected, the drug was stopped. Six months later, the echocardiogram and the cardiac magnetic resonance, showed a significant improvement of left ventricular function (EF 45-50%) and normalization of the left ventricle size. Cardiac disease can be associated with inflammatory bowel disease as an extraintestinal manifestation or as a consequence of drug-induced side effects. A review of the literature revealed some cases of cardiac toxicity with the use of mesalazine. In all of these cases, there had been, as in the present case, a clear improvement following the suspension of the medication. Although infrequent, cardiac involvement must be considered in patients with inflammatory bowel disease treated with mesalazine that show cardiac symptoms.

733

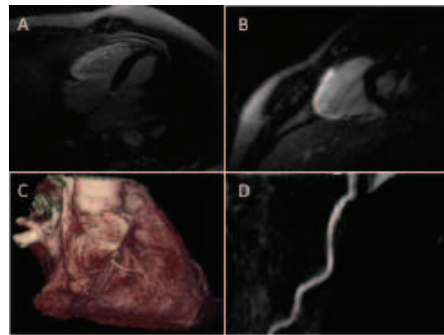
A curious case of chest pain

J De Juan Baguda¹; C Casanova Rodriguez¹; D Iglesias Del Valle¹; M Sarrion Caraballo¹; R Cano Carrizal¹; A Garcia Garcia¹; A Martin Penato¹; R Cadenas Chamorro¹; E Prieto Moriche¹; I Plaza Perez¹

¹University Hospital Infanta Sofia, Cardiology, Madrid, Spain

We present a 31 year-old-man, smoker, with no other personal or familiar background, that was admitted to our hospital due to chest pain. The physical examination was normal, the electrocardiogram showed a sinus rhythm with incomplete right bundle branch block and an isolated negative T wave in III but the laboratory test presented an elevated troponin I and C-reactive protein. During his stay at hospital the T waves of the right leads on the ECG were negative and the transthoracic echocardiogram showed a normal left ventricle with preserved ejection fraction and no regional abnormalities but the right ventricle was slightly dilated with a mild dysfunction. We were dubious about if the patient had an Acute Coronary Syndrome or a Myocarditis. Trying to resolve that diagnostic challenge we performed a Magnetic Resonance that revealed a normal left ventricle. The right ventricle was not dilated but showed an akinesia of the free and inferior walls and the ejection fraction was depressed (23%). On T2 weighted images there weren't suggestive images of edema but the late gadolinium enhancement was present in

all right ventricle (Images A and B). The perfusion images were normal and a mild pericardial effusion was present. Finally we did a Coronary Computed Tomography that reported no coronary stenosis with a well-visualized acute marginal branch (Images C and D), confirming our suspicion of isolated Right Ventricle Myocarditis. We didn't found any infectious cause of the myocarditis. The patient was treated with enalapril and bisoprolol due to the right ventricle dysfunction with good tolerance and was discharged from hospital. Two years later the patient is still asymptomatic and the right ventricle ejection fraction has improved to 40%. This case is a rare form of presentation of a common symptom, chest pain. To the best of our knowledge, there are only a few cases of isolated Right Ventricle Myocarditis in the literature, mostly described by necropsy. So this is probably the first one diagnosed with the novel image techniques, Magnetic Resonance and Coronary Computed Tomography.



734

Acute heart failure in meningococcal disease due to myocarditis and sepsis

L Celia Petersen¹; TR Reichert¹; CVE Drebes¹; JS Jardim¹; SVG Wanderley¹; M Crecenio¹; M Wiehe¹; LC Bodanese¹; JCVG Guaragna¹; LC Danzmann¹

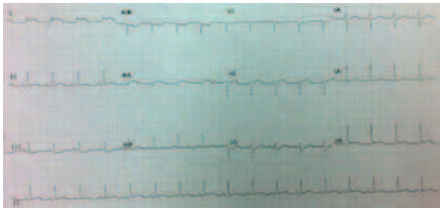
¹Hospital Sao Lucas, Cardiology, Porto Alegre, Brazil

Introduction: Acute heart failure presents with the challenge of many differential aetiologies that may not be cardiac in origin. Sepsis induced myocardial dysfunction is a major predictor of morbidity and mortality in sepsis. Myocarditis must be considered in patients with recent onset of heart failure in a context of infection.

Case report: A previously healthy 26 years-old male comes to the emergency department with progressive symptoms of sore throat, fever, headache, nausea, vomiting and malaise for 2 days. Initially he was confused with white spots on tonsils, nuchal rigidity, normal pupils and no focal neurologic deficits. There was no respiratory distress and normal cardiac and pulmonary auscultation. Vital signs were stable. Exams were ordered: Head Computed Tomography showed mild diffused cerebral edema. Laboratory work-up and cultures revealed an elevated young white blood cells count, creatinine and lactate levels. Chest radiography had a mild diffused infiltrate. Lumbar puncture was done and cerebrospinal fluid was pale with low glucose and high protein content with diplococci gram negative (identified as *Neisseria meningitidis*). The patient then became less responsive with hemodynamic compromise non-responsive to volume infusion. Orotracheal intubation was performed and norepinephrine infusion initiated with ceftriaxone / dexametasone treatment. An electrocardiogram was done (sinus rhythm with 1mm ST elevation on the lateral wall with reciprocal changes on inferior wall - attached) and Cardiology was called at 2:00am. A point of care ultrasound was performed and showed no pericardial tamponade and no right ventricle enlargement. The dilated left ventricle showed diffused hypokinesia with reduced ejection fraction estimated at 35%. The inferior vena cava was at 18mm with minimal ventilatory variation. The diagnosis of acute heart failure due to sepsis and myocarditis due to meningococcal meningoencephalitis was made. Maximum troponin value reached 8.660pg/ml. The patient was admitted to the ICU and developed purpura-fulminans in the extremities and an episode of atrial fibrillation was reverted with amiodarone. After 20 days of hospital admission, the patient was discharged with normal ventricular function and no neurologic deficits. Description of the problem / procedures - The use of point of care ultrasound by a trained physician applied with clinical judgment can aid to determine the etiology of shock and volume status. A dilated left ventricle with decreased ejection fraction in a septic patient with no other possible shock aetiology, indicates sepsis induced myocardial dysfunction. Possible differential diagnosis - Myocardial depression can result due to inflammatory mediators in septic shock and direct meningococcal virulence. Myocarditis is present in 50% of patients who die from meningococcal disease. A hyperdynamic state combined with a coagulation disorder of sepsis may induce an acute coronary syndrome.

Discussion: The interface of septic shock, myocarditis, acute coronary syndrome and others acute conditions that affect the heart of septic patients.

Conclusion: Myocardial dysfunction indicates a higher incidence of fatal outcome in meningococcal disease.



Electrocardiogram

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Eosinophilic fulminant myocarditis with coronary arterial spasm

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Introduction: Eosinophilic myocarditis is a clinical condition that can be mortal due to severe heart failure. Different factors such as leukemia, parasite infection,

allergic disease, granulomatous disease, connective tissue disease, vasculitis such as Churg-Strauss syndrome, or primary hypereosinophilic syndrome may play a role in the etiology. Certain diagnosis is based on endomyocardial biopsy.

Case presentation: A 18 year-old man was admitted to hospital because of chest pain, fatigue and syncope. Initial electrocardiography revealed ST segment elevations in lead D1, AVL, V2 through V6 with reciprocal changes in lead D2, D3, aVF. Echocardiography showed a left ventricular ejection fraction of 20% and wall thickening with severely decreased wall motion. His first angiography showed diffuse coronary spasm in LAD with a fully normal ventriculography. His general condition and left ventricular function deteriorated again so that the patient immediately received an intraaortic balloon pump. After confirming the diagnosis of myocarditis, high-dose corticosteroids were administered. After that his control angiogram showed completely normal coronary arteries. Right ventricular endomyocardial biopsy was performed in the acute phase and showed extensive eosinophilic inflammatory cell infiltration, severe interstitial edema and moderate myocardial necrosis. After starting high-dose corticosteroids, his ventricular functions dramatically improved, and the patient made a full recovery. To best of our knowledge this is the first case of eosinophilic myocarditis with diffuse coronary spasm in literature.

Conclusion: Acute eosinophilic myocarditis is extremely rare and rapidly progressive clinical condition with poor prognosis. Although observational series suggest potential clinical benefits of corticosteroid therapy, the best strategy is to remove causative agent when known.

Poster Session 2

Sunday 24 May 2015 08:30–18:00

Location: Poster Area

ACUTE HEART FAILURE

P748

Clinical and electrocardiographic features of heart failure with preserved ejection fraction

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¹Fattouma Bourguiba University Hospital, Cardiology, Monastir, Tunisia

Purpose: The purpose of our study was to compare the clinical and electrocardiographic data from patients hospitalized for heart failure with altered ejection fraction (HFaEF) to those hospitalized for heart failure with preserved ejection fraction (HFpEF).

Methods: This is a retrospective study of 234 patients admitted in our cardiology department for acute heart failure between January 2010 and March 2011. We classified our population into two groups according to LVEF, a first group with altered FE and a second group with preserved EF. We compared the clinical and electrocardiographic data between these two groups.

Results: Patients who have HFpEF represent 46.6% of our population (N = 102) and were more often female (63.1%). Medium age was similar into the two groups. The frequency of coronary heart disease, smoking and dyslipidemia is higher in patients with altered LVEF (respectively 45.6% vs 13.72%, $p < 0.0001$, 40% vs 25.49%, $P = 0.021$ and 30.4% vs 18, 62%, $p = 0.042$), whereas hypertension is more frequently observed in those with preserved LVEF (73.52% vs 48.8%, $p < 0.0001$). We also noted that patients with HFpEF have less dyspnea stage III / IV of NYHA (32% vs 56%, $p < 0.0001$), fewer signs of right heart failure (12.7% vs 44.8%, $P < 0.0001$), have higher blood pressure ($p < 0.0001$) and body mass index ($p = 0.001$) than patients with HFaEF. Regarding electrocardiographic data, patients with altered LVEF have a significantly higher frequency of left bundle branch block (32% vs 14.7%, $p = 0.002$) and wide QRS (37.6% vs 17.6%, $p = 0.001$).

Conclusion: A better understanding of the characteristics of patients with heart failure with preserved ejection fraction could allow us to provide a better management of this type of pathology

P749

New approaches to the therapy of acute heart failure

A Asel Isabekova¹; S Berkinbayev¹; G Junusbekova¹; A Mussagalijeva¹; A Rakisheva¹

¹Scientific Research Institute of Cardiology and Internal Diseases, Almaty, Kazakhstan

The Purpose: Evaluate the effectiveness of Levosimendan in patients with STEMI complicated by AHF compared with standard therapy.

Material and methods: The study included 50 patients. The Levosimendan group included 30 patients with STEMI complicated by AHF (18 men and 12 women) being hospitalized. The control group included 20 patients STEMI complicated by AHF who received standard therapy.

Results: According to the study design patients with AHF, which arose in 48 hours after PCI due to STEMI have received infusion of Levosimendan. Mean SBP after infusion of Levosimendan increased by 28.3%, and by the end of follow-up was $108,7 \pm 19,21$, as compared with the control group above 27.6%, $p < 0.05$. We obtained similar data by indices of DBP, because in a group of Levosimendan on DBP was 3.3% higher than the control group. HR in the Levosimendan group decreased by 12.8% in 48 hours after infusion. LVDd and LVDs dimensions in the Levosimendan group decreased by 15.3% in the control group by 13.3%. LVEDV and LVESV in the group of Levosimendan there were reduction for 3.2% of this parameters versus the control group. The EFLV significantly increased in 48 hours from the infusion and these indicators were stable during the whole follow-up, were $43,9 \pm 17,2\%$, which is 29.8% higher than the data of control group. Similar

changes we found in analysis of the MPA, which decreased by 30% in 48 hours and by the end of the follow-up amounted to $110,4 \pm 301,5$, which is 13.6% less than in the control group. Oxygen saturation after infusion increased by 12.9% and by the end of follow-up was $98,1 \pm 16,1\%$, which is 6.2% higher than in the control group. The number of patients of the Levosimendan group in whom we have been reached stabilization of clinical condition was 78.9% at the second day after infusion, whereas in the control group the stabilization of clinical condition we have been reached 45% of patients only after fifth day.

Conclusion: The treatment of patients with STEMI complicated by AHF with Levosimendan in addition to the standard therapy allow to reach stabilization of clinical condition faster compare to the standard therapy of AHF, which have been shown by improvement of hemodynamic parameters (SV, HR, mean BP, MPA), inotropic function, significant reduction of maladaptive remodeling, improve quality of life of patients.

P750

Determinants of acute left ventricular systolic dysfunction after percutaneous coronary intervention

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¹University Hospital Central de Asturias, Cardiology, Oviedo, Spain

Purpose: left ventricular systolic dysfunction (LVSD) after a ST-segment elevation myocardial infarction (STEMI) is known to be one of the main outcome predictors. Our aim is to identify potential determinants of LVSD which can help us on the prevention and prompt treatment, to avoid its deleterious effects.

	NORMAL LV SYSTOLIC FUNCTION (N = 301)	LV SYSTOLIC DYSFUNCTION (N = 161)	P VALUE
AGE	60,6 ± 13	66,4 ± 14	0,05
MALE SEX	219 (72,8%)	119 (73,9%)	0,78
DIABETES	44 (15,7%)	38 (24,7%)	0,02
HYPERTENSION	131 (43,5%)	82 (51,2%)	0,11
HYPERLIPIDEMIA	117 (38,9%)	51 (31,9%)	0,13
SMOKERS	164 (54,5%)	81 (51,3%)	0,51
RENAL DYSFUNCTION	5 (1,9%)	8 (5,5%)	0,04
PREVIOUS PCI	26 (8,7%)	18 (11,2%)	0,47
STENT THROMBOSIS	19 (6,3%)	13 (8,1%)	0,35
MULTIVESSEL DISEASE	133 (44,2%)	82 (50,9%)	0,16
EXITUS	2 (0,7%)	13 (8,5%)	<0,001*
STEMI PRESENTED AS SUDDEN DEATH	13 (4,3%)	13 (8,1%)	0,009

*Fischer exact test was used

Methods: we enrolled 462 consecutive patients who underwent an emergent percutaneous coronary intervention (PCI) and completed their hospitalization in our centre between 2011 and 2013, with a 2D-echocardiography done during the following 48h.

Results: Mean age was $62,3 \pm 14$ years. 73,2% were men. Preserved left ventricular (LV) ejection fraction was found in 301 patients (65,2%), mild LVSD in 48 patients, moderate in 84 (18,2%) and severe LVSD in 29 patients (6,3%). Mean age was

higher in the group that developed LVSD ($p=0.05$). Diabetes, renal dysfunction and significant obstruction of the main left coronary artery associated with LVSD ($p=0.02$, $p=0.04$ and $p=0.01$ respectively). Patients who developed LVSD were on significant higher risk of death during hospitalization ($p < 0.001$).

Conclusions: higher age, diabetes, renal dysfunction and main left coronary disease seems to confer higher risk to develop LVSD. That is associated with short term mortality after PCI.

P751

Renal insufficiency at admission predicts an ischemic etiology of acute heart failure

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¹Hallym Univ. Kangdong Sacred Heart Hospital, Seoul, Korea, Republic of; ²Hallym University Sacred Heart Hospital, Anyang-Si, Gyeonggi-Do, Korea, Republic of

Background: The majority of patients admitted with acute heart failure (AHF) have coronary artery disease (CAD), which independently has an adverse impact on prognosis. Although chronic kidney disease is known risk factor of cardiovascular disease, whether renal dysfunction (eGFR < 60 mL/min) at admission is associated with CAD in patients with AHF is not known.

Methods and results: This was a prospective single center cohort study. Of patients who admitted for de novo AHF, 454 patients underwent coronary angiography during index hospitalization (table 1). Sixty three percent of them had eGFR <60 mL/min at admission, and patients with renal insufficiency had CAD more than patients without renal insufficiency (67.8 vs. 35.7%, $P < 0.001$). With older age (odds ratio [OR] 1.05; 95% confidence interval [CI] 1.02-1.08; $P = 0.002$), male gender (OR 2.82, 95% of CI 1.29-6.18, $P = 0.010$), diabetes (OR 2.06, 95% of CI 1.04-1.08, $P = 0.038$), and high LDL-cholesterol level (OR 1.01, 95% of CI 1.00-1.05, $P = 0.032$), renal insufficiency was independently associated with CAD (OR 2.84, 95% of CI 1.34-6.04; $P = 0.007$).

Conclusions: Renal insufficiency at admission may represent a predictive factor of CAD in patients with AHF, so effort including coronary angiography should be paid for confirmation of CAD even with risk of contrast-induced nephropathy.

1 Baseline characteristics of patients

Clinical characteristics	GFR < 60ml/min (n = 286, 63.0%)	GFR ≥ 60ml/min (n = 168, 37.0%)	p value
Age (years)	73.7 ± 10.5	61.3 ± 13.4	< 0.001
Gender, male, n (%)	92 (32.2)	107 (63.7)	< 0.001
Diabetes, n (%)	129 (45.1)	42 (25.1)	< 0.001
Hypertension, n (%)	208 (63.1)	75 (44.9)	< 0.001
Smoking, n (%)	69 (24.2)	74 (44.3)	< 0.001
SBP (mmHg)	131.1 ± 29.3	125.5 ± 26.8	0.044
Heart rate (beats/minute)	89.8 ± 23.3	93.1 ± 26.2	0.176
Hemoglobin (g/dL)	11.8 ± 3.0	13.6 ± 2.1	< 0.001
HDL-cholesterol (mg/dL)	44.2 ± 14.5	41.9 ± 13.1	0.097
LDL-cholesterol (mg/dL)	99.1 ± 42.3	101.2 ± 43.8	0.627
Triglyceride (mg/dL)	91.7 ± 48.8	93.4 ± 41.1	0.709
BUN (mg/dL)	28.2 ± 16.9	14.9 ± 6.2	< 0.001
Creatinine (mg/dL)	1.6 ± 1.5	0.9 ± 0.3	< 0.001

P752

The predictors of worsening renal function in HFpEF versus HFREF: an analysis of the Korean acute heart failure registry

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Purpose: Worsening renal function (WRF) is associated with worse outcomes in patients with heart failure (HF). Amongst others, neurohumoral activation is partly accounted for the development of WRF. Heart failure with preserved ejection fraction (HFpEF) and heart failure with reduced ejection fraction (HFREF) are two distinctive diseases with a different degree of neurohumoral activation. The purpose of this study was to investigate the relationship between WRF and NT-proBNP and to identify the clinical predictors of WRF according to the two types of HF.

Methods: Korean acute heart failure (KorAHF) registry is a prospective observational multicenter cohort enrolling acute HF patients hospitalized in 10 tertiary university hospitals. A total of 5,536 patients were enrolled from 2011 March to 2014 February, who all had more than two creatinine levels measured during admission. HFpEF was

defined as an ejection fraction (EF) >50%, HFREF as an EF <40%. WRF was defined as an absolute increase in creatinine of >0.3 mg/dl.

Results: Overall, 2,885 patients had HFpEF and 1,413 patients had HFREF. HFpEF patients tended to be older, were more often females, had a higher proportion of hypertension, ischemic heart disease and chronic lung diseases. However, diabetes and renal diseases were more common in HFREF patients. Furthermore, HFREF patients had higher NT-proBNP (10560 ± 11600 vs. 6410 ± 8410, $p < 0.001$) and higher serum creatinine (1.51 ± 1.48 vs. 1.33 ± 1.16, $p < 0.001$) than those with HFpEF. In the HFREF group, there were 1,616 (56.6%) WRF patients which was significantly higher than the HFpEF group (738 (52.6%) WRF patients, $p = 0.015$). However in both groups, there was no correlation with the ejection fraction and increase in creatinine; ($r = 0.10$, $p = 0.583$ in the HFREF group; $r = 0.01$, $p = 0.979$ in the HFpEF group). In contrast, there was a significant correlation between Cr and NT-proBNP levels ($r = 0.497$, $p < 0.001$ in the HFREF group; $r = 0.510$, $p < 0.001$ in the HFpEF group). Using a multivariate logistic regression model, high BNP was the strongest predictor of the WRF in both HFREF and HFpEF groups amongst others. In ROC-curve analysis, the AUC of NT-proBNP to predict the WRF was 0.683 (95% CI 0.658-0.709, $p < 0.001$) in HFREF and 0.663 (95% CI 0.624-0.703, $p < 0.001$) in HFpEF patients.

Conclusion: From our registry, WRF was not an uncommon event during the admission of HF patients. WRF seemed to be related NT-proBNP levels, but not with left ventricular systolic function.

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Prognostic value of low plasma absolute lymphocyte count in patients admitted for acute heart failure

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Background: Low relative lymphocyte count is an important prognostic marker in acute heart failure (AHF), however it could be influenced by other abnormalities in white cells count. Our purpose is to evaluate if low absolute lymphocyte count (ALC) is an independent predictor of events in patients with AHF.

Methods: In a retrospective analysis, we included 309 patients with AHF, divided in 2 groups according to the median value of ALC at admission (1,410 cells/mm³). The primary end point was all-cause mortality within 1 year.

Results: Patients with low ALC were older and had more comorbidities, namely atrial fibrillation, chronic kidney disease, chronic obstructive pulmonary disease (COPD) and anemia. Low ALC was associated with higher all-cause mortality (27.1% vs 17.5%; $p = 0.020$). In a multivariable model, the independent predictors of mortality at one year were low ALC (HR 1.71; IC 95% [1.04-2.8]; $p = 0.035$), systolic blood pressure at admission (HR 1.17; IC 95% [1.04-1.33]; $p = 0.009$) and glomerular filtration rate (HR 0.96; IC 95% [0.95-0.98]; $p < 0.001$).

Conclusion: Low ALC in patients with AHF is an independent prognostic marker, underscoring that the immune system derangement may play an important role in the pathophysiology of this disease.

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Heart failure with preserved ejection fraction: not as common as you think

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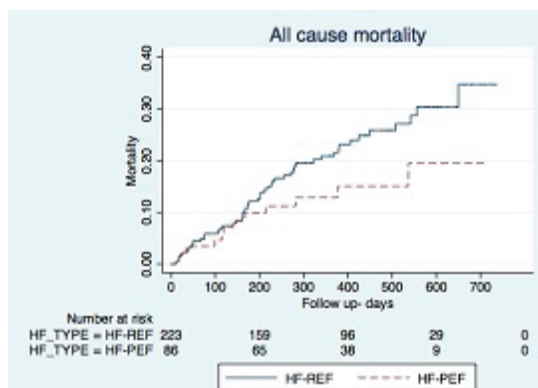
Purpose: Heart failure with preserved ejection fraction (HF-PEF) is frequently said to account for half of all patients with HF, with a similar mortality, although a recent meta-analysis has disputed the latter claim. Data from unselected, prospectively recruited patients, utilising natriuretic peptides and echocardiography to confirm the diagnosis are lacking. Therefore, we investigated this issue in a large, near-consecutive cohort of patients admitted to hospital with acute HF (AHF).

Methods: All admission wards were systematically searched on a frequent (usually daily) basis and any patient with possible HF was assessed. Patients meeting the ESC 2012 guidelines for the diagnosis of AHF without the following exclusion criteria were included: BNP < 100 pg/ml; confusion; and refusal to participate. Demographic data, BNP and a detailed and blindly-analysed echocardiogram were performed, including ventricular and atrial volumes, and markers of elevated LV filling pressure. Preserved EF was defined as > 50% by Simpson's biplane method. Patients were followed up for vital status.

Results: 309 unselected, near-consecutive, patients with AHF were recruited between 09/01/2013 and 02/12/2014. The majority (72%) of patients had HF with a reduced ejection fraction (HF-REF). Patients with HF-PEF were older, more often female, and less likely to have had a myocardial infarction. HF-PEF and HF-REF

patients were otherwise very similar. There was no difference in median BNP, haemoglobin, or eGFR. During a median follow up of 360 days, there were 62 deaths, with a numerically higher, although not statistically significant, mortality in HF-REF (Figure).

Conclusion: HF-PEF is much less common than HF-REF in patients admitted to hospital with AHF, and appears to have a better long term prognosis.



All cause mortality

P755

Evaluation of inappropriate hospitalizations in a cardiology department of a hospital in third level

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Heart Failure Schedule study in a Third Level Hospital

Purpose: Andalusian health system define a lot of fundamental measurements in heart failure: fraction ejection measuring > 66%, treatment with converting enzyme or angiotensin inhibitors (ACE/AIIRA > 66%, anticoagulant therapy in patients with atrial fibrillation > 80%.

Material and Methods: We analyzed the population of patients admitted to our hospital (University Hospital of third level with 1307 beds) during the period June 2013 to June 2014. We analyzed fundamental process parameters such as measuring the fraction of ejection, percentage of patients treated with ACE Inhibitors/AIIRA and percentage of anticoagulant therapy in patients with atrial fibrillation

Results: 1915 patients were entried with heart failure, 1167 patients in internal medicine and 6 45 in cardiology, the remaining patients are entried in a miscellanea of medical services. 44% of patients hospitalized in the internal medicine are taking ACEI/AIIRA, this figure reaches 80% in patients admitted for heart failure in cardiology. The completion of anticoagulation in patients with atrial fibrillation (479 patients) reaches 90%. Measurement of left ventricular ejection fraction is decreased, secondary to percentage in internal medicine (25%), whereas in cardiology is the 86%. The final result was 45%.

Conclusions: 1.-striking that the process continues with inadequate indicators because treatment with ACE Inhibitors only meets in 56%; This is below 66% the unit value, although the trend is towards increased. Currently only exceeded in Cardiology (80%) and having declined significantly in internal medicine (44%), unit value, while the same is not true in other specialties as with ACEI/AIIRA medication is below 40% and close to 0%.

2. the indicator of anticoagulant therapy in patients with atrial fibrillation is above the preferred unit value of 66% and reaches the 90%.

3.-The measurement of ejection fraction below the unit value of 66%, and it is in this cut of 40%, with ranges between 0 and 100%, just surpassing the 66% in Cardiology (86%); but it is very down in internal medicine (25%), measurements in this specialty have declined since the last cut, Nephrology (10%) and miscellaneous (0%).

4.- Finally the differences were significant depend on medical unit.

P756

Does the mode of arrival to emergency department predict the liability of acute heart failure patients assessed by systolic blood pressure categories

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Systolic blood pressure is a well-known prognostically significant factor which directs initial management of acute heart failure (AHF). However, it is not known whether the ambulatory patients have more normal blood pressure levels than those arriving to emergency department (ED) with ambulance.

Purpose: To compare admission blood pressure classes between patients arriving to ED by emergency medical services (EMS) and non-EMS patients.

Methods: We included patients with AHF from three academic emergency departments and grouped them to those transferred by emergency medical services (EMS group) and non-EMS group from July 2012 to 2013. Data was collected from electronic EMS and hospital databases. Vital signs on admission to ED were compared between EMS and non-EMS patients. Systolic blood pressure (SBP) was categorized to four ranges < 100, 100-119, 120-160 and > 160 mmHg (Table)

Results: 100 (11.5%) of 873 patients diagnosed with AHF in ED were EMS patients. The majority of AHF patients (56%) had normal to mildly hypertensive systolic blood pressure (SBP) (120-160 mmHg). Similarly, 53% of EMS patients and 56.4% of non-EMS patients had SBP between 120 and 160 mmHg (Table).

Conclusion: No difference was seen in SBP categories between EMS and non-EMS patients. Few patients had SBP < 100mmHg. Thus acuity according to admission SBP can't be predicted by the type of arrival to hospital. Equal caution has to be taken to both ambulatory and ambulance patients.

Comparison of blood pressure classes

Systolic blood pressure	All n(%)	EMS n(%)	Non-EMS n(%)	p-value
< 100 mmHg	45 (5.2)	6 (6.0)	39 (5.1)	0.700
100-119 mmHg	162 (18.7)	17 (17.0)	145 (18.9)	0.642
120-160 mmHg	485 (56)	53 (53.0)	432 (56.4)	0.520
> 160 mmHg	174(20.1)	24 (24.0)	150 (19.6)	0.300
total number of patients	866	100 (11.5)	766 (88.5)	

P757

Clinical outcomes differences between acute heart failure patients based on left ventricular ejection fraction

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Purpose: To compare clinical characteristics and outcomes of acute heart failure (AHF) between the Preserved ($\geq 45\%$) and Reduced ($< 45\%$) left ventricular Ejection Fraction patients.

Methods: This retrospective cohort study included data on 494 patients admitted to two tertiary care centers for AHF between July 2009 and June 2013.

Results: In the studied population, 67% of the patients showed reduced ejection fraction. Most of the patients were of ischemic (40.5%), Chagas disease (16%) and valvular (14.5%) etiology. The means of left ventricular ejection fraction (LVEF) among the studied individuals was 31% and 59.7% for reduced (REF) and preserved (PEF) ejection fraction, respectively. REF patients were older and showed more chronic renal failure. On the other hand, mean length of stay was higher among PEF patients. Table 1 shows the differences between patients according to LVEF.

Conclusion: In this study, our findings showed that Preserved Ejection Fraction was not a factor of improved prognosis among patients hospitalized for acute heart failure.

P758

Heart failure with intermediate left ventricular ejection fraction

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Purpose: Heart failure (HF) can be categorized with HF with reduced (HFREF) or preserved ejection fraction (HFPEF).

However, there is a lack of data regarding HF with intermediate EF. The aim of this study is to describe the clinical characteristics and outcomes of the patients with intermediate EF (HFIEF).

Methods: From KorHF Registry, clinical data of 2036 patients who admitted for acute heart failure and documented LVEF from June, 2004 to October were studied. Mean follow-up duration was 3.7 ± 2.5 years.

Table 61334. General characteristics of the sample

	Preserved Ejection Fraction (≥45%)	Reduced Ejection Fraction (<45%)	P (χ ²)	Odds ratio (95% confidence interval)
Male, % (n)	37.9 (58)	61.3 (190)	-	0.68 (0.32-1.46)
Mean Age±SD (range)	62.2 ± 18.6 (20-93)	63.8 ± 12.4 (22-93)	0.001	-
Ejection Fraction	59.7±10.2	31.0±7.7	000.1	-
Hypertension, % (n)	75.0 (114)	76.3 (232)	0.76 (0.96)	1.07 (0.68 - 1.69)
Atrial fibrillation, % (n)	43.1 (59)	36.4 (94)	0.19 (1.66)	0.76 (0.49-1.16)
Diabetes, % (n)	17.1 (26)	28.9 (88)	0.006 (7.58)	1.97 (1.2-3.2)
Chronic renal failure, % (n)	21.3 (32)	32.6 (99)	0.013 (6.17)	1.78 (1.13 - 2.82)
Mean Length of stay (range)	11 (2-88)	9 (2-82)	0.01*	-
Acute renal failure, % (n)	31.5 (47)	32.1 (99)	0.9 (0.17)	1.03 (0.68-1.57)
Vasoactive amine use, % (n)	21.6 (33)	21.0 (65)	0.88 (0.22)	0.97 (0.6-1.5)
Death, % (n)	5.2 (8)	7.1 (22)	0.44 (0.60)	1.39 (0.6-3.2)

Data are expressed as frequency (n) for categorical variables and median and interquartile range for continuous variables. * Mann-Whitney test. BB, beta blockers; OR, odds ratio; CI, confidence interval; P-value; χ²: Chi-square.

Results: Total 290 (14.2%) patients showed intermediate LVEF (over 40% and below 50%) while 1218 (59.8%) and 528 (25.9%) patients had reduced (≤40%) or preserved EF (≥50%).

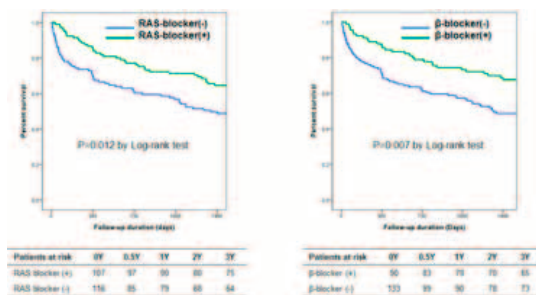
Their mean age was 69.3 ± 13.7 years and 152 (52.4%) patients were male. The patients with HFIEF showed higher prevalence of diabetes mellitus, chronic kidney disease, and ischemic heart disease (35.9%, 15.5%, 47.0%) compared to patients with HFREF (30.9%, 9.2%, 38.4%) or HFpEF (24.7%, 7.2%, 23.5%) (all p < 0.001).

Their estimated mean survival was 4.9 ± 0.2 years, which was not different with the patients with HFREF or HFpEF (p = 0.34). In Kaplan-Meier analysis, patients with beta-blocker or RAS blocker showed better overall-survivals compared with the patients without those medication (p = 0.012 and 0.007).

Follow-up echocardiography was available in 195 (67.2%) patients with mean follow-up of 2.5 ± 2.1 years.

Overall, mean EF was increased to 48.8 ± 12.1% (p < 0.001). Approximate half of the patients (93 patients, 47.7%) had EF ≥ 50%, while third of patients (56, 28.7%) had LVEF ≤ 40% at follow-up.

Conclusions: HFIEF patients seem to have worse cardiovascular risk profiles. The use of beta-blocker and RAS blocker may be profitable to those patients. Further study is needed to understand HF patients with EF in gray zone.



P759

Utilization of disease modifying therapies in heart failure patients in relationship to the ejection fraction - data from SONIC-RO study

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Background: Pivotal trials have shown that only patients suffering from heart failure with reduced ejection fraction (HF-REF) benefit from disease modifying therapies (DMT) to improve survival and reduce HF readmissions. The aim of the study is to evaluate prescription of DMT in relationship to ejection fraction (EF) in patients hospitalized for worsening heart failure (WHF).

Methods: Romanian National Observational Study of In-Hospital Heart Failure (SONIC-RO) enrolled 1222 consecutive patients, admitted with a primary diagnosis of WHF, from 41 hospitals, representative for the Romanian cardiology network. Rate of prescription for DMT were collected at admission and discharge and stratified by EF.

Results: The proportions of beta blockers, ACE inhibitors and aldosterone antagonists prescription on admission were 63%, 51%, and 43%; only 18% were taking all three classes. At discharge, proportions were 74%, 57%, and 54%, respectively, with only 26% of patients have been prescribed all. The mean EF evaluated by transthoracic echography was 41.4%. Differences in utilization of DMT between patients with reduced or preserved EF are depicted in Table 1.

Conclusions: A large proportion of patients with preserved EF received at discharge a beta-blocker or an ACE inhibitor, and only aldosterone antagonists were specifically allocated to HF-REF patients. Further trials investigating new therapies in heart failure patients with preserved EF may consider oral therapies already allocated to these patients.

Table 1

	FE≤40% (n = 632)	FE>40% (n = 590)	p value
Beta-blockers			
Admission rate (%)	62.4%	64.5%	p = 0.47
Discharge rate(%)	73.2%	75.2%	p = 0.42
ACEinh/ARBs			
Admission rate (%)	48.5%	54.2%	p = 0.05
Discharge rate(%)	55.0%	59.2%	p = 0.14
Aldosterone Antagonists			
Admission rate (%)	53.4%	32.9%	p < 0.001
Discharge rate(%)	64.8%	42.5%	P < 0.001

P760

Patterns of utilization of inotrope therapy in acute heart failure syndromes according to clinical profile at admission - insights from RO-AHFS registry

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Purpose: Clinical trials and registry data show that in patients admitted with acute heart failure syndromes (AHFS), inotrope therapy is associated with increased

	ADHF n = 1834	PE n = 924	CS n = 162	RHF n = 129	HTN HF n = 162	P value
SBP at admission(mmHg)	133±27#	167±43*#\$	89±29	125±21#	188±20	<0.01
Inotrope utilization (%)	12.7#	18.4#	94.2	13.3#	0	<0.01
Inotrope as initial therapy %	68%	33,8% *#	81%	57%	0	<0.01
Inotrope after initial therapy %	32%	66.2% *#	19%	43%	0	<0.01

P values adjusted for multiple comparisons;* versus ADHF;# versus CS; \$ versus RHF. (Separate Bonferroni analysis)

in-hospital mortality. However none of these studies described time frame initiation of inotropes in respect to hospital admission. This study aimed to characterize the pattern of inotrope utilization as part of initial management according to AHFS clinical profile at admission.

Methods: RO-AHFS registry enrolled 3224 consecutive patients admitted with a primary diagnosis of AHFS at 13 medical centers over a 12-month period of time. On admission patients were classified in five clinical profiles: acute decompensated heart failure (ADHF, 57%), acute pulmonary edema (PE, 29%), cardiogenic shock (CS, 5%), right heart failure (RHF, 4%) and hypertensive heart failure (HTN HF, 5%). Inotrope therapy utilization, by time of initiation, at presentation or later on during hospitalization was assessed in each group.

Results: 576 patients (17.7%) were treated with iv inotropes, 60.9% as initial treatment and 39.1% later on during hospitalization. As compared to other profiles, PE patients had higher systolic blood pressure (SBP) values at admission, and only a small proportion were initially treated with iv inotropes. Pattern of utilization of iv inotropes by clinical profile at admission is depicted in Table.

Conclusion: Pattern of inotrope therapy initiation in AHFS differs according to clinical profile. In contrast to other clinical profiles, in PE patients inotrope therapy is more frequently used after initial diuretic-vasodilator therapy. In this group of patients, severity of tissue hypoperfusion is probably not properly recognized at admission due to reactively increased SBP or maybe hypoperfusion occurs as result of overdiuresis or aggressive vasodilation.

P761

The music therapy in patients with heart failure and acute myocardial infarction after previous coronary artery bypass surgery; new experiences

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Patients who have clinical evidence of heart failure (HF) after coronary artery bypass surgery (CABS) have a poor prognosis in expression of acute myocardial infarction (AMI), as one of the MACE. Unrelieved anxiety can produce an increase in sympathetic nervous system activity leading to an increase in cardiac workload. The purpose of this study was to evaluate the effectiveness of music therapy on prognosis of patients with HF and AMI, after CABS.

Methods: 342 patients (males 76.4%, mean age 59.4 ± 2.4 yrs) with AMI after previous CABS have been selected from the patients consecutively submitted from January 2013 to December 2014. HF was registered in 154 (45.0%) pts with AMI after previous CABS. All patients with HF were randomized and divided in 2 groups: Study group of 77 patients treated with music therapy and Control group of 77 patients with no music therapy. Each patient in study group underwent two sessions of medical therapy (12 minutes) in a day. Both groups were similar in baselines, post-AMI characteristics and post-AMI medical therapy. The plasma cytokine and catecholamine were measured in both groups.

Results: In the Study group, heart rate was significantly decreased by music therapy (p = 0.3876). In the Control group, there were no significant changes in heart rate. Among cytokines (p = 0.4165), plasma interleukin-6 (IL-6) (p = 0.3384) in the Study group was significantly lower than those in the Control group, as well as plasma adrenaline (p = 0.4316) and noradrenaline (p = 0.4208) levels.

Conclusion: This study provides support for the use of musical therapy in patients with HF and AMI after previous CABS. The positive effects of music therapy, in these patients, are probably because of enhanced of parasympathetic activities and reduction of plasma cytokine and catecholamine levels.

P762

Cost effectiveness of lung impedance-guided preemptive treatment in chronic heart failure patients in the outpatient clinic

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Recurrent hospitalizations in patients with congestive heart failure (CHF) represent a major financial burden for the health care system. We previously found that preemptive treatment based on monitoring lung impedance (LI) can prevent 55% of hospitalizations for acute heart failure (AHF).

Aim: To assess the effect of LI-guided therapy as compared with conventional treatment in patients admitted for AHF on the incidence and cost of recurrent hospitalizations.

Method and Results: 250 patients [(68 ± 11 years-old, male- 80%, LVEF- 28 ± 9%, initial NT-proBNP level- 3594 ± 5114 pg/ml, follow-up duration- 36 ± 22 months (7500 visits), NYHA II/III/IV (107/100/43)] were randomized to the LI-guided group 1 (n = 124) and group 2 (n = 126) who were treated by clinical assessment. Hospitalizations for AHF were recorded annually for both groups during 8-years of follow up. Hospitalizations per year were divided by number of patients followed that year and normalized to 100 patients. We estimated the average cost of AHF hospitalization as 18000\$. Incidence of hospitalizations/100 patients during 1-8 year was 64, 31, 61, 57, 51, 15, 44, 77 in group 1 and 120, 68, 105, 111, 65, 73, 137, 150 in group 2 (p < 0.001).

Cumulative savings for the health care system by using LI-guided therapy in 100 patients during the first 8 years was 1, 1.7, 2.5, 3.5, 3.7, 4.7, 6.4 and 7.7 \$million, respectively. Cost of LI device for one patient was 1000\$ for the first year and 500\$ for each following year. The net profit of the health care system after 8 years of treatment was 7.7 million\$ (saved hospitalizations) - 0.45 million\$ (cost of devices with service) = 7.25 million\$. Calculated net profit for one patient treated according LI for one year was 9063\$.

Conclusion: The strategy of LI-guided therapy not only reduced significantly hospitalizations for AHF but also decreased the cost of therapy by 9063\$/year for each patient.

P763

Audit and clinical service evaluation for acute heart failure patients dying within 48 hours of admission

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Purpose: In the United States, better outcomes for acute heart failure (AHF) are found in higher spending hospitals with more Intensive Treatment Unit (ITU) and High Dependency Unit (HDU) resources. The National Heart Failure Audit shows that in-patient mortality for AHF is lower when care is delivered in cardiology than in general medicine.

Despite lower than the National average inpatient mortality, we reviewed all cases dying within 48 hours of non-elective heart failure admission to this Trust, to assess potential for improving service delivery.

Methods: Medical records were reviewed from July 2012 to June 2014 for all patients dying within 48 hours of non-elective admission to our Hospital with HF in the primary diagnosis code (n = 24).

Results: For 50% (n = 12) this was the first ever presentation with heart failure. Respiratory failure was documented in 88% (n = 21) on arterial blood gas (63% type 1, 25% type 2), and acute renal failure in 63% (n = 15). Only 21% (n = 5) were cared for in a Level 2 (ITU/HDU) area (13%, n = 3 in Cardiothoracic ITU, 8%, n = 2 in General ITU). Only 3 patients (13%) received invasive ventilation (non-invasive ventilation in 34% - CPAP 21%, BiPAP 13%).

Most (51%) died in general medical wards (38%, n = 9, acute medical unit, 13%, n = 3, medical ward). Care was delivered in cardiology for 21%. The majority died without senior cardiology review (13%, n = 3 received HF Consultant review, 16%, n = 4, non-HF Consultant Cardiologist review).

Left bundle branch block was present in 17% (n = 4).

Acute triggers for decompensation included infection in 42%, suspected acute coronary syndrome in 29% and arrhythmia in 13%. One patient received palliative care input (4%).

Conclusions: This audit of acute heart failure patients dying within 48 hours of admission demonstrates that despite multi-organ failure at presentation, most do not receive level 2 care or above and most die without senior cardiology review. Inpatient mortality is well below the national average at this Trust, indicating that the potential to improve acute heart failure management within the first 48 hours may be widespread. The data provides supportive evidence for investment in level

2 care capacity to manage these complex patients and to streamline care delivery to specialist heart failure teams.

P764

Risk assessment of re-hospitalizations for heart failure during 30 days after discharge for acute heart failure

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Background: Prevention of hospitalization for decompensation chronic heart failure (CHF) patients is an unresolved issue. The accuracy of implantable and non invasive devices in predicting deterioration before hospitalization is only 50%.

Aim: Evaluate the ability of a new non-invasive method for lung impedance monitoring to predict CHF decompensation.

Methods: CHF patients were monitored by a high sensitive device which enables to determine small changes in lung fluid content by measuring lung impedance (LI) instead commonly used trans-thoracic impedance. This device is 25-fold more sensitive than existing ones. A decreasing LI reflects accumulation of lung fluid. Changes in the clinical status of patients and LI were recorded monthly. The "normal" baseline LI was calculated according special algorithm for each patient. LI changes from baseline value are represented as percentage change.

Results: 250 CHF patients (68 ± 11 years-old, male- 80%, LVEF- 28 ± 7%) at NYHA II/III/IV (107/100/43) were recruited after index hospitalization for acute heart failure (AHF) and followed in an outpatient clinic for 36 ± 22 months (6940 clinical visits). Initial NT-proBNP level was 3594 ± 5114 pg/ml. Patients were treated according to guidelines. During follow-up, 63 patients (25%) died for cardiovascular death. Of study patients, 71 were not hospitalized for AHF while 179 required 548 re-hospitalizations for AHF.

At hospital admission for AHF, LI was -37.2 ± 10.6% from baseline LI. During hospital stay (4.4 ± 4.9 days) LI increased to -30.4 ± 12.5%. Study patients were divided by LI% improvement at discharge into groups. A: 0 < DLI < 5%; B: 5 < DLI < 10%; C: 10 < DLI < 20% and D: DLI > 20%. During the first month after discharge, re-hospitalization was required in 65% of group A, in 31% of group B, in 16% of group C and 2% of group D (p < 0.001).

Conclusions: Noninvasive LI monitoring may be used to evaluate effectiveness of therapy in hospitalized decompensated CHF patients. Small (less 5%) improvement in LI during hospitalization is a very strong predictor for re-hospitalization during next month.

P765

ADHERE risk score and acute heart failure: evaluation of its applicability in clinical daily practice, mortality prediction and inotropic support need prediction capacity

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Purpose: Acute Heart Failure (AHF) is a disease with high in-hospital mortality. Although there are well validated unfavorable prognostic predictors, the application of mortality scores is not easily used in daily practice. The ADHERE risk score entails a simple risk score stratification in AHF with the use of 1 clinical and 2 laboratory parameters (systolic blood pressure, blood urea and creatinine), estimating mortality between 2.14% and 21.95%. We aim to evaluate the applicability of the ADHERE score in a real world population and its capacity to predict in-hospital mortality and the need of use of inotropic support in AHF patients.

Methods: A retrospective study was conducted in a cohort of patients (P) admitted for AHF between Jan/2007 and 5/Dec/2013. For each patient the ADHERE score was calculated and a correlation with in-hospital mortality and the need of inotropic support use analysed.

Results: From a total of 234P, 71.4% male, 66.7 ± 12.5 years, 96 (41%) in NYHA class IV, 30P (12.8%) had an intermediate-1 to elevated ADHERE risk score. There were 13 deaths. In the superior risk ADHERE score, the P were older (72.2 ± 9.4 years; p = 0,0099), predominantly in NYHA class IV (p < 0,001), with lower incidence of new onset HF (p = 0,029), more patients in Afib rythm (p = 0,049) and with lower ejection fraction (EF 24,47 ± 8,55%; p = 0,016). A higher ADHERE score was also associated with higher in-hospital mortality (p = 0,015) and with the necessity of using inotropic support (p < 0,001). By univariate logistic regression, the ADHERE risk score showed to be and a mortality predictor (Odds Ratio 4,9; p = 0,009) and a predictor of the need of inotropic therapy (Odd Ratio 24,08, p < 0,001).

Conclusion: The ADHERE risk score is easy to use in daily clinical practice and has the ability to evidence the P with higher hemodynamic frailty, with the subsequent need of inotropic support, being a mortality predictor.

P766

Retrospective survey in patients <55 year old, admitted with an episode of acute heart failure

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Aims: Description of clinical epidemiology and patient's profile of patients admitted with an episode of acute HF. It is an initial phase of a survey aimed to continue into a permanent registry.

Methods: Retrospective observational survey conducted in one cardiology center in an emergency hospital in eastern European country. All patients admitted for an episode of acute HF are under the age of 55 and the two genders are presented equally. From 1.Jan.2014 to 1.Oct.2014 were included 56 patients.

Results: The survey shows that more than two thirds of the patients admitted for an episode of acute HF were with a history of arterial hypertension, with inadequate pharmacology treatment, 21% were with history of diabetes. The mean ejection fraction of the selected group is above 54%, which puts the group in the category of patients with HF with preserved ejection fraction.

Conclusion: HF with preserved ejection fraction, mainly due to inadequately treated arterial hypertension and diabetes, is the prevalent type of HF among patients under the age of 55, admitted for an episode of acute HF.

P767

Cardiorenhepatic interrelations in patients with acute decompensated heart failure

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Objective: Cardiorenal syndrome is a common and serious problem with negative impact on outcomes in patients with acute decompensated heart failure (ADHF). Over the last several years prevalence and prognostic value of cardiohepatic syndrome in this population has been discussed. The aim of the study was to assess possible relationship between renal and hepatic abnormalities in patients with ADHF.

Methods: In 200 patients with ADHF (184 male, 72.9 ± 10.7 years (M ± SD), arterial hypertension 79%, ischemic heart disease 65%, myocardial infarction 43%, atrial fibrillation (AF) 62%, diabetes mellitus 36.5%, known chronic kidney disease (CKD) 38%, chronic anemia 23.5%, chronic obstructive lung disease 23.5%, ejection fraction (EF) 45 ± 12%, EF < 35% 25%, chronic hepatic diseases 9.5%) alanine transaminase (ALT) and aspartate transaminase (AST) were measured baseline. TA were considered abnormal when levels exceeded 50 U/L (local upper normal limit (UNL)). CKD and acute kidney injury (AKI) were diagnosed based on KDIGO 2012 Guidelines. Mann-Whitney test and multivariate logistic regression analysis were performed. P < 0.05 was considered statistically significant.

Results: Mean baseline ALT and AST values in patients with versus without increase of TA were 95 ± 36 vs 21 ± 14 U/l and 87 ± 26 vs 25 ± 11 U/l respectively (p < 0.001). Increase of ALT and/or AST occurred in 29 (14.5%) patients (alone ALT/ alone AST/ both TA - in 42.3, 19.2, 38.5% respectively). Community-acquired AKI occurred in 36 (18%) patients. Patients with versus without community-acquired AKI had higher levels of ALT (38 ± 37 vs 21 ± 18 U/l, p < 0.001) and AST (41 ± 31 vs 25 ± 14 U/l, p < 0.001). Incidence of cytotoxicity was higher in patients with versus without community-acquired AKI (20 vs 2%, p < 0.001). Incidence of AKI was higher in patients with versus without cytotoxicity (70 vs 17.3%, p < 0.001). Combination of cytotoxicity with CKD or AKI was revealed in 10 (5%) patients. The independent predictors of cytotoxicity were AF at admission (odds ratio (OR) 11.3, 95% confidence interval (CI) 2.6-48.9), community-acquired AKI (OR 11.2, CI 4.1-30.3), CKD (OR 4.2, CI 1.6-11.0), chronic anemia (OR 2.7, CI 1.1-6.4), EF < 40% (OR 2.4, CI 1.1-5.7).

Conclusions: Cardiohepatic syndrome occurred in 14.5% of patients with ADHF. Community-acquired AKI was diagnosed in 18% of patients. Different phenotypes of cardiorenhepatic interrelations were revealed in 5% of patients. CKD and AKI along with AF at admission, chronic anemia, and EF < 40% were the independent predictors of TA increase.

Table P766

Females, %	Ischaemic aetiology of HF, %	SBP (mmHg)	EF %	EF > 45%	Treated hypertension n, %	Diabetes, %	History of atrial fibrillation, %	Anaemia, %	Creatinine > 1.5mg/dL, %
50	25	141,5	54,9%	73	48, 85%	21	17	14	16

P768

Incidence of cardio-hepatic syndrome in patients with acute decompensated heart failureA Anzhela Soloveva¹; A Aliev¹; S Villevalde¹; Z Kobalava¹¹ Peoples Friendship University of Russia (PFUR), Moscow, Russian Federation

Objective: The impact of acute decompensated heart failure (ADHF) on hepatic function has been described as cardio-hepatic syndrome that may reflect severity of HF. The aim of the study was to evaluate prevalence of liver transaminases (TA) increase in patients admitted with ADHF.

Methods: In 200 patients with ADHF (184 male, 72.9 ± 10.7 years (M±SD), arterial hypertension 79%, ischemic heart disease 65%, myocardial infarction 43%, atrial fibrillation (AF) 62%, diabetes mellitus 36.5%, known chronic kidney disease (CKD) 38%, chronic anaemia 23.5%, chronic obstructive lung disease 23.5%, ejection fraction (EF) 45 ± 12%, EF <35% 25%, chronic hepatic diseases 9.5%) alanine transaminase (ALT) and aspartate transaminase (AST) were measured at admission and further according routine clinical practice. TA were considered abnormal when levels exceeded 50 U/L (local upper normal limit (UNL)). Mann-Whitney test was performed. P < 0.05 was considered statistically significant.

Results: Increase of ALT and/or AST occurred in 29 (14.5%) patients (alone ALT/alone AST/ both TA - in 42.3, 19.2, 38.5% respectively). Mean baseline ALT and AST values in patients with versus without increase of TA were 95 ± 36 vs 21 ± 14 U/l and 87 ± 26 vs 25 ± 11 U/l respectively (p < 0.001). Increase of ALT and AST more than 1, 2 and 3UNL was found in 85.7%, 9.5% and 4.8% and 93%, 7%, 0% cases respectively. Increase of TA higher than 4 UNL was not observed. Transient increase of TA was observed in 80% cases, persistent - in 20% cases. Patients with vs without increased TA had lower weight (76 ± 15 vs 87 ± 11 kg, p < 0.05), body mass index (BMI) (27 ± 2 vs 30 ± 6 kg/m², p < 0.05), higher baseline serum creatinine (152 ± 44 vs 114 ± 44 mmol/l, p < 0.001), lower estimated glomerular filtration rate (eGFR) (34 ± 11 vs 53 ± 18 ml/min/1.73 m², p < 0.001), higher heart rate (115 ± 25 vs 92 ± 25 per minute, p < 0.001), left ventricular mass index (LVMI) (194 ± 40 vs 174 ± 48 g/m², p < 0.01), lower EF (40 ± 11 vs 45 ± 12%, p < 0.05), higher rate of comorbidities - CKD (11 vs 2.8%, p < 0.05), chronic anaemia (83 vs 24%, p < 0.05), AF (11 vs 1%, p < 0.001).

Conclusions: Increase of TA in patients with ADHF occurred in 14.5%, predominantly was mild (less than 2 UNL) and transient. Cardio-hepatic syndrome was associated with lower weight, BMI, higher baseline serum creatinine, lower eGFR, higher heart rate, LVMI, lower EF, higher rate of comorbidities (CKD, chronic anaemia, AF). There was no impact of chronic hepatic diseases on incidence of cardio-hepatic syndrome in patients with ADHF.

P769

Cardiohepatic syndrome is associated with congestion in patients with acute decompensated heart failureA Anzhela Soloveva¹; B Mamatov¹; E Tereshchenko¹; S Villevalde¹; Z Kobalava¹¹ Peoples Friendship University of Russia (PFUR), Moscow, Russian Federation

Objective: Recently the impact of acute decompensated heart failure (ADHF) on hepatic function has been described as cardio-hepatic syndrome. It is assumed that cytotoxicity is mainly associated with systemic hypoperfusion, whereas cholestasis - with volume overload. Systemic congestion is the known main driver for morbidity, mortality and hospital readmission of patients with ADHF. The aim of this study was to determine possible association of impaired liver function tests (LFT) with hydration status in patients with ADHF.

Methods: In 200 patients with ADHF (184 male, 72.9 ± 10.7 years (M±SD), arterial hypertension 79%, ischemic heart disease 65%, myocardial infarction 43%, atrial fibrillation (AF) 62%, diabetes mellitus 36.5%, known chronic kidney disease (CKD) 38%, chronic anaemia 23.5%, chronic obstructive lung disease 23.5%, ejection fraction (EF) 45 ± 12%, EF <35% 25%, chronic hepatic diseases 9.5%) alanine transaminase (ALT), aspartate transaminase (AST), total bilirubin, alkaline phosphatase (AP), gamma-glutamyl transpeptidase (GGT) were measured and hydration status by bioimpedance vector analysis (BIVA) was assessed using resistance (R) and reactance (Xc), standardized by height (h). LFTs were considered abnormal when levels exceeded local upper normal levels. Mann-Whitney and Spearman test were performed. P < 0.05 was considered statistically significant.

Results: Increase of ALT and/or AST occurred in 29 (14.5%) patients (alone ALT/alone AST/ both TA - in 42.3, 19.2, 38.5% respectively), increase of bilirubin, AP and GGT - in 68 (34%), 14 (7%), 20 (10%) patients respectively. Patients with versus without transaminases increase had higher rate of signs of congestion: echo-hydropericardium (33 vs 12%, p < 0.01), radiological signs of hydrothorax (72 vs 32%, p < 0.001), jugular venous distension (55 vs 21%, p < 0.001). The patients with versus without increase of bilirubin demonstrated higher volume overload: lower levels of both R/h and Xc/h (218 ± 44 vs 238 ± 54 Om/m, p < 0.01 and 16 ± 7 vs 19 ± 8 Om/m, p < 0.01). Negative correlations between serum bilirubin and BIVA parameters of hyperhydration were revealed (r = -0.38 for R/h and r = -0.29 for R/h, p < 0.05).

Conclusions: impaired LFT were common in patients with ADHF and were associated with signs of congestion (hydropericardium, hydrothorax, jugular venous distension). Increase of bilirubin was associated with higher volume overload assessed

by BIVA. The results of the study suggest that congestion may be important in the development of cardiohepatic syndrome in patients with ADHF.

P770

Predictors of onset of acute heart failure in ST-segment elevation acute coronary syndrome. Results from the ARIAM registryS Rufian Andujar¹; A Espinola Pardo²; E Blanco Ponce²; M Butron Calderon²; P Caravaca Perez²; J E Lujan Valencia²; J M Cruz Fernandez²; M Almendro Delia²; A Garcia Alcantara³; J C Garcia Rubira²¹Hospital Universitario Virgen de Valme, Cardiology, Sevilla, Spain; ²University Hospital of Virgen Macarena, Department of Cardiology, Seville, Spain; ³University Hospital Virgen de la Victoria, Malaga, Spain

Purpose: The occurrence of heart failure is one of the most frequent and serious complications associated with acute myocardial infarction. Our purpose is to identify the clinical variables associated with the onset of acute heart failure (AHF) in patients with Killip I class on admission.

Methods: Retrospective analysis of ARIAM registry data, collected from Intensive Care Units of Andalusian hospitals from January 2001 to January 2012. We analyzed 16511 patients admitted for STEMI categorized as Killip I class on admission, and 33 clinical variables associated with progression to Killip class III or IV.

Results: A total of 483 patients (2.9%) had AHF. They were older (mean age 69.7 vs 61.7, p < 0.001), and more often female (33.5% vs 21.3%, p < 0.001). In this group we found a significantly higher proportion of smoking, diabetes, hypertension, chronic heart failure, stroke, chronic respiratory disease and renal failure. These patients were more frequently treated with digoxin, diuretics, calcium-channel blockers and anticoagulants. In AHF group there was a higher mortality, both in ICU (35.2% vs 1.1%, p < 0.001), as during admission (36.9% vs 1.6%, p < 0.001). On multivariate analysis, age, female sex, diabetes, chronic respiratory disease, renal failure, atrial fibrillation or previous arrhythmia and anterior AMI were identified as significant independent predictive factors for AHF (table 1).

Conclusions: In our study group, obtained from the ARIAM registry data, 7 clinical variables easily collected at admission (age, female sex, diabetes, chronic respiratory disease, renal failure, atrial fibrillation and anterior AMI), were identified as significant independent predictive factors for AHF.

Variables associated to the onset of AHF

VARIABLE	P value	Odds ratio	95% confidence interval
Age	.000	1.050	[1.039-1.060]
Female sex	.005	1.367	[1.102-1.696]
Diabetes	.002	1.378	[1.129-1.682]
Chronic respiratory disease	.025	1.588	[1.060-2.381]
Renal failure	.001	2.554	[1.440-4.532]
Atrial fibrillation	.002	1.695	[1.218 -2.358]
Anterior AMI	.000	1.768	[1.465-2.134]

Table 1. Clinical variables associated to onset of acute heart failure.

P771

Heart-type fatty acid binding protein as a part of prognostic model of lethal results after myocardial infarctionY Yaroslava Giliova¹; N Tytarenko¹; M Kopytsya¹; O Petyunina¹; O Oparin¹;I Vyshnevskaya¹; L Peteneva¹¹National Institute of Therapy n.a. L.T.Malaya of NAMS of Ukraine, Cardiology Department, Kharkiv, Ukraine

Background: Heart-type Fatty Acid Binding Protein (H-FABP) is cytoplasmial protein. It releases in 30 minutes after onset of ischemia and enhances transport of fatty acids from cardiomyocytes.

Aim: to examine the prognostic value of biochemical and clinical markers and their sum in relation to development of lethal result in six months after AMI.

Methods and results. 189 patients with AMI were examined. They were divided in two groups: 1 - NSTEMI n = 36 (9%); 2 - STEMI n = 153 (81%), male 138 (73%). H-FABP was defined in blood plasma with ELISA, its concentration was measured using normal definitions till 1 ng/ml. During 6 months of follow-up 17 patients (9%) died. About 60 clinical biochemical markers were analyzed using sequential Wald-Genkin's procedure. Following factors in died patients and survivors had significant differences: H-FABP, class of heart failure (Killip), age, glucose level. The curves of sensitivity and specificity were made using method of ROC-analysis and the threshold values were chosen for each parameter. H-FABP had sufficient level of sensitivity 85.7%, but insufficient specificity (49.2%), and such markers as age, heart failure class (Killip) and glucose level had insufficiency sensitivity (50.0%; 66.7%; 43.7%) according to prognosis of lethal case. Every parameter was graded in points in relation to the

cut-off value and the scale for measurement of prognostic coefficient (PC) using Gubler's method was proposed. Positive value of PC is associated with lethal result in patients with AMI.

Conclusions: The mathematical model including the sum of markers - H-FABP level, age, glucose level, heart failure class (Killip) allows to prognose lethal result in patients with AMI with sensitivity 88% and specificity 78%.

Prognostic markers and model					
Marker	Se	Sp	AUC	p (AUC)	OR (±95% CI)
H-FABP	85,7	49,2	0,70	0,001	5,8 (1,2-19,7)
Glucose	66,7	66,7	0,68	0,033	4,0 (1,3-11,2)
Age	50,0	93,0	0,76	<0,0001	13,5 (4,3-39,1)
HF, Killip	43,7	90,8	0,70	0,066	7,7 (2,5-22,8)
Prognostic model	88,2	77,9	0,90	<0,0001	26,5 (5,4-86,4)

Se - sensitivity, Sp - specificity, AUC - area under ROC curve, P (AUC) - level of difference between AUC and 0,5, OR (±95% CI) - odds ratio with lower and upper limit 95% of confidence

P772

Factors associated with prolonged hospitalization, readmission and death in elderly heart failure patients

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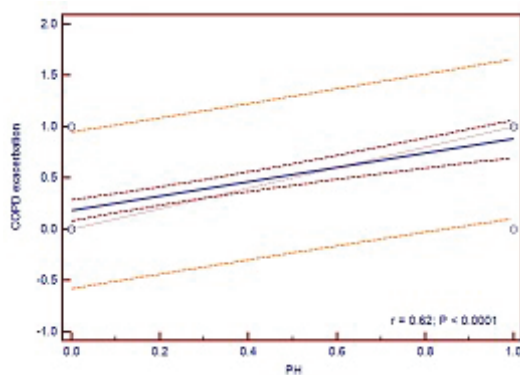
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Purpose: The purpose of this prospective study was to identify factors associated with prolonged hospitalization (PH), readmissions and death in elderly patients presenting heart failure with reduced ejection fraction (HFREF).

Patients and Methods: all consecutive patients aged ≥ 65 years, discharged with a diagnosis of acute new-onset heart failure with LVEF ≤ 45%, were included and followed-up for 1 year.

Results: 71 patients were included. Mean age was 72.5 years, 50% were female. PH was found in 34 (48%) patients and was independently predicted by the rural home of the patients (p=0.005), NYHA functional class 4 (p<0.001), the presence of comorbidities (p=0.023), COPD exacerbation (p<0.001) and chronic kidney disease (p=0.025). In multivariate analysis, only COPD exacerbation was independently associated with PH (p=0.003). 19 patients (27%) experienced readmissions during the 1 year follow-up, of which 12 (17%) had cardiovascular and 7 (10%) had non-cardiovascular causes. The variables associated with rehospitalizations were, in univariate analysis: infections (p<0.020), COPD exacerbation (p=0.015), comorbidities ≥1 (p<0.0001) and PH at baseline (p<0.0001). At multivariate analysis, independent predictors for readmissions were the presence of comorbidities (p<0.001) and PH at baseline (p<0.01). The 1 year mortality rate was 9.8% (cardiovascular deaths 5.6%, non-cardiovascular deaths 4.2%). The only independent predictive variable for mortality was NYHA functional class 4 at baseline hospitalization (p=0.001).

Conclusion: elderly patients are at high risk for prolonged hospitalization, readmission and death after a first hospitalization for HFREF. These outcomes have as independent powerful predictors the severity of HF, the presence of comorbidities and baseline PH.



COPD exacerbation and PH in HF patients

P773

Clinical and laboratory characteristics of short term mortality in acute heart failure patients

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Purpose: To identify variable clinical and laboratory characteristics of short term mortality in patients presented with acute heart failure.

Methods: We enrolled 120 patients presented with acute heart failure (HF) admitted to emergency and cardiac care unit and have undergone clinical evaluation, laboratory investigation, electrocardiography (ECG), and echocardiography.

Results: Mean age of the studied patients was 59.3 ± 10.1 years, mean body mass index was 27.9 Kg/m²

and 55.8% were males. Twenty nine patients (24.2%) died within 30 days (short term mortality), 14 patients (48.3%) of them died within one week. Patients with short term mortality were mainly males (72.4%), have higher BMI, lower oxygen saturation, tachycardia (HR> 100 bpm) and elevated jugular venous pressure (JVP). HF patients with short term mortality had significant statistical difference (P value < 0.05) compared to survived patients regarding these findings: increased serum creatinine (S.Cr.), anemia, hyponatremia, hypoalbuminemia, prolonged PR interval, wide QRS complex, poor R wave progression, atrial fibrillation (AF), left bundle branch block (LBBB), increased left ventricular & left atrial (LA) size, and low left ventricular ejection fraction (LVEF). Increased LV end diastolic and systolic dimensions (LVEDD & LVESD), LA size and S.Cr. had the highest area under the curve and strongest predictability for short term HF mortality.

Conclusion: This study revealed that there are different clinical and laboratory characteristics which are associated with short term mortality in patients with acute HF. These include: tachycardia, prolonged PR interval, wide QRS complex, poor R wave progression, AF, LBBB, impaired kidney function, anemia, hypoalbuminemia, dilated LV size and low LVEF. Of note, increased LVEDD, LVESD, LA size, and S.Cr. had the strongest predictability of short term HF mortality.

Predictors of short term mortality of HF						
	AUC	P value	95% CI	Cut off value	Sensitivity	Specificity
LVEDD	75%	0.001*	0.6 - 0.8	≥66.5 mm	89%	68%
LVESD	73%	0.001*	0.6 - 0.8	≥53.5 mm	75%	65%
Left atrial size	65%	0.01*	0.5 - 0.8	≥ 48 mm	72%	64%
Creatinine	65%	0.01*	0.5 - 0.8	≥ 1.6 mg/dl	62%	60%

LVEDD: left ventricular end diastolic dimensions, LVESD: left ventricular end systolic dimensions, mm: millimeter, mg: milligram, dl: deciliter, *: significant P value

P774

Determinants of improvement in functional status after a hospitalization for an acute heart failure syndrome; preliminary results

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Purpose: Patients hospitalized for an acute heart failure (AHF) syndrome have a high probability of readmission in the short-term with deterioration of their functional status. The aim of the present study was to identify determinants of functional status improvement at 6 months after optimal medical therapy in patients admitted for an AHF syndrome and investigate whether this may be related to changes in central hemodynamics and vascular function.

Methods: Our study included 45 patients (mean age 69 years, 84% males) who were admitted for AHF syndrome and were followed-up for 6 months after discharge. None of the patients had been admitted with heart failure in the meantime. Functional status (NYHA class) was recorded on admission and follow-up. A comprehensive echocardiographic study, a 6-minute walking test and peripheral vascular studies [assessment of brachial artery flow-mediated dilation, carotid-femoral pulse wave velocity, central augmentation index (AIx) and estimated central aortic pressures] were performed in all subjects 24-48 hours prior to discharge and at 6-month follow-up.

Results: Left ventricular ejection fraction (LVEF) was 35 ± 13% and 73% of patients had heart failure with reduced LVEF (<40%, HF-REF). Most patients (62%) had ischemic etiology of heart failure and 22% of patients appeared with NYHA IV on admission. At follow-up a significant increase in the use of furosemide (78 vs 47%, p<0.005), aldosterone antagonists (64 vs 38%, p=0.017) and beta blockers (91 vs 56%, p<0.001) was observed. An increase in peripheral (p=0.003) and central (p=0.001) systolic blood pressure, peripheral (p=0.014) and central (p=0.003) pulse pressure, AIx (p=0.002), LVEF (p<0.001), LV stroke volume index (p=0.009)

and 6-minute walking distance ($p < 0.001$) and a decrease in inferior vena cava (IVC) diameter ($p = 0.026$) and pulmonary artery systolic pressure ($p < 0.001$) were found at follow-up compared to baseline. Twenty seven (60%) patients improved NYHA class. Functional improvement was associated with the presence of HF-REF, use of aldosterone antagonists, beta-blockers and furosemide ($p < 0.05$ for all), and an increase in LV stroke volume index ($p = 0.012$).

Conclusion: In patients hospitalized for an AHF syndrome, no changes in vascular function indices were observed at 6-month follow-up despite optimal therapy. Peripheral and central systolic and pulse pressure and Alx increased indicating probably the increase in LV stroke volume. Improvement in functional status at 6 months was associated with improved LV performance and the use of life-saving therapies, mostly evident in patients with HF-REF.

P775

Heart failure complicating acute coronary syndromes in Montenegro

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Montenegro, the state of 650 000 inhabitants has ten hospitals, only one hospital is with catheterisation laboratory and capabilities for primary percutaneous cardiac intervention and Center for cardiac surgery. All patients who need this type of interventions are referred to Podgorica. The aim of this study was to examine which are the risk factors for congestive heart failure (CHF) in acute coronary syndrome (ACS) in 415 patients with ACS. The group 1, $n = 236$ were patients from hospital with cath lab. The group 2 included 179 patients from other hospitals without cath lab. They were treated in their local hospitals, 5-20 days. Number of patients with CHF (Killip classes II or III) on admission was greater in group 2 (34,6% vs. 27,7%). Patients with CHF were older ($76 \pm 10,9$ vs. $61,6 \pm 11,1$ $P < 0,001$), were more likely to be hypertensive, to have a prior CABG, had longer time to hospital presentation ($2,2 \pm 1,6$ vs. $3,2 \pm 1,1$ h), had higher prevalence of STEMI, diabetes (32,1% vs. 18,5%), fewer received β -blockers and statins. CHF on admission was associated with increase in mortality rates during hospitalization (12,2% vs. 3,0% (with vs. without CHF). Hospital development of CHF was also associated with an even higher in-hospital mortality rate (16,9% vs. 9,0%, $P < 0,0001$). Patients with ACS presenting with CHF required more aggressive treatment. Despite this, they are less likely to be treated with reperfusion therapy and medications with proven mortality benefit.

P776

Clinical characteristics and predictors of mortality at six months of patients hospitalized for acute heart failure

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Introduction: Heart failure is known as a major cause of morbidity and mortality in developed countries. Few data are currently available on the demographic and clinical characteristics and prognosis of patients hospitalized for acute heart failure.

Objective: To determine the clinical characteristics and predictors of 6-month mortality of patients admitted for acute heart failure.

Methodes: Retrospective Study on 234 patients hospitalized for acute heart failure. The demographic, clinical, echocardiographic and laboratory were collected and tested first by univariate analysis and then multi variables studies to identify prognostic markers.

Results: The mean age was $65 \pm 13,8$ years, 65% were male. Hypertension was noted in 60,3% and 51,7% diabetes. Most of our patients (60,3%) had a clinical congestive heart failure. We were able to determine the causal heart disease in almost all cases (97,4%). The main causes of IC were ischemic heart disease (48,7%), Hypertension (21,4%) and dilated cardiomyopathy (14,5%). The precipitating factor most frequently noted was ischemic attack (35%) followed by pulmonary disease (20,5%). Most of our patients (97%) had received transthoracic echocardiography, among them 46,6% had a normal ejection fraction ($\geq 50\%$) and 17,2% had a severe left ventricular dysfunction ($< 30\%$). At the exit, the use of an inhibitor of the renin angiotensin system (ACE inhibitors or ARBs) was observed in 86,8% and that of beta-blockers in 41,5% of patients. The mortality rate at 6 months was 11,2%. Several clinical and biological prognostic factors were identified in univariate studies. In multivariate analysis, independent predictors of mortality at 6 months were: QRS width > 130 ms (OR, 6,15; 95% CI, 1,25-30,15; $p = 0,025$), hyperglycemia on admission (OR, 1,32; 95% CI, 1,12- 1,56; $p = 0,001$), higher A1C (OR, 0,49; 95% CI, 0,39- 0,67; $p < 0,0001$), worsening of renal function during the stay (OR, 13,87; 95% CI, 3,54-54,24; $p < 0,0001$) and non-use of beta-blockers to the output (OR, 0,06; 95% CI, 0,007-0,58, $p = 0,015$).

Conclusion: the predictive prognostic factors for mortality in the medium and long terms are still poorly studied. In our study, independent predictors of mortality at 6 months were: wide QRS > 130 ms, hyperglycemia on admission, a high A1C, worsening of renal function during the hospitalization and non-use of beta-blockers on exit.

P777

The role of hepatic dysfunction in clinical course and prognosis for patients with decompensated systolic heart failure

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The purpose of this study is to evaluate the role of liver function markers combined with BNP and hs-CRP levels as predictors for the course of disease in a short time and in a 1-year follow-up prognosis for patients with decompensated systolic heart failure (DSHF).

Methods and materials: we examined 450 patients divided into 2 groups: I) 214 patients, 129 males and 85 females (average age $67,2 \pm 10,2$ years), with total bilirubin level ≥ 20 $\mu\text{mol/l}$; and II) 236 patients, 106 males and 130 females (average age $71,4 \pm 10,5$ years) with total bilirubin level < 20 $\mu\text{mol/l}$ who had been hospitalized with DSHF of ischemic or hypertensive origin. EF at admission was $29,3 \pm 3,9\%$ vs $30,1 \pm 3,2\%$ respectively. Serum total and direct bilirubin, AST, ALT, ALP, hs-CRP, WBC and BNP were taken at admission (D1) and discharge (D10 ± 4). We obtained data about re-hospitalizations due to DSHF and cardiovascular deaths in a 1-year follow-up (D360).

Results: mean levels of bilirubin were higher in group I - $39,8 \pm 7,5$ $\mu\text{mol/l}$ - $21,4 \pm 4,6$ $\mu\text{mol/l}$ vs $11,9 \pm 3,6$ - $10,6 \pm 2,3$ $\mu\text{mol/l}$ in group II, (p -value = 0,02 for admission and p -value = 0,03 for discharge). ALT and AST levels were slightly elevated in both groups: ALT - $36,8 \pm 9,6$ vs $35,0 \pm 6,8$ U/L; AST - $38,1 \pm 7,0$ vs $36,6 \pm 8,9$ U/L, (p -value = 0,54 for admission and p -value = 0,61 for discharge). ALP was elevated on D1 in group I to $144 \pm 4,7$ vs $132,5 \pm 5,0$ $\mu\text{mol/l}$ in group II. BNP levels were elevated in both groups - 1706 ± 191 - 980 ± 92 pg/ml vs 1522 ± 166 - 1127 ± 139 pg/ml, (p -value = 0,25 for admission and p -value = 0,21 for discharge). Hs-CRP was higher in group I: $38,9 \pm 2,5$ - $25,9 \pm 1,7$ mg/l vs $28,4 \pm 2,6$ - $16,3 \pm 2,4$ mg/l, (p -value = 0,033 for admission and p -value = 0,041 for discharge). WBC were not significantly elevated in both groups. Average daily doses of i.v. furosemide were $36,4 \pm 6,9$ vs $25,6 \pm 4,0$ mg (p -value = 0,044). Hospital mortality was 5,6% vs 5,5%, (p -value = 0,79). By 1 year follow-up, mortality rate in group I = 43,8%, in group II = 36,6%, which is significantly lower as p -value = 0,047. The rates of re-hospitalizations due to DSHF about the same in both groups ($0,64 \pm 0,11$ vs $0,55 \pm 0,13$ per 1 patient in a 1 year, p -value = 0,36).

Conclusion: hepatic dysfunction has a negative impact on the clinical course of DSHF reflected in the higher demand of i.v. loop diuretics and is associated with induction of systemic inflammatory response marked by elevated hs-CRP levels. However, at the moment we find no significant correlation of hepatic dysfunction and in-hospital mortality. In the long run (1-year follow-up) the risk of cardiovascular death is higher for those patients who suffered from hepatic dysfunction.

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Liver function abnormalities, clinical profile and outcome in acute decompensated heart failure

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Aim: alteration in liver function tests (LFTs) is a recognized feature of acute decompensated heart failure (ADHF), the aim of this study was to assess the prevalence of abnormal LFTs and the associated clinical profile in ADHF patients.

Methods: 185 consecutive patients admitted with acute heart failure between 2013 and 2014 were selected; LFTs: alkaline phosphatase (AP), alanine transaminase (ALT), aspartate transaminase (AST) and bilirubin were performed at baseline. Demographics characteristics, functional, echocardiography and hemodynamic variables were evaluated. $P < 0,05$ was considered statistically significant. Follow up at 90 days was performed.

Results: mean age was 52 (± 13) years and 79,7% were males; 109 patients (58,9%) had an abnormal LFTs, abnormal AST/ALT was present in 41 (37,6%) patients, total bilirubin/AP in 80 (73,4%) and total bilirubin 57 (52,3%). Patients with cardiogenic shock and/or low cardiac output at admission had higher prevalence of abnormal LFTs (93,8% vs 55% $p = 0,011$) and that was mainly due to abnormal TGO/TGP values (43,8% vs 21,1% $p = 0,039$). Also, abnormal LFTs were associated with more inotropic use (89,5% vs 10,5% $p = 0,014$). There was not any significant association between abnormal LFTs and systemic congestive presentation. Abnormal LFTs were not associated to death and/or ADHF re-hospitalizations at 90 days.

Conclusions: almost 50% of our population had abnormal LFTs at baseline, the most frequent feature was a total bilirubin and AP elevation but these parameters were not related with systemic congestion; an elevated TGO and TGP value was associated to a high risk clinical profile at admission, this could be related with hepatocyte necrosis.

P779

Cockcroft-gault versus modification of diet in renal disease: importance of glomerular filtration rate formula for prognosis in acute heart failure

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Introduction: the deterioration of renal function reflects the hemodynamic status of the patient and proved to be a risk factor for morbidity and mortality in cardiovascular diseases and particularly in heart failure (HF).

Aims: to determine which of creatinine-based calculation using the MDRD Study formula or Cockcroft Gault (C-G) that influences the rates of death / readmission for "new" episode of HF at 24 months of follow-up.

Methods: The study started in April 2009 in acute HF registry level. We included 600 patients (51.5% women) in the analysis. Carried out follow-up at 24 months with combined endpoint: death or readmission for HF. the multivariate Cox regression was used to determine the best estimated glomerular filtration rate (eGFR) formula that is associated with worse prognosis. Statistical analysis with SPSS. Statistical significance at $p < 0.05$.

Results: The study population consisted of 52% women. The age was 77 ± 10 years. The average ejection fraction was $48 \pm 16.1\%$.

The mean estimated glomerular filtration rate was 55.4 ± 23.6 ml/min/1.73m² by MDRD and was 50.3 ± 27.7 ml/min by Cockcroft-Gault.

By univariate Cox regression found that eGFR by C-G was predictive of events at 24 months (HR = 1.7; CI (1.3-2.2), $p < 0.001$) and also the eGFR by MDRD was predictive of events at 24 months (HR, 1.5; CI (1.3-1.8), $p < 0.001$). After multivariate analysis eGFR by C-G was the best predictor of events at 24 months (HR, 1.8; CI (1.3 2.5); $p < 0.001$) compared with the MDRD formula ($p = NS$).

Through the analysis of Kaplan-Meier survival curves the eGFR: stage 4 and 5 of chronic kidney disease (CKD) were associated with worse prognosis (log rank $p < 0.001$).

Conclusions: estimated glomerular filtration rate by Cockcroft Gault formula is preferable because was associated with worse prognosis in decompensated HF.

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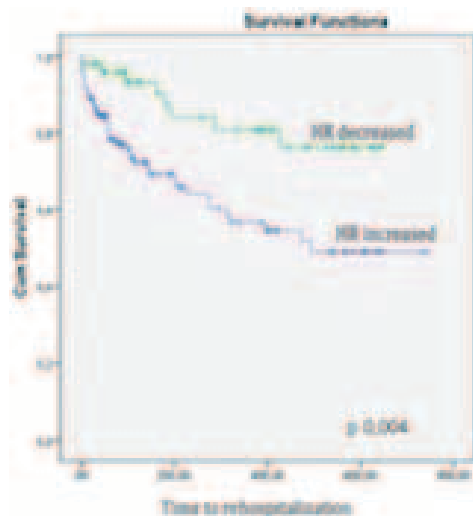
Decrease in heart rate during hospitalization is associated with lower readmission rates

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The aim of this study was to evaluate whether the improvement in the heart rate (HR) in patients with a reduced ejection fraction (REF) hospitalized for acute heart failure predicts readmission rates for heart failure (HF).

Methods: A prospective cohort study of 176 patients admitted to our centre for acute heart failure was conducted. All hospital readmissions within 18 months of discharge were reviewed. We divided the study population in two groups, one in which the HR decreased during hospitalization and the other in which HR increased.



HR and time to readmission

Patients with non-sinus rhythm were excluded from the analysis. Ejection fraction (EF) was measured with echocardiography by Simpson's rule and HF-REF was defined when EF was $< 45\%$. Kaplan-Meier was used to analyse readmission rates for HF.

Results: The study population had a mean age of 67 ± 13 years. Most patients were men (76%). The mean EF was $24 \pm 10\%$. The mean HR at admission in the study population was 83 ± 16 bpm and 74 ± 15 bpm at discharge.

During the 18-month follow-up, the readmission rate for the group with improvement of the HR during hospitalization was 15.4% compared with 34.1% for the other group - a difference of 18.7%.

The median time period to readmission was higher in the group with a good control of HR during hospitalization being 645 days compared to 494 days in the other group. The readmission rate was lower in the group in which HR improved during hospitalization being 10% at 6 months, 19% at 12 months and 24% at 18 months compared with the group with worse control of HR (31%, 43% and 51% at 6, 12 and 18 months respectively) $p < 0.004$.

Conclusions: Improvement of HR during hospitalization for acute heart failure in patients with HF-REF is associated with a lower readmission rate for heart failure.

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Hyponatremia in acute heart failure in Spain: comorbidities, mortality and readmissions

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Objective: Hyponatremia (HNA) is the most common electrolyte disorder in clinical practice. Besides being an independent predictor of morbidity in patients hospitalized for heart failure (HF), many studies have reported an increase in hospital mortality associated with this entity. The aim of our study was to determine the incidence, average stay, comorbidities, readmissions and mortality of hyponatremia in acute HF cases recovered from the national basic minimum data set (MDS) registry.

Material and Method: National data from the MDS registry of patients discharged from the services of Internal Medicine (MI) after admission to the Hospitals of the National Health System (NHS) for HF (ICD-9: 428; DRGs 127 and 544) were analyzed between 2005 and 2011. A descriptive analysis of the data was performed, comparing the diagnostic codes and administrative variables between patients with HF with and without HNA. The chi-square test for qualitative variables and t-student for quantitative variables was used. We performed a bivariate analysis to detect differences between groups in mortality, mean age, Charlson index, mean stay and readmission rates. A multivariate analysis, using logistic regression as the dependent variables in-hospital mortality and hospital readmission and as the independent variables age, sex, and comorbidity standardized according to the Charlson index and the presence of HNA was performed.

Results: 504.860 patients with acute HF were identified, 11.095 of which had HNA. The overall mortality from all causes in patients with HNA series stood at 17% (1.937 patients), compared to 11% in non-Hyponatremic (53.820 patients). The probability of readmission was 22%, and 17% in the HNA and normonatremic group respectively. Hyponatremia was associated with increased mortality during hospitalization for acute HF with an odds ratio (OR) of 1.58, 95% CI 1.50 to 1.66 ($p < 0.05$). HNA remained statistically significant in the regression model after adjusting for sex 0.919 (95% CI 0.902 to 0.936), age OR 1.061 (95% CI 1.060 to 1.062) and Charlson index OR 1.388 (95% CI 1.361 to 1.461). The level of statistical significance in all the analysis described was $p < 0.05$.

Conclusions: In our observation, HNA was associated with increased mortality and readmission rates in subjects hospitalized for heart failure. In our study, a statistically significant association between HNA and increased hospital mortality was found independently associated despite sex and Charlson comorbidity index. We also found an increase in the codification of the diagnosis of HNA in the discharge sheets during the study period.

CHRONIC HEART FAILURE

P782

The use of the quadropole left ventricular electrode for cardiac resynchronization therapy in treatment of congestive heart failure

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Objective: To explore the advantages of the quadropole left ventricular electrode for cardiac resynchronization therapy in the treatment of congestive heart failure.

Materials and Methods: On 07.09.2013 for the first time in our country was held implantation of CRTD with quadropole left ventricular electrode UNIFY QUADRA.

This system has several configurations for stimulation and allows physicians to optimize the system depending on patients' individual features. Furthermore, it allows to control complications without any surgical reposition of electrode. QUARTET lead is used as a part of UNIFY QUADRA and has four electrodes with intervals of 4.7 cm and has up to 10 stimulation options.

Results: The device was implanted to 73-year-old patient with hypertensive left ventricular remodeling, congestive heart failure III class NYHA and left bundle branch block (LBBB). Patient noted the increase of dyspnea, edema of the lower extremities and low exercise tolerance since the beginning of 2013. ECG: LBBB, PQ-180 ms, QRS-160 ms, QT-410 ms. Echocardiography: ESD-5.1 cm. EDD-6.0 cm, ESV-130 ml. EDV-187 ml. EF-30% NT proBNP-612 pg/ml. Despite optimal medical therapy, the patient continued to suffer from congestive heart failure. Then, it was decided to implant a cardiac resynchronization device with a defibrillator function. During the operation, there were difficulties associated with the high threshold of stimulation and phrenic nerve stimulation. We used 4 vectors of stimulation (1,2,7,9) from 10 configurations. Only the use of seventh vector of stimulation, from medium second 2 to the proximal fourth electrode, we reached optimal left ventricular stimulation. Afterwards, the stimulation threshold in left ventricular electrode was lower than 1V and phrenic nerve stimulation was not observed. CRT implantation led to a narrowing of QRS to 120 ms. On Echocardiography after 3 months: ESD-4.9 cm. EDD-5.8 cm, ESV-98 ml. EDV-160 ml. EF-39% NT proBNP decreased to 310 pg/ml.

Conclusions: Thus, our experience demonstrates that quadropole stimulation technology provides more opportunities of stimulation of the left ventricle and cope with common complications of stimulation, such as stimulation of the phrenic nerve stimulation and high thresholds.

P783

The effect of thyroid function on clinical outcome in patients with chronic heart failure

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Objective: To determine the clinical effects of thyroid dysfunction on patients with chronic heart failure.

Methods: Patients with a diagnosis of heart failure (n=1613) were followed for cardiac-related hospitalizations and death for 2 years. Patients with thyroid dysfunction were compared with those with normal thyroid function.

Results: Nineteen patients (1.17%) had thyroid dysfunction. In this group, 52.6% had hypothyroidism and 47.4% had hyperthyroidism. The mean age was 62 ± 17 years. Severe systolic dysfunction was present in 47% of patients, moderate systolic dysfunction in 31.6% and mild systolic dysfunction in 21.1%. The number of hospitalizations for cardiac decompensation was significantly higher in the group with thyroid dysfunction compared with the group who had normal thyroid function, with successively (26.3% and 6.58%, p=0.003). No mortality was observed in this study.

Conclusions: The results showed that thyroid dysfunction can predict Acute decompensated heart failure.

P784

Lack of specialist involvement in heart failure diagnosis and care leaves concerning gaps in management; a cross-jurisdictional analysis

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Purpose: This study sought to determine the characteristics of patients with a label of heart failure in the community without a record of previous specialist assessment in an ongoing cross-jurisdictional review in Northern Ireland (NI) and Republic of Ireland (ROI)

Methods: Patients with a coded diagnosis of heart failure were identified in 11 general practice electronic health records. Records were reviewed and data was extracted on those patients which had no previous record of cardiology specialist assessment on file.

Results: To date we have 131 patient files from 11 general practices were reviewed. 52 patients met the criteria for inclusion which were that they had not had a specialist review for management of their heart failure. The details are outlined in Table 1.

Conclusion: Patients with heart failure in the community who have not had specialist assessment represent a substantial proportion of patients coded as having heart failure in general practice. There was insecurity of diagnosis because of lack of echocardiography which also gives rise to difficulties in ensuring appropriate therapy is applied as it is not possible to determine if patients have heart failure and if so whether it is HF-REF or HF-PEF. Strategies to reach this patient group need to be developed to confirm diagnosis and implement appropriate management strategies.

Table 1

	NI (Total n = 55)	ROI (total n = 76)
Number of Patients	17 (31%)	35 (46%)
Age average	76	82
Female	13 (76%)	23 (66%)
Cardiology Review	0	0
Known to Nurse-led HF service	0	0
ECHO	3 (18%)	14 (40%)
ECHO in last 5 years	0	5
NT-Pro BNP	9 (53%)	15 (42%)
NT-Pro BNP level	896	1570
Beta Blocker	9 (53%)	22 (63%)
ACEI/ARB	8 (47%)	22 (63%)
MRA	2 (12%)	0 (0%)
Loop	13 (76%)	30 (85%)

P785

Do early follow-up appointments combined with the use of beta-blockers reduce 30-day hospital readmissions in an underserved multi-racial population?

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Purpose: Based on data collected by the Centers for Medicare & Medicaid Services, congestive heart failure (CHF) is the most common reason for hospitalization in the Medicare program, accounting for 1.4 million hospitalizations and nearly \$17 billion in 2010. The rate of readmission in minority populations is high. The disparity between races is prevalent in Camden, where minorities make up nearly 95% of the population. It has been shown that early follow-up (post discharge visit within seven days) was associated with lower rates of 30-day readmission among Medicare beneficiaries. The current practice has been to take measures that ensure early follow-up, prescribe appropriate medications at the time of discharge, and provide patient education as dictated by the American Heart Association (AHA).

Methods: Patients of all races admitted to a tertiary urban medical center from the Camden, NJ zip code with acute decompensated volume overloaded heart failure (ADVOHF) from January 2011 to December 2011 were selected (n = 174). A retrospective chart review was conducted. All patients were followed to determine if readmission occurred within 30 days.

Results: The study populations' demographics were minority mean age of 63 and white mean age of 61, male (59%), minority (70%). Early follow-up appointments for all patients occurred in 114 patients (65%). Of the patients that were prescribed beta-blockers and seen as early follow-up, 90 (79%) had no readmission within 30-days and 20 (17.5%) had one readmission during that period. In the 60 patients (34%) who were prescribed beta-blockers but did not receive an early follow-up appointment, 38 (63%) no readmission within 30-days and 13 (22%) had one readmission. 51 (84%) patients of the patients who received a beta-blocker and early follow up, had a readmission within one-year (p = 0.029)

Conclusion: In a city such as Camden, where many disparities exist between races, beta-blockers along with early follow-up, regardless of race shows a significant reduction in the rate of readmission within 30-days. Efforts to ensure early follow-up appointment is scheduled at the time of discharge will lead to better outcomes and a reduction in healthcare spending for patients with CHF.

P786

Ivabradine treatment in octogenarians with chronic heart failure: improvement in quality of life

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Purpose: Chronic heart failure (CHF) is associated with high mortality and morbidity. High values of resting heart rate (HR) are a risk factor for adverse outcomes. Ivabradine reduces HR through the selective and specific inhibition of cardiac pacemaker current If, that controls spontaneous diastolic depolarization in sinus node, regulating HR. The aim of our study is evaluate effectiveness of Ivabradine in reducing HR and improving outcomes in over 80 years of age, suffering from CHF.

Methods: We enrolled 25 patients aged over 80 years (Age 80 to 87 years), with left ventricle ejection fraction (LVEF) ≤ 40% (36%), affected by symptomatic CHF and referring to our CHF clinic. Patients were in sinus rhythm (SR), with resting HR >70 bpm and intolerant to beta-blockers or already in treatment with beta-blockers, without reaching target HR. Ivabradine target dose (5 mg bid) was associated at the pre-existing treatment. After 6 months follow-up, patients were evaluated by heart failure symptoms (NYHA class) and their quality of life (QOL) in daily activities by

Minnesota questionnaire score at 0 and 6 months. The results were analyzed using descriptive statistical methods.

Results: In these 25 patients (11 M and 14 F) ivabradine after 6 months of treatment reduced HR by a mean of 10 bpm (HR baseline 80 +/- 10 bpm). This was accompanied by not worsens NYHA class and improvement in Minnesota questionnaire score. Ivabradine was well tolerated. Reducing rest HR, Ivabradine improves well being and compliance to treatment.

Conclusion: In elderly patients with CHF increased HR worsens QOL and reduces compliance to therapy; patients are confined in the performance of daily physical activity and the resulting emotional state reduces daily life activities and social life. Introduction of Ivabradine in treatment of patients over 80 years of age, suffering from CHF symptoms, contributes to HR target improvement, enhancing compliance to treatment and it is a valid alternative to beta-blockers.

P787

Heart and liver: a tense relationship

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Purpose: Patients with chronic heart failure have a variety of liver abnormalities, known as cardio-hepatic syndromes. The aim of the study was to evaluate the prevalence and importance of liver function tests (LFT) abnormalities in a group of patients with chronic heart failure.

Methods: The study included 436 patients with chronic heart failure consecutively hospitalized in the Internal Medicine Clinic of a University Emergency Hospital over a period of 8 months.

Results: The mean age of the patients was 59.2 ± 17.4 years. The distribution by sex: 233 (53.4%) men and 203 (46.6%) women. Liver function tests abnormalities were frequent in patients with chronic heart failure: low albumin in 16.97% of the patients, increased total bilirubin in 13.30%, elevated alkaline phosphatase in 11.92%, elevated aspartate aminotransferase in 4.12%, alanine aminotransferase elevation in 3.66% of patients. The proportion of patients with reduced ejection fraction (≤40%) who had elevations in total bilirubin was 15.8%, almost double that of patients with preserved ejection fraction (>40%) (9.4%). Other liver tests were similar in patients with reduced and preserved ejection fraction. In hospital mortality of the whole study group was 5.9%. Baseline abnormalities in bilirubin, alkaline phosphatase and albumin were more common in patients who died during hospitalization.

Conclusions: Mild abnormalities of LFT are relatively frequent in patients with chronic heart failure, with a greater elevation of bilirubin than aminotransferases. Patients with reduced ejection fraction had a higher prevalence of increased bilirubin than those with preserved ejection fraction. Total bilirubin was a predictor of adverse prognosis during hospitalization.

P788

Predictors of heart failure and death after acute coronary syndrome

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Background: Patients with acute coronary syndrome (ACS) have an increased risk of hospitalization for heart failure (HF). The objective of this study is to evaluate predictors of HF and death in patients hospitalized for ACS.

Methods: Observational retrospective study of 508 patients admitted to the coronary care unit for ACS for 3 consecutive years. The follow-up lasted until October 31st, 2014 or until a new event (new ACS, stroke, hospitalization for HF, hospitalization for arrhythmic event or death). The primary endpoint was defined as hospitalization for HF and the secondary endpoint as a composite of death or hospitalization for HF.

Results: The study included 508 patients, 72.3% male, mean age 66 ± 13 years. During follow up (medium of 30 ± 18 months), 15 hospitalizations for HF and 43 deaths were recorded. On Cox multivariate analysis adjusted for potential confounding factors [gender, age, previous events, diabetes, hypertension, dyslipidemia, obesity, smoking, systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR) at admission] only Killip class, hemoglobin, maximum troponin, and left ventricular ejection fraction (LVEF) were independent predictors of the primary endpoint [with respective Hazard Ratios (HzR) of 1,642; 0,785; 1,007 and 2,004 with p < 0.05]. Cox multivariate analysis adjusted to the same confounding factors showed that the only predictors of the secondary endpoint were age, Killip class, glycemia on admission and LVEF (with respective HzR of 1,064; 2,170; 1,004 and 1,972 with p < 0.00). The analysis of Kaplan-Meier survival curves showed an association between lower DBP classes (<70 mmHg) and the primary endpoint (log rank 8,358 with p < 0.015) and also with the secondary endpoint (log rank 18,046 with p < 0.000).

Conclusion: Killip class, LVEF and the DBP shown to have predictive value for hospitalization for HF and death in patients hospitalized for ACS.

P789

Iron status in patients with chronic heart failure

Annual grant for Young Scientists "Club 30" Polish Cardiac Society M Marcinkiewicz-Siemion¹; K Ptaszynska-Kopczynska¹; A Lisowska¹; M Jasiewicz¹; A Szpakowicz¹; E Waszkiewicz¹; M Witkowski¹; WJ Musial¹; KA Kaminski¹

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Purpose: The changes in iron status are frequent among patients with chronic heart failure (HF). We investigated disease severity, exercise tolerance and changes in basic laboratory and hematological parameters in regards to absolute and functional iron deficiency (ID) in HF patients.

Methods and Results: We prospectively studied 60 optimally treated patients with stable chronic HF (62 ± 10 years, 93% males, 59% ischemic etiology, ejection fraction 24 ± 6.57%, New York Heart Association Class - NYHA II/III 40/60%) and 25 age- and gender-matched subjects without the disease (62.9 ± 10 years, 80% males, ejection fraction 62.8 ± 5.7%). Serum iron concentration, ferritin and transferrin saturation (Tsat) were assessed as the biomarkers of iron status. ID (absolute: ferritin < 100 ug/L, functional: ferritin 100-300 ug/L with serum transferrin saturation < 20%) was present in 30% (n = 18) of heart failure patients and in 40% (n = 4) of those with coexistent anemia (hemoglobin level < 12 g/dL in women and < 13 g/dL in men). Compared with the control group, stable heart failure patients had significantly lower hemoglobin and serum iron level (14.78 ± 0.96 vs 14.19 ± 1.17; 114, 42-196 vs 93.5, 75-120, respectively; in both p < .05). With increasing heart failure severity (II vs III) the percentage of anemia risen (4% vs 25%, p < .05) being expressed mainly by lower hemoglobin (14.73 ± 1.09 vs 13.84 ± 1.10, p < .05) and red blood cells level (RBCs; 4.88 ± 0.50 vs 4.63 ± 0.43, p < .05). The incidence of iron deficiency was the same in both NYHA class groups: II - 50% (n = 9) vs III - 50% (n = 9). Female gender, elevated B-type natriuretic peptide level (BNP; 190.7, 131-585 vs 164.95, 71-254; p < .05), lower mean corpuscular volume (MCV; 87.7 ± 3.52 vs 90.7 ± 4.46; p < .05) and higher unsaturated iron binding capacity (UIBC; 256.9 ± 76.2 vs 177.8 ± 65.1; p < .05) were characteristic to HF patients with ID.

Conclusions: Among HF patients ID is observed more often than anemia. The incidence of anemia, unlike ID, increases with the severity of the chronic HF. Biomarkers of iron status should be evaluated in addition to simple hematological parameters irrespectively of NYHA class.

P790

The first results of register of patients with decompensated chronic heart failure

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Purpose: Evaluate the effectiveness of the use of inotropic agents (IA) such as dopamine and dobutamine in patients with end-stage heart failure (HF) in a cardiology department, as well as the possibility of combined use IA with β-blockers. **Methods.** We analysed 64 medical histories of patients with end-stage HF with LVEF ≤ 30%, who were hospitalised in special cardiological department of heart failure and have indications for treatment with IA. **Results.** Patients aged 50.0 ± 11.5, 89% men. HF due ischemic heart disease 47% (n = 30), dilated cardiomyopathy 37% (n = 24), 13% (n = 8) - postmyocarditis cardiosclerosis, 3% (n = 2) - non-compact myocardium. Before initiating therapy with IA blood pressure (BP) was 90 ± 5 (60-110) mm Hg, heart rate (HR) 88 ± 9 (60-130) beats per minute. At baseline, patients were treated with β-blockers - 74% (n = 47), combined diuretic therapy - 100% (55% (n = 35) on the background of continuous furosemide infusion therapy (infusion pump), spironolactone - 65% (n = 42), ACEI / ARB - 19% (n = 12), amiodarone - 38% (n = 24), ivabradine 22% (n = 14). Indications for treatment with IA were multiple organ dysfunction, symptomatic arterial hypotension, resistant edema. In patients who achieved stabilisation of clinical status, but cannot undergo discontinuation of inotropic treatment this treatment was prolonged. After stabilisation 26% of patients (n = 16) without β-blockers were started taking β-blockers at a dose equal to 1,5 - 3% of the recommended for treatment of HF. Titration of β-blockers was performed in the presence of a stabilisation with the level of systolic BP ≥ 85 mm Hg during infusion of IA and after their discontinuation. Hospital mortality was 23% (n = 15), 19% (n = 12) were undergoing heart transplantation, 6% (n = 4) were excluded from heart transplantation list due to improvement of clinical status and 52% (n = 33) patients were discharged from hospital in II-III functional class HF. At the time of discharge all patients were treated with β-blockers at a dose equal to 32% (3-75%) of the recommended for HF treatment. At the time of discharge IA BP was 115 ± 9 (85-125) mm Hg, HR 70 ± 7 (60-90) beats per minute. Follow-up 1 year - mortality was 6,3% (n = 4), rehospitalised 9,4% (n = 6).

Conclusions: The use of IA in patients with HF in special cardiological department of heart failure like a bridge therapy before heart transplantation can improve clinical status even in end-stage HF. Initiation of treatment with β-blockers while continuing is possible in stable patients with positive diuresis.

P791

A score of optimal medical treatment achievement (SOMTA) in systolic heart failure patientsS Sergio Perna¹; D Petrovai¹¹General Hospital Meaux, Department of Cardiology, Meaux, France

Background: International Guidelines recommend full dose treatment by appropriate betablockers agents (BB) and renin-angiotensin system antagonists (RASA) as the mainstay of long term treatment for patients with systolic heart failure (1). It is a common findings, even in large international trials, that effectively administered doses are lower than target doses (2), suggesting suboptimal titration as well as side effects driven dose limitation.

Purpose: To propose a score of optimal medical treatment achievement (SOMTA) in patients with systolic heart failure.

Methods: SOMTA for any given patients is calculated as follows:

SOMTA = BB dose/ BB target dose × 0.5 + RASA dose / RASA target dose × 0.5 ;

Then, SOMTA value was 1.0 if BB and RASA doses reached the target, and zero if neither treatment was taken by the patient.

For instance, a patient treated by bisoprolol 5mg/day and ramipril 10 mg/day will have SOMTA value of $5/10 \times 0.5 + 10/10 \times 0.5 = 0.75$

Discussion: SOMTA could be useful in many domains. First of all, in daily clinical practice, a SOMTA target placed at 1.0 it will focus medical attention on the importance to achieve full doses of appropriate drugs in as many patients as possible. Moreover, average SOMTA calculated in the whole cohort of heart failure patients followed in standard of care outpatient clinics could be considered a reference value to target in fee-for-performance programs.

Conclusion: SOMTA appears an interesting tool to encourage dose titration of life-saving drugs in systolic heart failure and a potential objective index to evaluate the average adequacy of the pharmacologic treatment of chronic heart failure patients in outpatients clinics. Further studies should address these topics.

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P792

The safety and effectiveness of carvedilol high doses treatment of patients with chronic heart failureD V Dmitrii Ryabenko¹; EV Onishchenko¹; ES Rey¹¹NSC "Institute of cardiology named acad.Strazhesko" NAMS of Ukraine, Kyiv, Ukraine

Purpose: to explore the possibility of achievement and effectiveness of carvedilol (C) high doses in the treatment of patients with chronic heart failure (CHF).

105 patients (96 men and 9 women) with systolic II-III functional classes (FC) according to NYHA (61% of patients III FC) were examined after stabilization of clinical symptoms after achievement and at least 6 months treatment with target doses of C (100 mg/day) and enalapril (E) (20 mg/day). The raw mean value were: patients FC 2.6 ± 0.1 ; LV EF - $34.5 \pm 0.5\%$; LV EDV - 249.0 ± 4.0 ml; index of LV EDV - 124.6 ± 3.3 ml/m². Mean value of CHF manifestations duration was 25.0 ± 3.5 months. It was used the slow scheme titration (C daily dose was increased to 6.25 mg per week) and "intensive" approach to patients learning and outpatient examination.

Results: It was revealed that the target dose C 100 mg/day was achieved by 76.7% of patients (the average dose for the group was 92.3 ± 1.7 mg/day) and it was necessary 12.1 ± 1.0 months. By the end of the study (total duration of the titration and treatment of 19.5 ± 1.6 months) 74.4% of CHF patients continued receiving high doses of C. The treatment regimen was well tolerated by CHF patients, did not cause any serious side effects. As a result of treatment with high doses of C we detected the reduction of HR by 13.6% (79.1 ± 1.5 to 68.3 ± 2.1 in minutes) and dose of furosemide (153.8 ± 12.2 to 69.3 ± 14.0 mg/week) ($p = 0.0028$) and blood pressure level increase ($114.6 \pm 1.6\%$ to 120.4 ± 2.7 mm Hg) ($p = 0.003$). It was revealed that at the end of research the functional state of 81.3% of CHF patients met NYHA I FC (mean 1.2 ± 0.1) ($p = 0.0011$).

During the study 9 patients died (8.6%) - all during the period of dose titration. Analysis of the results with the help of Kaplan-Meier method showed that 5-year survival rate of patients was 88%.

Conclusion: Thus, as a result of slow schema titration 76.7% CHF patients can safely reach high doses of carvedilol (100 mg/day). Prolonged C high dose treatment leads to persistent and significantly improvement of patients NYHA FC and has a beneficial effect on 5-year survival of patients with systolic CHF.

P793

Coronary blood flow after LVAD implantation: first results of a prospective evaluationM Maria Goetjes¹; P Krings¹; N Pizanis¹; T Neumann¹¹University of Duisburg-Essen, West German Heart Center, Cardiology, Essen, Germany

Background: Left ventricular assist devices (LVAD) are a growing therapeutic option for patients with end-stage or acute decompensated left ventricular heart failure. More than 1000 implantations of LVADs last year surpasses the number of heart transplantations significantly. In spite of the fact, that non-pulsatile flow devices show a great clinical importance, still less is known about their influence on coronary hemodynamics. Therefore we analysed the effects of left ventricular assist devices on coronary perfusion including coronary flow reserve with the help of invasive evaluation before and after the implantation. Currently three patients have been surveyed exemplarily.

Methods: Coronary perfusion was measured immediately before and after LVAD implantation as well as 3 and 6 months after the procedure. While coronary perfusion data were acquired by invasive Doppler measurements, hemodynamic results were determined by right-heart catheter simultaneously. All measurements were repeated at four different rotorspeeds (capacity levels) of the LVAD system (2200 rpm - 2800 rpm).

Results: Coronary flow significantly increased after receiving a LVAD. Subsequent to the implantation coronary flow reserve (CRF) showed an increase from 1.8 ± 0.3 to 2.3 ± 0.8 . Data from 3 and 6 month after implantation revealed a CFR of 4.3 ± 0.5 (3 months) and 3.5 ± 0.7 (6 months). Higher capacity levels such as 2600 rpm and 2800 rpm came along with a better coronary flow reserve in contrast to the lower ones of 2400 rpm and 2200 rpm. Data from 6 month after implantation were most impressive by presenting a difference of CFR of $4.5 - 5$ (2600 - 2800) to a CFR of $2.5 - 3$ (2400 - 2200).

Summary: The results give a hint towards the influence of LVAD therapy and different capacity levels of this system on coronary perfusion. In summary we can assume a considerable effect of myocardial perfusion, further data are necessary, before we might be able to encourage and push on the process of vascular remodeling.

P794

Entire approach including social problems for stage D heart failure by multidisciplinary heart failure teamK Kodama¹; K Nishigami¹; T Sakamoto¹; T Honda¹; K Nakao¹¹Saiseikai Kumamoto Hospital, Cardiology, Kumamoto, Japan

Background: Stage D heart failure (HF) patients continue progress in spite of optimal medical therapy and tend to require the repeated hospital admissions. Although HF conditions and advanced medical treatment tends to be focused, the social profiles and supports of the patients with stage D HF might not be fully paid attention. We constructed a multidisciplinary HF team made up of not only health care providers but also MSW (medical social workers) and nursing care managers so as to reduce readmissions of stage D HF patients.

Patients and Methods: Over the 12 months from November 2013, 401 acute decompensated HF patients were admitted to our hospital, and our HF Team applied screening and general intervention to all cases. Of them, 33 cases that required particular social considerations got additional intervention by the same team. The team made a comparative review of the periods before readmissions, scales for depression, adherence to internal medicines and hospital visits, assuming the same group of patients before interventions to be the historical control group.

Results: The patients were aged 73 ± 12.8 . Of them, 24 (72.7%) were male with 6.6 ± 5.7 past hospital admissions due to HF. Intervention by the team into social backgrounds effectively extended periods between discharge and readmission from 149.4 ± 13.3 days to 170.2 ± 27.4 days ($p < 0.05$). There was no difference between the historical control group and the current group about the content of HF treatment, including drug therapy and implantable device. However, it turned out an improvement in the European heart failure self-care behavior scale and in the depression scale (Patient Health Questionnaire-9) contributed to a reduction in the periods between discharge and readmission. ($p < 0.05$)

Conclusions: Extended management including social support for stage D HF patients by multidisciplinary HF team could be effective to improve the patient's self-care and mental status, and reduce hospital readmissions.

P795

Visit-to-visit systolic blood pressure variability predicts adverse outcomes in stable heart failure with reduced ejection fractionE Elena Troitskaya¹; YV Kotovskaya¹; LA Babaeva¹; ZD Kobalava¹¹Peoples Friendship University of Russia (PFUR), Moscow, Russian Federation

Objective: There is a growing evidence of the prognostic significance of visit-to-visit BP variability in different groups of patients. Several studies evaluated prognostic significance of 24-h BPV in patients with heart failure. The aim of the study was to evaluate prognostic significance of visit-to-visit BPV in patients with stable HF and reduced ejection fraction.

Methods: Retrospective analysis included 100 pts (80 men, age 64.4 ± 9.3 yrs, BP $127.6 \pm 15.1/77.9 \pm 8.3$ mmHg, HR 72.3 ± 10.4 bpm) with stable II-III NYHA class HF with EF $< 40\%$ (mean $32.3 \pm 4.3\%$). Median of baseline NT-proBNP was 1200 pmol/l ($402.0-20524$ pmol/l). Patients received stable standard therapy for HF with ACE inhibitors, beta-blockers, verospirone and furosemide. BP was measured with a

validated oscillometric device. Visit-to-visit BPV was calculated as SD for 5 visits during 18 months. The endpoints included death, myocardial infarction (MI), stroke, hospitalization for HF.

Results: At the end of the study BP was $123,6 \pm 12,6/74,8 \pm 8,9$ mmHg, HR $69,3 \pm 9,1$ bpm. Visit-to-visit SBPV varied from 2,3 to 20,0 mmHg, DBPV from 1,5 to 13,0 mmHg. 47 endpoints in 37 patients were registered (21 deaths, 17 hospitalizations for HF, 6 MI and 3 strokes). There was no significant difference between groups with and without endpoints in age, gender, history of MI, baseline BP, severity of HF, EF ($33,1 \pm 3,5$ vs $31,0 \pm 5,1\%$, respectively, $p > 0,05$). A trend to higher baseline NT-Pro-BNP level was observed in patients with endpoints (median 1921 pmol/l vs 993 pmol/l, respectively, $p = 0,17$). The patients with endpoints had higher visit-to-visit SBPV ($11,2 \pm 4,0$ vs $9,5 \pm 3,5$ mmHg, $p < 0,05$). Endpoints occurrence significantly correlated with DM ($r = 0,20$), NYHA grade ($r = 0,21$) and visit-to-visit SBPV ($r = 0,22$), $p < 0,05$ for all. Nonlinear logistic regression analysis revealed higher risk of adverse outcomes in patients with higher level of visit-to-visit SBPV (OR 1,13, 95% CI 1,0-1,27, $p = 0,03$). Area under curve (AUC) for visit-to-visit SBPV $> 10,9$ mmHg was 0,74, 95% CI 0,53-0,94 (sensitivity 72,7%, specificity 80%, $p = 0,02$).

Conclusion: Visit-to-visit SBPV may predict adverse outcomes in patients with stable HF with reduced EF. The threshold of visit-to-visit systolic BPV $> 10,9$ mmHg may be used as prognostic criteria in this patient population.

P796

Non invasive evaluation of right atrial pressure by near-infrared spectroscopy: preliminary experience. A report from the SICA- HF study

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Aims: Jugular venous pressure reflects right atrial pressure (RAP) and, when increased, is a classical sign of heart failure (HF). However, its clinical assessment can be difficult.

Methods: RAP was measured non-invasively using near-infrared spectroscopy (NIRS) over the external jugular vein in patients with chronic HF enrolled in the "Studies Investigating Co-morbidities Aggravating Heart Failure" (SICA-HF) programme.

Results: Comparing 243 patients with HF (mean age 71 years; mean left ventricular ejection fraction (LVEF) 45%, median (inter-quartile [IQR] range) NT-proBNP 788 (280-1841) ng/l) to 49 controls (NT-proBNP ≤ 125 ng/l), RAP was higher in patients (7 [IQR: 4-11] mmHg) than in controls (4 [IQR: 3-8] mmHg, $p < 0.001$). Patients with RAP ≥ 10 mmHg were older, had worse clinical congestion and renal function, higher plasma concentrations of natriuretic peptides, larger left atrial volumes and higher systolic pulmonary artery pressure, were more often in atrial fibrillation but their LVEF was similar to patients with lower RAP.

During a median follow-up of 413 (IQR: 302-512) days, 35 patients (14%) died or were hospitalized for heart failure. Compared to patients with RAP ≤ 5 mmHg, those with RAP ≥ 10 mmHg had a greater risk of an event during follow-up (HR 2.38, 95% CI: 1.03-5.48, $p = 0.042$).

Conclusions: Evaluation of RAP by using NIRS identifies out-patients with heart failure who have a higher risk of an adverse outcome. This device might be used for rapid, objective clinic evaluation of the severity of residual congestion in patients with HF.

P797

Effect of a group orientation in self-care and compliance of patients with heart failure

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Background/Introduction: High rates of hospitalization and mortality for heart failure in Brazil and the world determine the research for strategies to improve self-care and compliance to therapy. The orientation group is an alternative to information about the disease and treatment.

Purpose: Compare the effect of a nursing intervention orientation group and nursing consultation on compliance and self-care of patients with chronic heart failure.

Methods: A randomized clinical trial with patients with chronic heart failure in a specialized clinic, conducted between September 2012 and November 2013. The intervention group participated 3-8 sessions and the control group received nursing consultation. The data are presented as mean and standard deviation and compared between groups was performed by Student's t-test.

Results: 56 patients were randomized, having as a final sample of 27 patients (GI = 11 and GC = 16). The initial scores were: adherence ($14,11 \pm 3,41$), maintenance ($43,82 \pm 15,54$); management ($56,26 \pm 29,10$) and confidence ($62,01 \pm 23,94$). Ladies and greater than or equal to 60 years of age gender were associated with greater self-care management, ($p = 0,01$ and $p = 0,02$), respectively. After

completion of the follow-up demonstrated that there was no significant beneficial change in these scores in the intervention group. The score of self-care confidence was lower at the final moment in GI (initial = $74 \pm 16,18$ and final = $59,14 \pm 14,97$). The other scores did not significantly change.

Conclusion: Perhaps the change in confidence self-care can mean difference in perception of patients about the disease and self-care. The strategy steering group as a nursing intervention did not show effective results in the outcomes assessed and should be further studied.

P798

Coronary revascularization in senior patients with left ventricular systolic dysfunction

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Purpose: Senior patients with left ventricular systolic dysfunction (LVSD) benefit less from the recommended therapies. The prognostic impact of revascularization in elderly patients with ischemic LVSD is not well established, therefore revascularization is less frequently carried out. We aim to study the prognostic impact of revascularization in the elderly.

Methods: We enrolled all senior patients (> 75 year old) who were diagnosed with LVSD (ejection fraction $\leq 35\%$) between January 2008 and April 2012. After the follow-up, we identified variables associated with mortality and cardiovascular events (total mortality and hospitalization for cardiac cause) with multivariate analysis of survival. Furthermore we determined the variables associated with left ventricular ejection fraction improvement (LVEF $> 35\%$) with logistic regression.

Results: 472 senior patients (≥ 75 years old) were diagnosed of LVSD (LVEF $\leq 35\%$) during the inclusion period. 25% of them did not undergo etiological study, 28% resulted to have non-ischemic, while 47% (223 patients) had an ischemic origin. Our study group of these 223 ischemic patients had a mean age of 82 ± 5 years, and 72% of them were male. After a mean follow-up of 24 ± 15 months, 42% of the patients died and 58% presented a cardiovascular (CV) event. In the survival analysis, variables independently associated with CV events were renal insufficiency (RI) (OR 1.8 [1.3-2.7]), LVEF at inclusion (OR 0.97 [0.94-0.99]), betablocker therapy (BB) (OR 0.5 [0.4-0.8]), and LVEF improvement during the follow-up (OR 0.5 [0.3-0.8]). Variables related to total mortality were RI (OR 1.9 [1.2-2.9]), LVEF at inclusion (OR 0.95 [0.92-0.99]), BB (OR 0.5 [0.3-0.7]), and LVEF improvement (OR 0.2 [0.1-0.5]). Coronary revascularization resulted to be related to mortality (OR 0.5 [0.3-1.1]), without reaching statistical significance. Variables related to LVEF improvement during the follow-up were BB (OR 3.3 [1.2-9.1]), narrow QRS complex (OR 2.5 [1.2-5.1]), resynchronization therapy (OR 6.7 [1.4-31.7]) and coronary revascularization (OR 2.5 [1.03-5.6]).

Conclusion: LVEF improvement was strongly associated with a better prognosis in our study population. Revascularization decreased mortality but without reaching statistical significance, nevertheless it was associated with LVEF improvement, reducing secondarily the CV event rate and mortality. One fourth of our patients did not undergo etiological study of LVSD. Higher percentage of etiological studies, and a proper indication for revascularization in the senior patient population could improve prognosis through LVEF recovery.

P799

Periodic breathing in heart failure patients

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Objectives: 30-50% of heart failure (HF) patients with III-IV functional class (FC) safe from periodic breathing (PB) - a condition associated with cyclic waxing and waning of tidal volume (VT). Periodic breathing independently predicts cardiac mortality in CHF patients.

Aim: The present study was designed to examine effect of cardiac resynchronization therapy (CRT) on systolic function, exercise capacity, peak oxygen consumption and PB severity in patients with systolic heart failure in 3-12 month after implantation of CRT-device.

Methods: 55 HF patients III-IV functional class, mean age 49 ± 11 years, 52 men, mean left ventricular ejection fraction (LVEF) $- 21 \pm 5\%$ performed exercise tests with breath-by-breath gas analysis before CRT and 3-12 month after implantation of CRT-device. Current medication included angiotensin converting enzyme inhibitors (88%), furosemide (88%), betablockers (10%), amiodarone (11%), spironolactone (100%). PB was established according to the following criteria: 1) three or more regular oscillations; 2) regularity was defined if the standard deviation of three consecutive cycle lengths (time between 2 consecutive nadirs) was within 25% of the average; 3) minimal average amplitude of ventilatory (VE) oscillation of 5 L (peak value minus the average of two in-between consecutive nadirs). Mean and standard deviations (SD) were obtained for values in subjects grouped according to time:

before and after CRT. The p value of a type I error was established at 0.05 for all hypothesis tests.

Results: All patients presented PB before CRT. Maximal exercise capacity was 40±13 W, actual peak VO₂ values were 11,7±2,0 ml/min/kg. In 3-12 month after CRT: 1) LVEF was 35±8%, in compare with basic LVEF (21±7%), p<0,05; 2) peak VO₂ values were 14±2,5 ml/min/kg, p<0,05; 3) maximal exercise capacity was 50±10 W, p<0,05; 4) standard deviation of three consecutive cycle lengths was within 9,5±1,3% of the average, p<0,05; 5) minimal average amplitude of VE oscillation was less than 5 L.

Conclusion: Cardiac resynchronization therapy leads to a reduction of PB severity in patients with systolic HF in 3-12 month after implantation of CRT-device.

P800

Heart failure with reduced ejection fraction: should we submit patients without angina to coronary angiography?

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Purpose: Coronary artery disease (CAD) is the main cause of heart failure with reduced ejection fraction (HFrEF). The recommendations for the diagnostic approach of HFrEF patients without angina do not include the performance of coronary angiography routinely. We aimed to determine the clinical variables associated with the presence and severity of CAD in patients with HFrEF without angina and no previous myocardial infarction.

Methods: We retrospectively identified consecutive patients submitted to coronary angiography in a Heart Failure (HF) clinic. Patients with preserved ejection fraction and those reporting angina, with known CAD or submitted to coronary angiography for other purposes, were excluded. Demographic and cardiovascular risk factors data were abstracted from clinical records.

Results: Of 168 patients with HFrEF analyzed, 30.9% had significant CAD among whom 23.1% had severe CAD. Patients with CAD were older, more frequently male, and had a higher prevalence of multiple cardiovascular risk factors: diabetes mellitus (DM), arterial hypertension, dyslipidemia and history of smoking. Significant CAD was more than twice as prevalent in the presence than in the absence of risk factors. In males, 14.3% of those without cardiovascular risk factors had significant CAD and this percentage rose to 40.0% in those with at least one risk factor (DM, dyslipidemia or smoking). Angiography identified significant CAD in 12.5% of women without risk factors.

Conclusion: In patients with HFrEF without angina, the prevalence of significant CAD was high. Although we found a strong association between CAD risk factors and CAD, coronary angiography identified a high proportion of patients with coronary disease in HFrEF patients without clinical or known CAD even in the absence of traditional risk factors.

P801

Prevalence and predictors of hand grip weakness in a cohort of chronic heart failure patients

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Purpose: To evaluate hand grip strength (HGS) in patients with chronic heart failure (HF) based on values of a reference population; and to determine clinical, anthropometric and bioelectrical predictors of HGS.

Methods: Cohort study evaluating 403 patients with stable HF and NYHA functional class I-III. Measurements of weight, height, arm muscle circumference (AMC), hand grip strength (HGS) using a dynamometer, lean mass (LM) and phase angle (PA) by bioelectrical impedance were performed by a trained nutritionist. Clinical variables were collected during medical appointment. Spearman correlation was used to evaluate the relationship of HGS with continuous variables. Multiple linear regression was performed to identify independent predictors of HGS.

Results: HF patients were predominantly male (63%), of non-ischemic etiology (56%), had moderate to severe LV systolic dysfunction (mean left ventricular ejection fraction [LVEF]=35±13%) and 60±13 years old. Higher values of HGS were observed in man (p<0.001) with NYHA I e II (p=0.002). HGS was positively correlated with AMC (rs=0.49; p<0.001), BMI (rs=0.2; p<0.001) LM (rs=0.63; p<0.001) and PA (rs=0.33; p<0.001) and inversely correlated with age (rs=-0.24; p<0.001). HGS was not associated to LVEF. In a multiple linear regression model, HGS was independently associated with age (p<0.001), gender (p<0.001), NYHA functional class (p<0.001), AMC (p=0.006) and LM (p=0.03). These predictors explained 56% of the HGS variation (p<0.001). According to a reference population, using the 10th percentile as cutoff, 40% of HF patients were classified with loss of muscle strength for the right arm and 38% for the left arm.

Conclusion: HGS is an easy and feasible parameter of peripheral muscle strength that is related to clinical and muscle mass parameters in a stable population of

chronic HF patients. When compared to a healthy reference population, more than a third of the HF patients had muscle weakness.

P802

Impact of lipid disorders on mortality among saudi patients with heart failure

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Background: Dyslipidemia, which is a known cardiovascular risk factor, is extremely common among Saudis, both children and adults. The impact however of dyslipidemia and several other lipid disorders in patients with congestive heart failure in this particular population has not been documented. This study aims to fill this gap.

Methods: This retrospective, single center study was done at our Medical City in Saudi Arabia from 2002-2008. 392 of the 500 cases seen were included. Charts were reviewed and information on medical history, medications and lipid status were documented.

Results: Having a low HDL-cholesterol level was the most common lipid disorder with 82.9%, followed by hypertriglyceridemia (35.2%), atherogenic dyslipidemia (27.8%) and hypercholesterolemia (9.2%). Diabetes mellitus is the single most significant predictor for mortality (p=0.001). Among the lipid disorders, only low-levels of HDL-cholesterol contributed to significant mortality risk [OR 1.29 (Confidence Interval 1.04-1.59)] (p-value <0.01) adjusted for age, gender and statin use.

Conclusion: The results of the present suggest that emphasis should be given in elevating HDL-cholesterol levels among subjects with congestive heart failure, without compromising current management on LDL-lowering drugs. Current management should not be limited to conventional statin use and should promote other treatments that would elevate HDL-cholesterol levels.

P803

The effects of dyslipidemia in patients with chronic heart failure

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Background: Dyslipidemia is a high risk factor of heart disease. Among heart disease, the prevalence of heart failure is increasing in recent years. We aim to investigate the association between lipid profile and age, gender, clinical and echocardiographic characteristics and the influences of dyslipidemia on heart failure.

Methods: This retrospective study including 583 patients (72 years, 338 were male) admitted in the therapeutic unit of heart failure. All patients underwent measurement of serum lipid profiles. They were divided into two groups based on combining dyslipidemia or not. Clinical characteristics, biochemical data and echocardiography were analyzed in both groups.

Results: There were 246 (45%) patients diagnosed with dyslipidemia in this study. Mean serum levels of total cholesterol and triglycerides were 2.31g/l and 2.59 g/l respectively in group with dyslipidemia. Young age, diabetes, hypertension, stroke attack, and coronary heart disease were associated with dyslipidemia (p value <0.001).

Patients with dyslipidemia had a significantly diastolic dysfunction (p=0.035) and lower functional capacity during six - minute walk. Higher level of glucose was also noted in dyslipidemia population. No sex-related difference in dyslipidemia and nondyslipidemia (p=0.17) and no correlation between dyslipidemia and cardiac decompensation were found (p=0.36).

Conclusions: Dyslipidemia is associated with others risk factors of coronary heart disease. These results demonstrate a correlation between functional capacity, left ventricular diastolic dysfunction and dyslipidemia.

P804

Predictors of functional capacity in chronic heart failure: echocardiography versus six-minute walk test

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Background: Six-minute walk test (6MWT) constitutes a suitable alternative for Cardio-pulmonary exercise testing to assess functional capacity in patients with heart failure (HF). Echocardiography has always been considered as the most useful easy test for evaluation of these patients.

Purpose: to determine the echocardiographic predictors of six-minute walk distance (6MWD) in patients with chronic systolic heart failure as an objective assessment of functional capacity.

Methods: This study included 40 patients with HF, ejection fraction (EF) <40% presenting with grade I to II NYHA (New York Heart Association) classification. All performed simultaneous transthoracic echocardiographic study and 6MWT.

Results: The mean 6MWD was 340.25 ±88.64 meters. 26 patients (65%) walked more than 300 meters (group I) while 35% (14 patients) did not (group II). Right ventricular systolic pressure (RVSP) and E/e' were significantly higher in (group

II), ($p=0.04$ and 0.05 respectively). There were significant negative correlations between 6MWD and each of LVESV ($r=-0.34$, $p=0.03$), E/e' ($r=-0.36$, $p=0.02$) and RVSP ($r=-0.34$, $p=0.03$). Linear regression analysis showed RVSP as the only independent predictor of 6MWD, thus an independent predictor of functional capacity in HF patients. Furthermore this study suggested a predictive model of estimation of 6MWD from a given value of RVSP: $6MWD = a + (b \times RVSP)$; (a and b are constants) with a standard error of ± 42 m.

Conclusion: RVSP, LVESV and E/e' were correlated with 6MWD in chronic HF patients. Among different echocardiographic parameters, RVSP can be used as an independent predictor of functional capacity in HF patients. Further studies are still needed to ascertain the sensitivity and specificity of this model in prediction of functional capacity in HF patients in everyday practice.

P805

Heart failure in elderly patients: experience of a cardiology department

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Purpose: Heart failure in elderly is a quite frequent and severe condition in Africa, yet few African data available that take into account that specific profile of heart failure. This study aims to characterize epidemiological, clinical, etiologic and therapeutic features of heart failure in the elderly in Morocco.

Methods: A descriptive study was carried from May 2006 to September 2014. Nine hundred and sixty one patients aged ≥ 65 years presenting clinical and echocardiographic signs of heart failure and followed at the heart failure unit were included, among with 608 men and 353 women mean aged 77 years.

Results: Heart failure in the elderly represents 59, 57% of our heart failure population. Dyspnea was a constant symptom (91%). 25, 3% of patients were in class III of NYHA and 1, 9% in class IV.

48,9% had a dilated cardiac cavities and had diastolic heart dysfunction accounted for 28,3% of cases. Ischemic heart disease was the main etiology (56,1%). Other etiologies were myocardial infarction (6,1%), valvular disease (3,5%) and hypertension (1,7%). Medical treatment consisted of beta blockers (98%) angiotensin-enzyme converting inhibitor (97,7%) and spironolactone (49,1%).

Conclusion: The clinical syndrome of heart failure in the elderly constitutes a major public health problem in Morocco. Echocardiography is of paramount importance in confirming the diagnosis and precisating its etiology. Preventive and public health strategies need to be defined according to the local characteristics.

P806

Long-term changes of PQ interval and its association with mortality in chronic heart failure with reduced ejection fraction

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Background: The different ECG parameters have diagnostic, prognostic and therapeutic influences in chronic heart failure with reduced ejection fraction (HFrEF). The effect of QRS duration on prognosis is well known. However less data is available on the effect of the PQ interval.

Aim: To investigate PQ interval at the time of diagnosis of the disease in different patient subgroups, the long-term changes of this ECG parameter and its association with mortality in a real-life HFrEF patient cohort.

Patients and Method: Parameters of 245 pts with HFrEF managed at our heart failure outpatient clinic (age: 60.1 ± 14.3 years, male: 75.1%, ischemic etiology: 59.6%, NYHA functional class: 2.83 ± 0.98 , diabetes: 33.1%, left ventricular ejection fraction (LVEF): $30.2 \pm 8.1\%$, systolic blood pressure: 127.1 ± 21.8 mmHg) were assessed. Pts with pacemaker and atrial fibrillation or flutter were excluded. Every pt received the current guidelines recommended optimal medical treatment of HFrEF. PQ intervals were obtained from 12-lead ECGs performed at the time of diagnosis of HFrEF and their changes were assessed every 6 months for up to 5 years follow up. At baseline the proportion of pts with normal PQ (nPQ) (<200 ms) and prolonged PQ (pPQ) (≥ 200 ms) intervals were assessed in different patient subgroups (male/female, diabetic/non-diabetic, $LVEF \leq 35\%$ / $LVEF > 35\%$, ischemic/non-ischemic etiology). We evaluated the five-year survivals with Kaplan-Meier analysis and compared them with log-rank test.

Results: At the time of diagnosis of HFrEF 26.1% of pts had pPQ interval, which increased to 34.8% at the end of the follow-up period. In the subgroup of males, the proportion of pts with pPQ was significantly higher ($p=0.02$) than the proportion of pts with nPQ. In the other subgroups there was no difference in the proportion of the pts with nPQ and pPQ. The five-year survival rate in pts with nPQ was more favourable than in pts with pPQ (77.45% vs 61.44%, $P=0.02$).

Conclusions: The presence of pPQ interval is common in HFrEF. During long-term follow-up period the proportion of pts with pPQ increases. Like the wide QRS, the pPQ interval also has an unfavourable effect on survival. The pPQ together with a wide QRS, or even without it can be a therapeutic target in HFrEF.

P807

Predictors of one-year outcome of patients with heart failure and prior coronary revascularization: results from the polish part of the heart failure pilot survey of the european society of cardiology

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Purpose: The aim of the study was to evaluate clinical predictors of long-term outcomes of patients (pts) hospitalized for heart failure (HF) with or without previous coronary angioplasty (PCI) or coronary artery bypass graft (CABG).

Methods: Primary endpoint (PE) was all-cause death at 12 months. Secondary endpoint (SE) was a composite of all-cause death and readmission for cardiac causes at 12 months.

Results: The final analysis included 649 pts hospitalized for HF. History of prior PCI/CABG had 212 from 649 pts (32.7%). Compared to pts without prior coronary revascularization (non-PCI/CABG), pts with previous PCI/CABG more frequently were male, smokers, had a previous HF hospitalization, lower left ventricle ejection fraction (LVEF), myocardial infarction, hypertension (HT), peripheral artery disease, diabetes; were more likely to have acute coronary syndrome (ACS) as a cause of admission; had lower heart rate at admission and at discharge; more frequently required PCI/CABG and implantation of cardioverter-defibrillator during hospitalization; had more often prescribed beta-blockers, statins and antiplatelets at discharge. Non-PCI/CABG pts more often had cardiogenic shock and died in-hospital. The PE occurred in 33 of 212 of PCI/CABG pts (15.6%) and in 56 of 437 non-PCI/CABG pts (12.8%; $p=0.334$). The data on hospital readmission at 12 months were available for 516 pts. The SE occurred in 82 of 170 PCI/CABG pts (48.2%), and in 122 of 346 non-PCI/CABG pts (35.3%; $p=0.005$). In multivariate analysis in pts with prior PCI/CABG predictor of PE were lower LVEF (hazard ratio [HR] 0.953; 95% confidence interval [CI] 0.913-0.996; $p=0.032$); use of antiplatelets at discharge had protective value (HR 0.309; 95%CI 0.111-0.859; $p=0.024$); predictors of SE were diabetes (HR 1.833; 95%CI 1.146-2.930; $p=0.011$) and higher NYHA (New York Heart Association) at admission (HR 1.502; 95%CI 1.062-2.124; 0.021); HT (HR 0.362; 95%CI 0.216-0.607; $p=0.0001$) had protective value. Lower serum sodium concentration at admission was a predictor of PE and SE in both groups. In non-PCI/CABG pts predictors of PE were higher age (HR 1.050; 95%CI 1.020-1.081; $p=0.001$) and ACS at admission (HR 2.065; 95%CI 1.157-3.685; $p=0.014$); predictors of the SE were higher NYHA class (HR 1.429; 95%CI 1.087-1.880; $p=0.012$) and lower hemoglobin at admission (HR 0.872; 95%CI 0.790-0.963; $p=0.007$). Higher heart rate at discharge was a predictor of PE and SE in those pts.

Conclusions: HF pts who were revascularized had similar mortality and higher risk of death or rehospitalizations at 12 months compared with non-PCI/CABG pts.

P808

Inferior vena cava diameter in ambulatory outpatients with chronic heart failure: relationships and prognostic significance

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Purpose: The inferior vena cava (IVC) diameter and degree of inspiratory collapse are used as echocardiographic indices in the estimation of right atrial pressure.

Therefore it might represent an index of heart failure severity independent of left ventricular ejection fraction. The relation between IVC diameter and other clinical variables and its prognostic significance in patients with HF has not been explored. The aim of this study was to assess the relation between IVC diameter, clinical variables, and outcome in patients with chronic heart failure.

Methods: This retrospective study including 1841 patients (65 years, 1146 were male) admitted in the therapeutic unit of heart failure from 2006 to 2014. All patients underwent transthoracic echocardiography.

Results: Patients with heart failure with dilated IVC diameter had a more ischemic heart disease, were more likely to have atrial fibrillation ($p=0.02$), to be treated with high doses of diuretics ($p=0.00001$); had higher pulmonary pressures ($p=0.00004$), significant tricuspid regurgitation (0.00001) and right ventricular systolic dysfunction. There was a good correlation with NYHA functional class and diastolic dysfunction. However male sex, age, severity of systolic dysfunction did not differ among the groups. A negative correlation with glomerular filtration right was detected in the IVC highest.

Conclusion: In patients with chronic heart failure, increasing IVC diameter identifies patients with an adverse outcome.

P809

Ventricular dysfunction as a complication in 5-year follow-up of our patients with adult congenital heart disease

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Objectives: To assess the incidence of ventricular dysfunction that appears in adult patients followed in an office of adult congenital heart disease.

Methods: We reviewed patients followed for five years in an office that follows patients with adult congenital heart disease in a tertiary hospital that is not a referral center in our community for this condition.

Results: Of the 135 patients reviewed 79 (58%) were male. The average age was 36 years with a range between 16 and 77 years. Within the classification of congenital heart disease in 37 patients (27%) had simple congenital heart disease, 79 patients (58%) of moderate complexity, and 19 patients (14%) complex congenital heart disease. The most prevalent congenital heart disease was aortic coarctation (15 patients) followed by tetralogy of Fallot (15 patients), congenital aortic valve disease (13 patients), transposition of great arteries (12 patients) and atrioventricular canal (11 patients). The most frequent complications appeared in monitoring were atrial arrhythmias in 10% and the appearance of non-symptomatic ventricular dysfunction 7%. 13 patients (10%) have required some type of intervention: 7 surgeries (4 replacement of pulmonary valve in Fallot tetralogy, 1 venous sinus type atrial septal defect closure, and one intervention in subaortic stenosis), 4 percutaneous interventionism (3 to close ostium secundum atrial septal defect and 1 aortic coarctation) and 2 pacemaker implants because atrioventricular block. 2 patients presented pregnancy to term without significant complications. 3 patients (2%) died (2 cerebral hemorrhage and 1 pneumonia).

Conclusions: 1) Patients with congenital heart disease in adulthood have a non-negligible rate of complications (mainly arrhythmias and ventricular dysfunction).

2) It is not uncommon the need for intervention during follow-up.

3) It seems appropriate for these patients to be followed in a specific office in their area. Moreover, more complex patients should be followed in referral centers.

P810

Racial differences in clinical treatment and self-care behaviors of adults with chronic heart failure

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Purpose: Most European countries are racially diverse, with a rising proportion of individuals of African descent. In the US, the highest prevalence of heart failure (HF) is in Blacks followed by Whites. Compared to Whites, Blacks have a higher risk of HF-related morbidity and mortality and HF-related hospitalization. Little research has focused on explaining the reasons for these disparities. The purpose of this study was to examine racial differences in demographic and clinical characteristics in Blacks and Whites with HF and to determine if these characteristics influenced treatment, or together with treatment, influenced self-care behaviors.

Methods: This was a secondary analysis of existing data collected from adults (n = 272) with chronic HF enrolled from out-patient sites in the northeastern US and followed for 6-months. Clinical characteristics were abstracted from the medical record by registered nurses. Race, demographic characteristics, and support quality were self-reported. HF knowledge and premorbid intellect were assessed with valid methods. Medication names and doses were determined by direct observation of medicine bottles by research staff. Medication adherence was measured objectively with the medication-event monitoring system (MEMS).

Results: After adjusting for sociodemographic and clinical characteristics within reduced (HF_rEF) and preserved ejection fraction (HF_pEF) groups, there were two significant racial differences in clinical treatment. Blacks with HF_rEF were prescribed ACE inhibitors and isosorbide dinitrate (H-ISDN) more often than Whites. In the HF_pEF group, Blacks were taking more medications and were more likely to be prescribed digoxin and a diuretic when symptomatic. Deficits in HF knowledge and poor medication adherence were more prominent in Blacks and these racial differences were not explained by sociodemographic or clinical characteristics or clinical treatment variables. Comorbidity, premorbid intellect, and the quality of support received contributed to clinical treatment and self-care.

Conclusions: Although few differences in clinical treatment could be attributed solely to race, knowledge about HF and medication adherence are lower in Blacks than Whites. Further research is needed to explain these observations, which may be targets for future intervention research.

P811

The impact of T(-786)C endothelial nitric oxide synthase on endothelial-dependent vasodilatation in chronic heart failure

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Background: Chronic heart failure (CHF) is associated with marked deterioration of endothelial function (EF). The pivotal role of nitric oxide bioavailability in maintenance of EF is well-known. However, corresponding role of genetic factors and, in part,

polymorphisms in endothelial nitric oxide synthase gene (eNOS), in such patients (pts) is still unclear.

Aim: To investigate eNOS T(-786)C gene polymorphism in relation to flow-mediated (FMD) vasodilatory response in CHF pts.

Methods: 157 stable (NYHA II-III) CHF pts of ischemic origin with left ventricular systolic dysfunction (ejection fraction \leq 45%) on standard treatment were examined. FMD vasodilatation of a. brachialis was carried out by standard cuff test. eNOS T(-786)C polymorphism was genotyped by polymerase chain reaction-restriction fragment length polymorphism analysis.

Results: The frequency of T(-786)C genotypes was: TT - 41,4% (n = 65), TC - 45,2% (n = 71), CC - 13,4% (n = 21). FMD in pts with TT genotype was $7,2 \pm 1,0\%$, in pts with TC - $6,8 \pm 0,6\%$, whereas FMD in pts with genotype CC was $4,7 \pm 1,1\%$. The difference between FMD was significant: TT vs CC - $p = 0,026$; TC vs CC - $p = 0,039$.

Conclusion: In stable ischemic systolic CHF poor flow-mediated vasodilatory response is associated with CC genotype of eNOS T(-786)C.

P812

Uric acid levels and chronic heart failure

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Background: Elevated uric acid (UA) is associated with increased cardiovascular morbidity and mortality in the general population. In cohort studies UA has been shown to have a strong prognostic value as a predictor of mortality in patients with chronic heart failure. In fact, UA is often elevated in these patients. The reasons for this are multifactorial: reduced UA excretion by the kidneys due to reduced kidney function, treatment with diuretics, and increased production. We evaluated the prognostic effect of UA on clinical outcome in patients with heart failure. In addition, we looked at the relation of UA to echocardiographic parameters in a subset of these patients.

Methods: Totally 309 consecutive patients with chronic heart failure symptomatic class II, III, or IV were retrospectively studied. Clinical, electrocardiographic, echocardiographic and biological data were investigated. 84% of the patients had elevated UA (>70 mg/L in men and > 60 mg/l in women). We divided patients on 2 groups: group 1 with hyperuricemia and group 2 without hyperuricemia. Mean UA levels were 71.4 mg/l in group 1 and 42.2 mg/l in group 2.

Results: Male sex, diabetes mellitus, hyperlipidemia, and ischemic heart disease were associated with higher UA levels. Increased urea and creatinine were also associated with higher UA levels, whereas reduced estimated glomerular filtration rate, hyponatremia treatment with furosemide were seen with higher UA levels. An increase in UA levels was a predictor of increased cardiac hospitalizations ($p = 0,0001$) and mortality ($p < 0,00039$). Echocardiographic data demonstrated a significant correlation between UA levels and E/A ratio, a marker of diastolic dysfunction ($p < 0,0001$).

Conclusion: Increased UA level was independent predictor of increased morbidity and mortality in a cohort of ambulatory patients with chronic heart failure.

P813

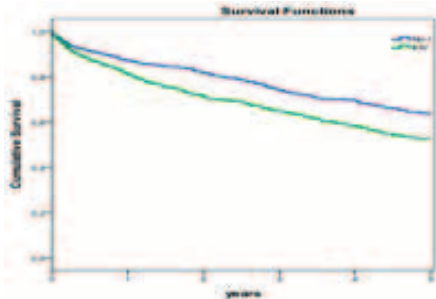
Characteristics and outcome of patients with functional mitral valve regurgitation and systolic heart failure

Grant from the Spanish Ministry of Science and Innovation, Redes de Investigación del Instituto de Salud Carlos III, (REDINSCOR, RD06/0003) M D M Dolores Garcia-Cosio Carmena¹; E Roig¹; A Ferrero¹; S Mirabet¹; R Vazquez²; J Delgado³; JR Gonzalez-Juanatey⁴; LA Alonso-Pulpon⁵; D Pascual⁶; JR Cinca¹
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Functional mitral regurgitation (FMR) is present in 25% of heart failure (HF) patients (P) with reduced ejection fraction and it implies poor prognosis if it persists despite optimal therapy. A better understanding of FMR may play a role in prognostic evaluation and/or to develop specific therapies to slow down disease progression. 2507 P with persistent symptomatic HF from 18 hospitals were prospectively included in a registry (2007-2011). We selected 1526 P with left ventricular (LV) ejection fraction <40% without organic valvular disease or hypertrophic cardiomyopathy. The cohort was divided according to FMR grade as significant (II-IV) and non-significant (0-I).

Significant FMR was present in 47%. Variables independently related to FMR were male gender (OR 0.34; 0.25-0.47), body mass index (OR 0.94;0.91-0.97), HF decompensation (OR 1.33;1.01-1.174), LV diameter (1.04;1.02-1.05), left atrium (OR1.05; 1.03-1.07), natremia (OR 0.97;0.94-1) and BNP (OR1.57;1.17-2.1) (AUC 0.70; 0.67-0.74). Five-year mortality was 36% mostly due to cardiac causes. P with FMR had worse survival than P without FMR at 1, 3 and 5 years (81.5 VS 87.1%;

64.9 VS 74.3%; 52.7 VS 63.5%, $p < 0.001$) Figure 1. Factors independently related to mortality in stable P were: FMR (HR 1.5; 1.14-2.1), arterial pressure (HR 0.98; 0.98-0.997), LV diameter (HR 1.01; 1-1.03), renal failure (HR 0.98; 0.982-0.996), BNP (HR 2.1; 1.4-3.06) and beta-blockers (0.5; 0.33-0.76). FMR was predictor of cardiac mortality (1.8; 1.3-2.7) and refractory HF mortality (2.6; 1.6-4.4). Functional mitral regurgitation is present in nearly half of HF with reduced ejection fraction and it poses a poor prognosis in clinically stable patients. There's a need of prospective studies to confirm FMR prognostic implication in different clinical scenarios.



Survival Curve

P814

The efficacy of the heart failure follow-up clinic in the management of chronic heart failure: an Australian centre study

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Purpose: Heart failure (HF) remains one of the most common causes of hospitalization and mortality. The primary aim of this single centre retrospective cohort study is to assess the short-term and intermediate effects of a nurse-led HF Follow-up Clinic (HFFC) with respect to hospital representation and survival.

Methods: In this study [n=674], patients who had attended the HFFC [n=50] at a tertiary Australian institution were compared to non-clinic attenders [n=624] following an index hospitalisation with diagnosed HF and followed for 12 months. Clinical appraisal with respect to HF aetiology, cardiac risk factors, hospital representations and survival analysis was undertaken.

Results: With respect to baseline patient characteristics, patients in the HFFC group were found to have a lower mean LVEF at time of entry ($P=0.04$). There were no significant between-group differences in terms of frequency of coronary artery disease, previous myocardial infarction, hypertension, diabetes mellitus, psychiatric illness or NYHA FC on entrance ($P=ns$). A predominance of ischaemic cardiomyopathy was noted in the HFFC cohort, relative to a more heterogeneous distribution of HF substrate in the comparison arm. A statistically significant reduction in total representations to Emergency Department within 12 months was noted in the HFFC group [1.46 vs. 2.32, $P=0.042$]. With respect to representations related to HF, a stronger association was discovered [0.74 vs. 1.39, $P<0.001$]. A trend towards divergence in survival was noted on Cox-Hazard regression, however failed to reach statistical significance on Mantel-Cox analysis [$P=0.130$]. (Figure 1)

Conclusion: Our study reveals that utility of the HFFC reduces hospital representations. Longer-term follow-up is required for further analysis of survival.

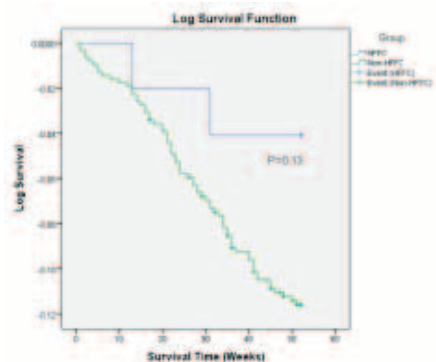


Figure 1. Cox-Hazard Regression Survival

P815

The impact of iron deficiency and anaemia on exercise capacity and outcomes in patients with chronic heart failure

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Background: Anaemia and iron deficiency are important co-morbidities and both may lead to reduced exercise capacity.

Methods: A total of 331 patients with stable chronic HF (mean age: 64 ± 11 y, 17% female, left ventricular ejection fraction [LVEF] $35 \pm 13\%$, body mass index [BMI] 28.5 ± 5.2 kg/m², New York Heart Association [NYHA] class 2.2 ± 0.7 , chronic kidney disease 35%, glomerular filtration rate 61.7 ± 20.1 mL/min) were enrolled from 2010 and followed until April 2014 or death. Anaemia was defined according to World Health Organization criteria [Hb <13 g/dL in men, <12 g/dL in women], microcytic anaemia as mean corpuscular volume (MCV) ≤ 80 fl, macrocytic anaemia as $MCV \geq 96$ fl. Iron deficiency (ID) was defined as serum ferritin <100 μ g/L or ferritin <300 μ g/L with transferrin saturation (TSAT) $<20\%$. Exercise capacity was assessed as peak oxygen consumption (peakVO₂) by spirometry and 6-minute walk distance test (6MWT).

Results: A total of 91 (27%) patients died from any cause during a mean follow-up of 17 months. At baseline enrolment, 98 (30%) patients presented with anaemia, 149 (45%) patients presented with ID. Of the anaemic patients 72 were found to have normocytic, 12 macrocytic and 14 microcytic anaemia. Moreover we observed a significant reduction in exercise capacity in parallel to decreasing haemoglobin levels ($r=0.24$, $p<0.001$). In patients with ID and anaemia together ($n=63$, 19%) exercise capacity was significantly lower than in patients with ID or anaemia alone. Cox regression analysis showed higher risk of mortality in patients with microcytic anaemia (hazard ratio [HR]: 2.434, 95%CI: 1.10-5.38, $p=0.02$) and with higher NYHA class (HR: 1.938, 95%CI:1.41-2.67, $p<0.0001$) and lower risk in patients without anaemia (HR:0.46, 95%CI:0.31-0.70, $p=0.0003$), with higher TSAT (HR: 0.976, 95%CI:0.956-0.99, $p=0.01$) without renal failure (HR: 0.38, 95%CI:0.25-0.57, $p<0.0001$), with higher LVEF (HR:0.938, 95%CI: 0.92-0.96, $p<0.0001$), with higher peak VO₂ (HR:0.856, 95%CI: 0.81-0.90, $p<0.0001$). After adjusting for NYHA, age, BMI and hsCRP anaemia is an independent predictor of mortality in patients with heart failure.

Conclusion: Anaemia and ID are associated with reduced exercise capacity. The impact of anaemia on reduced exercise capacity and on mortality is stronger than that of ID. Patients with microcytic anaemia showed a 2 fold higher risk of death.

P816

Cytokines aggression in patients in chronic heart failure with anaemic syndrome

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Purpose: The aim of investigation to study relation to levels of erythropoietin (EPO) and pathological cytokines of patients in CHF with anemic syndrome, and erythropoietic effect of continuous erythropoietin receptor activator methoxy polyethylenglicol-epoietin beta (MEB) its impact on this relation and on regress of symptoms CHF.

Methods: 94 patients with CHF of NYHA class III-IV a LVEF of 40% or less with anaemia were included in investigation. Mean age of patients 59.7 ± 1.6 years (58 males,36 females). The Hb level of less 120 g/l by males and less 110g/l by females. 46 patients were treated basis treatment of CHF (I group) and 48 patients were treated with MEB (II group).

Percutaneous MEB in dose 50 IU in day in one months patients without iron deficiency to receive in follow-up on 6 months. Plasma NT pro BNP, cytokine, EPO, ferritin, echocardiographic indices of LV systolic and diastolic function and 6 minute walked distance were assessed at baseline and posttreatment.

Results: Analysis of the received results, showed that lowering EPO level to $2,01 \pm 0,3$ ME/ml and $1,87 \pm 0,1$ ME/ml in blood is accompanies with sharp cytokine aggression respectively in CHF patients with anemia: increase IL-1 up to $9,46 \pm 1,16$ pg/ml and $7,04 \pm 0,71$ pg/ml respectively, IL-6 up to $12,41 \pm 2,2$ pg/ml and $11,8 \pm 2,6$ pg/ml, $10,41 \pm 2,9$ pg/ml and $11,67 \pm 3,1$ pg/ml. On the patients CHF with anemic syndrome in II group MEB treatment the level Hb increased on 22,4% ($p<0,05$) and EPO levels in plasma increased to $29,3 \pm 4,3$ IU/ml ($p<0,001$). The increase the level of EPO connected with the decrease of level cytokines: IL-1 on 36,6% ($p<0,001$), IL-6 on 54,3% ($p<0,05$), TNF- α on 48,3% ($p<0,05$) compared with of patients receiving I group. MEB treatment had a significantly increase LVEF on 19,04% ($p<0,05$) as compared with of patients receiving I group. A greater 6-minute distance walked on exercise testing increased on 76,6% ($p<0,05$) after treatment MEB. There was also a significant fal in serum NT pro BNP levels from $387,4 \pm 52,3$ fmol/ml to $198,1 \pm 30,3$ fmol/ml ($p<0,01$). Lowering of activation of cytokines was accompanied by reverse development of clinical symptoms of HF.

Conclusion: EPO insufficiency in patients with CHF with anemia is accompanied by cytokine aggression, which is increased much more in comparison with the patients without anemic syndrome.

Correction of anemic syndrome with application of percutaneous MEB in dose 50 IU in day in one month in follow-up 6 months effective increased EPO levels, suppressed cytokine aggression and to improve clinical symptoms and quality of life in anaemic CHF patients.

P817

SCAMP for non-invasive ventilation implementation by nurses in acute cardiogenic pulmonary edema

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Background: Standardized Clinical Assessment & Management Plans (SCAMPs) are care pathways designed for standardization of care of heterogeneous patient population, such as of ACPE, for quality of care improvement and resource utilization reduction.

Purpose: The development of an evidence based nurse led SCAMP protocol for non-invasive ventilation (NIV) implementation in acute cardiogenic pulmonary edema (ACPE).

Methods: The protocol/algorithm consists of actions concerning initial patient assessment, ventilator checks, implementation, monitoring, parameters' titration, corrective measures and NIV release. The targeted data collection elaborated in two ICUs in Cyprus, where trained nurses initiated and run NIV, according to the protocol/algorithm, under intensivists' supervision. The researchers-observers were recording process, without interfere in treatment decisions and deviations. ACPE patients were recruited (n=20), in two pilot applications (n=10). Each application was followed by data processing and modification of the protocol/algorithm, based on deviation, observations and literature review. The procedure was evaluated by the professionals involved, through a questionnaire.

Results: The participants were presented with dyspnea, tachypnea, hypoxemia, acidosis, generalized crackles in all lung fields, and imaging documentation of ACPE. Twelve patients were released of NIV in four hours, with a mean duration of 7.43±5.6hours. In four hours' recordings, improvement was shown in the rest study variables, compared with baseline, such as hypoxemia (PO₂/FiO₂:296±92.9mmHg, F29.89 p<0.0001), acidosis (pH:7.4±0.05, F14.8 p=0.029), RR (19.3±3.7/1', F7.513 p<0.0001), heart rate (HR) (81.8±20.1, F92.3 p<0.049), blood pressure, systolic (SBP:119,5±11.3mmHg, F8.662 p=0.01) and diastolic (DBP:67±9.8mmHg, F7.253 p=0.131), and recovery in level of consciousness (100%). The mean ICU length of stay (37.9±24.9 hours) was shorter in patients without concomitant diseases (35%) (22.7±13.9, p=0.042). Lack of NIV tolerance (10%) and vomiting (5%) were managed by removing NIV. Nurses and intensivists who were involved (n=56), seem keen to participate again in a SCAMP (93%) and found the SCAMP protocol/algorithm as an adjuvant in improving NIV practices (96%).

Conclusions: The present protocol/algorithm is demonstrated to be safe and feasible, enhancing the quality of care and clinical outcomes, through standardization of NIV management by nurses, in the heterogeneous population of ACPE.

P818

Is exercise right heart catheterization useful for the assessment of chronic heart failure patients?

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Background: In patients with heart failure with reduced ejection fraction (HrEF), prognostic value of hemodynamic parameters at rest has been well documented. By contrast, there is little information regarding exercise.

Methods: We retrospectively analyzed long-term survival in 190 HrEF patients [54±10 years, 78% men, LVEF 21±8% and peak VO₂ 10±2ml/min/kg] referred for right heart catheterization (RHC). Blood tests, functional respiratory tests, echocardiogram and RHC (resting and cycle ergometer exercise) were recorded.

Results: During a mean follow-up of 3.2±3.3years, 46 patients died: 36 cardiovascular (78%), 7 non-cardiac and 3 unknown deaths. In univariate analysis, size, high creatinine level, ischemic cardiomyopathy, left atrial size (LA), low cardiac index (CI), mean pulmonary arterial pressure (mPAP) and mean pulmonary capillary wedge pressure at rest were significant predictors of mortality. Predictive parameters at exercise were: low CI, peak oxygen consumption (V_{O2}) and mPAP. In a multivariate Cox regression model, the most robust predictor of mortality was mPAP at rest (HR: 1.04; 95% CI: 1.02-1.07; P<0.019). LA size (HR: 1.06; 95% CI: 1.02-1.09; P<0.001), ischemic cardiomyopathy (HR: 2.08; 95% CI: 1.16-3.74; P<0.014) and high level of creatinine (HR: 1.23; 95% CI: 1.01-1.51; P<0.04) were also associated with long-term survival. A worse outcome was observed in

subgroup with mPAP≥25mmHg. A subgroup of 112 patients without transpulmonary gradient (TPG) and diastolic pulmonary gradient (DPG) at rest developed a TPG and DPG at exercise. The appearance of these gradients don't affect the survival of this population.

Conclusions: In HrEF patients with very low EF, mPAP at rest combined with LA size, creatinine and ischemic cardiomyopathy were the most robust predictive factor. Invasive exercise testing did not improve prediction of long-term mortality and is not cost-effective to evaluate HrEF patients.

HEART FAILURE DIAGNOSIS

P819

Clinical significance of leg edema and added value of monitoring fluid weight gain during follow-up of patients with established heart failure

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Purpose: The use of bilateral leg edema as a predictor of heart failure (HF) is a simplest sign of right-sided congestion, but not specific enough to use as the sole basis for an accurate diagnosis of worsening HF status. The present study examined the clinical characteristics of leg edema and determined the added value of monitoring fluid weight gain during follow-up of HF patients.

Methods: Clinical records of HF patients were retrospectively examined. HF-related signs/tests included leg edema, pulmonary rales, S3, fluid weight gain (body weight gain≥1.5 kg with decreased%body-fat), and ultrasound pleural effusion (US-PLE).

Results: 83 HF patients (39% men, 77±12 years) were enrolled. Over a mean follow-up of 652±456 days, 1826 visits (mean interval, 28 days) were evaluated. Among the 83 study patients, at least one of the following events presented at 161 visits of 75 patients: fluid weight gain (n=107), leg edema (n=90), US-PLE (n=85), rales (n=29), and S3 (n=16). Severity of leg edema was mild in 58 patients, moderate in 31, and severe in 1. Appearance of each HF-related sign/test and the cumulative number of HF-related signs/tests did not differ significantly (p=0.49) between events of mild (1.36±1.09; n=58) and moderate/severe leg edema (1.53±1.11; n=32). Compared with the events of isolated leg edema (n=23), leg edema events with additional HF-related signs/tests (n=67) were associated with symptomatic worsening (7% vs. 55%, p<0.0001), and a higher incidence (61% vs. 96%, p=0.0002) and magnitude of BNP increase. Presentation of the events led to 2 (8%) extra/urgent clinic visits and 1 (4%) HF-related hospitalization among the isolated leg edema events compared to 43 (46%) and 40 (43%) events, respectively, among those with 2 or more HF-related signs (p=0.03 and 0.05 in each). Among a total of 67 leg edema events with additional HF-related signs/tests, 56 events (84%) coexisted with fluid weight gain. Therefore, additional monitoring of fluid weight gain distinguished most of the clinically significant leg edema events from insignificant isolated leg edema events. When taking worsening of symptoms into consideration, 5 additional events of leg edema with coexistent HF sign(s) other than fluid weight gain (n=11) were differentiated from the isolated leg edema events.

Conclusions: During follow-up of HF patients, isolated leg edema presented in ~30% of the leg edema events, which might appear to be clinically insignificant. Additional monitoring of fluid weight gain and symptoms could indicate that this physical sign is more clinically relevant as evidence for HF worsening.

P820

VE/VCO₂ slope as a marker of right ventriculo-arterial unit dysfunction in patients with heart failure reduced ejection fraction

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Background: It is well known the prognostic value and diagnostic potential of the minute ventilation (VE)/carbon dioxide production (VCO₂) relationship (VE/VCO₂ Slope) in patients with chronic heart failure reduced ejection fraction (HFREF). In this population prognosis is aggravated by the development of pulmonary hypertension (PH) and right ventricular (RV) dysfunction. So in the evaluation of HFREF patients is important the wider investigation of the coupling between RV function and pulmonary artery pressure (PAP) because is the loss of balance of these two components, functionally integrated with each other, that determines the rapid clinical deterioration in these patients.

Aim: we hypothesized a correlation between VE/VCO₂ Slope and the morphological /functional echocardiographic parameters of RV. We also evaluated the correlation between VE/VCO₂ Slope and the right heart catheterization data.

Methods and Results: 165 patients with HFREF underwent incremental cardiopulmonary exercise test (CPET) and echocardiographic evaluation, of these we analyzed data from 76 patients (mean±SD age: 54±10; % male: 92%; nonischemic: 57%; LVEF: 30,83±8,38%; Peak Oxygen uptake: 17,56±4,62 mL/Kg/mn; VE/VCO₂ Slope: 35,34±8,22). All RV echocardiographic data analyzed correlated with the

VE/VC02 Slope (RV basal end diastolic diameter RVEDD: $R = -.39$, $P = .000$; tissue Doppler systolic velocity of tricuspid annulus S': $R = -0.3$, $P = .009$; RV Fractional Area Change FAC: $R = -.422$, $P = .000$; Tricuspid annular plane systolic excursion TAPSE: $R = -.38$, $P = .001$; Systolic PAP: $R = .42$, $P = .000$; RV free wall longitudinal strain RVLS: $R = -.38$, $P = .001$). The VE/VC02 Slope correlated also with the LVEF ($R = -0.46$, $P = .000$) and the ratio of transmitral Doppler velocity to early diastolic tissue Doppler velocity of mitral annulus E/E' ($R = .3$, $P = .000$). Multivariable analysis revealed that only LVEF, TAPSE and RVEDD were independently associated with VE/VC02 slope. Invasive hemodynamic data were available on 33 patients; only pulmonary vascular resistances (PVR) showed a statistically significant correlation with the VE/VC02 Slope ($R = 0.368$, $P = 0.021$).

Conclusion: high VE/VC02 Slope value is associated both with RV dysfunction than with increased PVR. Accordingly this parameter, non invasive and easily obtainable with a CPET, could be considered expression of the more complex "right ventriculo-arterial unit" functional status and it could be used as a noninvasive follow-up tool helping in choosing the best moment for a new right heart invasive and noninvasive evaluation.

P821

Barriers to diagnosis and treatment of sleep disordered breathing in patients with heart failure: perceptions and experiences of healthcare professionals

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Purpose: Sleep disordered breathing (SDB), both obstructive (OSA) and central sleep apnoea (CSA), is an important risk factor for cardiovascular disease (CVD). 40% of patients with heart failure (HF) suffer from SDB and up to 80% of these patients may be undiagnosed. Reasons for this have not been previously explored. In this study, using qualitative methodology, we identify the barriers experienced by healthcare professionals in the diagnosis and treatment of SDB.

Methods: We conducted 12 semi-structured interviews with health professionals in the NHS (England): 6 cardiologists (4 secondary & 2 tertiary care), 2 respiratory physicians (tertiary care), and 4 HF nurses (2 from each). Interviews lasted 30mins, were conducted one-to-one using a digital voice recorder, and transcribed verbatim. Then a thematic analysis was performed with the aid of a qualitative data analysis package (NVIVO 10).

Results: Most health professionals (10) stated that there was a strong association between CVD and SDB, and treatment with CPAP/mask therapy had patient benefit, but diagnosing CSA compared to OSA was challenging. 3 major barriers to diagnosis and treatment were identified. Firstly, there was a limited understanding about SDB among health professionals and poor cross-speciality communication, resulting in a lack of clear responsibility in the management of patients with SDB. Secondly, there was a difference in organisational resources between secondary and tertiary care; secondary care had a reduced capacity and poorer access to sleep services. Thirdly, a lack of effective screening tools to identify patients with SDB needing specialist assessment and lack of objective evidence that treatment of CSA in HF has mortality benefits, had an impact on health professionals time. In addition, cardiologists and HF nurses, in contrast to respiratory physicians, perceived patients were poorly compliant with CPAP therapy and mask therapy to be an 'invasive' type of treatment.

Conclusions: Our study has identified perceived barriers to better diagnosis and treatment of SDB in patients with HF. From these findings, we can build strategies to improve care pathway design including improved communication between specialities and better screening tools empowering health professionals to direct these patients to specialist centres. Further, recognising the significance of CSA and educating health professionals about the importance and ease of mask therapy will likely optimise effective treatment.

P822

Clinical features of peripartum cardiomyopathy

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The aim. To explore the clinical and hemodynamic parameters and characteristics in patients with peripartum dilated cardiomyopathy (PPCM).

Methods: For 12 years, we examined 514 pts with DCM. The ratio of male to female was 294/158. According to the results of anamnesis and clinical and functional research peripartum cardiomyopathy form was established in 68 (13.2%) pts. For comparative evaluation of hemodynamic parameters and prognosis of life 2 groups ($n = 50$ pts with PPCM form and $n = 43$, women with idiopathic DCM) were formed. Assess of the clinical status, echocardiography, and the clinical course during prolonged observation were performed.

Results: The analysis of demographic characteristics showed that the average age of pts with PPCM was 28.2 ± 0.8 years and was significantly less than in the comparison group (38.1 ± 2.1 years; $p = 0.001$). The timing from the start of symptoms manifestation up to the admission (6.9 ± 1.1 and 14.8 ± 2.1 months, $p < 0.05$) was also significant, with no difference in the average NYHA class (3.4 ± 0.1

and 3.3 ± 0.1) respectively. Analysis of the intracardiac hemodynamic parameters showed that the pts with PPCM form had lower values of LV ESD ($5.3 \pm 5.9 \pm 0.1$ cm vs. 0.1 mm) and LVEDD (6.5 ± 0.1 cm vs. 7.1 ± 0.1 cm, both $p < 0.01$), with the prevalence of average LVEF to 7.5% (36 ± 1.4 vs. 33.3 ± 1.3 ; $p > 0.05$). The study of the disease dynamics revealed that in the PPCM group 19 (38%) cases had complete recovery of left ventricular function after 12 month of OMT (EF was greater than 55%), while in patients with idiopathic dilated cardiomyopathy it was observed only in 4 (9.3%) cases (both $p < 0.01$).

Thus, the incidence of PPCM form is 13.2%, in women compared with idiopathic dilated cardiomyopathy. It has a relatively younger age and disease duration, as well as less marked dilatation of the left heart, associated with more stable duration of CHF.

P823

Predicting heart failure in the community: role of 12-lead electrocardiography

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Purpose: Many patients attending their primary care physician with symptoms suggestive of new onset heart failure have a 12 lead electrocardiogram (ECG) as part of an initial triage work up. However, the role of ECG in predicting heart failure in the community is not yet defined. We thus examined the ability of ECG to predict heart failure in this patient population.

Method: All 733 patients attending the rapid access clinic for possible heart failure in our University Hospital from the period of 2000 till 2012 were included in this study. 12-lead ECG was performed using the Agilent Page Writer 100 ECG machine and interpreted by independent cardiologists. The ECGs were analysed along side the diagnosis of heart failure. ROC curves were performed to assess the robustness of the ECG in predicting heart failure.

Result: The heart failure group in this population had significant prolonged QRS duration (100ms [89:119] vs 89ms [81:98], $p < 0.05$), prolonged QT duration (393ms [360:431] vs 384ms [358:409], $p < 0.05$), prolonged QTc (431ms [407:457] vs 416ms [399:438], $p < 0.05$) and more rightward T wave axis (69degree [19:109] vs 45degree [23:68], $p < 0.05$) compared to the non heart failure group.

Heart failure patients also had significant ECG evidence of prior myocardial ischaemia (20.5% vs 12.8%, $p < 0.05$), intraventricular conduction disorder (37.3% vs 22.1%, $p < 0.05$), abnormal axis (21.7% vs 13.3%, $p < 0.05$), ventricular hypertrophy (11.8% vs 6.1%, $p < 0.05$) and atrial fibrillation (47.9% vs 8.9%, $p < 0.05$). Using the ECG evidence of myocardial ischaemia, intraventricular conduction disorder, atrioventricular disorder, abnormal axis, atrial enlargement, ventricular hypertrophy, ventricular arrhythmia and atrial fibrillation as a predictive model, the ROC analysis showed that the ECG model is a reasonable test (AUC = 0.81) to help predict heart failure in the community. Adding BNP to the model increased the robustness of the model in predicting heart failure (AUC = 0.88).

Conclusion: The utility of the 12-lead ECG in predicting heart failure in the community is under appreciated. This study showed that this simple test is useful and can offer primary care physicians the ability to expedite the diagnosis of heart failure in order to start relevant further investigation and treatment in the community. In conclusion, ECG is a useful test in predicting heart failure in the community, however addition of BNP into the model helped to increase the robustness of the test.

P824

Usefulness of contemporary echo and bnp assessment during early hospitalization in patients with acute heart failure

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Purpose: The Combined Use of BNP and Echocardiography (CUBE) in acute heart failure (AHF) diagnosis is poorly employed because of sonographers and expert physicians lack in the Emergency Department. The aim of the present study is to evaluate relation among hormone levels systolic and diastolic dysfunction by the contemporary assessment of BNP and Echocardiography during early HF management

Methods: We performed echocardiography and BNP measurement within 24 hours of hospital admission in 310 patients with AHF in order to evaluate those with left ventricular (LV) systolic dysfunction and enlargement calculated by Simpson biplane formula. We also studied the correlation among BNP and degree of diastolic dysfunction evaluated by pulsed Doppler transmitral flow velocity during early diastole velocity (E wave) late diastole velocity (A wave) E/A ratio, deceleration time (DT) of E, and by the ratio of peak early diastolic filling velocity and septal Tissue Doppler early diastolic velocity (E/e'). Finally we investigated the relation among BNP and the right systolic longitudinal ventricular function (TAPSE) and the systolic Pulmonary Arterial Pressure (PAPs).

Results: BNP levels were 1410 [CI: 1004-1830], 1082 [CI: 869-1294], 494 [CI: 291-888] pg/ml, respectively, for patients with EF \leq 25%, EF 25-40% and EF 40-50% (p=0.005). The correlation between BNP and EF was negatively significant (p < 0,001; r = -0,24). 150 patients (49%) had HF with preserved EF: BNP levels were 582 [CI: 488-676], 712 [CI: 569-854] and 1694 [CI: 1388-2001] pg/ml, respectively, in patients with impaired relaxation (E/A<1; DT>240msec), pseudonormal (E/A 1-1,5; DT 140-200msec) and restrictive (E/A>1,5; DT<140 msec) filling pattern (p < 0.001). BNP levels were 357 [CI: 265-488], 626 [CI: 544-709] and 1321 [CI: 1112-1531] pg/ml, respectively, for patients with E/e' \leq 8, E/e' 8-15 and E/e' >15 (p < 0.001). The correlation between BNP and E/e' was positively significant (p < 0,001; r = 0,63). BNP levels were significantly increased in patients with right systolic ventricular dysfunction (TAPSE<18 mmHg; p = 0.006) and in patients with PAPs \geq 40mmHg (p = 0.001).

Conclusions: BNP levels correlate linearly with LV systolic dysfunction as well as with impaired degree of diastolic dysfunction suggesting that BNP increase occurs in more advanced systolic impairment and higher LV filling pressure. Right ventricular dysfunction and PAPs are further parameters influencing BNP elevation. Our CUBE protocol confirmed the importance of the combined Echo and BNP assessment to optimize the diagnostic approach during early hospitalization phase.

ADVANCED HEART FAILURE

P825

Predictors of advanced heart failure in patients who underwent primary angioplasty and long term mortality rates

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Aim: The aim of our study is to identify the predictors of post-discharge advanced heart failure (AdHF) (LVEF \leq 30 and/or NYHA class III - IV symptoms despite optimal medical treatment and/or rehospitalization), in patients who underwent primary angioplasty (P-PCI) for acute myocardial infarction (STEMI) and to determine long term (median follow-up: 5 years) mortality.

Study population: Of the 3205 patients who admitted to our center with STEMI between January 2006-January 2010 within first 12 hours of chest pain and underwent P-PCI, 119 patients were excluded due to in-hospital mortality. Remaining 3086 patients (650 females, mean age 58.3 years) who could be discharged, formed the study population (AdHF, n = 233; no-AdHF, n = 2853).

Results: In the AdHF group, advanced age, presence of diabetes, hypertension, renal failure, anemia, delayed reperfusion, anterior infarct location, Killip class>1, neutrophil to lymphocyte ratio (NLR), baseline glucose, uric acid, B-type natriuretic peptide (BNP) levels, baseline SYNTAX score, peak troponin I levels, postprocedural mitral regurgitation (\geq 2) were significantly higher and baseline TIMI 2/3 grade flow, complete ST segment recovery (>70%, STR), final TIMI grade 3 flow and myocardial blush grade 2/3 were significantly lower (p < 0.05, for all). In the multivariate analysis, baseline BNP \geq 80 (Odds Ratio [OR] 2.01, 95%Confidence Interval [CI] 1.22 - 3.04, p = 0.002), NLR \geq 6 (OR 1.88, 95%CI 1.25 - 2.82, p = 0.003), anterior MI (OR 1.87, 95% 1.13 - 3.07, p = 0.014), anemia (OR 1.53, 95%1.07 - 2.20, p = 0.020), glomerular filtration rate <60 ml/min/1.73m² (OR 2.11, 95%CI 1.24 - 3.61, p = 0.006), SYNTAX score \geq 20 (OR 1.89, 95%CI 1.12 - 3.27, p = 0.027), peak troponin I >125 (OR 1.56, 95% CI 1.04 - 2.36, p = 0.030), mitral regurgitation \geq 2 (OR 2.76, 95%CI 1.66 - 4.59, p < 0.001), STR<70% (OR 7.24, 95%CI 4.18 - 12.55, p < 0.001) were identified as the independent predictors of AdHF. In the AdHF group, 1 year (27% vs 2.3%) and 5 year (56.7% vs 9.4%) mortality rates were significantly higher (p < 0.001, for both).

Conclusion: In patients who underwent P-PCI, development of AdHF is related to very high long term mortality rates and the presented parameters are found to be beneficial in the prediction of AdHF.

P826

Outcome predictors in hospitalized patients with advanced heart failure: usefulness of INTERMACS profile

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Purpose: There is a growing interest in reduction of Heart Failure (HF) Hospitalizations. Identifying outcome predictors is of paramount importance. We aimed to investigate in-hospital variables and INTERMACS (IM) scale as prognostic tools to predict adverse events.

Methods: We prospectively studied consecutive 131 acutely decompensated HF patients (pts) with ejection fraction (EF) less than 40%, admitted to Advance HF Care Unit. IM profile was divided into 3 groups: A (IM 1 - 2), B (IM 3 - 4) and C

(IM 5 - 7). Median time of follow-up was 7.3 (3.1 - 11.5) months. Adjusted hazard ratios for Death, Transplant and Rehospitalization were estimated by Cox Regression analysis.

Results: Mean age: 56.1 \pm 17 years, 75% were male, ischemic cardiomyopathy were found in 33.6%. Mean EF: 21.4 \pm 6.1%. Low cardiac output and right-sided HF at admission were more frequent in group A. Renal failure, hepatopathy and hyponatremia were more prevalent in groups A and B. Compliance for HF medication, group C: 78% and group B: 39%; p < 0.001. Survival (months): Group A: 0.8, Group B: 5.8 and Group C: 12.2; p < 0.001. 30-day Readmission: 19.1%. Pts eligible for heart transplant: 25% and 65% were successfully transplanted after a median of 39 days.

Conclusions: Our data shows that past medical history and HF medication tolerance predict adverse events in hospitalized Advanced HF patients.

Cox Regression.Adverse Events Predictors

Variable	Hazard ratio (95% CI)	p value
Previous HF admission	2.6 (1,5 - 4,4)	0.001
Previous inotropic requirement	2.3 (1,3 - 3,8)	0.002
Furosemide dose at discharge > 120 mg/d	2.0 (1,03 - 3,9)	0.041
ACE-Inhibitors and β -blockers intolerance at discharge	5.1 (2,2 - 11,7)	0.001

P827

Tolvaptan improves symptoms in advanced heart failure with hyponatremia

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Introduction and objectives: Tolvaptan have showed to increase diuresis in the presence of hyponatremia. We evaluated the effectiveness of tolvaptan in improving symptoms.

Methods: We analyzed patients with NYHA functional class III-IV, despite optimal treatment and hyponatremia \leq 130 mg/dl admitted between November 2010-November 2014. We measured diuresis, dyspnea and systemic congestion before initial dose of tolvaptan, at 24 hours treatment, at discharge and during follow-up. Statistical analysis with SPSS19.

Results: 31 pts (80% males, mean age of 61.4 \pm 13.11 years). Baseline characteristics are shown in the table with an overall mortality rate of 58.06% (18 pts). 23 pts (76%) with concomitant inotropic treatment and average dose of intravenous furosemide of 304 \pm 212.3 mg/day. Tolvaptan dosage used were 15 mg (23 pts; 74.2%), 5 pts (16.12%) 30 mg and the rest 7.5 mg (3 pts; 9.6%). 15 pts (48.3%) were discharged with Tolvaptan. Basal diuresis is 2026.92 \pm 967.59 cc/day and increased significantly (p < 0.001) after 24 hours of treatment (4546.80 \pm 1731.8 cc/day). At discharge basal diuresis is recovered (2406.94 \pm 1055.65 cc/day). Of the 24 pts (77.42%) with dyspnea prior to the start of tolvaptan, 15 pts (62.5%) improve significantly (p < 0.001) at 24 hours after initiation of treatment and was sustained at discharge. Baseline, 19 (61.3%) pts with severe congestion, 4 (12.9%) moderate and 4 (12.9%) slight congestion. At 24 hours after starting, the congestion decreases significantly (p < 0.001): 5 pts slight congestion (16.13%), 14 moderate (45.16%) and 7 (22.6%) severe, which improves at discharge, as half the pts have no congestion (16; 51.6%). 5 persists severe congestion (16.1%).

Conclusions: Tolvaptan is significantly effective in improving dyspnea and congestion in patients with advanced heart failure and allowing hospital discharge.

BASELINE CHARACTERISTICS OF PATIENTS

NYHA Functional Class III/IV	70.96% (22 patients)
IV/IV	29% (9 patients)
Etiology Ischemic cardiomyopathy	48.4% (15 patients)
Idiopathic dilated cardiomyopathy	16.1% (5 patients)
Others (valvular, restrictive, others)	38%(11 patients)
Mean Ejection Fraction	35.39% \pm 17.44%

P828

Preoperative tricuspid regurgitation and short-term outcomes in CF-LVAD recipients

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Purpose: Tricuspid valve regurgitation (TR) in patients undergoing implantation of continuous left ventricular assist device (CF-LVAD) can result in post-operative right ventricular (RV) dysfunction, leading to right ventricular assist device implantation (RVAD), renal impairment, prolonged ICU and hospital stay, early and in-hospital mortality. The aim of our study was to evaluate if severity of pre-operative TR may predict outcomes (morbidity and mortality) in CF-LVAD recipients in order to do better patient selection for biventricular devices or concomitant tricuspid valve repair.

Methods: We reviewed the data of 67 consecutive patients who had CF-LVADs implanted between May 2012 and June 2014 at our institution, without concomitant tricuspid valve (TV) repair. HeartMatell was implanted in overall 46 patients (68%). 27 patients had no, trivial or mild TR (Group 1) and 40 patients had moderate, moderate-to-severe, or severe TR (Group 2). Between these two groups we compared patients' demographics, treatment strategies and outcomes.

Results: Between groups 1 and 2 there was no statistical significance in age (56 ± 13 years vs. 55 ± 13 years, $p = 1$), median INTERMACS score (2 vs. 2, $p = 0.54$), and model of end-stage liver disease (MELD) IX score (39 ± 25 vs. 40 ± 16 , $p = 0.312$). Groups 1 and 2 had similar percentages of patients receiving CF-LVAD as bridge-to-transplant therapy (55.6% vs. 62.5) and destination therapy (44.4% vs. 37.5%), $p = 0.57$. No differences ($p < 0.05$) were seen with respect to gender, RVAD implantation, 30-day overall mortality, 30-day cardiovascular (CVS) mortality, post-operative renal failure, except in total hospital length of stay ($p = 0.009$) (Table 1).

Table 1 Patients' short-term outcomes

	No/Trivial/Mild TR (N = 27)	Moderate/Severe TR (N = 40)
Male (N)	25 (92.6%)	37 (92.5%)
RVAD, yes (N)	1 (3.7%)	1 (2.5%)
Renal failure, yes (N)	2 (7.4%)	5 (12.5%)
30-day mortality, yes (N)	3 (11.1%)	1 (2.5%)
30-day CVS mortality, yes (N)	2 (7.4%)	1 (2.5%)
Median hospital length of stay, days (range)	18 (12-216)	29 (13-85)

P829

Pulse pressure can predict mortality in advanced heart failure?

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Background and Objectives: Pulse pressure (PP) is the difference between systolic and diastolic blood pressure (BP) values. Pulse pressure markedly rises after the 5th decade of life, due to arterial stiffening with increasing age.

Several studies have shown a close relationship between high PP and the occurrence of cardiovascular (CV) death. Furthermore, high PP is a risk factor for the development of coronary heart disease, myocardial infarction, and heart failure in normotensive and hypertensive persons.

The aim of this study was to evaluate if Pulse pressure can be used as a prognostic marker in advanced heart failure.

Methods: We retrospectively studied 824 NYHA II-IV heart failure patients who were hospitalized in a single advanced heart failure unit, between June 2009 and August 2013. Pulse pressure was calculated as the difference between systolic and diastolic BP, and the patients were divided into 2 groups (PP > 40 mmHg and PP < 40 mmHg). All patients underwent standard clinical, laboratorial, echocardiographic evaluation or radionuclide angiography (RNA).

Median follow-up time was 2 years.

We analysed the cardiovascular mortality and heart transplantation.

Results: During follow-up time were hospitalized 824 NYHA II-IV heart failure patients who were divided into 2 groups: Group I: PP > 40 mmHg with 469 patients; Group II: PP < 40 mmHg with 350 patients.

The mean ages of the patients were 60 ± 19.1 years old, which 73% were man and 27% were women.

At admission, 62.4% of the patients were in IV/IV NYHA class, with a mean ejection fraction $43 \pm 12.7\%$ and BNP 1300 ± 328 pg/mL.

The mean hospitalization time was 12 ± 11 days.

On Kaplan-Meier analysis, group 2 (PP < 40 mmHg) had the highest mortality (38% vs 24% mortality, logrank $p = 0.002$), during the follow-up time.

Conclusions: Pulse pressure is easily calculated, and it enables the prediction of CV death in patients who have advanced heart failure. We believe that PP can be used reliably as a prognostic marker in daily clinical practice.

P830

Does revascularization in ischaemic patients with severe left ventricular dysfunction admitted for heart failure decompensation improve survival?

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Purpose: Given the lack of evidence on how PCI improves symptoms and survival in ischaemic patients with severe left ventricular dysfunction admitted in hospital for decompensated HF, we hereby present our experience on how these patients were managed.

Methods: We retrospectively selected the patients with known ischaemic heart disease and a LVEF ≤ 0.35 , who were admitted for decompensated HF and made a coronariography to rule out ischaemia as a leading factor. The decision of PCI over the suspected culprit arteries, apart from adjusting medical treatment (increase doses or start new drugs), was consensuated by the heart team. The main outcome in the follow-up was death for any cause.

Results: 53 patients (44 male) were followed-up, with an age of 70 years old. The cause of the myocardiopathy was only ischaemic in 38 patients, with also other causes in 15. Twenty nine patients had been previously revascularized (14 with PCI and 15 with CABG). The mean left ventricular EF was 0.27. All of them were receiving optimal tolerated treatment at home (ACE-I/ARB in 35, Betablocker in 32, MRA in 13 and TRC in 12).

In the coronariography, 46 patients had significant occlusions, and 26 were made a PCI over the suspected culprit arteries. There were no major complications related to the coronariography in any patient. The mean follow-up in PCI group was 56 months, and 65 months in the only medical treatment group. 16 died during the follow-up. There were no statistical differences between the groups (Breslow and Tarone Ware tests $p > 0.05$), as it is presented in figure 1.

Conclusions: In our sample, revascularization in patients with severe left ventricular dysfunction admitted for decompensated heart failure is reasonable and safe, but it does not improve survival compared to optimal medical treatment.

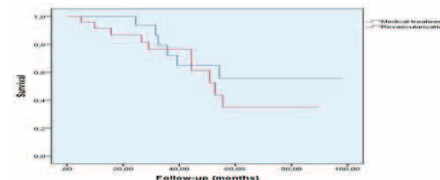


Figure 1. Survival curves.

P831

Levosimendan infusion in outpatients with advanced heart failure

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Background: Patients with advanced chronic heart failure are hospitalised frequently because of clinical deterioration. Levosimendan is an inodilator indicated for the treatment of acutely decompensated heart failure. There are a few small-scale studies, in which levosimendan was administered to ambulatory patients with advanced heart failure. However, there is still controversy about the security and beneficial effect of this approach.

Purpose: To analyse our experience with levosimendan infusion in outpatients with chronic advanced heart failure.

Methods: We included all pts with advanced heart failure treated with ambulatory levosimendan infusion between January 2011 and December 2014 in our Heart Failure Unit. All patients received a 6 hours continuous infusion of 0.05 to 0.2 mcg/kg/min of levosimendan (depending on patient tolerance). Continuous ECG and blood pressure were monitored during the infusion.

Results: A total of 23 pts were included. The mean age was 68 ± 13 years and 69,6% were males. Ischaemic etiology of chronic heart failure was 52%. The mean left ventricle ejection fraction was $28 \pm 7\%$. Medical treatment included beta-blockers in 87% of pts, ECA inhibitors/ARB in 87%, aldosterone antagonists in 74% and ivabradine in 17%. Mitral regurgitation was present in 91% of patients (mild 19%; moderate 62%; important 19%) and pulmonary hypertension in 78% (mild 33%; moderate 44%; important 23%). The NYHA functional class was: 61% III and 39% IV. The treatment with levosimendan was well tolerated without hypotension or arrhythmic events. At the first control post-infusion, 74% of the patients expressed subjective improvement, and in 17% of pts diuretic treatment could be reduced. However, 35% need intravenous diuretic within the first month and 52% within the first three months. Levosimendan was re-administered in 52% of pts. At one month 65% of the patients were free of hospitalization and 90% were alive. During de follow-up (mean of 277 ± 254 days) 5 pts died (21,7%), 2 patients were heart transplanted and 2 patients are still in the waiting list for heart transplantation.

Conclusions: 1/ Ambulatory infusion of levosimendan is well tolerated in patients with advanced decompensated heart failure. 2/ 74% of our patients expressed subjective improvement after infusion. 3/Further studies are necessary to determine the role of levosimendan in outpatients with advanced heart failure.

P832

Safety of tolvaptan in advanced heart failure: a single-center experience

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Introduction and Objectives: Some studies have showed that tolvaptan improves hyponatremia in heart failure. We evaluated its safety profile in advanced heart failure.

Methods: We analyzed 31 patients with congestive heart failure in NYHA functional class III-IV despite optimal treatment and hyponatremia ≤ 130 mg/dl admitted between November 2010-November 2014. It was made a control of renal function and ions 24 hours after beginning treatment, at discharge and during follow-up. Statistical analysis with SPSS19.

Results: 31 patients (80% males, mean age 61.4 ± 13.11). Baseline characteristics are shown in the table with an overall mortality rate of 58.06% (18 pts). 23 pts (76%) with concomitant inotropic treatment and average dose of intravenous furosemide of 304 ± 212.3 mg/day. Tolvaptan dosage used was 15 mg (23 pts; 74.2%), 5 pts (16.12%) 30 mg and 3 pts. 7.5 mg (9,6%). There was intolerance in 2 patients: in 1 patient dosage reduced because of thirst, and 1 with asthenia which forced to remove and restart with a lower dose. 15 pts (48.3%) were discharged with Tolvaptan. There were no significant differences in renal function after the start of tolvaptan nor during follow-up: initial GFR 55.8 ± 34.96 , at 24 hours 63.51 ± 43.5 , at discharge 71.65 ± 53.46 and at follow-up 70.56 ± 89 . There were significant differences in serum sodium prior to taking tolvaptan (Na 126.93 ± 4.36), 24 h of onset (Na 132.6 ± 5.15)($p=0.001$), and at discharge (133.37 ± 5.41)($p=0.001$), remaining stable at follow-up (132.8 ± 6.4)($p=0.001$). We found no significant differences in baseline potassium (4.34 ± 0.86), at 24 hours (4.283 ± 0.66), at discharge (4.18 ± 0.59) and at follow-up (4.873 ± 0.25).

Conclusions: Tolvaptan is safe and well-tolerated in advanced heart failure. It improves hyponatremia significantly without ionic disorders nor worsening renal function.

BASELINE CHARACTERISTICS OF PATIENTS	
NYHA Functional Class III/IV	70.96% (22 patients)
IV/IV	29% (9 patients)
Etiology Ischemic cardiomyopathy	48.4% (15 patients)
Idiopathic dilated cardiomyopathy	16.1% (5 patients)
Others (valvular, restrictive, others)	38%(11 patients)
Mean Ejection Fraction	$35.39\% \pm 17.44\%$

P833

Outcome of conservative management versus assist device implantation in patients with advanced refractory heart failure

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Background: In patients with advanced refractory heart failure (HF) cardiac transplantation (HTX), conservative medical management and the implantation of a ventricular assist device (VAD) represent valuable options. The determination of the best therapeutic destination strategy remains a challenge.

Aim: The aim of the present study was to assess the clinical outcome in advanced refractory HF patients either managed conservatively receiving optimal contemporary medical therapy including i.v. prostaglandin E1 ("conservative"), or underwent pulsatile flow VAD ("pVAD") or continuous flow VAD ("contVAD") implantation.

Methods: 118 patients with INTERMACS profile >1 at baseline, who died, or fully completed a 24 month follow-up free from HTX were included into this retrospective analysis. All-cause mortality at 24 months was assessed and compared between the three groups.

Results: 50 (42%) patients were managed conservatively, 25 (21%) received a pVAD and 43 (36%) a contVAD. NT-proBNP values were comparable between the three groups (median 25-75th percentile: 4402 (2730-13390)pg/mL, 3580 (1602-6312)pg/mL and 3693 (2679-8065)pg/mL, $p=0.256$). Mean survival was 18.6 (95% CI 16.2-21.0) months for patients managed conservatively, 7.0 (3.9-10.0) for

pVAD and 20.5 (18.2-22.8) for contVAD (Log-rank test $p < 0.001$). Conservatively managed patients spent a mean of 22.4 (95%CI 22.1-22.8) months, pVAD 17.7 (15.4-20.1) months and contVAD 21.6 (21.2-22.1) months out of hospital (conservative vs pVAD $p < 0.001$; conservative vs contVAD $p=0.015$; pVAD vs contVAD $p < 0.001$).

Conclusion: contVAD resulted in a significantly better clinical outcome than pVAD implantation. Conservative management with current optimal medical therapy appears to remain a valuable option for patients with advanced HF.

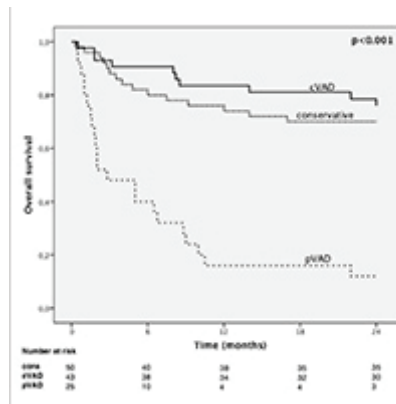


Figure 1

P834

Ambulatory intermittent levosimendan in patients with advanced heart failure not candidates for advanced therapies is effective to improve functional capacity and reduce hospital admissions

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Advanced heart failure in patients not candidates to heart transplant or ventricular assist device is a clinical challenge. The aim of this study was to determine whether intermittent ambulatory treatment with levosimendan is effective to improve functional capacity, decrease the Nt-ProBNP and hospital admissions in patients with heart failure, high prevalence of comorbidities and no response to an optimized treatment whom are not candidates for advanced therapies.

Methods: This was a prospective, observational study of pulsed infusions of levosimendan in 38 consecutive outpatients.

Levosimendan was administered at 2-week intervals over 6 weeks, in total 4 sessions. In patients with response to this initial treatment, levosimendan was administered as maintenance once a month. The improvement in functional capacity and decrease in Nt-ProBNP was evaluated in week 6. The decrease in hospital admissions was evaluated at week 24. Continuous variables were compared by Student t test for paired samples and chi square for categorical.

Outcomes: In the basal evaluation 92% of the patients were in functional class NYHA III-V, at the week 6 this proportion was reduced to 21% ($p=0.626$).

The 6 mWT week 6 vs 6mWT basal improve significantly, 300.3 ± 64.5 vs 223.4 ± 84.9 ($p 0.001$).

The Nt-ProBNP week 6 vs basal decrease but not significantly, $4793.3\text{pg/ml} \pm 4799.9$ vs $6224.7\text{pg/ml} \pm 3480.2$ ($p 0.066$).

At the week 24, the comparison between hospital admissions in the 6 months before and 6 months after levosimendan treatment evidenced a significant reduction in hospital admissions from 1.2 ± 0.99 vs 0.6 ± 0.9 ($p 0.03$).

In the total follow-up of this cohort (343 ± 265.8 days) the survival was 68.4%, and the causes of death were in 66.7% by heart failure.

Demographic and clinical characteristics					
Age	73 ± 9.8	Ischemic cardiomyopathy	42%	Beta-blockers	76.3%
Males	84.2%	LVEF	$28.3\% \pm 9.6$	NYHA III-IV	92%
HTA	76.3%	Atrial fibrillation	50%	6minWT mts	211.8 ± 88.6
DM	47.4%	ICD-CRT	7.9%	Nt-ProBNP pg/ml	6571 ± 5064
Charlson Comorbidity Index	12.8 ± 1.9	ACEi/ARB	55.3%	Prior hospitalizations 6 months	2 ± 1.6

Table 1

Conclusions: Levosimendan in patients with advance heart failure improve the functional capacity and decrease the hospital admissions. This strategy represent an effective alternative of treatment in these every time more prevalent population of heart failure patients.

P835

Ventilation of CO2 slope in the evaluation of heart failure patients. Does it add something to peak VO2?

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Purpose: peak VO2 is the most validated parameter in ergopirometry, with a cutoff value of 12-14 ml/Kg/min indicating a worse prognosis or need for a heart transplant. Although less used, the ventilation of carbon dioxide slope (VE/VCO2) that evaluates ventilatory efficiency plays also an important role in evaluating the results of cardiopulmonary stress test. The aim of our study is to analyze the correlation between peakVO2 and VE/VCO2 and their accuracy predicting events.

Methods: patients referred to our laboratory for an ergoespirometry during 2011 and 2012 were included. The primary endpoint was death, and the secondary endpoint a combinated of death, heart transplantation or peritoneal dialysis as treatment of refractory heart failure.

Results: 113 patients were included, 81,4% were male. Mean age was 57,6 (SD 10,3) and most common diagnosis was dilated cardiomyopathy (49,6%). Mean EF was 31,8% (SD 11,3). 92% received treatment with betablockers and ACE inhibitors or ARBII. VO2 and VE/VCO2 showed a lineal and negative correlation (Pearson Coef -0,53; p < 0,01). There were no differences in VO2 for the 1° endpoint, but mean VO2 was significantly lower for patients that presented the secondary endpoint (14,9 vs 18,7; mean diff 3,7 p < 0,05). VE/VCO2 was higher in patients that died (45,25 vs 40,37; mean diff -4,87 p < 0,05) and for the group with the combineate of death, transplant and dialysis. (45,81 vs 39,44; mean diff -6,36 p < 0,05).

CONCLUSION: VO2 and VE/VCO2 are inversely correlated. Both variables were associated with the secondary endpoint, but only VE/VCO2 showed an statistically significant correlation with death. Integrating VE/VCO2 in the evaluation of ergoespirometry in heart failure patients could improve our accuracy to predict events, and should therefore be evaluated in larger cohorts of patients.

P836

Which patients die due to acute heart failure?

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Background: Acute heart failure (AHF) is characterized by its heterogeneity and complexity, being associated with both high morbidity and mortality. Despite multiple treatment options, in-hospital mortality remains high.

Purpose and Methods: From a population admitted to a cardiac intensive care unit, in the setting of AHF, the cases resulting in death were studied. Clinical parameters and therapeutic strategies were evaluated.

Results: 140 consecutive patients (P) (74% male, age 69 ± 14 years) were admitted along 5 years. The in-hospital mortality was 19% (26 P - 69% male, age 74 ± 10 years).

The most frequent aetiology of HF in the deceased P was ischemic heart disease. The median evolution time of HF was 5 years and 50% of those P had been previously admitted with decompensate HF. 65% had concomitant chronic kidney disease, 77% were hypertensive and 38% diabetic. 15% had an ICD and 3.8% a CRT-D.

At admission, 23% of P were in acute pulmonary oedema and 23% in cardiogenic shock. Infection was the precipitating factor in 50% of patients. Analytically: 54% had lower haemoglobin (<12.0 g/dL); 54% had a lower glomerular filtration rate (GFR) (<30 ml/min/1.73m²) and 39% had a GFR 30-60 ml/min/1.73m²; 31% of P had hepatic cholestasis and 15% hypoperfusion and NTproBNP 29.0744 ± 27.490 pg/nl.

Transthoracic echocardiography showed LVEF < 35% in 58% of P and a restrictive pattern of filling in 23%; moderate/severe mitral regurgitation was present in 38% and 62% had moderate to severe pulmonary hypertension.

Regarding therapy: furosemide infusion was used in 69%, being the maximum daily dose 294 ± 203mg, despite association with other diuretic; 27% were treated with levosimendan, 35% with dobutamine and 15% required noradrenaline. Non-invasive ventilation was used in 65% and invasive in 19%; renal replacement therapy was required in 23% of patients

Hospitalization was complicated with cardiorenal syndrome in 85% and with hospital acquired infection in 54%.

Hospital length of stay was 15 ± 13 days.

The cause of death was end stage heart failure in 69% of P and infection in 31%.

Conclusions: Our study highlights the progressive deterioration of patients with chronic heart failure, being admitted several times previously to the final admission, when they present with multi-organ dysfunction.

This population deserves a special look concerning how far we should go with them in escalating therapies, and when is it time to start palliative care.

P837

Weaning from inotropic support in advanced heart failure patients who referred for heart transplantation evaluation

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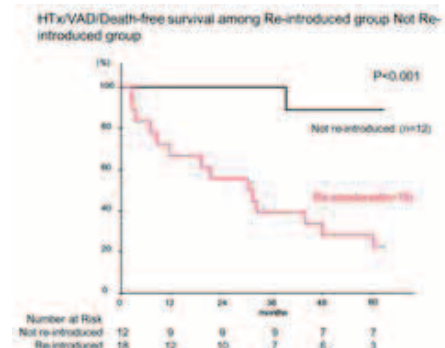
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Background: Heart transplantation (HTx) provides an effective treatment for selected patients with end-stage heart failure (HF). Candidate patients have a high mortality risk and require inotropic agents. The aim of this study was to examine the outcome of advanced HF patients who required inotropic agents and evaluated for HTx.

Methods: We retrospectively studied 75 inotropy-dependent HF patients (55 men, 35 ± 10 years) who evaluated for HTx in our hospital between 1997 and 2014.

Results: During a median follow-up of 3.4 years, 30 (40%) patients were successfully weaned from inotropic agents. However, 45 patients could not be weaned and received ventricular assist device (VAD) or HTx, or died. Among patients successfully weaned from inotropic agents, 18 (60%) patients were reintroduced inotropic agents (RI) during follow-up, while 12 (40%) patients were not reintroduced (NRI). At discharge after weaned from inotropic agents, the RI group had lower systolic blood pressure (BP) (88 ± 13mmHg vs. 105 ± 11mmHg, P < 0.05) than the NRI group. The HTx/VAD/death-free survival rate of the RI group was significantly higher than the NRI group (89% vs. 8%, p < 0.01).

Conclusion: In advanced HF patients who could be successfully weaned from inotropic agents, patients in the NRI group had a good prognosis. However, patients in the RI group showed low BP after the weaning from inotropes and had a bad prognosis.



HTx/VAD/Death-free survival

ATRIAL FIBRILLATION

P838

Correlation of serum potassium and vitamin B12 with the event atrial fibrillation

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Introduction-Purpose: The primary objective of this study is to investigate the correlation of serum potassium and vitamin B12 in the event of persistent atrial fibrillation. Secondary purpose of the present study was to evaluate whether correction of potassium levels contributed to the recovery of sinus rhythm.

Methods: The study included 37 patients with persistent atrial fibrillation aged <60 years who restored sinus rhythm. Full medical history was obtained from all participants who subsequently underwent blood tests, electrocardiogram and heart triplex. Inclusion criteria in the study were absence of other cardiac, pulmonary, thyroid disease, absence of a recent surgery and normal heart triplex. Patients were divided into 2 groups according to the presence(subgroup 1) or the absence (subgroup 2) of non-cardiac risk factors for atrial fibrillation, such as diabetes, hypertension, dyslipidemia and positive family history. The levels of potassium and vitamin B12 were evaluated in both subgroups during the follow up period.

Results: The first subgroup consisted of 17 patients, who had at least one of the above factors. The second subset included 20 patients with no risk factors. The mean potassium at the onset of the study was statistically significantly lower

TABLE 1

subgroup	Amiodarone + b-blocker	Amiodarone	Amiodarone + b-blocker+propafenone	b-blocker + K i.v	Amiodarone + b-blocker+ K	Amiodarone + propafenone	Amiodarone + K	electrical cardioversion	Propafenone + K i.v	Ki.v
1	29,4%	6%	6%	6%	6%	12%	6%	6%	-	-
2	-	-	-	30%	-	-	15%	-	15%	40%

Methods Rehabilitation Sinus Rhythm in both subgroups

in the second subgroup (3.2 ± 0.18 mmol / lt) compared to the first subgroup (3.8 ± 0.23 mmol/lt). ($P < 0.001$) Moreover, the second subset had lower levels of vitamin B12 (211.7 ± 72.58 pg/ml) compared to the first subgroup (309.3 ± 123.2 pg/ml) ($P = 0.008$). In both subgroups, methods rehabilitation sinus rhythm demonstrated at the following Table 1.

Conclusions: The idiopathic atrial fibrillation is associated with lower levels of potassium and vitamin B12 compared to sustained atrial fibrillation associated with classical risk factors. The intravenous administration of potassium resulted in restoration of sinus rhythm in a substantial proportion of patients with idiopathic AF. Further studies are needed to confirm these findings and to investigate the role of intravenous potassium and perhaps the administration of vitamin B12 as therapeutic agents in persistent idiopathic atrial fibrillation.

P839

Efficacy of omega-3 polyunsaturated fatty acids for the prevention of atrial fibrillation recurrence

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Background: Atrial fibrillation (AF) remains to be one of the most common arrhythmia. It is associated with low quality of life, increased risk of thromboembolic complications and death. Traditional pharmacological treatment of AF is limited by low efficacy and risk of the serious adverse events. We suggest that omega-3 polyunsaturated fatty acids (PUFAs) may exert beneficial effects for the prevention of AF recurrence.

Purpose: To evaluate the efficacy of omega-3 PUFAs for the prevention of AF recurrence.

Methods: We prospectively studied 58 patients (34 men and 24 women, mean age 56.8 ± 6.6 years) with stable coronary artery disease and moderate arterial hypertension who had a history of paroxysmal AF and sinus rhythm at the baseline. All patients regularly took standard therapy with ACE inhibitors, beta-blockers, statins, anti-platelet drugs and amiodaron. Participants were assigned to omega-3 group (1 g/day; n = 28) or control group (n = 30) for 6 months.

Results: During 6-month follow-up in 10 participants (33%) of the omega-3 group and in 18 (64%) patients of the control group AF recurrence were documented ($\chi^2 = 4.39$; $p = 0.036$). Omega-3 group had significantly ($p < 0.05$) less the mean number of AF episodes per one patient (4.4 ± 1.0 vs 7.0 ± 1.4) and the mean duration of AF episode (76 ± 38 vs 121 ± 56 min) compared to control group. Omega-3 PUFAs intake was associated with 29% (95% confidence interval 7.0-47.7%, $p = 0.02$) reduction in AF recurrence.

Conclusions: Supplementation with omega-3 PUFAs during 6-month reduces AF recurrence in patients with paroxysmal AF.

P840

The correlation of uric acid level with left atrial diameter in paroxysmal atrial fibrillation

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Background: The positive association between uric acid level and atrial fibrillation has been demonstrated in some studies. There has been a great deal of interest in the role of serum uric acid in left atrial diameter.

Purpose: To study the correlation between uric acid level with left atrial diameter in paroxysmal atrial fibrillation.

Methods: Two hundred patients (pts) were enrolled in the study, 100 of them with paroxysmal atrial fibrillation (PAF) and 100 pts without PAF (control group), who were admitted in the Emergency Department of our University Hospital Center. Exclusion criteria included: presence of valvular and congenital heart disease, gout, severe heart failure. Demographic, clinical, and echocardiographic characteristics were recorded for every patient. Serum uric acid (UA) levels were measured.

Results: There was a significant difference between two groups in the age: 67.5 ± 10.18 years in pts with PAF vs 59.67 ± 10.63 in control group, $p = 0.0001$. Pts with PAF had more heart failure, pulmonary disease, thyroid disease, $p < 0.05$. Diuretics were prescribed significantly less in the control group, $p = < 0.0004$.

The left atrial diameter in pts with PAF was 43.3 ± 5.8 mm vs 39.5 ± 4.6 mm, $p = 0.0001$ and serum uric acid levels was significantly higher in pts with PAF than

control group, 6.72 ± 2.2 mg/dL vs 5.23 ± 1.56 mg/dL, $p = 0.0001$. In the two groups of the study there was a positive correlation between serum uric acid level with left atrial diameter. In pts with PAF, $r = 0.323$, determinant coefficient $r^2 = 10\%$, and $p = 0.001$. In the control group, there was a weak correlation, $r = 0.237$, determinant coefficient $r^2 = 5.6\%$ and $p = 0.01$.

Conclusions: There was a significant positive correlation between serum uric acid level with left atrial diameter in paroxysmal atrial fibrillation.

P841

Does atrial fibrillation limit the efficacy of betablockers in patients with chronic heart failure? Suggestions from an observational study

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Introduction: The use of beta blockers in heart Failure is widely demonstrated. However, according the last results of study "META-BB" the utilization of beta-blockers on patients with heart failure and atrial fibrillation is controversial.

Objectives: We compare the prognosis impact of beta-blockers use on patients with heart failure and atrial fibrillation with that of those patients with heart failure and sinus rhythm.

Methodology: we studied patients seen in the first four years of our heart failure specific outpatient clinic. We assessed patient features, where they were referred from, sex, age, heart failure etiology, functional class and left ventricle ejection fraction on patients with auricular fibrillation or sinus rhythm. The primary endpoints were major cardiovascular events (dead/readmission) and improvement of left ventricle ejection fraction.

Results: 141 patients were seen in the four first years of the outpatient clinic. Our patients had an average age of 59.6 years (CI 57.2 - 62), 75.2% male sex. Average follow up time was 856.5 days (CI 802.2 - 910.9). Important symptoms of heart failure were found in most patients, with II or worse NYHA class in 77.3% of patients. Median LVEF was 34% (CI 31.6 - 36.5), 63.8% of patients had severe systolic dysfunction (LVEF < 35%). The most frequent etiology was ischemic dilated cardiomyopathy (36.9%), followed by idiopathic dilated cardiomyopathy (31.9%), enolic dilated cardiomyopathy (5.7%), other causes of dilated cardiomyopathy (13.5%), and other non-dilated causes (11.3%). 64.5% of the patients were in sinus rhythm and 31.2% were in atrial fibrillation.

128 patients of the total (128 [90,7%]) were treated with betablockers. From these patients we assessed the ecg rhythm. 86 patients (61%) were sinus rhythm (SR), 38 (27%) were in atrial fibrillation (AF). The general mortality in the beta blocker group was 14%, 16,2% in the AF group and 13% SR group ($p = 0.77$ Fisher test). Readmissions were not different between the two groups (AF 38% vs SR 45% $p = 0.54$ Fisher test). There was no significant difference on LVEF change during follow up both groups. Patients with AF had similar NYHA class ($p = 0.82$). Mean follow up time were similar (861 days in SR group vs 849 days in the AF group $p = 0.84$).

Conclusion: In our study, atrial fibrillation in patients on long-term beta-blocker therapy is not associated with significant increased subsequent risk of mortality, readmissions and improvement LVEF. There is a need for further investigations to clarify this issue.

P842

Atrial fibrillation, heart failure and renal failure: a lethal combination

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Atrial fibrillation (AF), heart failure (HF), and renal failure (RF) share many risk factors coexisting frequently in clinical practice.

The purpose of this study was to evaluate the effect of HF and RF on the mortality and hospitalization rates in a population of patients with AF, in a two year period.

The data was collected by reviewing the digital records of all patients discharged in 2011 with the diagnosis of AF and complemented by telephonic interview. Renal function was estimated using the MDRD (Modification of Diet in Renal Disease) formula, RF.

Our population was composed by 340 patients, was 43,8% male and had average age of 75.5 years. Both HF and RF were common, 30.5% of the patients were

diagnosed with HF and 38.7% had a glomerular filtration rate (GFR) below 60 mL/min/m², predominantly moderate renal with only 2.1% in stage V renal failure. For the entire population the mortality rate was 35% at two years, 21.8% in the first year and 16.9% in the second. The presence of HF was associated with a significant increase in mortality in the first year (from 14.1% to 26.8%, $p < 0.01$) but not in the second year (17.2% to 16.9%, $p = 0.9$) or in the entire follow-up (28.9% to 39%, $p = 0.056$). As for RF, it was linked to a significant increase in mortality at two years in the total population (42.7% to 30.3%, $p < 0.05$) and in the patients without HF (45.5% to 23.8%, $p < 0.05$).

On the other hand, HF was associated with a significant increase in the percentage of patients with at least one hospitalization, from 45.2% to 62.4% ($p < 0.01$), and in the average number of hospitalizations, from 0.85 to 1.34 ($p < 0.05$), in the two years of follow-up. RF was also linked to a significant increase in average number of hospital admissions (0.99 to 1.44, $p = 0.014$) in the general population but not in patients with both AF and HF (1.18 to 1.53, $p = 0.13$).

In conclusion, heart failure and renal failure are important comorbidities in patients with atrial fibrillation leading to a worst prognosis in these patients.

P843

Features of warfarin dose titration in long term atrial fibrillation according to VKORC1 genotyping and severity of heart failure

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Purpose: To study the influence of polymorphism G (-1639) A VKORC1 gene and the severity of heart failure (HF) at the therapeutic dose of warfarin (Wf) and the incidence of anticoagulation.

Methods: Study included 84 patients (63.1% men) with a long-lasting (mean 5.2 ± 6.1 years) atrial fibrillation, > 2 risk factors for thromboembolism and who didn't receive Wf before. All patients received basic therapy of the underlying disease, in accordance with the guidelines of the ESC. Wf was administered at the starting dose of 2.5 mg/day under the INR control. Hypocoagulation noted, if INR > 3.0. Functional class (FC) of HF by NYHA was determined based on 6-minute walking test: 47 patients had HF I - II NYHA FC and 37 patients had III- IV FC. Identification of allelic variants of G (-1639) A VKORC1 gene performed using the polymerase chain reaction with subsequent study of restriction fragment length polymorphism technique. Genotype G/G "wild type" had 27 patients, genotype A/G or A/A (defective genotypes) was revealed in 57 patients. To achieve the goal, the patients were divided into 4 groups: 1 group (gr) consisted of patients with genotype G/G and I - II HF FC ($n = 16$); 2 gr with genotype G/G and FC III - IV heart failure ($n = 11$); 3 gr with genotypes A/G or A/A and I - II HF FC ($n = 31$); 4 gr patients ($n = 26$) with genotype A/G or A/C and FC III - IV HF.

Results: All patients achieved the recommended INR average 2.30 ± 0.31, with a maintenance dose of Wf 3.25 ± 1.16 mg/day at the end of 1 month. Hypocoagulation noted in 51 (60.7%) patients: 44.4% versus 68.4% in those with a wild and defective genotypes, respectively ($\chi^2 = 3.468$; $p = 0.063$). Incidence of hypocoagulation noted in 43.8%, 45.5%, 74.2% and 61.5% respectively in patients of 1st 2nd 3rd and 4th gr. Maintenance daily dose of Wf provides therapeutic hypocoagulation (INR 2-3) in 4th gr was lower 2.65 ± 0.95 mg/day than in the 2nd gr 3.75 ± 1.08 mg/day ($p = 0.004$) and 3rd gr 3.33 ± 1.25 ($p = 0.027$), respectively. Dose of Wf, which cause excessive hypocoagulation was significantly lower in 4th gr compared with 2nd and 3rd gr, 2.65 ± 0.62 vs. 4.09 ± 1.04 ($p = 0.000$) and 4.21 ± 0.99 ($p = 0.000$), respectively.

Conclusions: 1. Incidence of hypocoagulation noted 1.54 times more frequently in patients with defective alleles compared with wild genotype. 2. The highest risk of hypocoagulation revealed in patients with A/G or A/A genotypes and HF I - II FC, and the lowest risk in patients with G/G genotype and HF I - II FC by NYHA. 3. Maintenance dose of Wf was the lowest in 4th group and the highest dose of Wf in 1st gr.

P844

The impact of new onset atrial fibrillation on mortality in patients with acute coronary syndrome and heart failure with reduced ejection fraction

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Background: There is a strong evidence that patients with atrial fibrillation (AF) and myocardial infarction constitute a high-risk population for cardiovascular morbidity and mortality. However, the importance of new onset atrial fibrillation (AF) in patients with acute coronary syndrome (ACS) and heart failure with reduced ejection fraction (HFREF) remains unclear.

Aim: The aim of this study was to determine long-term mortality in patients with acute coronary syndrome, HFREF and new onset AF.

Methods: We conducted the cohort study, which included consecutive 360 patients with ACS and HFREF (EF ≤ 50%) diagnosed according to the ESC guidelines, hospitalized in the Department of Coronary Disease and Heart Failure between January 2008 and June 2010. We excluded patients with valvular heart disease, LV

hypertrophy, pericarditis, permanent AF, active thyroid disease and cancer. Patients were divided into two groups: 1st group - patients with new onset AF during ACS (25 M, mean age 74 ± 9.3) and 2nd group - patients without new onset AF during ACS (221 M, mean age 63.9 ± 11.4). After the follow-up period of 43-73 months we phoned 41 (78.8%) patients from 1st group and 152 (49.3%) patients from the 2nd group.

Results: Patients with AF in comparison to the patients from 2nd group were characterised by: older age (74.1 vs. 63.9 yrs, $p < 0.001$), women prevalence (48 vs. 72% M; $p < 0.001$), higher heart rate on admission to the hospital (111 vs. 81/min.; $p < 0.001$). Blood examination revealed higher serum creatinine level (107 vs. 89 umol/l; $p = 0.004$). In these patients we also observed higher rate of cardiac arrest during hospitalization (9.8 vs. 1.6%; $p < 0.001$). In-hospital mortality rate in the 1st group was 1.9 vs. 1.3% in the 2nd group ($p = 0.72$). Follow up revealed differences in both groups in all-cause mortality (45 vs 11.1%, $p < 0.001$), stroke-related mortality (9.3 vs. 0.7%, $p = 0.003$) and combined stroke and cardiovascular disease-related mortality (27.3 vs. 6.5%, $p < 0.001$). Cox proportional hazards model revealed three independent predictors of all-cause mortality in both groups: new onset atrial fibrillation during ACS (RR 2.6; 95% CI (1.3-5.3); $p = 0.008$), age (RR 1.07; 95% CI (1.04-1.12); $p < 0.001$), serum creatinine level (RR 1.01; 95% CI (1.0-1.02); $p < 0.001$).

Conclusions: In patients with ACS, HFREF and new onset of AF follow-up revealed higher rate of all-cause mortality, stroke-related mortality and combined stroke and cardiovascular disease-related mortality. AF during ACS, age and serum creatinine level were independent predictors of all-cause mortality in patients with ACS and HFREF.

P845

Heart rate is not related to survival in patients with heart failure and atrial fibrillation

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Introduction: Atrial fibrillation (AF) is common in patients with chronic heart failure (CHF), and is associated with significant morbidity and mortality. Although there is robust evidence that heart rate is a risk factor in CHF and that reducing elevated heart rates improves survival in patients who are in sinus rhythm, the importance of strict heart rate control in AF is still not clear. This study sought to investigate the influence of resting ventricular rate on survival in CHF, comparing those who are in sinus rhythm to those in AF.

Methods: A total of 1415 CHF patients (mean age 76 ± 11 years, 36% females, 65% IHD, 41% NYHA II, 44% NYHA III, 14% NYHA IV), of whom 62% ($n = 875$) were in sinus rhythm and 38% ($n = 540$) in permanent AF were evaluated from the BIOSAT-CHF Scotland study. Patients from both in-patient and out-patient settings were included. We analysed the heart rate and rhythm data recorded on a 12 lead ECG at the baseline review. Multivariate Cox proportional hazards models & Kaplan-Meier curves were used to assess the influence of heart rate on survival in CHF patients with AF or sinus rhythm.

Results: During a median per-person follow-up of 1.5 yrs (QIR 0.7-2.2), there were 330 (23%) all-cause deaths. Although Kaplan-Meier survival curves displayed significant differences between the AF and sinus rhythm groups (log-rank test $p = 0.014$), multivariate Cox survival models showed no significant difference between the 2 groups (hazard ratio [HR]: 0.98, 95% CI: 0.75-1.29; $p = 0.9$). When assessing the influence of heart rate, multivariate Cox models showed that higher heart rates (per 10 beats/min increments) were associated with worse survival in patients in sinus rhythm (HR: 1.14, 95% CI: 1.03-1.25; $p = 0.008$), but not for those in AF (HR: 0.98, 95% CI: 0.91-1.07, $p = 0.7$), for both preserved and reduced ejection fraction heart failure. When separated into two categories (heart rate < 80bpm vs. ≥ 80bpm), those in sinus rhythm with a heart rate ≥ 80bpm had a significantly worse survival than those with a heart rate < 80bpm (HR: 1.57, 95% CI: 1.10-2.23, $p = 0.012$).

Conclusion: Although higher heart rate was associated with worse survival for CHF patients in sinus rhythm, it does not appear to be associated with survival in those who are in AF. These findings question the value of strict heart rate control in CHF patients with atrial fibrillation, thus necessitating further research in this area.

P846

Atrial fibrillation versus sinus rhythm in patients with ischemic heart failure: prevalence, clinical and therapeutic profile

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Background: Ischemic heart disease is known to be the first cause of cardiac heart failure world wide, atrial fibrillation is the most frequent heart rhythm disorder encountered in clinical practice, the prevalence of the atrial fibrillation in heart failure population varies widely, the data treating the prevalence of this rhythm disorder

specifically in ischemic heart failure population remain scarce, also the intersection of those two cardiovascular disease may have clinical and therapeutic implications.

Objectives: The aims of this study were to identify the prevalence of Atrial fibrillation in ischemic heart failure population, describe the clinical and the therapeutic profile of the atrial fibrillation versus sinus rhythm patients with ischemic heart failure.

Methods: We conducted a retrospective descriptive study based on the heart failure registry of the Cardiology department of our University Hospital of from 2006 to 2014, all cases of ischemic heart failure were recorded and we proceeded to a comparative analysis between patients with Atrial fibrillation and Sinus rhythm.

Results: In this period 893 patients with ischemic heart failure were recorded, the prevalence of Atrial Fibrillation was 5,9%. The patients in AF group was significantly older than in Sinus rhythm group (72,64±12 Vs 68,67±11 respectively, $p=0,013$), Hypertensive patients were significantly more frequent in AF group (56,6% Vs 34,9%, $p=0,001$), more strokes was recorded in AF group (32,1% Vs 17,6%, $p=0,009$), there was no difference between the two groups about the other cardiovascular risk factors, the HASBLED score was significantly higher in AF group (2,47±1,11 Vs 2,11±0,87, $p=0,007$), cardiac heart rate at admission was significantly higher in AF group (84,5±21 bpm Vs 77,21±16 bpm, $p=0,002$), Diastolic arterial pressure at admission was significantly higher in AF group (mean 77,4±14 mmHg Vs 72,40±13 mmHg, $p=0,018$), the Aspirin use was significantly lower in AF group (83% Vs 94%, $p=0,003$), the Clopidorel use was significantly lower in AF group (7,5% Vs 22%, $p=0,009$).

Conclusion: In our knowledge this is the largest study treating the prevalence of atrial fibrillation in ischemic heart failure population in Morocco, the prevalence of atrial fibrillation in ischemic heart failure population was lower than described in the literature, also the atrial fibrillation and ischemic heart failure patients had higher bleeding risk profile which may influence the anticoagulant therapy options in such population.

P847

Evaluation of the antiarrhythmic therapy efficiency in patients with atrial fibrillation depending on the parameters of the left atrium structural remodeling

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Purpose: To evaluate the effects of amiodarone and sotalol on the left atrium LA remodeling in arterial hypertension (AH) and coronary artery disease (CAD) patients with recurrent atrial fibrillation (AF).

Materials and Methods: The study included 60 patients, mean age 66,3 ± 8,6 years, with stable CAD and either paroxysmal or persistent AF, who were randomized into 2 modes of 3 month antiarrhythmic therapy. The first group (n=30) received 200 mg amiodarone (A) plus 100 mg metoprolol (M) daily, the second one (n=30) received 160 mg sotalol (S) daily. Concomitant therapy was comparable in both groups and included ACE inhibitors, aldosterone antagonists, diuretics and warfarin. To assess LV diastolic dysfunction (LVDD), Doppler patterns of early filling peak velocity (E), atrial peak velocity (A), E/A ratio, mitral annulus velocity (E'), E/E' ratio. Apical four- and two- chamber views images of 6 myocardial segments in the filling phase were obtained to assess globPALS; LA volume index (LAVI) was also calculated by biplane method. The patients were divided into the groups with normal (n=29) and increased (n=31) antero-posterior dimension of the left atrium, with normal (n=14) and increased LAVI (n=46), with moderate (n=26) and considerable (n=34) decrease in the LA global longitudinal strain (><14%). All measurements were performed in the sinus rhythm period.

Results: Assessment of the antiarrhythmic drugs efficiency depending on the baseline morphofunctional state of the left atrium showed that the frequency of full antiarrhythmic effect in patients with normal antero-posterior dimension of the left atrium (n=12, 69%) and LAVI (n=9, 65%) was slightly higher than in the compared groups (n=15, 48% and n=26, 56,5%), but these differences were not statistically significant ($p=0,1$ and $p=0,6$). At the same time, the dependence of antiarrhythmic drugs on the baseline values of the LA global strain appeared to be more evident. So in patients with moderately decreased globPALS full antiarrhythmic effect was achieved in 23 (88,5%) cases, while in patients with significantly decreased globPALS - only in 12 (35,3%) cases ($<0,0001$). Under antiarrhythmic treatment recurrence of atrial fibrillation in patients with normal LA was significantly lower than in patients with the changed indices of antero-posterior dimension of LA - $0,67 \pm 0,06$ and $1,26 \pm 0,10$, respectively ($p=0,038$) and LAVI $00,85 \pm 0,07$ □ $1,69 \pm 0,10$ ($p=0,032$), the global deformation of LA $-0,72 \pm 0,07$ □ $1,35 \pm 0,18$ ($p=0,039$).

Conclusion: Full antiarrhythmic effect of amiodaron and sotalol significantly correlated with global longitudinal strain left atrium (globPALS).

P848

Permanent atrial fibrillation is associated with higher hospitalization and mortality in chronic heart failure patients despite adequate rate control

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Background: Rate control is well accepted strategy in pts with atrial fibrillation (AFib) and chronic heart failure (HF), but its role in terms of morbidity and mortality is still debated.

Methods and results. We evaluated 376 consecutive pts attending our HF clinic. By excluding PMK pts we selected 309 pts with the following baseline characteristics: 37.2% in permanent AFib, 30.1% female, mean age 71.5 ± 14.4 yrs, 62.1% ischemic etiology, mean EF(%) 36.5 ± 12.2 , in optimal medical therapy (96,8% on beta-blockers and 94,5% on ACE-I or ARBs, up-titrated to a mean percentage of 73.2 ± 30.8 and 83.4 ± 23.7 of maximum daily drugs dosage respectively). AFib pts had more HF hospitalization compared to the sinus rhythm group (80.0% vs 68.0%; HR 1.88; 95% CI, 1.09-3.24; $p=0.025$). After a mean follow-up period of 629.6 ± 264.1 days, 27 patients (23.5%) in permanent AFib group died, as compared with 14 (7.2%) in the sinus rhythm group (HR 3.94; 95% CI, 1.97-7.89; $p < 0.001$). Pts in AFib were older compared to sinus rhythm group (77.4 ± 9.5 vs 68.5 ± 15.0 years; $p < 0.001$) but they did not differ for other clinical risk factors, EF, HF etiology, and optimal beta-blockers therapy (98.3% vs 95.9%, up-titrated to a mean percentage of 73.6 ± 30.4 vs 72.9 ± 31.2 of maximum daily dosage). AFib pts heart rate was on goal according to the ESC guidelines (mean heart rate 76.6 ± 16.0 bpm). In a multivariate analysis AFib resulted independently related to a higher mortality (HR 2.53; 95% CI, 1.31-4.88; $p=0.006$).

Conclusions: Our study demonstrated that permanent AFib is an independent risk marker in chronic HF pts because is associated with higher hospitalization and higher mortality despite an adequate rate control by optimal beta-blockers treatment. The role of rate control strategy in this setting needs to be better addressed.

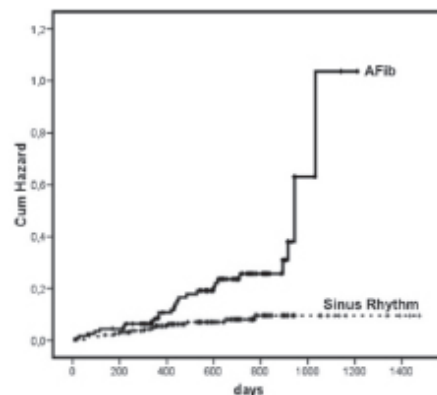


Figure 1

CARDIOMYOPATHY

P849

Possible new homoplasmic mutation of mtDNA as the aetiology of a familial hypertrophic cardiomyopathy

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Objective: To describe the case of a familial hypertrophic cardiomyopathy (HCM) possibly related to a non reported homoplasmic mutation in the gen MTTV.

Methods and Results: We present a female patient, 14 years old, referred for the study of a possible HCM in the context of a familial cardiomyopathy. She was born at the 35th week of gestation; her weight was 1,7 kg. She walked at 16 months and spoke at 20 months of age. At 6 years old she was referred to occupational therapy and pedagogic support. Now she is in school according to her age. She can exercise without limitations.

Her father had died at 30 years old of meningitis; her mother is 35 years old and has no cardiomyopathy but mild ocular ptosis and low stature. She has two half sisters (same mother but a different father) who died at 4 months from refractory heart failure secondary to HCM. A genetic test in one of them and in her mother found the homoplasmic mutation MTTV 1638T>C (tRNA Val).

Her physical exam showed an aortic systolic murmur that did not change with position or Valsalva maneuvers. She had alata scapulae, a slight basculant gait and no ophthalmoplegia.

Her lab tests were normal; her EKG showed mild signs of left atrium overload and left ventricle hypertrophy. Her Doppler echocardiogram showed a slight increase in mass index and normal systolic and diastolic function. A cardiac magnetic resonance showed a normal heart.

We ordered the molecular test for m.1638T>C in blood, urothelial and mouth cells from both the patient and mother. A microfluidic PCR-RFLP (chipDNA 1000 y Bioanalyzer 2100, Agilent Technologies) was performed and confirmed the homoplasmic change m.1638T>C in all samples.

Conclusions: Mitochondriopathies must be considered when studying the aetiology of HCM, especially in familiar forms. According to the type of DNA that has the mutation (nuclear DNA vs mtDNA), heritage of these diseases can be mendelian or matrilineal. In general, mitochondriopathies caused by a mutation of mtDNA are heteroplasmic: two different mtDNA populations coexist in each cell, the mutant and the wild type. When mtDNA shows only the mutant variant and it is present in all the cells, we say there is homoplasmic. In this situation it is difficult to know if this change is pathogenic or it is a polymorphism of the mtDNA. There are previous reports of homoplasmic mutations of mtDNA in genes that encode for many tRNAs as the cause of cardiomyopathies. The variant found in this family is highly suspicious of being pathogenic, but it is necessary to complete functional studies in order to confirm it.

P850

Predictive value of the prognostic markers in the hypertrophic cardiomyopathy

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Background: Hypertrophic cardiomyopathy is the first cause of sudden death in young adults. One of the relevant challenges in this pathology is represented by the risk stratification of sudden cardiac death.

Our aim was to evaluate the risk stratification and to identify the risk factors of sudden death in hypertrophic cardiomyopathy.

Methods: We report a retrospective, descriptive and analytic study about 48 patients with hypertrophic cardiomyopathy followed in the Department of Cardiology in the Military hospital of Tunis between 1997 and 2013

Results: The mean age of the patients was 37 ± 16 years with a sex-ratio of 1.8. The mean follow-up period was 5 years. The initial tests showed a mean parietal thickness of 23 ± 8 mm and a left ventricular obstruction in 23% of the cases. The prevalence of the delayed enhancement was 79%. Eighteen patients (38%) had an implantable cardioverter defibrillator. The percentage of the appropriate shocks was 39% (11.7%/year) and of inappropriate shocks 16.7% (5%/year). The mortality rate caused by sudden death was 1.2%/year. A multivariate analysis based on the Cox regression identified 2 predictive factors of severe rhythmic events: familial past medical history of sudden death (odds ratio = 6; p = 0.011) and unexplained syncope episodes (odds ratio = 5.4; p = 0.019). The presence of a delayed enhancement was associated to severe rhythmic events only when the analysis of the Kaplan-Meier curves was performed (Log Rank, p = 0.049). The prevalence of the occurrence of a severe rhythmic event was 5% in patients with no rhythmic risk factor, 23% in patients presenting one risk factor and 50% in patients with at least 2 risk factors.

Conclusion: The risk stratification of sudden death in hypertrophic cardiomyopathy remains challenging particularly in patients with only one risk factor. We think that the proposed algorithm of recommendations needs some improvements and that the therapeutic management should consider other factors such as the presence of extensive myocardial fibrosis especially in patients with only one risk factor.

P851

Predictors of heart failure on hypertrophic cardiomyopathy - a portuguese multicenter study

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Introduction: Hypertrophic cardiomyopathy (HCM) may lead to the development of heart failure. Little is known about the predictors of heart failure in HCM.

Aim: To identify predictors of heart failure in patients with HCM.

Methods: A Portuguese multicenter study involving 9 hospital centers and including all patients diagnosed with HCM. We evaluated demographic, clinical, genetic, electrocardiographic, echocardiographic and cardiac magnetic resonance data. We determined the factors that were associated with the development of heart failure and then conducted a multivariate analysis to establish the independent predictors of heart failure in patients with HCM.

Results: We included 356 patients with HCM.

Heart failure was present in 45% of patients.

In patients with HCM, the factors associated with the development of heart failure were female gender (55% vs 31%, p < 0.001), older age (67 ± 13 vs 58 ± 14 years, p < 0.001), left ventricular outflow tract obstruction at rest (31% vs 14%, p < 0.001), mitral valve regurgitation (61.9% vs 45.4%, p = 0.002), reduced left ventricular ejection fraction (64 ± 9% vs 67 ± 9%, p = 0.018), history of surgical miectomy (6.2% vs 0%, p < 0.001), diabetes mellitus (19% vs 11%, p = 0.032) and atrial fibrillation on clinical presentation (16% vs 8.2%, p = 0.019).

Patients with HCM and heart failure had higher frequency of death in the 5 years of follow up (3.8% vs 0.0%, p = 0.006).

In the multivariate analysis, female gender (p = 0.015) and left ventricular outflow tract obstruction at rest (p = 0.003) were identified as independent predictors of heart failure in HCM.

Conclusion: Heart failure is a common complication of HCM. The development of heart failure in patients with HCM was associated with female gender, older age, left ventricular tract outflow obstruction at rest, mitral valve regurgitation, reduced left ventricular ejection fraction, history of surgical miectomy, diabetes mellitus and atrial fibrillation on presentation. Female gender and left ventricular outflow tract obstruction at rest were identified as independent predictors of heart failure in patients with HCM.

P852

Could male sex be a risk factor for sudden cardiac death in hypertrophic cardiomyopathy?

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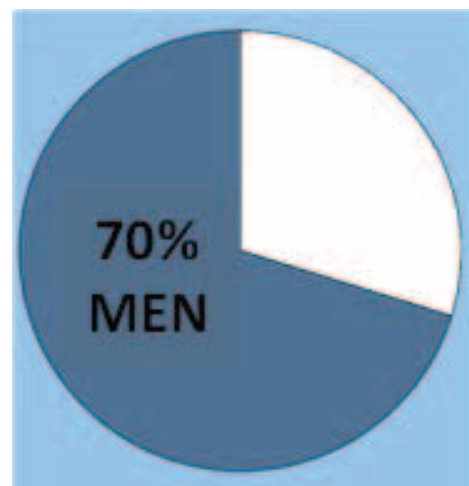
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Purpose: Hypertrophic cardiomyopathy (HCM) is a relatively frequent disease (1:500 individuals) and potentially devastating. It is considered one of the main causes of sudden cardiac death (SCD) among young adults. While HCM is most frequently transmitted as an autosomal dominant trait, small male preponderance, that remains unexplained, is reported in most studies. Our study aimed to review HCM patients with cardioverter-defibrillators implanted (ICDs), due to their known high risk clinical profile.

Methods: we retrospectively studied 47 consecutive patients with HCM from our hospital or referred to our center in order to receive an ICD, from 2008 to the end of 2014.

Results: The mean age of our study population was 55.8 ± 16 years. 76.7% of ICDs were implanted for primary of SCD and 23.3%, for secondary. Positive familiar antecedents for HCM and/or SCD in the same patient in 72.7%. Within the genetically studied group (63.8%), HCM mutations were identified in almost 76.7%. A surprising 70.2% of our population were men, (56.6-83.8), finding these differences significant (p < 0.05). This proportion remains the same in the genetically studied group and in the non-studied one. Nevertheless, all MCH genetically studied without identified mutations were men.

Conclusions: In general, HCM is considered an autosomal dominant inherited heart disease. However, in our population of HCM with high SCD risk, a striking male preponderance was found, statistically significant. As these differences remain unexplained, genetic and hormonal modifiers should be considered. This small sample is insufficient to draw definitive Conclusions: Further studies are essential, especially in patients at high risk clinical profile in order to study possible penetrance differences related.



P853

Clinical features and long-term outcomes of apical hypertrophic cardiomyopathy in a mediterranean population

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Purpose: Apical hypertrophic cardiomyopathy (AHC) is a phenotype variant of HC, with hypertrophy predominantly affecting the apex, which was initially described 30 years ago. It comprises approximately 1% to 10% of the total HC population in non-Asian populations, and may have different clinical implications compared with other subsets of HC. The aim of this study is to summarize clinical characteristics and outcomes of a Mediterranean population with this condition.

Methods: We retrospectively studied all patients with diagnosis of AHC in our Cardiology Unit, since January 2003 until December 2014. Patients with uncontrolled hypertension or non-compaction cardiomyopathy were excluded. Presenting symptoms and associated clinical features were characterized, and cardiovascular morbidity and mortality were determined on follow-up. All diagnoses of AHC required technically adequate apical views during TTE or a cardiac magnetic resonance (MR) image.

Results: 24 consecutive patients with diagnosis of AHC could be included. Our cohort had a mean age of 55,7 years. 13 patients (54,2%) had hypertension at the time of presentation, 2 had diabetes, 1 had a previous cerebrovascular accident (CVA), and 7 familial history of AHC or sudden death (29%). Presenting symptoms were dyspnea (6 patients, 25%) or angina (7 patients, 29,2%), and 11 were asymptomatic. Atrial fibrillation (AF) was present in 4 patients (16,7%), and giant negative T-waves (GNT) in 15 (62,5%). "Pure apical" pattern was identified in 4 patients, "medio-apical" in 20 (83,3%), and an apical aneurysm was found in 3 patients (12,6%). 12 had dilated left atrium, no patients had evidence of LV outflow obstruction, and one patient had moderate mitral regurgitation on TTE. 10 patients (41,7%) had late gadolinium enhancement (LGE) in MR. Genetic test was performed in 8 patients, finding mutations in 5 (4 involved sarcomeric genes). The diagnosis of AHC was initially missed in 10 patients due to inadequate image quality of the apex, a lack of awareness of the condition, or incorrect diagnoses. After a median follow-up of 68 months there were 1 death, 2 ischemic events, 2 CVAs and 3 ICD implantations.

Conclusions: 1. To our knowledge, this is the first study of AHC carried out in a Mediterranean population.

2. HTN, AF, familial history and LGE are highly prevalent. Furthermore, AHC may be less benign than previously suspected.

3. The diagnosis, when not carefully considered, can be missed. AHC should be suspected in patients with GNT. Although echocardiogram is an adequate approach, cardiac MR image should always be considered.

P854

Clinical status, structure and functional parameters of the heart in patients with hypertrophic cardiomyopathy and persistent atrial fibrillation

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Atrial fibrillation (AF) is the most common arrhythmia in patients with hypertrophic cardiomyopathy (HCM) and one of the causes of heart failure (HF) development.

Purpose: to assess the clinical status, structure and functional parameters of the heart in patients with nonobstructive hypertrophic cardiomyopathy (HCM) and persistent atrial fibrillation (AF).

Methods: we examined 20 patients with nonobstructive HCM (16 women (80%), average age 57.0 ± 16.5 years treated with bisoprolol (5.5 ± 1.8 mg). All patients had evidence of chronic heart failure (HF) I stage I-III functional class (FC) of chronic by NYHA. All patients underwent clinical examination, echocardiography with tissue doppler imaging (TDI) and evaluation of the level of brain natriuretic peptide (BNP). The patients were divided into 2 groups: group I - 5 patients with persistent AF and group II - 15 patients with sinus rhythm.

Results: There were no significant difference in gender, age, bisoprolol dose between two groups. Patients of group I had higher BNP level (404.0 ± 246.4 and 274.2 ± 136.2, pg/ml, p=0.02) and higher FC of chronic HF by NYHA (2.3 ± 0.5 □ 2.0 ± 0.5, p=0.05), higher left atrial (LA) size index (2.4 ± 0.3 □ 2.1 ± 0.3 cm, p=0.048), lower lateral systolic mitral annulus (MA) s' (7.4 ± 0.5 □ 8.9 ± 1.5 cm/s, p=0.01), lower septal systolic MA s' (8.0 ± 0.5 □ 9.4 ± 2.0 cm/s, p=0.04), lower posterior systolic MA s' (7.5 ± 1.0 □ 9.4 ± 2.0 cm/s, p=0.04), lower anterior systolic MA s' (8.3 ± 1.3 □ 9.0 ± 1.4 cm/s, p=0.05), lower lateral tricuspid annulus s' (12.1 ± 3.2 □ 14.0 ± 1.9 cm/s, p=0.03). There was a significant and high positive correlation between AF and BNP level (r=0.42, p=0.01) and LA size (r=0.37, p=0.01) and negative correlation between AF and lateral systolic MA s' (r=-0.33, p=0.01), septal systolic MA s' (r=-0.40, p=0.01), tricuspid annulus lateral s' (r=-0.34, p=0.04).

Conclusion: The presence of persistent AF in patients HCM associated with a higher

functional class of chronic heart failure by NYHA, higher BNP level and LA size. AF followed by decreased of longitudinal ventricular systolic dysfunction.

P855

The immunological status of patients with dilated cardiomyopathy depending on the severity of heart failure

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The **Aim:** Examine the nature of immunological disorders in pts with dilated cardiomyopathy (DCM) with different NYHA classes of heart failure.

Methods: The study included 96 pts with DCM in age from 18 to 61 years (mean 38,8 ± 1,2 years old). For studying of the state of cellular immunity pts were divided into 4 groups depending on the NYHA class: I gr - 7 pts with DCM diagnosed in preclinical stage, II gr - 14 pts with NYHA class II, III gr - 42 pts with NYHA class III and IV gr - 33 pts with NYHA class IV. The control group consisted of 29 volunteers. Clinical laboratory testing, immunological status was performed.

Results: It was showed a significant inhibition of cellular immunity in pts with DCM during the progression of HF, which was expressed in reducing of the total population of T-lymphocytes (CD3 +) (59,4 ± 1,5 vs. 52,2 ± 1,9; 50,6 ± 2,1 and 48,7 ± 1,1 g, respectively. control and II-III-IV gr. all p < 0.01) and T-helper cells (CD4 +) (33,8 ± 1,08 vs. 28,1 ± 1,3; 26,1 ± 0,7 and 26,7 ± 1,1; all p < 0.01). It was interesting to note that in pts identified in preclinical stage it was revealed very low levels of T-lymphocytes and T-helper cells (43,7 ± 1,1 and 24,1 ± 0,5 respectively). In all groups were showed increased levels of T-suppressors (18,4 ± 0,05 vs. 20,1 ± 1,1; 24,2 ± 1,0; 22,6 ± 0,8 and 23,8 ± 1,1 respectively, control and I-IV gr (all p < 0.001). Consequently, the IRI in all groups was statistically significantly lower (1,3 ± 0,1; 1,2 ± 0,07; 1,2 ± 0,05; 1,2 ± 0,06) compared with the control group (1,5 ± 0,05; all p < 0.01). Changes in the humoral immunity also indicated the violation in the immunological response. Thus, during the progression of CHF, indicators of autoimmune reactions progressively were growing, for example, the average concentration of the major circulating immune complexes were significantly higher in all groups (8,5 ± 1,3 19,7 ± 4,5 against 19,5 ± 1,4; 28,2 ± 2,5 and 23,6 ± 1,6; all p < 0,01) than in control group, as well as small immune complexes (14,2 ± 1,1 vs. 30,1 ± 2,3, 36,4 ± 1,8; 49,9 ± 3,5 and 44,8 ± 2,1 p < 0,01), having auto-aggressive properties.

Thus, in pts with DCM, regardless of NYHA class it was observed the imbalance of cellular immunity, accompanied by a more pronounced decrease of T-helper cells at pts in preclinical stage. During the disease progression it was showed a significant increase in both large and small circulating immune complexes in serum.

P856

Long-term myocardial recovery in patients with idiopathic dilated cardiomyopathy

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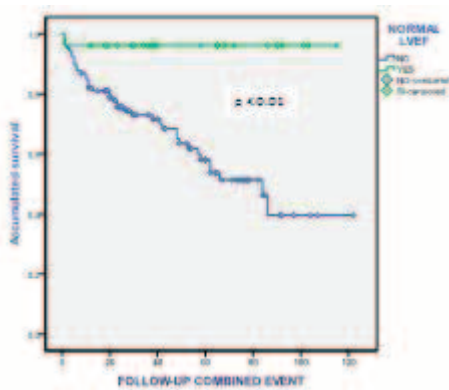
Purpose: Myocardial recovery is a process comprising left ventricular reverse remodeling added to a clinical course free from heart failure symptoms and events. Our goal was to know if myocardial recovery is possible in the long-term follow-up of patients with diagnosis of idiopathic dilated cardiomyopathy (DCM).

Methods: A cohort of 132 consecutive outpatients with diagnosis of idiopathic DCM was analyzed. We considered that there was reverse remodeling of the left ventricle when the left ventricular ejection fraction (LVEF) was over 55% during follow-up.

Results: Mean age was 65.87 ± 12.45 years and female gender was 35.6%. Mean follow-up was 48.66 ± 29.01 months. LVEF was normalized in 21.2% of patients. No mortality happened in this group vs 22.6% mortality in the group of patients without normalization of the LVEF (p=0.03). Only 3.8% of patients with reverse remodeling had a heart failure related event vs. 24.8% in patients with maintained depressed LVEF (p < 0.001). Mean number of hospitalizations for HF was 0.04 for patients with reverse remodeling of the LVEF whereas it was 0.58 for patients without normalization of the LVEF (p=0.04).

Improvement of the NYHA Functional Class during follow-up period (OR 2.88 IC 95% 1.05-7.91; p=0.040), NYHA class at the end of the follow-up (OR 0.38 IC 95% 0.15-0.94, p=0.037) and the combined event (death, heart transplant or heart failure hospitalization) (OR 0.096 IC 0.01-0.77; p=0.027) were independently related to normalization of the LVEF.

Conclusion: LV reverse remodeling was associated with an important improvement in NYHA Functional Class as well as with absence of mortality and a very significant reduction heart failure related events, so we consider that myocardial recovery is a fact in our cohort.



Kaplan-Meier of combined event

P857**The influence of left ventricular midwall fibrosis on torsional mechanics**

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Background: Left ventricular (LV) mid-wall fibrosis (MWF), which occurs in about a quarter of patients with non-ischemic cardiomyopathy (NICM), is associated with poor outcomes with higher rates of hospitalisation and reduced survival.

Objectives: To determine the effect of MWF on LV torsional mechanics.

Methods: Patients with NICM (n = 116; age: 62.8 ± 13.2 yrs; 67% male) underwent late gadolinium enhancement CMR and were categorized according to the presence (+) or absence (-) of MWF. Feature tracking (FT) CMR of apical and basal short axis cine was used to assess myocardial torsion.

Results: Both cohorts had similar LVEF (24.3 vs 27.5%, p=0.20). Whilst basal rotation was unaffected by MWF (3.00° vs. 3.30°, p=0.51), apical rotation was reduced (-1.99° vs. -3.50°, p=0.024). This reduction in the magnitude of apical rotation led to an overall reduction in LV twist (peak LV twist: 4.65° vs. 6.31°, p=0.004; LV twist per unit length: 0.94 °/cm vs. 1.34 °/cm, p=0.005; torsional shear angle: 0.52 vs. 0.83, p=0.008). The rate of LV twist (36.1 °s⁻¹ vs. 48.4 °s⁻¹, p=0.001) and untwist (30.5 °s⁻¹ vs. 44.5 °s⁻¹, p<0.001) was also reduced in patients with MWF. Rigid LV body rotation was more frequently observed in patients with MWF (64 vs 28%, p<0.001).

Conclusion: MWF is associated with disordered torsional dynamics in both systole and diastole. A reduction on apical rotation drives overall reduced LV twist. Apical and basal rotation are likely to be in the same direction in MWF. These systolic and diastolic disturbances, which are likely to be permanent, may explain the poorer outcomes in patients with NICM and MWF

P858**Mildly dilated cardiomyopathy: a distinctive disease or the effect of early diagnostic strategies?**

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Background: to characterize and assess the long-term natural history of Mildly Dilated Cardiomyopathy (MDCM). MDCM is a particular subgroup of dilated cardiomyopathy (DCM) characterized by systolic dysfunction but normal or slightly dilated left ventricle (LV). The characterization and long-term evolution of MDCM are currently unknown.

Methods: From 1988 to 2008 we analyzed all DCM patients consecutively enrolled in the Trieste Heart Muscle Disease Registry. MDCM was defined as LV ejection fraction ≤ 50% and index LV end-diastolic volume ≤ 86 ml/m².

Results: Among a whole population of 659 patients, 252 (38%) fulfilled the criteria for MDCM. At baseline MDCM patients presented a less advanced disease. At 10 years follow-up, all-cause mortality/heart transplant (HTx) death was 21% in MDCM and 39% in DCM (p < 0.001); heart failure death/HTx and sudden death/malignant ventricular arrhythmias rates were also significantly less frequent in MDCM (p = 0.004 and p = 0.04, respectively). Even if the status of MDCM patients initially improved under optimal therapy, in the long-term they gradually approached DCM patients. Furthermore, MDCM was not independently associated with a better outcome at multivariable analysis for all the study end-points.

Conclusions: MDCM identifies a consistent subgroup of DCM patients initially characterized by an apparent better evolution, but later by a long time progression similar

to non-MDCM. Despite a less adverse long-term outcome, MDCM did not show an independent protective effect after multivariate adjustment. Further studies are warranted to identify MDCM patients at higher-risk, for which early genetic testing could be indicated.

P859**A case of dilated cardiomyopathy with heart failure with reduced ejection fraction as a form of presentation of graves thyrotoxicosis**

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Objective: To analyze a case of thyrotoxicosis (TTx) debuting as dilated cardiomyopathy (DC) with low-output heart failure with reduced ejection fraction (LOHFrEF).

Background: DC with LOHFrEF is an extremely rare manifestation of TTx.

Methods: A detailed case report is presented. In addition, a review of the few similar cases published up to 2014 is performed.

Results: A 53-year-old man represented Graves' TTx (TSH = 0.001 IU/mL; FT4 = 4.04 ng/dL), LOHFrEF (NYHA functional class III), severe pulmonary hypertension and systemic congestion. Cardiovascular risk factors were absent, and screening for cardiotoxicity, other autoimmune diseases, myocarditis, or nutritional deficits was negative. The patient showed sinus tachycardia, CO Index = 2.4 L/min/m², LVEF = 30%, LV diastolic diameter = 65 mm, and PASP = 65 mmHg. Coronary angiography was normal. After 12-months conventional treatment (furosemide, carvedilol, eplerenone, ACEI and thiamazole administration), his clinical condition was dramatically improved with thyroid function normalization, and reversal of cardiopulmonary abnormalities. 25 similar cases from the literature plus our currently described patient had a mean age of 45 years, a male-to-female ratio of 1:1.2, Graves' disease as the principal cause of hyperthyroidism, and post-treatment LVEF improvement from 29% to 58%.

Discussion: DC with LOHFrEF is a paradoxical manifestation of hyperthyroidism since a high-output circulatory state represents the most common manifestation in thyrotoxic cardiomyopathy. The cause of systolic LV dysfunction in this condition remains unclear but both cardiac (genomic and non-genomic) and extracardiac (pulmonary and systemic vascular abnormalities) effects of T3 hormone excess have been argued as possible pathophysiological mechanisms.

Conclusion: Healing of cardiovascular abnormalities with appropriate treatment in thyrotoxic DC highlights the importance of early recognize this condition as an unusual cause of LOHFrEF.

P860**Prognostic biomarkers of mortality in patients with non-ischemic dilated cardiomyopathy**

This work was supported by a grant (No.MIP-086/2012) from the Research Council of Lithuania and the European Union, EU-FP7, SarcoSi project(nr:291834)| Zasytyte¹; D Vitkus²; E Zurauskas³; D Bironaitė⁴; K Rucinskas¹; J Celutkienė¹; D Karčiauskaitė²; V Grabauskienė³

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Aims: To evaluate the performance of biomarkers and endomyocardial biopsy (EMB) results to predict mortality and readmission in patients with non-ischemic dilated cardiomyopathy (DCM).

Methods and Results: 57 patients (44 men, 47.7 ± 10.9 years) with non-ischemic DCM (average left ventricle diastolic diameter 6.86 ± 0.89 cm, left ventricle ejection fraction 26.3 ± 9.43%, mean pulmonary wedge pressure (PCWP) - 22.06 ± 8.97 mmHg) were enrolled in the study. Standard demographics, echocardiography, blood samples were obtained shortly after admission. All patients have undergone endomyocardial biopsy (EMB) and were studied for inflammation with histological (Dallas) and immunohistological criteria. During a follow-up period of one year 11 patients (19.3%) died and 15 patients (28.1%) were readmitted because of heart failure (HF) recurrence, including those who had died because of HF. Multivariate analysis identified adiponectin (APN) (hazard ratio (HR) 1.045; 95% confidence interval (CI) 1.010 - 1.082, p < 0.05), interleukin-6 (HR 1.049; 95% CI 1.012-1.088; p < 0.01), number of CD3+ T cells in EMB (HR 1.091; 95% CI 1.027-1.158; p < 0.01) as independent predictors of mortality. APN (HR 1.039; 95% confidence interval (CI) 1.012 - 1.065, p < 0.01), interleukin-6 (HR 1.057; 95% CI 1.021-1.093; p < 0.01), were predictors of readmission due to HF.

Conclusion: For patients with non-ischemic dilated cardiomyopathy adiponectin, interleukin-6, number of CD3+ T cells in EMB can predict mortality and readmission for heart failure.

P861

New ways of clinical management in familial cardiomyopathy: utility of next-generation sequencing in the diagnosis of familial dilated cardiomyopathy

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Purpose: Nowadays, genetic testing is a widely used technique for the clinical management of cardiomyopathy. Next-generation sequencing allows us to analyze a large number of genes in a safe, quick and economical way. The aim of our study was to test the usefulness of this technique in the identification of genetic mutations in patients with familial dilated cardiomyopathy.

Methods: We studied all the index cases diagnosed of familial dilated cardiomyopathy and their first-degree relatives in our familial cardiomyopathy consultation, recording the results of the genetic studies. We compared the diagnostic performance of conventional sequencing technique (Sanger method) versus next-generation sequencing with specific genetic panels.

Results: Of the 111 patients (48 years, 43% women), the presence of any gene mutation was observed in 57.7%, presenting classical gene mutations 60.7% and combined mutations 39.3% (26.8% two genes mutations and 12.5% more than two genes). The most frequent mutations were those in sarcomeric genes (67.9%), followed by desmosomal genes (12.5%) and membrane genes (10.7%). Of the 38 index cases studied, 63.2% had at least one genetic mutation, presenting positive results 55% of the studies performed by Sanger method compared to 77.8% in those made with next-generation sequencing ($p = 0.182$).

Conclusions: 1. Genetic mutations were identified in a high percentage of the patients analyzed.

2. A significant percentage showed combined and non-classical gene mutations.

3. Next-generation sequencing improves diagnostic efficacy in the identification of genetic mutations.

P862

Safety, feasibility and short-term results of two minimally invasive procedures of left ventricle volume reduction and reshaping by means of novel myocardial anchoring system

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Background. Surgical approaches that correct left ventricular (LV) aneurysm may reduce wall stress by restoring a normal LV elliptical geometry, but have an high morbidity and mortality. Aim of this study: to evaluate the safety, feasibility of two minimally invasive procedures of LV volume reduction and reshaping by means of novel myocardial anchoring system (MAS). **Methods.** Patients (pts) with LV dysfunction (LVEF $\leq 45\%$) and LVESV $> 60 \text{ ml/m}^2$ due to ischemic dilated cardiomyopathy (IDC) and with a discrete anteroseptal LV scar were enrolled. MAS consists in titanium anchors pairs implanted, using fluoroscopic imaging, into the scarred portion of the heart, from the right side of ventricular septum and on the LV free wall creating a fold of tissue that excludes the non-functioning area. In 3 pts surgical procedure was performed by means of median sternotomy beating heart (Less Invasive Ventricular Enhancement-LIVE); in 1 pt closed chest endovascular delivery of the same MAS (Transcatheter Ventricular Restoration-TCVR) was performed. At baseline (T0) and at 3-6 month follow-up (T3-T6), all pts underwent CT-scan for the assessment of LV function and volumes, Minnesota Living Heart Failure (MLHF) questionnaire for the assessment of quality of life (QoL) and 6-minute walk test (6MWT). **Results.** At T0 all pts (mean age 69.75 ± 6.55) were in NYHA class III with mean LVEF 26% and mean LVEDVi $165.5 \pm 43.92 \text{ ml/m}^2$. Procedure was successfully completed in all cases: there were no intraoperative complications and no bleeding through the anchoring area. The postoperative course was uneventful and all pts were discharged within 7 days. Short term results are reported in Table 1. **Conclusion.** This novel MAS seems to be efficient to improve LVEF,

functional capacity and QoL in pts with IDC. In our experience both surgical procedures can be performed safely and effectively with no perioperative complications. Further evaluation of long term results are needed for a widespread application of this technology.

P863

Inverted TakoTsubo cardiomyopathy: a rare form of acute cardiac dysfunction

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Purpose: TakoTsubo cardiomyopathy is a transient acute left ventricular dysfunction, typically with apical akinesis and ballooning, in the absence of coronary artery disease. The basal variant - also named inverted - is an unusual form of presentation, described mainly in women with neurological dysfunction or pheochromocytoma. The authors present a rare case of inverted TakoTsubo cardiomyopathy.

Methods: A 59-year old woman, with history of cardiovascular risk factors (hypertension, dyslipidemia, smoking and stress), paroxysmal atrial fibrillation (under amiodarone) and reactive depression presented in the Emergency Department with thoracic pain irradiating to both arms and back, aggravated by efforts and associated with nausea, with several hours of duration. Physical examination was unremarkable. The EKG revealed ST segment depression in anterior and inferior leads. Blood sample analysis revealed an elevation in cardiac biomarkers (myoglobin and cardiac troponin T) and mild hyperthyroidism. Patient was admitted in Cardiac Intensive Care Unit with a suspicion of acute coronary syndrome. Cardiac catheterization was performed 12h after admission: no coronary artery disease was seen. In the ventriculography: akinesis of the basal segments in contrast with hyperkinesis of the medial and distal segments of the left ventricle. The transthoracic echocardiogram confirmed these alterations. Four days after admission, a cardiac magnetic resonance was performed: no myocardial scar was detected, but a remarkable recovery of the basal akinesis was seen and confirmed by echocardiography.

Results: The patient had a favourable clinical course and was discharge seven days after admission. At 3-months follow-up she was asymptomatic, in a functional class I of New York Heart Association.

Conclusion: We present a case initially interpreted as an acute coronary syndrome, but with a final diagnosis of an inverted TakoTsubo cardiomyopathy. It is noteworthy the rapid clinical and structural improvement and the favourable outcome. One can hypothesize that iatrogenic hyperthyroidism and stress are possible precipitating factors.

Despite the benign clinical course of the majority of the patients, some may have acute heart failure or a fatal outcome. The optimal interval of clinical and imagiologic re-evaluation and the type and duration of drug therapy remain to be addressed in future researches.

P864

The effects of obesity on morphological and functional changes of the heart

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Purpose: The aim of this study was to evaluate if obesity can lead to morphological and functional changes of the heart, predisposing to an evolution towards a systolic and diastolic dysfunction.

Methods: Forty-eight consecutive young patients (average age 31 ± 5) referred to our hospital, from October 2014 to December 2014, were prospectively enrolled. Twenty-four (20 female and 4 male) of them presented a morbid obesity (average BMI 42.2) (obese group OG), and twenty-four (13 female and 11 male) a normal body mass index (average BMI 22.9) (normal group NG). All these patients underwent to a good quality echocardiographic evaluation; we estimated morphological parameters (systolic and diastolic diameter of right and left ventricle), functional parameters (systolic and diastolic function of right and left ventricle) and hemodynamic parameters (systolic pulmonary artery pressure, cardiac output and stroke volume).

Results: We found a significant statistical difference in left ventricular diameter between the two group (average LVDD in NG was 44 mm vs 48 mm in OG; $p < 0.001$; for LVSD these values was 37 mm vs 39 mm; $p = 0.04$; average diastolic diameter of septal wall in NG was 8 mm vs 9 mm in OG, $p = 0.01$; for posterior wall 8,01 mm in

Table 1.

Patients	Type of surgery	LVEF%		Distance walked at 6MWT (meters)	MLHF QoL Score								
		To	T3		T6		To		T3		T6		
A	LIVE	34%	45%	45%	103	83	77	455	500	520	19	8	2
B	LIVE	19%	30%	37%	169	153	142	296	330	340	52	27	6
C	LIVE	26%	30%	39%	187	177	159	260	300	330	48	11	8
D	TCVR	25%	43%	43%	203	180	164	400	416	420	43	15	8

NG and 8,84 mm in OG; $p=0,006$). For right ventricle diameters we found significant statistical difference between basal diameter (27,8 mm vs 32,6 mm, $p=0,002$) and right ventricular wall thickness (5,7mm vs 6,7mm; $p<0,001$). Same results we obtained with left ventricular volume: average LVDV was 77ml in NG and 92ml in OG ($p=0,007$); LVSV was 34 ml vs 40 ml in NG and OG respectively ($p=0,05$); SV was 43,7ml in Ng vs 52 ml in OG ($p<0,01$) but there was no significant difference in ejection fraction and cardiac output. For right ventricular volume we have had the following results: average RVDV in NG was 29,6 ml vs 46,4 in OG ($p<0,001$); RVSV was 18 ml vs 22 ml respectively ($p=0,01$). We also noted a worsening of left ventricular diastolic function in OG (average E/A = 1,51 in NG and 1,04 in OG; $p=0,01$). Same results for right ventricular diastolic function with average E/A in NG 1,51 vs 0,97 in OG. In addition to this we have had a significant statistical difference in systolic pulmonary artery pressure values (21,7 mmHg in NG and 27,8 in OG, $p=0,02$)

Conclusion: these results clearly demonstrate the negative influence of body mass index on the heart; the alteration of all the parameters that we analyzed starting from a young age may lead to an unfavorable cardiac remodeling which in turn could be responsible for the appearance of an obesity-related cardiomyopathy.

P865

A broken heart of 'body or soul'?

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Introduction: Takotsubo cardiomyopathy (TC) is characterized by a transient left ventricular (LV) dysfunction, often associated with precipitating factors, either from physical or emotional nature. It is unknown if physical and emotional precipitating factors have different impact on the development of heart failure in patients with TC.

Aim: To determine the impact of physical and emotional stress factors on the development of heart failure in TC.

Methods: Portuguese multicenter study involving 11 hospitals centers and including all patients diagnosed with TC in the last 10 years. We evaluated demographic, clinical, electrocardiographic and echocardiographic data. We evaluated the impact of physical and emotional stress factors on the development of heart failure in TC.

Results: We included 142 patients with TC, predominantly women (89.4%). The mean age was 67 ± 12 years.

A precipitating factor was clearly identified in 82 patients (57.7%), 68 patients (82.9%) had emotional factors and 22 patients had physical factors (8 patients had physical and emotional factors).

Patients with TC associated with a physical precipitating factor were predominantly men ($p < 0.001$), had worse LV dysfunction ($p = 0.046$) and higher incidence of acute pulmonary edema (22.7% vs 4.6%, $p = 0.003$) and cardiogenic shock (9.1% vs 0.9%, $p = 0.019$) than patients without physical stress factors. No differences were found regarding heart failure or in-hospital death.

Patients with TC precipitated by an emotional situation had a lower incidence of acute pulmonary edema (1.6% vs 13.2%, $p = 0.012$) than patients without emotional stress factors. No differences were found regarding heart failure, cardiogenic shock or in-hospital death.

Conclusion: The presence of a physical precipitating factor is associated with the development of acute pulmonary edema and cardiogenic shock, while the presence of an emotional precipitating factor is associated with less development of acute pulmonary edema. So in TC, the heart is more broken "by the body than by the soul."

P866

Clinical picture of patients with heart failure of restrictive origin

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Purpose: Purpose of the study was to analyse causes, clinical picture, morphological features and prognosis of restrictive cardiomyopathy (RCM). The usefulness of new diagnostic tools such as brain natriuretic peptide (NT-proBNP) and cardiac magnetic resonance (CMR) was assessed.

Methods: 29 patients, 11 males, mean age 53 (± 13) yrs, with advanced heart failure were diagnosed with RCM, using thoracic echocardiography. 21 pts (72%) underwent CMR. Immunohistochemistry of tissue specimen was used to

confirm primary cardiac amyloidosis (cardiac biopsy in 3 pts, other tissue biopsy in 3, autopsy in 4). Fabry disease was diagnosed by gene sequencing and alpha-galactosidase concentration measurement.

Results: 10 pts were diagnosed with primary cardiac amyloidosis, 8 pts - with remarkably restrictive phenotype of hypertrophic cardiomyopathy, 2 pts - with Fabry disease, 1 pnt had desmoplakin pathology and 1 pnt had an inherited defect. The remaining 7 pts were diagnosed with idiopathic RCM. Heart failure stages distribution was as following: 14 pts (48,3%) were diagnosed with heart failure NYHA II class, 12 pts (41,4%) - NYHA III class, 3 pts (10,3%) - NYHA IV. Mean concentrations of NT-proBNP, troponin I and troponin T were 4765,6 (± 5222) pg/ml, 0,172 ($\pm 0,367$) ng/ml and 43,36 ($\pm 55,37$) ng/l, respectively. Significant positive correlations between NT-proBNP and troponins were observed (troponin I - 0,581, troponin T - 0,908, $P < 0,05$). There was a positive correlation between NT-proBNP and posterior wall thickness measured in CMR (0,636, $P < 0,05$), while similar correlation for echocardiographic findings was not found. However, a negative correlation was noticed between NT-proBNP and left atrium area measured by CMR, but not by echocardiography ($- 0,601$, $p < 0,05$). From among 21 pts who underwent CMR, late gadolinium enhancement was revealed in 16 pts (76%). Heart failure symptoms improved in 14 patients, resulting in NT-proBNP decrease in 8 pts. The remaining 15 pts did not improve, including 10 pts (34%) who died during mean 16,5 months (from 1 day to 31 months) of follow-up.

Conclusions: Restrictive cardiomyopathy results in advanced heart failure with remarkably increased NT-proBNP concentration and high mortality. Primary cardiac amyloidosis is the most common cause of RCM in the referral centre setting. NT-proBNP and CMR are new valuable diagnostic tools in RCM management.

P867

Does an admission BNP value greater than 100 ng/L correlates with the prognosis of takotsubo cardiomyopathy? A multicenter portuguese study

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Introduction: Takotsubo cardiomyopathy (TC) is characterized by a transient left ventricular (LV) dysfunction. BNP has been used as a marker of heart failure (HF) and LV dysfunction. There are no studies to determine if the cut-off of BNP used for HF is suited for TC.

Aim: To determine whether patients diagnosed with TC presenting an admission BNP value greater than 100 ng/L have worse in-hospital and medium term prognosis.

Methods: A multicenter Portuguese study involving 11 hospital centers and including all patients diagnosed with TC in the last 10 years. We analyzed the BNP value at hospital admission. The defined cut-off was 100 ng/L, the cut-off used for HF. It was determined if patients with BNP higher than 100 ng/L had a worse in-hospital and medium term prognosis.

Results: We included 79 patients with TC with a mean follow up of 39.7 ± 30.7 months.

A BNP value higher than 100 ng/L at admission was not associated with the occurrence of atrial fibrillation (7.4% vs 0%, $p = 0.353$), ventricular tachycardia (1.5% vs 0%, $p = 0.686$), complete AV block (1.5% vs 9.1% $p = 0.136$), LV thrombus (2.9% vs 0%, $p = 0.565$), stroke (1.5% vs 0%, $p = 0.686$), HF (26.5% vs 27.3%, $p = 0.955$) or in-hospital death (0% vs. 0%; $p = 1.000$).

A BNP value higher than 100 ng/L at admission was not associated with death (1.8% VS0%, $p = 0.673$) or stroke / TIA (1.8% VS10%, $p = 0.158$) or TC recurrence (0% VS0% $p = 1.000$) in the follow-up.

Conclusion: In this multicenter Portuguese study, patients with TC presenting BNP greater than 100 ng/L on admission did not present a worse in-hospital or medium term prognosis. This study suggests that the cut-off of 100 ng/L, for the BNP at admission, is not the most appropriate cut-off for predicting the in-hospital and medium term prognosis of patients with TC.

P868

Congenital heart disease and downs syndrome: a confirmed association but various aspects

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Background: Congenital heart disease is frequently described in Down's syndrome population, this associated malformation is the main cause of death during the first two years of life in this population, the spectrum of congenital heart disease patterns varies widely world wide, this variation could be due to demographic, genetic, and geographic factors.

Objectives: We try through this study to explore the spectrum of congenital heart disease in a Moroccan population with downs syndrome.

Methods: We conducted a retrospective descriptive study based on the congenital heart disease registry of the Pediatric Unit Of cardiology department of the our University Hospital in Morocco, we proceeded to a screening from December 2008 to October 2014 of all patients having congenital heart disease and having Down's syndrome which was phenotypically diagnosed in all our patients, and we collected clinical, echocardiographic features and outcomes of this population.

Results: From 2156 patients of the congenital heart disease registry we identified 128 patients with Down's syndrome (6%). The median age of diagnosis was 9.5 months (2days to 16 years). Sex ratio was 1. The most common CHD was the atrioventricular septal defect (AVSD) (42.2%), followed by ventricular septal defect VSD (31.3%) then atrial septal defect ASD (28,9%) and patent ductus arteriosus PDA(24,2%). The most common associations of CHD were: AVSD+ASD(10%), VSD+ASD(7,8%), VSD+PDA(7,8%), ASVD+PDA(7%) and ASD+PDA(6%). Surgery was the most common treatment's modality (54.3%) and the total mortality was 20%.

Conclusion: Our study showed that the distribution of congenital heart disease features in Moroccan Downs syndrome population was similar to most European countries and USA, and differs from most Asian countries this geographic distribution suggest that ethnicity may have an implication in the repartition of associated congenital heart disease in Down's syndrome population.

P869

The state of immunological status in patients with peripartum cardiomyopathy

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The **Aim:** To evaluate the parameters of the immune status (IS) in patients with peripartum cardiomyopathy (PPCM) complicated by high NYHA classes of HF
Methods: The study involved 29 pts with PPCM, aged 23 to 44 (31,8 ± 1,8) years. The disease duration ranged from 1 to 12 months (median 4,4 ± 0,8 months). The clinical laboratory testing and immunological status were determined (IC), as well as ECG, EchoCG, 6-minute walking test (6MWT). In all cases, the disease developed from 1 to 5 months after the delivery. NYHA class III was observed in 13 (44,8%), IV C - in 16 (55.1%) pts (mean 3,3 ± 0,1). The control group - 29 healthy volunteers.

Results: The analysis of intracardiac parameters showed a significant increase of the heart in PPCM pts. So the size of the LP was 4,3 ± 0.1 sm, the EDD LV 6,7 ± 0.1 cm, SDD LV 5,3 ± 0.2 sm, EF LV 37,1 ± 1,2%. The average 6MWT for all groups were amounted to 218,1 ± 15,5m. The level of leucocytes (6140 ± 521 and 6500 ± 295) and the percentage of lymphocytes (32,7 ± 1,8 and 33,1 ± 0,9%) compared with the control gr showed no differences. However PPCM pts showed a significant reduction of T lymphocytes (CD3) on 17,8% (59,4 ± 1,5 vs. 48,8 ± 1,3%; p = 0.00) and T-helper (CD4) on 22,8% (33,8 ± 1,08 and 26,1 ± 0,8%; p = 0.00), so the T-suppressors (CD8) cytotoxic lymphocytes were on 23.4% higher (18,4 ± 0,5 and 22,7 ± 1,1%; p = 0.001), and as a consequence, the immunoregulatory index (IRI) (CD4/CD8) at PPCM pts dropped on 20%, compared with control gr (1,5 ± 0,05 and 1,2 ± 0,07; p = 0.001). At the same time there was a statistically significant increase in natural killer cells (NK cells) (CD16) to 22,8% (18,4 ± 1,1 vs. 22,6 ± 1,02 p = 0.02) and B-lymphocytes 11,7% (19,6 ± 0,59 vs. 21,9 ± 0,5; p = 0.02) compared with the gr of control. The indicators of humoral immunity also testified about depression of IS at PPCM pts. Thus, the level of IgA was on 24% higher (120 ± 8,5 vs 148,8 ± 8,9; p = 0.04) than a comparison gr. This also indicates the presence of inflammation in pts with PPCM. The level of IgM, IgG what are the nonspecific factors of protection were within normal limits. The average concentrations of the major circulating immune complexes (CIC) were significantly higher than the corresponding parameters of the control group (respectively: 30,4 ± 5, 03 8,5 ± 1,35; p = 0.00), as well as small CIC (50,3 ± 7,02 and 14,2 ± 1,2; p = 0,01).

Conclusions: There is an imbalance on the part of cellular and humoral immunity at PPCM patients, accompanied by a decrease in the IRI and the formation of "small" and "large" CIC having autoaggressive properties.

P870

Advanced cardiac AL amyloidosis: the role of Bortezomib

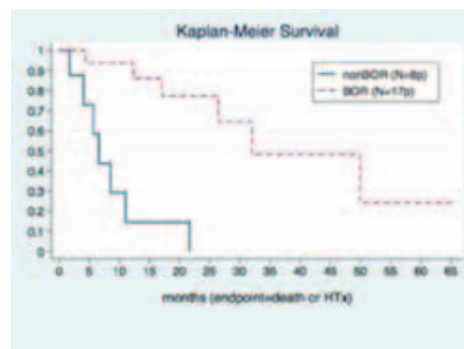
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Purpose: Cardiac AL amyloidosis (ALCAm) carries a poor prognosis. Combinations of alkylators and steroids have a limited role in ALCAm. Heart transplantation (HTX) and autologous stem cell transplantation improve long-term S but most of ALCAm patients(p) are not candidates due to comorbidities. Bortezomib(BOR),a proteasome inhibitor, has shown significant benefits in systemic AL amyloidosis, but its efficacy in ALCAm is not well known.The aim of our study is to compare BOR with other therapeutic strategies.

Methods: This is a retrospective analysis of a series of 34 consecutive ALCAm p treated in our hospital from July 2005 to October 2014.The analysis of prognostic variables was carried out in the entire series. The cohort, after excluding those with S<1m, was divided:p who received BOR(BOR=17)and those who did not(nonBOR=8). We compared outcomes.

Results: Median follow-up was 8m and estimated OS during the first year(y) of follow-up was 53%. Variables with a significant impact on the combined outcome(death and HTx) in the multivariate analysis were age≥70y,NT-proBNP≥8.500 ng/L and pericardial effusion. A hematologic response was observed in 15p(94%) in BOR versus 2p(25%) in nonBOR(RR 3,75(CI 95% 1,12-12,5);p=0,001).Ten p(71%) from the BORgroup reached at least one cardiac response criteria versus none of p in the other group(p=0,011).S at 6m,1 and 2y for BOR p was 94%,94% and 77% versus 58%,15% and 0%,respectively, in nonBOR p(log-rank, p=0.001). S at 1, 2 and 3y, including those who received a HTX,was 94%,94% and 73% with BOR vs 34%,0% and 0% in nonBOR p(log-rank, p=0.003).

Conclusion: ALCAm carry a poor short-term prognosis. In our experience, BOR is associated with greater absolute S as well as S without HTx. Nowadays, its use should be considered in ALCAm.



Survival by treatment

P871

Predictors of cardiogenic shock in Takotsubo cardiomyopathy, a portuguese multicenter study

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Introduction: Takotsubo cardiomyopathy (TC) is characterized by a transient left ventricular (LV) dysfunction that may lead to cardiogenic shock. Cardiogenic shock is one of the most prevalent and serious acute complications of TC. Little is known about the predictors of cardiogenic shock in TC.

Aim: To identify predictors of cardiogenic shock in patients with TC.

Methods: A Portuguese multicenter study involving 11 hospital centers and including all patients diagnosed with TC in the last 10 years. We evaluated demographic, clinical, electrocardiographic and echocardiographic data. We determined the factors that were associated with the occurrence of cardiogenic shock and then conducted multivariate analysis to establish the independent predictors of cardiogenic shock in patients with TC.

Results: We included 142 patients with TC. During the hospital stay (7.2 ± 6.9 days), cardiogenic shock occurred in 9.9% of patients. Other complications: heart failure (25.4%), atrial fibrillation (8.5%), complete AV block (2.8%), acute pulmonary edema (3.5%), Stroke / AIT (2.1%), ventricular tachycardia (VT) (2.1%), LV thrombus (1.4%) and death (1.4%).

In patients with TC, the factors associated with the occurrence of cardiogenic shock were the history of heart failure (14.3% vs 0%, p < 0.001), chronic renal failure (21.4% vs 4.7%, p = 0.015), the clinical presentation with dyspnea (42.9% vs 16.4%, p = 0.017), the in-hospital occurrence of VT (14.3% vs 0.8%, p = 0.001) or complete AV block (14.3% vs 1.6%, p = 0.006).

In the multivariate analysis, chronic renal failure was identified as an independent predictor of the occurrence of cardiogenic shock during hospitalization of patients with TC (p = 0.007).

Conclusion: In this Portuguese multicenter study, the occurrence of cardiogenic shock in patients with TC was associated with a history of heart failure and chronic renal failure, as well as with dysrhythmic complications such as VT or complete AV

block. Chronic renal failure was the only independent predictor of cardiogenic shock in patients with TC.

P872

Heart failure during hospitalization is associated with takotsubo cardiomyopathy recurrence at follow-up. a portuguese multicenter study

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Purpose: Takotsubo cardiomyopathy (TC) is characterized by a transient left ventricular (LV) dysfunction. Recurrence of TC has been described in several studies, but the risk factors associated with the recurrence of TC are still unknown.

To identify the risk factors for recurrence of TC and specifically to determine if the occurrence of in-hospital heart failure (HF) is associated with recurrence of TC.

Methods: A Portuguese multicenter study involving 11 hospital centers and including all patients diagnosed with TC in the last 10 years. We evaluated demographic, clinical, electrocardiographic and echocardiographic data. We determined the risk factors for recurrence of TC by univariate analysis.

Results: We included 142 patients with TC with a mean follow up of 39 ± 31 months. Recurrence of TC was diagnosed in 4.3% of cases.

The following factors were associated with recurrence of TC: a history of angina (40% vs 10.8%, p = 0.050), the presence of ST-segment depression in the initial ECG (40% vs 6.3%, p = 0.006) and the occurrence of HF during hospitalization (60% vs 21.6%, p = 0.047).

Conclusion: A history of angina, ST-segment depression in the initial ECG and occurrence of HF during hospitalization were associated with recurrence of TC.

P873

The difficult diagnosis of cardiac AL amyloidosis: is the endomyocardial biopsy necessary?

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Purpose: AL cardiac amyloidosis (ALCAm) carries a poor prognosis so early diagnosis is essential for better therapeutic approach. Diagnosis of ALCAm requires either demonstration of AL amyloid deposit in myocardial tissue or a positive biopsy (B) in other tissue plus cardiac ultrasound involvement criteria. B of non-clinically affected organs such as abdominal fat aspiration, salivary gland or rectal mucosa, is usually performed, but its sensitivity (S) is low and could result in delay of diagnosis and treatment of ALCAm. The aim of our study is to analyse the S of B obtained from different tissues in the diagnostic workup.

Methods: This a retrospective analysis of a series of 34 consecutive ALCAm patients treated in our hospital from July 2005 to October 2014. We analysed the diagnostic yield of B taken from different tissues for the identification of amyloid deposits (table). There were no complications associated with any B.

Results: Sensitivity of non-clinically affected organs B was 22% versus 98-100% of affected organs. The need for more than 2 B delayed the diagnosis after the onset of symptoms (5 months vs 10 for the group with >2 B, p = 0,04)

Conclusions: Our experience shows the poor yield of B from nonaffected organs thus delaying the final diagnosis. Endomyocardial B (or from another clinically affected organ) performed and analysed in experienced centres is recommended for the certain diagnosis of ALCAm.

Diagnostic yield of biopsies

BIOPSIES	TOTAL	NEGATIVES	POSITIVES	SENSITIVITY	CI 95%
Subcutaneous fat	22	16	6	27%	10,7 - 50,2
Salivary gland	10	7	3	30%	6,7 - 65,3
Submucosae (rectal, lip)	9	9	0	0%	0
Bone marrow	30	12	16	53%	33,8 - 72,9
EMB	21	1	20	95%	76,1 - 99,9
Clinically involved tissues (colon, lung, kidney, liver, tongue, lymph node)	12	0	12	100%	100

EMB: endomyocardial biopsy

P874

Cardiac involvement in alcoholic liver cirrhosis is independent of duration and quantity of alcohol abuse

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Purpose Non-cardiac aetiology is relevant cause of heart failure (HF). Alcohol induced cardiomyopathy remains insufficiently researched and conflicting reports ranging from left ventricle (LV) dilatation to LV hypertrophy with impaired diastolic function are available. We aimed to investigate cardiac function in patients with liver cirrhosis due to significant alcohol abuse and HF like symptoms.

Methods In this prospective study, 101 patients (57 ± 11y, 70% men) with alcohol induced liver cirrhosis underwent main diagnosis best practice assessment and cardiovascular assessment including complex echocardiography. Based on echocardiography 4 groups were defined: 1) LV dilatation/reduced ejection fraction; 2) LV hypertrophy with diastolic dysfunction; 3) portopulmonary hypertension; 4) normal echocardiography or hyperdynamic pattern.

Results HF symptoms were assessed as the NYHA class I to IV in 44, 37, 19, and 1 patient, respectively. Echocardiographic criteria for HF were met in 41 (41%) of patients. Uneven distribution and significant differences among 4 phenotypes were apparent - Table 1.

Duration of alcohol abuse (p=0.6) and alcohol units consumed per day (p=0.4) had no influence on echocardiography findings. Liver cirrhosis severity according to classification was not associated with cardiac involvement (p=0.3 for all).

Conclusion Cardiac involvement is common in subjects with alcohol induced liver cirrhosis. Different echocardiographic phenotypes, unrelated to alcohol burden and severity of liver disease were detected.

P875

Perforin is an independent risk factor for survival in patients with suspected inflammatory cardiomyopathy

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Objective: To analyse the prediction of intramyocardial perforin on long-term mortality of patients with suspected inflammatory cardiomyopathy (CMi).

Background: Intramyocardial inflammation is considered to be an independent risk factor for cardiovascular death. The impact of perforin on survival of CMi patients remains elusive. In the present study we investigated the influence of perforin-positive cells detected in EMB on mortality or need for transplantation in CMi patients.

Methods and Results: Between 2003 and 2013, 2389 consecutive patients with clinically suspected CMi were enrolled, who underwent EMB. EMBs were performed upon first hospital admission for assessment of cardiac inflammation after exclusion of coronary artery disease. The observation period was up to 10.0 years (median 5.0 [2 - 31.0] month). Hemodynamic measurements were quantified by two-dimensional echocardiography. Information on vital status of patients was obtained from official resident data files.

Upon the observation period 128 patients died or need heart transplantation. Perforin, quantified in EMBs by immunohistochemistry, on the optimal cut off point of 2.95 positive cells/mm², was associated with increased mortality or need for transplantation. Multivariable Cox regression analysis showed that perforin-positive cells predict mortality independently of other parameters (CD3, Mac-1, HLA-1, baseline LVEF, baseline LVEDD, and age (hazard ratio 1.14; P = 0.03)). Importantly, the other examined immunohistochemical parameters (CD3, Mac-1, HLA-1) made minor or insignificant contributions to survival or need for transplantation in these 2389 patients. Viral genome detection (Humanes Herpesvirus 6) alone had no predictive meaning for the end points.

Conclusion: Perforin-positive cells detected in EMB predict long-term mortality in patients with suspected inflammatory cardiomyopathy independently of LV function or other inflammatory factors.

P876

Chest pain with normal coronary angiography evolving to ventricular dysfunction: a challenging diagnosis

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Introduction: Chest pain is a common complaint with extensive differential diagnosis, ranging from anxiety to life-threatening cardiovascular disease. Workup for chest pain is usually straightforward but sometimes it can be more demanding.

Case report: A 55-year-old woman presented with rest constrictive chest pain. She had a 1-week history of effort chest pain. Her medical history was relevant for multiple cardiovascular risk factors and carpal tunnel syndrome. Electrocardiogram (ECG)

Table 60178: Echocardiographic phenotypes

	Age	% men	Child-Pugh	LVEF % ± SD	SWTd mm ± SD	Diastolic Dysfunction N /grade	AF N	NTpro BNP ng/L	PASP mmHg	AVDP (mm)	
Phenotype 1	22 patients	55.7	86.4	A = 6 B = 10 C = 6	37.5 ± 13	12.3 ± 1.8	3 grade I 4 grade II 1 grade III	7	4038	<35	10.9
Phenotype 2	60 patients	60	71.6	A = 11 B = 26 C = 23	56.8 ± 8	14.5 ± 1.2	35 grade I 20 grade II 3 grade III	3	876	<35	12.4
Phenotype 3	3 patients	64.6	66.6	B = 1 C = 2	43.7 ± 21	12.4 ± 0.5	2 grade I	1	4538	51	9.4
Phenotype 4	16 patients	51.7	50	A = 4 B = 7 C = 5	56.8 ± 4.8	12 ± 0.5	0	0	345	<30	14.8

Child-Pugh class A: 5-6 points, class B: 7-9 points, class C 10-15 points; LVEF- left ventricular ejection fraction; SD - standard deviation; SWTd-septal wall thickness diameter; AF - atrial fibrillation; N - number; PASP- pulmonary artery systolic pressure, AVDP- atrioventricular plane displacement

showed sinus rhythm, poor R-wave progression and T-inversion in the inferior leads. Troponin I and BNP were mildly elevated. Echocardiogram (ECHO) revealed normal left ventricular (LV) function with segmental contractility changes. She was admitted with the diagnosis of non-ST-elevation myocardial infarction. Coronary catheterization did not show atherosclerotic disease. During the next 6 months, the patient had recurrent episodes of chest pain and progressive exertion dyspnea, orthopnea and lower limb edema. She also referred anorexia, weight loss, and intermittent diarrhea. The ECG exhibited lower voltage in the limb leads and ECHO revealed LV thickening with infiltrative speckles, biatrial enlargement and LV systolic dysfunction. Cardiac magnetic resonance imaging confirmed infiltrative cardiomyopathy. Myocardial biopsy stained positive for amyloidosis with the immunohistochemical study inconclusive. Serum and urine protein immunofixation were unremarkable. Serum free light-chain assay demonstrated an abnormal kappa/lambda ratio with high levels of lambda. Bone marrow biopsy exposed normal cellularity with 1.8% of plasma cells, most of them were monoclonal lambda. Diagnosis of AL amyloidosis with cardiac involvement was assumed. There was no evidence of renal disease. The patient progressed with low arterial pressure and progressive signs of hypervolemia requiring higher doses of diuretics. She initiated therapy with dexamethasone and melphalan. There was a mild clinical improvement in the beginning of treatment, with partial hematologic response. However, in the following months, the patient's condition declined quickly with frequent hospital admissions and increasing difficulty of diuretic titration. She died 6 months after the diagnosis.

Conclusion: Cardiac amyloidosis is an uncommon cause of heart failure, often with a poor prognosis, particularly in the AL amyloidosis. Atypical and indolent presentation can delay the diagnosis, as in this case. In the ending stage, with limited therapeutic options, the management of these patients is problematic.

CO-MORBIDITIES

P877

Proposed diagnostic algorithm for patients with heart failure and sleep disordered breathing

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Sleep Disordered Breathing (SDB) is a highly prevalent comorbidity in heart failure (HF) patients, that weighs on HF high morbimortality. Both HF and SDB overlap of symptoms and difficulty in scheduling a laboratory for the diagnostic gold standard, the polysomnography (PSG), are responsible for the underdiagnosis of SDB in HF patients. The use of a validated type 3 home sleep testing diagnostic device, allows an early intervention and initiation of treatment, aiming towards better outcomes.

Objective: To compare the diagnostic accuracy of the portable diagnostic device as a screening test for SDB in stabilized inpatients "versus" outpatients with HF, previously validated against PSG, and to propose a diagnostic algorithm. Hospitalization period is a crucial moment for treatment optimization in HF.

Methods: Observational, prospective study of consecutive patients discharged from an HF unit of a central university hospital during one year. The diagnostic test was performed just before discharge, on stable optimized treatment and repeated while outpatient. Outpatient diagnostic test has previously shown a good correlation with PSG. Specificity (Sp), Sensibility (S), positive predictive value (PPV) and negative predictive value (NPV) for both central apneas (CA) and obstructive apneas (OA) diagnosis were obtained to validate inpatient diagnostic test in order to take advantage of the hospitalization period, a precious moment for treatment optimization.

Results: 38 patients were included, 23 women, age 71.2 ± 10.2 years, avg BMI 27.6 ± 5.1 kg/m². For an apnea-hypopnea index (AHI) > 15/h as cut-off, the portable

diagnostic test at discharge had NPV of 0.92 and Sp of 0.88 for CA and NPV of 0.95 for Cheyne Stokes respiration. PPV for OA was 0.89.

Conclusion: Using AHI > 15/h as cut-off, the portable diagnostic test applied to inpatients with stabilized HF and drug treatment revealed to be a trustworthy method for detecting SDB and, therefore, allowing early treatment, dismissing the PSG.

P878

Cardiovascular risk factors in hypertensive patients with heart failure and preserved systolic function combined with rheumatoid arthritis

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Background: In view of the aging of population and steady increase in the prevalence of hypertension and comorbid diseases, the proportion of patients with heart failure with preserved systolic function (PSF) is growing. Cardiovascular risk factors evaluation in hypertensive patients with heart failure and PSF combined with rheumatoid arthritis (RA) can be useful for management this patients.

Objectives: To determine cardiovascular risk factors in hypertensive patients with heart failure and PSF combined with RA.

Methods: The study included 20 hypertensive patients with heart failure and PSF (>50%) with a mean age of 54,63 ± 5,64 years (17 female and 3 male). The 1st group made up 14 pts with comorbid RA, 2nd group - 20 hypertensive patients without RA. The mean duration of HT was 8,8 ± 5,31 years, mean duration of RA - 8,5 ± 6,23 years. Patients with verified diagnosis of ischemic heart disease and diabetes weren't included in the study. The risk of fatal cardiovascular disease was calculated using modified SCORE for RA. The levels of total cholesterol, triglycerides, C-reactive protein, serum creatinine, BMI, DAS-28 were determined. Intima-media thickness of common carotid artery and endothelial-dependent flow mediated vasodilatation of brachial artery were measured by high-resolution ultrasonography, echocardiography was performed to all pts.

Results: Dyslipidemia were established in 7 (50%) pts of 1st group and 5 (83,33%) 2nd group pts (mean levels of total cholesterol 5,4 ± 0,36 mmol/l and 5,9 ± 0,36 ± 0,11 mmol/l respectively p < 0.05). The obesity were determined in 11 (78,57%) hypertensive patients with RA and 3 (50%) hypertensive patients without RA. Sub-clinical manifestations of atherosclerosis and endothelial dysfunction were established in the majority of patients - 13 (65%) and 15 (75%) respectively. 1st group pts showed significantly higher mean BMI 31,12 (±5,85) vs. 28,17 (±3,23), p < 0.05, SCORE risk level 4,32 (±2,92) vs. 1,64 (±0,65), p < 0.05, and higher level of rheumatoid factor (68,52 ± 11,62 vs. 53,4 ± 14,14, p < 0.05), uric acid (282,73 ± 33,23 vs. 251,75 ± 29,23, p < 0.05), C-reactive protein (13,52 ± 4,62 vs. 3,4 ± 1,14, p < 0.05).

Conclusions: Hypertensive patients with heart failure and preserved systolic function combined with rheumatoid arthritis have a high prevalence of cardiovascular factors such as obesity, hyperuricemia, increased C-reactive protein and rheumatoid factor level.

The stratification and prevention of traditional and non traditional risk factors of CVD and control for disease activity may be useful for managing this group of pts.

P879

Features of myocardium remodeling and type of diastolic dysfunction in patients with anemic syndrome on a background of chronic heart failure and chronic kidney disease

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Purpose: to examine the features of the remodeling of the myocardium and estimate the parameters of diastolic dysfunction in patients with anemia of varying severity that developed on the background of chronic heart failure (CHF) and chronic kidney disease (CKD).

Materials and Methods: The study involved 90 patients with CHF II-IV FC (NYHA) of ischemic origin (mean age 71.42 ± 8.66 years), with anemia and CKD stage II-III. Causes of CKD were chronic pyelonephritis and diabetic nephropathy. Availability and CKD stages were determined according to the classification of the National Kidney Foundation U.S. (NKF) K / DOQ. Diagnosis of anemia was determined according to the criteria of the Medical Committee of Standards of Hematology (ICST, 1989). Mild anemia was diagnosed in 50 pts, moderate -25 pts and severe -12 pts. Types of remodeling were defined by Ganau classification. The nature of transmitral flow was determined by following parameters of left ventricular diastolic function: maximum peak velocity of early transmitral blood flow - E, cm / sec and the maximum speed of atrial systole - A, cm / sec; diastolic ratio - E / A.

Results: In patients with mild anemia, CHF and CKD concentric remodeling (CR) was found in 47%, concentric hypertrophy (CG) in 53%. The normal geometry and eccentric hypertrophy (EG) was not found in any patient. In patients with moderate anemia defined by CR in 23% of patients, CG in 68% pts and EG in 9%. Study of the structural myocardial changes in patients with severe anemia showed the presence of EG in the majority of patients-72%, CG in 28%, CR was absent. The study of diastolic dysfunction (DD) showed the presence of transmitral flow changes in 20% of patients, which is specific for pseudonormal type, a violation of relaxation in 80% of patients. In patients with moderate anemia structural and functional features are characterized by heterogeneity, patients with DD type pseudonormalisation (24%) prevailed, violation of relaxation was diagnosed in 15% of pts, 27% had DD of restrictive type. Patients with severe anemia mostly had restrictive type of DD 23%, pseudonormal DD type was observed in 28% pts, while the violation of relaxation was observed in 39% of patients.

Conclusions: The presence of anemia in patients with CHF and CKD have a negative impact on the structural and functional parameters of the myocardium, characterized by enlargement of the heart chambers, an early type of adverse remodeling of myocardium and DD.

P880

Crossing of drugs in patients with chronic heart failure and chronic obstructive pulmonary disease during in-hospital time

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Background: Using of many drugs at the same time is common in patients with chronic heart failure (HF) and chronic obstructive pulmonary disease (COPD). But little is known about the prevalence and significance of drug-drug crossings (DDCs). This study evaluates DDCs in hospitalized patients.

Material and Methods: We retrospectively screened medical charts over a 3-month period for diagnosis of chronic HF and COPD. Potential DDCs were evaluated using SPSS software.

Results: 398 patients were included in the study (median age 72 years, 66% men). The median number of drugs on admission and discharge was 5 (interquartile range (IQR) 3-9) and 6 (IQR 4-11), respectively ($p=0.13$). We recorded 5.6 ± 4.5 potential DDCs per patient on admission and 6.7 ± 5.1 on discharge ($p=0.34$). From admission to discharge, type-C and type-X potential DDCs increased ($p < 0.05$ for both). Type-X interactions were rare ($< 1\%$), with the combination of a β -blocker and a β 2-agonist being the most common (68%). There were significantly more type-C and type-D potential DDCs in patients with chronic HF as compared to patients with COPD ($p < 0.01$). Patients with concomitant chronic HF and COPD had more type-C and type-X potential DDCs when compared to those with individual disease ($p < 0.005$). An aldosterone antagonist and iACE/ARB were prescribed to 17% of chronic HF patients with estimated glomerular filtration rate < 45 ml/(min \times 1.73m²).

Conclusion: The DDCs are common in patients with chronic HF and COPD, but only a few appear to be of clinical significance. The increase in potential DDCs from admission to discharge may reflect better guideline implementation rather than poor clinical practice.

P881

Iron deficiency is highly prevalent in patients with heart failure with preserved ejection fraction

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Background: Iron deficiency is highly prevalent in patients with heart failure with reduced ejection fraction (HFrEF), while its prevalence in patients with preserved ejection fraction (HFpEF) remains elusive. Thus, we sought to assess the prevalence of iron deficiency in outpatients with HFpEF.

Methods: Consecutive patients referred for heart failure outpatient management at two centers were prospectively enrolled. HFpEF was defined with signs and symptoms of heart failure, a LVEF $> 50\%$, echocardiographic signs of diastolic dysfunction, and an NT-proBNP level > 500 pg/ml [??]. [ML2] Iron deficiency was defined as ferritin < 100 mcg/L or ferritin 100-300 mcg/L and transferrin saturation $< 20\%$.

RESULTS: A total of 339 patients (71 ± 12 years, 42% females) were analysed and 207 (61%) were classified as having HFpEF. Iron deficiency was diagnosed in 183 (54%) patients and was evenly distributed among HFpEF and HFrEF patients (56% vs. 52%, respectively; $p=0.613$). Increased levels of NT-proBNP (OR per log unit 1.65; 95%CI 1.02-2.67, $p=0.041$); and female gender (OR 2.16; 95%CI 1.25-3.89, $p=0.006$) - but not NYHA class $> II$, age or glomerular filtration rate - predicted iron deficiency, but failed to retain statistical significance after multivariate adjustment.

Conclusions: Iron deficiency is highly prevalent in both HFrEF and HFpEF. None of routine clinical parameters was independently associated with iron deficiency.

P882

The effect of arterial hypertension on a patient population with heart failure

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Purposes: Arterial hypertension (AHT) is a prevalent pathology and a known risk factor for various cardiovascular diseases, including heart failure. This study evaluates the different clinical outcomes (mortality and hospital readmission) in two groups, those without a known previous diagnosis of AHT (GA) and those with a history of AHT (GB), after an initial hospital admission for heart failure.

Methods: A retrospective study of patients admitted to a central hospital for heart failure between 2009 and 2014. Patients' symptoms, blood work and echocardiogram were evaluated. Statistical analysis was done with SPSS 17.0. Data was considered statistically significant when $p < 0,05$.

Results: Total of 831 patients, 49,3% men, median age of 77 ± 10 years. A total of 68,1% of the population had known AHT. GA was a predominantly male population, with a majority of patients having a history of diabetes mellitus, dyslipidemia and coronary artery disease. No statistical difference was found between age and previous history of chronic kidney disease or heart failure. It was noted that GA patients tended to be medicated with loop-diuretics and spironolactone, while GB patients were treated with angiotensin converting enzyme inhibitors (ACEI) or angiotensin II receptor blockers (ARB-2).

Blood work revealed higher sodium values in GB and greater potassium and cerebral natriuretic peptide in GA. Echocardiogram evaluation revealed that GB patients had a higher left ventricular ejection fraction (LVEF) than GA patients. In-hospital complications, such as worsened renal function, cardiac arrhythmias and nosocomial infections, were similar in both groups. At discharge, patients in GA were more frequently prescribed loop-diuretics and spironolactone, while GB patients were prescribed ACEI and ARB-2 and beta-blockers.

No statistical difference was observed when comparing in-hospital mortality and hospital readmission rates. Post-discharge, GA patients presented a higher mortality rate at 3 months (8,3% vs 3,6%, $p=0,012$), at 6 months (10,8 vs 6,2%, $p=0,041$), at 12 months (14,4% vs 9,1%, $p=0,044$), at 18 months (16,0% vs 10,0%, $p=0,030$) and at 24 months (16,8% vs 10,3%, $p=0,021$). Multivariable analysis concluded that statistical mortality rate difference is independent of LVEF, prescribed medication and blood work values.

Conclusion: In this population of patients with heart failure, the presence of AHT did not have a negative impact on patient outcome: no statistical difference was observed when comparing hospital readmission rate and the post-discharge mortality rate was lower in patients with known AHT.

P883

Anemia and acute heart failure with preserved ejection fraction in adult patients with cardiorenal syndrome: a pilot study

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Purpose: Anemia is a common comorbidity in heart failure (HF) patients and is an independent risk factor for mortality. Among patients with acute HF, anemia is more prevalent in patients with preserved (HF-PEF) than reduced (HF-REF) ejection fraction. However, information on whether this relation is maintained among patients with chronic kidney disease (CKD) and acute HF (cardiorenal syndrome type 4) is

limited. This pilot study was designed as a preliminary analysis to identify the relation between anemia and ejection fraction among patients with CKD admitted with acute HF.

Methods: A prospective, cross-sectional, multicenter analysis of consecutive patients with CKD admitted with acute HF was performed at two private teaching hospitals in Argentina between July 2014 and January 2015. Patients with eGFR <60 mL/min/1.73 m² by CKD-EPI equation for over 3 months were considered to have CKD. Acute HF was defined as signs and symptoms of HF according to Framingham criteria along with increased ventricular filling pressures determined non-invasively by natriuretic peptide serum levels or echocardiographically by E/E'. The primary outcome was the prevalence of anemia, defined according to 2011 WHO criteria, in patients with HF-PEF versus HF-REF. The secondary outcome was hemoglobin levels among both groups. Given the expected proportion of 30% of anemia in the HF-PEF group, with an expected difference across groups of 10%, our study had an 11% power. Significance was set at 5%.

Results: 55 patients were included in the analysis, of which 41.8% had HF-PEF. There were statistically significant differences regarding age (86.2 versus 79.5 years; $p=0.00$) and gender (69.6% versus 25.0% females; $p=0.00$) among groups, with a higher prevalence of elder females in the HF-PEF group. There were no differences regarding chronic (41.4 versus 44.0 mL/min/1.73 m²; $p=0.40$) or admission (38.3 versus 40.0 mL/min/1.73 m²; $p=0.83$) eGFR. The primary outcome of prevalence of anemia was higher in the HF-PEF group (69.6% versus 56.3%), with a crude OR based on univariate logistic regression of 1.52 (95%CI 0.48-4.81; $p=0.47$). The secondary outcome of hemoglobin levels was lower in the HF-PEF group (11.5 versus 12.2 g/dL; $p=0.11$), though non-statistically significant.

Conclusions: These results suggest that, among patients with CKD admitted for acute HF (cardiorenal syndrome type 4), anemia is more prevalent in patients with HF-PEF than in HF-REF. These results need to be confirmed with a larger sample size and with a multivariate logistic regression model.

P884

Prognostic value of anemia in patients hospitalized for acute heart failure

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Purpose: The purpose of our study is to investigate the presence of anemia among patients admitted for acute heart failure and to evaluate its short and medium term prognostic value.

Methods: This is a retrospective study of 234 patients admitted in the cardiology department of our hospital between January 2010 and March 2011. Anemia was defined according to the criteria of the World Health Organization (WHO): Haemoglobin <13 g / dl in men and <12 g / dl in women.

Results: The mean hemoglobin (Hb) was 12.1 ± 2.26 g / dl. The prevalence of anemia in our population is 55.6% (N = 130 cases). A significantly higher frequency of anemia is found among subjects older than 75 years (71.18% vs 50.28%, $P=0.005$), patients with impaired renal function (72.46% vs 48.48%, $p=0.001$) and among those who had shown signs of right heart failure (72.18% vs. 48.48%, $p=0.001$) whereas no statistically significant difference was found among hypertensive diabetics or those with impaired LVEF.

17 of our patients died during hospitalization. 10 Among these patients had anemia. The relative increase in hospital mortality in anemic patients was not significant. Nevertheless, the rate of rehospitalization during follow-up of 6 months and the rate of mortality at 6 months were significantly higher in patients who had anemia; Respectively 14.28% vs 3.68%, $p=0.001$ and 7.83% vs 3.68% $p=0.019$.

Conclusion: Anemia is frequent in patients admitted for acute heart failure and seems to be related to an increase in readmission and mortality at 6 months in our study.

P885

Frailty in a colombian heart failure population

the study has the financial support of our hospital C I Clara Ines Saldarriaga¹; AM Lopez²; AC Alvarado²; J Garces²; J Mejia²

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Frailty is a biological syndrome characterized by a decrease in functionality. The prognostic role of frailty in heart failure has not been comprehensively studied in Latin American population. The evaluation of frailty might be important in HF patients because it can predispose to more adverse events.

Objective: To describe the prevalence of frailty and pre-frailty state using the FRAIL SCORE in a Colombian population of heart failure patients.

Results: The study included 233 elderly patients who were followed in a multidisciplinary heart failure program with a mean age of 76.4 ± 6.97 years, 33.9% were male, the mean ejection fraction was $30.83 \pm 12.97\%$. A high rate of comorbidities was found with an average of 4.4 ± 1.75 per patient, the most common were

hypertension (42,5%) Atrial fibrillation (27%) and chronic kidney disease (19,7%). 48,7% of the population had frailty criteria and 34,6% had pre-frailty state.

Conclusions: There is a high prevalence of frailty in our population of heart failure patients that is explained by the increase of the life expectancy in Colombia and Latin America. The use of frailty scores must be implemented in the multidisciplinary heart failure programs as a screening tool to detect patients at risk of emergency department visits and hospitalizations.

P886

Diabetes mellitus in cardiology hospitalization for heart failure: prevalence, diagnostic tools, active search and involvement by the cardiologist

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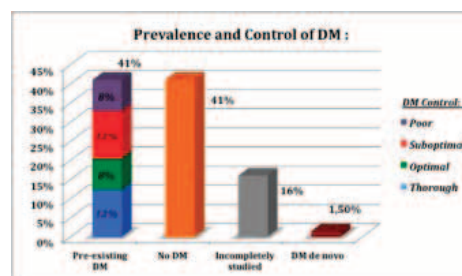
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Purpose: Diabetes mellitus(DM) is a common disease, growing with important cardiovascular implications. DM prevalence in hospitalization for heart failure(HF), use and interpretation of diagnostic tools and performance by the cardiologist is analyzed.

Methods: All patients admitted in cardiology 3° center between 1/1-3/31/2013 were reviewed. Selecting those with discharge diagnosis of HF. Variables related to CV risk, diagnosis and management of DM were collected. Diagnose DM de novo itself glycosylated hemoglobin(HbA1c)>6.5% and/or basal glucose(Glcb)>126mg/dl; and patient studied if both tests are requested.

Results: Population: 63 patients among 427 reviewed, mean age 72 ± 12 y, 62% male, 83% hypertension, 49% dyslipidemia, 36% smoking, 27% ischemic heart disease, 25% stroke and renal failure 58%. Represented 15% of discharges and died 6%. Prevalence of pre-existing DM was 41% (1/3 Insulin), DM de novo 1.6%, 41% no DM and 16% incompletely studied. PreDM(HbA 5.7-6.4% or Glcb 110-125) was 64% of no DM. HbA 78% and 92% Glcb requested without difference between groups. Application HbA1c no increase significantly the time of stay. DM group 50% had suboptimal control(HbA>7%), 40% of these poor control(HbA>8%). 50% with optimal control, 60% had thorough control(HbA<6.5%). Endocrinology consultation was requested in 11%, to adjust insulin, significantly increasing the time of stay adjusted for complexity(W Wilcoxon $p=0.01$). DM controlled by cardiologist: 78% not make any changes, 13% urge diet, 8% adjusted ADO. Modifications of insulin were performed by endocrine.

Conclusion: DM is a very prevalent disease among patients admitted for heart failure. The request Glcb and HbA1c is not low, but along with the optimization of glycemic control and diabetes treatment involve areas of needed improvement to the cardiologist.



Prevalence and control of DM

P887

The role of influenza virus infection in acute decompensated heart failure

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Background: Respiratory tract infections are associated with acute exacerbations of heart failure (HF). However, the role of the influenza virus (Inf), a major agent of such infections, in this population remains unclear.

Methods: Prospective case-control study. The sample was obtained during two influenza seasons, and included all patients hospitalized for management of an acute decompensated HF, matched by sex and age with patients with compensated HF. Influenza virus testing was performed on nasopharyngeal swab samples by qualitative RT-PCR for Influenza (A/H1, A/H12009pdm, A/H3 and B).

Results: 61 patients with decompensated HF (58.0%) were sequentially assessed for Influenza virus infections and matched with 43 compensated HF patients (42.0%). The two groups had overall similar characteristics. The mean age was 57.1 years (± 13.8) and 59.0% were males; 37.2% had AF and mean EF was 35.5%.

Only patients with decompensated HF were positive for Influenza virus (9.8%). These patients were more likely to receive antimicrobials (OR 5.078, $p=0.005$) and mechanical ventilation (OR 7.858, $p=0.003$). There was no difference in mortality among the groups (34.3%; 10.9%, $p=0.173$).

Conclusions: Influenza virus infection was a frequent finding among patients with acute decompensated heart failure. In this group of patients, the presence of Influenza virus infection has resulted in worst outcomes. Immunization and antiviral treatment may positively impact their clinical outcomes.

P888

Prevalence, factors associated with and prognostic effects of preoperative anemia on short and long-term mortality in patients undergoing transcatheter aortic valve implantation

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There is little information on the prevalence and factors associated with preoperative anemia in patients undergoing transcatheter aortic valve implantation (TAVI) and whether it is associated with mortality. We sought to determine the prevalence and factors associated with preoperative anemia in addition to the prognostic effects on mortality undergoing TAVI.

Methods: 441 patients with aortic stenosis who underwent TAVI 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 TAVI procedure, 279 patients (67.7%) were classified as anemic with a mean hemoglobin of 10.8 ± 1.5 g/dl vs. 13.3 ± 1.03 g/dl in the no-anemia group, $p < 0.001$. Anemic patients were more frequently transfused (40.7% vs. 9.8%, $p < 0.001$) after procedure. At discharge, the value mean of hemoglobin levels was 10.3 ± 1.5 g/dl in group anemic vs. 11.5 ± 1.4 g/dl, $p < 0.001$.

The patients with anemia had more comorbidities compared with no-anemia group: Charlson index 3.5 ± 1.9 vs. 2.8 ± 1.1 , $P = 0.001$; Karnosky index 59 ± 18 vs. 65 ± 17 , $P = 0.002$, Logistic EuroSCORE 18.3 ± 12 vs. 15.4 ± 9 , $P = 0.029$ and lower left ventricular ejection fraction 59 ± 15 vs. $62.7 \pm 13\%$, $p = 0.019$. Preoperative anemia was not associated with 30-days mortality, 2.9% vs. 1.5%, $p = 0.400$ and late mortality 15.1% vs. 12.2%, $p = 0.432$. The risk of anemia significantly increased in patients with chronic kidney injury (adjusted Odds ratio [OR]: 2.41; 95% CI: 1.36 to 4.29), $p = 0.002$ and treatment with diuretics 94.3% vs. 84.2% [OR = 3.08 (95% CI 1.551-6.126), $p = 0.001$], but it was not associated with antiplatelet or anticoagulant treatment, ($p > 0.5$ for both).

Conclusions: The presence of anemia and lower haemoglobin levels is frequent co-morbidities in patients with aortic stenosis who underwent TAVI, but it was not associated with any increase in overall or cardiovascular death

P889

Growth differentiation factor 15 as a predictor of cardiorenal syndrome development

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Development of cardiorenal syndrome (CRS) significantly worsens the prognosis of patients with acute coronary syndrome (ACS). Stress-induced marker growth differentiation factor 15 (GDF 15), a member of the transforming growth factor- β cytokine superfamily is being actively studied.

Purpose: to determine prognostic significance of GDF 15 and other biochemical markers in prognosis of development of CRS in patients with ACS.

Methods: 70 patients with different forms of ACS were included in the study, they were admitted to hospital from 2012 to 2013: 77% men and 23% women, mean age was $61, 8 \pm 1, 3$ years. Among them, 54% patients with Q-wave myocardial infarction (Q-wave MI), 20% - with non-Q-wave myocardial infarction (non-Q-wave MI), 26% - unstable angina (UA). All patients underwent a baseline investigation which includes: standard electrocardiography, echocardiography, angiography, determination of marker of myocardial necrosis - cardiac troponin T, marker of inflammation - C-reactive protein (C-RP) GRACE score has been used for risk stratification. The glomerular filtration rate (GFR) was estimated by MDRD. In addition, the level of GDF 15 was determined during the first day of hospitalization via ELISA test.

Results: The effect of 60 variables of clinical, instrumental and laboratorial status were assessed on formation of CRS in patients with different level of GFR. We calculated the GFR, the average was $57, 4 \pm 3, 5$ ml/min. In patients with Q-wave MI the average of GFR was $58, 2 \pm 3, 7$ ml/min, with non-Q-wave MI - $49, 7 \pm 3, 5$ ml/min, UA - $60, 0 \pm 3, 2$ ml/min. There was significant difference between level of GFR in

patients with non-Q-wave MI and UA ($p \geq 0.02$). For identification of the main risk factors for CRS, we have used logistic regression (LR): CRP (area under curve (AUC) 0.817; $p < 0.0057$; 95% confidence interval (CI): 0.592 - 1), GDF 15 (AUC 0.754; $p < 0.017$; 95% CI: 0.546-0.962) were main risk factors for predicting development of CRS. We have developed a prognostic model for predicting CRS formation (AUC 0.839; $p < 0.0007$). This model with 88% of sensitivity and 76% of specificity can predict development of CRS in patients with different level of GFR after ACS.

Conclusions: The prognostic multifactor model was the best for predicting the risk formation of CRS and can be used in clinical practice to improve risk stratification in patients with ACS to prevent formation of CRS.

P890

Risk factors of acute kidney injury in patients with non-ST-elevation acute coronary syndrome and non-invasive strategy

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Objective: Acute kidney injury (AKI) is a common and serious problem associated with poor prognosis. The aim of the study was to assess the prevalence and predictors of AKI in patients with non-ST elevation acute coronary syndrome (NSTEMI-ACS) with non-invasive strategy.

Methods: 288 patients (36% male, 72 ± 12 years (M \pm SD), arterial hypertension 92%, previous myocardial infarction (MI) 42%, diabetes mellitus (DM) 23%, heart failure 36%, atrial fibrillation 23%, chronic kidney disease (CKD) 16%, baseline serum creatinine (SCr) 108 ± 55 mmol/l, GFRCKD-EPI 61 ± 23 ml/min/1.73 m²) were examined. Based on ESC Guidelines NSTEMI-ACS was qualified as NSTEMI or unstable angina (UA) in 186(64.5%)/102(35.5%) patients. AKI was diagnosed according to KDIGO 2012 Guidelines. Mann-Whitney test and multivariate logistic regression analysis were performed. $P < 0.05$ was considered statistically significant.

Results: Incidence of AKI in NSTEMI-ACS was 36%: stage 1/2/3 - in 73/14/13% of cases. Patients with versus without AKI were older (75 ± 10 vs 70 ± 12 years, $p < 0.001$), had higher SCr (129 ± 73 vs 95 ± 29 mmol/l, $p < 0.001$), urea (11.1 ± 7.1 vs 7.8 ± 3.8 mmol/l, $p < 0.001$), plasma glucose at admission (9.0 ± 4.1 vs 7.8 ± 3.7 mmol/l, $p < 0.001$), higher rate of DM (31 vs 19%, $p < 0.05$), CKD (20 vs 11%, $p < 0.05$) anemia (35 vs 19%, $p < 0.01$), low left ventricular ejection fraction (EF) (44 ± 9 vs $48 \pm 9\%$, $p < 0.01$), higher rate of acute heart failure (47 vs 24%, $p < 0.01$), MI (83 vs 55%, $p < 0.001$), recurrent MI (11 vs 2%, $p < 0.001$), in-hospital mortality (17 vs 5%, $p < 0.01$). Independent predictors of AKI were known CKD (odds ratio (OR) 3.9; 95% confidential interval (CI) 1.09-14.02, $p < 0.05$), GFRCKD-EPI < 59 ml/min/1.73 m² (OR 3.9; CI 1.53-6.31, $p < 0.001$), urea > 7.5 mmol/l (OR 3.8; CI 1.85-7.85, $p < 0.001$), MI (OR 3.6; CI 1.68-7.68, $p < 0.001$), EF $< 35\%$ (OR 2.6; CI 1.19-5.67, $p < 0.01$), plasma glucose > 7 mmol/l at admission (OR 2.6; CI 1.28-5.35, $p < 0.01$), DM (OR 2.4; CI 1.02-5.73, $p < 0.01$).

Conclusions: 36% of patients admitted to the hospital with NSTEMI-ACS developed AKI. AKI stage 1 was prevalent. Known CKD, GFRCKD-EPI < 59 ml/min/1.73 m², urea > 7.5 mmol/l, MI, EF $< 35\%$, plasma glucose > 7 mmol/l at admission, DM independently predicted AKI.

P891

The kidney blood flow and functional state in the patients with chronic heart failure with kidney dysfunction

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Purpose of investigation was to study kidney functional state and kidney blood flow in the patients with chronic heart failure (CHF) of functional class II-III.

Material and methods: This investigation included 28 males with ischemic heart disease (IHD) associated with CHF II-III functional class. Control group consisted of 10 healthy individuals.

The kidney functional state was evaluated by the level of blood serum creatinine (Cr), glomerular filtration velocity (GfV) and fermenturia. The GfV was calculated by formulae MDRD in ml/min/1,73m² Evaluation of the renal blood flow was performed with use of color Doppler mapping with measurement of peak systolic velocity (Vs), maximal end diastolic velocity (Vd) and mean velocity of the blood flow (V mean), resistive index (RI), pulse index (PI), were studied at the level of right (RRA) and left renal artery (LRA) as well as of the interorgan (segmentary, lobular) arteries.

Results: The results of investigation showed that in patients with FC II-III CHF parameters of creatinine were $95, 62 \pm 10, 26$ and $103, 9 \pm 9, 4$ mcmol/l, GfS by formulae MDRD was $68, 4 \pm 11, 3$ and $58, 1 \pm 9, 3$ ml/min/1,73 m², respectively.

Analysis of the values of renal hemodynamics showed that in all patients with FC II-III CHF at the level of RRA and LRA there was noted increase in RI by 11,9% and 7% ($p < 0,001$ and $p < 0,005$) as well as PI - by 20% and 13% ($p < 0,001$ and $p < 0,005$), respectively, in comparison with control. The Vd at the level of RRA and LRA was lower by 91,3% and 43,2% ($p < 0,001$ and $p < 0,001$), respectively, in comparison with control. The Vs was lower by 45,6% and 40,5% ($p < 0,001$) at the level of RRA and LRA, respectively, in contrast to control parameters. As far as reduction of the level

of arteries there was noted decrease in velocity parameters at the level of right and left segmentary arteries in the systole by 38,4% and 30,7% ($p < 0,001$ and $p < 0,001$) in diastole by 77,9% and 66,8% ($p < 0,001$ and $p < 0,001$), respectively, in comparison with control. At the level of segmentary and lobular renal arteries there was noted reliable increase in RI and PI, respectively, in comparison with control.

Conclusions: In the patients with CHF II-III FC there were found changes in the renal hemodynamics with reduction of linear and volumetric velocities of the blood flow and increase in the indices of the peripheral renal resistance, and they were closely interrelated with disorders of the renal function state.

The reduction of GFS and changes of the renal hemodynamic in the patients with CHF seem to be early predictors of the kidney dysfunction.

P892

Renal function, acute kidney injury and effect on mortality in cardiogenic shock

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Aim: To investigate the incidence and effect on prognosis of acute kidney injury (AKI) in an unselected cohort of patients with cardiogenic shock (CS)

Methods: Creatinine was measured at baseline and serially in 159 patients from the prospective, multicenter CardShock study. AKI was defined as a creatinine increase > 0.3 mg/dL within 48 hours and all-cause mortality at 90 days evaluated.

Results: The mean age was 67 years and 26% were women. Median eGFR was 63ml/min (IQR 41-87 ml/min), with 47% having eGFR < 60 ml/min and 15% eGFR < 30 ml/min. Impaired renal function (eGFR < 60 ml/min) was associated with higher mortality compared to patients with preserved renal function (57% vs. 28%; $p < 0.001$).

AKI occurred in 30% of the study population, more frequently in patients with impaired renal function (57% vs 37% in patients with eGFR > 60 ml/min; $p = 0.02$). The incidence of AKI was related to more elevated blood lactate levels, but not to age, gender, systolic blood pressure, CS etiology, or left ventricular ejection fraction.

Mortality was significantly higher in AKI than in patients with stable renal function (70% vs 26%; χ^2 27.8, $p < 0.001$). The group with eGFR < 60 ml/min on admission and subsequent AKI had significantly worse prognosis than patients with AKI and normal renal function (78% vs. 50% mortality; $p = 0.02$). Patients not experiencing AKI had the most favorable outcome (18% mortality; $p < 0.001$ compared with both AKI groups); Figure 1. In multivariable regression analysis adjusting for age, gender, medical history, LVEF, eGFR and blood lactate, AKI was independently associated with mortality (OR 12.9, 95%CI 4.1-40.3; $p < 0.001$)

Conclusion: In CS, both the incidence of and mortality associated with AKI is related to baseline kidney function. AKI is a strong predictor of mortality, independently of eGFR.

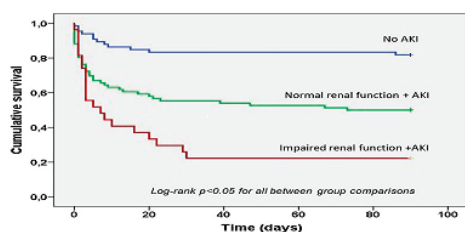


Figure 1: AKI and survival

P893

Epidemiological, clinical, paraclinical and therapeutic features of patients with cardiorenal syndrome type 2

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Introduction: Renal failure is common in patients with chronic heart failure, with a prevalence ranging from 20% to 57%, and a poor prognosis and a high risk of readmission.

The purpose of our study is to show the epidemiological, clinical, paraclinical and therapeutic features of patients who had developed a chronic renal failure during chronic heart failure.

Materials and Methods: We conducted a prospective study on 563 patients with chronic heart failure during a period of 2 years between July 30, 2012 and July 30, 2014.

Patients were divided into two groups, with cardiorenal syndrome and without cardiorenal syndrome.

Results: 262 patients (46.5%) had developed a renal failure. their mean age was 67 years (vs. 61). Higher frequency of male (24.7%) was observed. Concerning their risk factors, 13.7% were smokers, 25.7% hypertensive, 19.5% diabetic and 8.5% were dyslipidemic.

Clinically, New York Heart Association class III and IV was reported in 11.9%. The mean heart rate was higher in the group with cardiorenal syndrome (69.42 vs. 68.58). 8% of patients were on atrial fibrillation. The Ischemic cardiomyopathy was the predominant etiology (31.8%).

The mean levels of serum sodium, serum calcium, and hemoglobin were significantly lower in the group with cardiorenal syndrome, respectively 139, 91 and 12.3 vs. 140.1, 93.5 and 13.05. And the mean levels of serum potassium, uric acid and CRP were higher respectively 4.8, 71.4 and 24.6 vs. 4.5, 53.3 and 11.5.

The mean EF, left atrial dimension and deceleration time of mitral flow were significantly lower in the group with cardiorenal syndrome, respectively 33.50%, 43.6 and 137.70 vs. 37.57%, 39.96 and 161.59. Systolic RV function was impaired in 8.9% with cardiorenal syndrome, and 26.3% of patients who developed a renal failure had a pulmonary hypertension ($p < 0.0001$).

In the group with cardiorenal syndrome, 0.9% of patients were not under ACE inhibitor or ARB vs. 0.9% ($p = 0.289$), 4.4% were not under β Blocker vs. 2.5% ($p = 0.17$), 24.5% were under Aldactone vs. 24%, 9.8% of patients were under calcium channel blocker to control hypertension vs. 6.9% ($p = 0.007$) and 21.3% required the use of loop diuretics vs. 9.4% ($p < 0.0001$).

Rehospitalization for heart failure was higher in the group with cardiorenal syndrome, observed in 14% of patients vs. 2.8% ($p < 0.0001$).

Conclusion: The interaction between the heart and kidneys among patients with heart failure is a complex relationship. A complete understanding of the bidirectional interactions between the two organs remains elusive.

P894

Renal function markers in acute heart failure

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Introduction: Renal function plays a key role in the clinical outcome from acute heart failure (AHF). However, the markers we use are imperfect in acute dysfunction situations.

Objectives: Evaluate which of the renal function markers best predicts outcomes in AHF situations.

Methods: Retrospective study of all consecutive admissions in a single cardiology unit in a 5 years period. We only evaluated the first episode of each patient during this period. Urea, creatinine and filtration rates estimated by MDRD formula (eGFR), on admission were evaluated, and compared with hospitalization times and in-hospital mortality.

Results: We evaluated 835 admissions, corresponding to the same number of patients, mean age 77.2 ± 10.1 years, 50.7% female, 19.8% had previous known chronic renal disease. The average hospital stay was 8.5 ± 6.6 days and in-hospital mortality rate was 6.8%. The mean serum creatinine at admission was 1.34 ± 0.72 ; the average urea 68.7 ± 34.7 and 57.9 ± 34.4 eGFR.

Higher urea and creatinine levels were associated with in-hospital death (Test T-Student, $p = 0.000$ and $p = 0.025$, respectively); and the same association was not observed with eGFR ($p = 0.395$).

When evaluating the length of stay, a positive correlation was observed with urea and creatinine (Index Pearson correlation, $R = 0.152$, $p = 0.000$, $R = 0.124$, $p = 0.000$), while there was none with eGFR ($R = -0.048$, $p = 0.173$).

Conclusion: This study confirms the correlation between renal dysfunction and worst outcome in terms of hospital mortality and length of stay for AHF. Urea appears to be superior to creatinine in predicting mortality and longer hospital stay. Renal function estimates from MDRD formula do not appear to be useful in this acute situation.

P895

Early identification of impaired left ventricular function in hemodialysis patients: a 2D speckle tracking echocardiography study

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Background: Our aim was to investigate left ventricular (LV) myocardial function throughout the cardiac cycle with 2D speckle tracking echocardiography (2D-STE) in end-stage renal disease (ESRD) patients undergoing chronic hemodialysis (HD).

Methods: The study population consisted of 30 maintenance HD patients. These patients were examined just before and after HD. LV global longitudinal (GLS), circumferential (GCS) and radial (GRS) peak systolic strain was measured with 2D-STE. BNP levels were measured before and after HD.

Results: Increased LV mass index (LVMI) and a decreased E/A ratio were found in hemodialysis patients. LV global longitudinal and radial peak systolic strain was decreased in the study group population. Strain values improved in longitudinal and radial directions after HD [pre- vs. post-HD; GLS: -16.43 (1.7) vs. -18.49 (1.9)%, $p < 0.001$, GRS: 23.94 (9.2) vs. 30.41 (10.4)%, $p < 0.001$, GCS: -20.23 (3.4) vs. -21.46 (4.9)%, $p = 0.1$]. LVMI was inversely related to pre-HD GLS ($r = -0.418$, $p = 0.02$) and post-HD GLS ($r = -0.406$, $p = 0.03$). Serum BNP levels were also inversely correlated with pre-HD GLS ($r = -0.433$, $p < 0.05$) and post-HD GLS ($r = -0.456$, $p < 0.05$).

Conclusion: 2D-STE may be used to identify early abnormalities in patients with ESRD undergoing hemodialysis who have preserved LV ejection fraction. HD treatment results in immediate improvement in all strain directions. LV hypertrophy may play a role in the deterioration of LV mechanics in patients with ESRD.

P896

Heart failure and acute kidney injury in infective endocarditis

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Infective endocarditis (IE) is often associated with kidney and heart damage. However, acute kidney injury (AKI) in IE have not been largely discussed until now.

Objectives: To study the epidemiology of AKI and its clinical significance in patients with IE.

Methods: The study included 122 patients [76 (52.8%) men] with IE (Duke criteria 2009), mean age 52.3 ± 20.2 years, 44 (36.1%) drug users. Patients with the history of structural kidney disease were excluded. Patients were divided into 2 groups by the presence of acute kidney injury: group 1 (AKI present, n = 61), group 2 (no AKI, n = 61). Medical history, types of IE, clinical, laboratory and echocardiography parameters, and total mortality were evaluated.

Results: Both groups had comparable demographic characteristics. There were no differences in other types of IE and the prevalence concomitant pathology (hypertension, CAD, diabetes) between groups. In both groups left-sided native valve IE was predominant ($p > 0.05$). However, prosthetic valve IE was significantly more frequent in Group 1 [11 (18%) vs. 4 (6.6%), $p < 0.05$]. Mean GFR value on admission in Group 1 was 52.6 ± 30.2 ml/min, in Group 2 79.7 ± 32.6 ml/min ($p < 0.001$). More (35, 57.3%) patients in Group 1, than in Group 2-19 (31.1%) reported class III-IV heart failure symptoms ($p < 0.05$). Mean left ventricular ejection fraction was similar 55.9 ± 8.3 vs. 58.0 ± 7.1 ($p > 0.05$). Nt-proBNP values were higher in AKI patients: 2397 ± 691.1 vs. 492.5 ± 171.8 pg/ml ($p < 0.05$). When adjusted for the presence and severity of heart failure the difference in Nt-proBNP levels remained statistically significant: in mild heart failure patients (class I-II) with AKI 258.2 ± 72.6 vs. 187.6 ± 46.8 pg/ml in non-AKI group, $p < 0.05$; in those with severe heart failure (class III-IV) with AKI 3985.8 ± 882.5 vs. 1166 ± 294.1 pg/ml in non-AKI group, $p < 0.05$. AKI patients had higher C-RP (166.6 ± 101.1 vs. 142.4 ± 318.7 mg/l, $p < 0.05$) and rheumatoid factor (68.2 ± 4.7 vs. 44.9 ± 4.5 U/ml, $p < 0.05$) levels than those without AKI. Proteinuria occurred in 41 (67.2%) in Group 1, in 53 (86.9%) in Group 2 and microhaematuria in 25 (41.0%) vs. 35 (57.4%), respectively, $p > 0.05$. Overall mortality was similar: 12 (19.7%) in Group 1, 19 (31.1%) in Group 2, $p > 0.05$.

Conclusion: Acute kidney injury is highly prevalent in patients with infective endocarditis and is associated with higher disease activity. Patients with AKI had significantly more heart failure symptoms and Nt-proBNP levels than those with normal kidney function, although the overall Nt-proBNP increase in this group cannot be explained by the severity of heart failure alone.

VALVULAR HEART DISEASE (DIAGNOSIS, MANAGEMENT AND INTERVENTIONAL THERAPIES)

P897

Clinical characteristics and outcome in patients with severe aortic stenosis

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Background: Aortic stenosis is the most prevalent form of valvular heart disease in western countries. The purpose of this study was to describe the main clinical characteristics of patients with symptomatic aortic stenosis.

Methods: This was a single-center retrospective study of consecutive patients who were hospitalized with symptomatic severe aortic stenosis, between October 2009

and November 2013. Patient's demographic, clinical and echocardiographic data were collected. Severe aortic stenosis was defined as an valve area $\leq 1 \text{ cm}^2$. Patients with a mean transvalvular gradient $< 40 \text{ mmHg}$ were included in present of systolic left ventricular dysfunction. Patients with other significant valvular disease were excluded. The main outcome measure in this study was all-cause-mortality.

Results: 145 patients with isolated severe aortic stenosis were included, mean age 73.9 ± 8.9 years; 55.2% were female. At admission, all patients presented heart failure symptoms, mean NYHA functional class 2.6 ± 0.7; 31% had associated angina symptoms and 6.9% syncope. Hypertension was present in 58.6% of patients; 44.8% had hypercholesterolemia and 24.8% had diabetes; significant coronary lesions were present in 34%. A-Fib was also frequent, observed in 24.8% of patients. 12 patients had a bicuspid aortic valve. Mean aortic valve area was 0.7 cm², with mean transvalvular gradient 55.1 mmHg; 16 patients (11%) present a low-gradient aortic stenosis (mean transvalvular gradient $< 40 \text{ mmHg}$). The mean left ventricular end-diastolic diameter was 50.8 mm; 29.6% present left ventricular systolic dysfunction; 33.8% had moderate to severe left ventricular hypertrophy. Median of length of stay was 10.2 ± 10.3 days. Surgical aortic valve replacement (AVR) was performed in 95 patients (65.5%); the other 50 patients were treated with medical therapy only. Mean follow-up was 28.2 ± 16.1 months. Overall, all cause mortality rate was 31% of patients died. In the non-AVR group, patients 70.6% died; in the AVR group mortality rate was 9.5%.

Conclusion: Despite demonstrated symptomatic and survival advantages, in the studied population, approximately one-third of patients with severe symptomatic aortic stenosis did not undergo aortic valve replacement, resulting in poor long-term prognosis.

P898

Comparison of the effectiveness of transcatheter aortic valve implantation in patients with stenotic bicuspid versus tricuspid aortic valves

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Patients with bicuspid aortic valves (BAVs) are considered a relative contraindication to transcatheter aortic valve implantation (TAVI). One of the main reasons is the presumed risk for residual aortic regurgitation (AR). However, case reports have suggested that TAVI can be successfully performed with acceptable clinical outcomes in high risk patients with BAV. We sought to evaluate TAVI in older high-risk patients with BAV.

Methods: From April-2008 to December 2014, a total of 441 patients with severe aortic stenosis undergoing TAVI. For the present analysis, patients with valve-in-valve procedures were excluded. The patients with BAV (n = 5, 1.2%) were compared with those with tricuspid aortic valve (n = 422, 98.8% 97%).

Results: Patient characteristics did not markedly differ in both groups, except the patients with BAVs were more younger 68 ± 8 years vs. 79 ± 6 years, $p = 0.001$.

There was a higher time of procedure and deployment of prosthesis in patients with BAVs: 129 ± 35 min vs. 99.7 ± 36, $p = 0.07$ and 10.6 ± 5 vs. 5.5 ± 2 min, $p = 0.001$.

The final position of prosthesis was more lower in patients with BAVs 75% (mean depth in LVOT 9.7 ± 5 mm) vs. 14.9% (7.1 ± 5 mm), $p = 0.002$.

There was a higher rate of relevant aortic regurgitation ($\geq 2+$ Sellers) after TAVI among patients with BAV (60% vs. 25.3%, $p = 0.003$), whereas pacemakers were more often implanted in patients with BAVs (75% vs. 14.9%, $p = 0.002$).

In-hospital mortality was higher in group with BAVs 40% vs. 3.6%, $p = 0.014$ and the late mortality (beyond 30 days) rate were a little better in those BAVs 0% vs. 15.2%, $p = 0.463$.

Conclusions: In selected patients with BAV, TAVI can be performed with a satisfactory clinical result. Although the procedure is more complicated and the risk for relevant aortic regurgitation and not correct position of the prosthesis seems to be greater among patients with BAV, The long-term outcome is favourable compared with patients with TAV.

P899

Gender differences in clinical presentation and outcome of severe aortic stenosis

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Background: Aortic stenosis (AS) is the most prevalent valvular heart disease in developed countries and has been extensively studied in the past years. Only a limited number of studies have been conducted to clarify differences between male and female patients with aortic stenosis (AS). The aim of this study was to evaluate gender differences in clinical characteristics and outcome in patients with symptomatic severe aortic stenosis.

Methods: Analysed clinical, demographic, echocardiographic characteristics and outcome in patients with symptomatic aortic stenosis, hospitalized in a single centre, between October 2009 and November 2013. The main outcome measure in this study was all-cause-mortality. Patients with other associated major valvular conditions were excluded. Comparisons between groups were performed with an unpaired Student t test. Categorical variables were compared with a chi-square test and Fisher's test. Survival analysis was based on the Kaplan-Meier method. A value of $p < 0.05$ was considered statistically significant.

Results: 145 patients with isolated severe aortic stenosis were included, mean age 73.9 ± 8.9 years; 55.2% were female. At presentation, women were older (76.8 years vs 70.3 years; $p = 0.0001$) and presented with smaller valve areas estimated by echocardiography (0.65cm^2 vs 0.77cm^2 ; $p = 0.0001$) and smaller end-diastolic left ventricular diameter (53.4mm vs 48.3mm ; $p = 0.003$). Bicuspid aortic valve were more frequent in male sex ($p = 0.026$); A-fib was more frequent in female sex ($p = 0.016$). Presence of left ventricular systolic dysfunction ($p = 0.18$), mean transvalvular pressure gradient ($p = 0.572$) and presence of significant coronary lesions were similar in females and males. There was no difference in the frequency of angina, syncope or dyspnea between genders. There were no significant differences between groups for presence of arterial hypertension ($p = 0.73$), diabetes ($p = 0.56$) or hypercholesterolemia ($p = 0.6$). Rates of aortic valve replacement were similar between groups. There was no significant difference in the survival of the patients between the two groups ($p = 0.478$) throughout the follow-up period. There was no difference in the frequency of angina, syncope or dyspnea between genders.

Conclusions: In our population of patients with symptomatic isolated severe aortic stenosis, female patients were older, had smaller aortic valvular area and left ventricular diameter. Despite older age and more advanced disease in women, there was no significant difference in overall survival.

P900

Tissue inhibitor of metalloproteinase 2 (TIMP2) is related to hypertension in patients with aortic valve stenosis

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Background: Aortic stenosis (AS) and hypertension (HT) are both associated with chronic pressure overload and left ventricular hypertrophy. Matrix metalloproteinases (MMPs), specific tissue inhibitors of metalloproteinases (TIMPs) and inflammatory cytokines are involved in left ventricular remodeling. Local expression of TIMP-1 and TIMP-2 was found to be related to cardiac interstitial fibrosis and left ventricular overload.

Objectives: The aim of study was to compare the serum level of metalloproteinase inhibitors (TIMP1, TIMP2) and selected mediators of inflammation and tissue remodeling (IL-1b, IL-6, monocyte chemoattractant protein 1 (MCP-1), TNF α , osteoprotegerin (OPG), osteopontin (OPN), NT-proBNP) in hypertensive and non-hypertensive stenotic patients and to evaluate the relationship of examined clinical and biochemical parameters to hypertension.

Patients and Methods: Sixty six patients accepted for surgical aortic valve replacement with moderate ($n = 27$) and severe ($n = 39$) aortic stenosis were included. There were fifty two (78.8%) cases with concomitant arterial hypertension. In all patients we performed transthoracic echo with typical projections, severe AS in 33 (50.0%) patients with mean gradient $\geq 50\text{mmHg}$ with left ventricular ejection fraction LVEF $\geq 50\%$, moderate AS 27 (40.9%) patients with mean gradient $< 50\text{mmHg}$ with LVEF $< 50\%$.

The panel of serum biomarkers: IL-1b, IL-6, TIMP1, 2 TIMP2, MCP-1, TNF α , OPG, OPN, NT-proBNP was measured using multiplex method based on Luminex technology (Flexmap 3D analyser). The data were analyzed with Mann-Whitney test, chi-squared/Fisher's exact test. Variables were also tested in multivariate logistic regression models.

Results: The comparison of hypertensive and non-hypertensive patients disclosed the following significant differences: age (years) 67 (61-73) [median (inter-quartile range)] vs 57 (53-72); body mass index (BMI) 29.1 (26.9-32.1) vs 25.3 (22.8-29.6); IL-6 (pg/ml) 1,291 (0.82-2,872) vs 0.802 (0.563-1.17); TIMP2 (ng/ml) 113.6 (98.95-128.35) vs 95.73 (83.34-105.85) respectively. There were no significant differences in severity (moderate/severe) of aortic stenosis between hypertensive and non-hypertensive patients. In multivariate logistic regression analysis TIMP2 was the only factor significantly contributed to hypertension (OR = 1.05, 95% CI = 1.001-1.09, $P = 0.046$).

Conclusions: In our study the level of TIMP2 is related with arterial hypertension in patients with moderate to severe aortic stenosis influencing on pressure overload of the left ventricle.

P901

Infective endocarditis: predictors of in-hospital severity

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Introduction and Objective: The infective endocarditis (IE) incidence has not changed in the past few decades. Indeed, its morbidity and mortality cannot be underestimated. The aim of this study was to conduct an epidemiological, clinical and echocardiographic analysis on IE patients in order to identify early predictors of adverse outcome.

Methods: This study was based on a retrospective analysis of 65 consecutive patients admitted in a tertiary center for definite or possible diagnosis of IE, conducted between July 2013 and July 2014. Data were collected from the electronic clinical process and registered in a uniform base. The primary endpoints were systemic embolism, a composite outcome of major complications (shock, new heart failure, heart block, systemic embolism and neurologic complications) and death during hospital stay.

Results: Mean age was 64.2 ± 17.1 years, 61.5% males. According to modified Duke criteria, 50 cases were classified as definite IE. Only 6.2% of IE cases were right-sided. Most patients (55.4%) had native valve IE and device-related IE was diagnosed in 10.8% of the cases. The major causative microorganisms were Staphylococaceae (43.1%), followed by Streptococaceae (12.3%) and Enterococaceae (12.3%); no microorganism was identified in 18.5% of the cases. The absence of fever at admission (43.8 vs. 17%, $p = 0.043$) and the presence of large ($> 10\text{mm}$) or multiple vegetations (31.7% vs. 8.3%, $p = 0.031$) were significantly more frequent in the group of patients who developed systemic embolism. The variables significantly associated with the composite outcome were the evidence of predisposing valvular conditions (79.1% vs. 44.4%, $p = 0.008$), the absence of fever at presentation (93.8% vs. 59.6%, $p = 0.011$) and new valvular regurgitation at admission (83.3% vs. 48.3%, $p = 0.003$). In-hospital mortality was significantly higher in the female gender (44.0% vs. 17.5%, $p = 0.020$), the elderly (38.9% vs. 13.8%, $p = 0.025$) and the heart failure group (50.0% vs. 15.6%, $p = 0.018$).

Conclusion: Our study points out as predictors of severity of IE the absence of fever at admission, large or multiple vegetations, predisposing valvular conditions and new valvular regurgitation. Moreover, female sex, advanced age and heart failure were good indicators of mortality. The identification of patients at risk of deleterious outcome may improve therapeutic approach of IE in the future.

P902

Percutaneous closure of periprosthetic paravalvular leaks in patients with acute heart failure: an alternative to surgery?

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Purpose: Paravalvular leaks (PVL) are a common and potentially serious complication after surgical valve replacement. Although most patients remain asymptomatic, some may present with acute heart failure or signs of hemolysis. Percutaneous closure has been utilized as an alternative treatment option in patients with high surgical risk. We aim to assess the feasibility and efficacy of percutaneous PVL closure and report the clinical outcomes.

Methods: Retrospective review of a Centre's experience in percutaneous closure of mitral and aortic PVL, based on clinical and technical data of procedures performed over a 58-month period. Planning, orientation and evaluation of the procedure was achieved by 3D-echocardiography.

Results: A total of 17 percutaneous PVL closures were performed in 15 patients (median age 70.0 years-old, 46.7% males).

Successful PVL closure was achieved in 12 procedures (70.6%): 11 in mitral valves (6 biological and 5 mechanical valves) and one in a biological aortic paravalvular leak.

On immediate post-procedural echocardiographic evaluation, a decrease in leak severity was seen in 47% of the leaks closed.

On clinical evaluation, 45.5% of the patients in which the leak was closed improved their functional class and the prevalence of transfusion-dependent hemolytic anemia decreased from 27.3% to 9.1%.

Major hemorrhage on the site of the vascular access was the main complication (11.8%). There were no embolizations, dissections, infections, conversions to surgery or deaths related to the procedure.

Survival rates after the procedure were 92.3% at 6 and 12 months and 84.6% at a 24-month period of follow-up.

Conclusion: In selected patients, percutaneous PVL closure is feasible and effective in improving symptoms of heart failure and hemolytic anemia. In the future, integrated imaging modalities and the development of specific devices for the closure of PVL will contribute to improve clinical and technical results.

P903

The rheumatic myocarditis in pure mitral stenosis: myth or reality?

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Introduction: Left ventricle function is usually considered as unchanged in pure mitral stenosis (MS), but as the main cause of mitral stenosis is rheumatic fever, we

suggest that the subclinical systolic function may be impaired, even in lack of atrial fibrillation. We conducted so this study to analyze systolic function in patients with isolated mitral stenosis via new echocardiographic technics.

Materials: We included prospectively patients with isolated mitral stenosis and sinus rhythm. We excluded patients with conditions modifying left ventricle function (diabetes, hypertension, kidney failure...). We compared echocardiographic findings (global longitudinal strain, S wave on the lateral wall of LV and Tei index) between our patients and a control group (same age and sex).

Results: 37 patients (P group) were compared to 27 healthy subjects (H group). Left ventricle ejection fraction was similar in both groups (P group = $56.1 \pm 10\%$ vs H group = $60 \pm 9\%$, $p=0.2$). However, the longitudinal global strain (P group = $-16 \pm 4\%$ vs H group = $-20 \pm 2\%$, $p < 0.001$) and the s wave on the left ventricle lateral wall were significantly lower in patients with mitral stenosis (P group = 8 ± 2 cm/s vs H group = $12 \pm 2\%$, $p < 0.001$); there were no correlation between severity of mitral stenosis and subclinical longitudinal function. The Tei Index was similar in both groups (P group = 0.48 ± 0.25 vs H group = 0.40 ± 0.10 , $p=0.18$).

Conclusion: We demonstrated that patients with MS had lower LV functions using 2D strain imaging, and this is independent of the hemodynamic severity of MS. Many hemodynamic and myocardial factors have been put forward regarding the LV dysfunction in MS chronic myocardial inflammation, scarring of subvalvular apparatus and abnormal right-left septal interaction.

P904

Percutaneous annuloplasty successfully treats type IIIb mitral regurgitation

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Background: Several valvular and ventricular alterations are associated with higher risk for failure of surgical annuloplasty. The Cardioband percutaneous annuloplasty system aims to reproduce surgical annuloplasty.

Objectives: To assess the impact of the Cardioband on mitral regurgitation (MR) severity, valvular alterations and left ventricular (LV) remodeling at one year post implantation, and whether the success of the procedure can be predicted based on baseline echo parameters.

Methods: Initial experience with six patients with moderate or severe functional MR were implanted with Cardioband through trans-femoral, trans-septal delivery system in a supra-annular position, and secured to the mitral annulus using anchor elements. MR grade, valvular alterations and LV remodeling were measured at baseline and one year following implantation.

Results: MR grade decreased in all patients from median 3.5 (3-4) to 1 (1-3) at 1 year follow up ($p=0.002$) irrespective of baseline valvular alterations, LV size or sphericity. Annular diameter, and tenting area decreased significantly from 3.7 ± 0.5 cm to 2.5 ± 0.2 cm ($p=0.0004$) and from 1.4 ± 0.3 cm² to 0.9 ± 0.2 cm² at baseline and at one year respectively ($p=0.0004$). There was a trend for decrease in anterior leaflet angle from $26 \pm 7^\circ$ to $20 \pm 5^\circ$ ($p=0.1$), but no change in tenting height ($p=0.8$) or posterior leaflet angle ($p=0.6$). LV end diastolic diameter decreased significantly from 62 ± 6 cm at baseline to 57 ± 7 cm at one year follow up ($p=0.02$), but there was no change in inter-papillary muscle distance ($p=0.5$) or sphericity index ($p=0.8$). Ventricular and valvular changes were linked to improved symptoms as seen by the decrease in NYHA from baseline 3 (2.75- 3) to 2 (1- 3) ($p=0.04$) at one year and longer 6 minute walk test distance from 302 ± 92 meters at baseline to 499 ± 79 meters at one year follow up ($p=0.04$).

Conclusions: Cardioband percutaneous annuloplasty implantation is associated with mid-term improvement in MR grade, LV size, symptoms and effort capacity irrespective of recognized risk criteria for failure of surgical annuloplasty.

P905

Left atrial volume changes and left atrial 2D strain measurements for diagnostic and prognostic evaluation of heart failure patients with MR undergoing percutaneous mitral valve repair using mitralclip

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The aim of this study was to evaluate left atrial function in heart failure patients undergoing percutaneous mitral valve repair using mitralclip using 2D speckle-tracking

echocardiography and also to investigate the prognostic role of LA size and function for this procedure.

Methods: 75 patients with heart failure symptoms (NYHA class >2) and significant mitral regurgitation (MR 2+) undergoing mitralclip procedure were investigated. Conventional 2D echocardiography and two-dimensional speckle-tracking analysis were performed to determine LA volumes (max and min) and LA function (EF, LA systolic strain and diastolic strain rate) at baseline (BL) and at six-months follow-up (FU).

Results: Primarily, mitralclip implantation resulted in significant reduction of MV regurgitation (BL: 2.5 ± 0.4 vs. FU: 1.4 ± 0.7 , $p < 0.001$) and ameliorated NYHA functional class (3.0 ± 0.5 vs. 2.3 ± 0.6). Echocardiography revealed reduced left atrial (LA) minimal (75 ± 31 vs. 70 ± 32 ml) and maximal volumes (106 ± 39 vs. 96 ± 35 ml), LA volume index (57 ± 19 vs. 51 ± 19 ml/m²) accompanied by decreased pulmonary systolic artery pressure (PASP 52 ± 12 vs. 44 ± 14 mmHg) and increased LA systolic strain (10.2 ± 4.1 vs. $12.3 \pm 6.1\%$).

However, patients with preserved left ventricular ejection fraction undergoing mitralclip procedure (LVEF >50%) showed an increase in LA systolic strain (11.3 ± 4.6 vs. $13.9 \pm 5.7\%$, $p < 0.01$), LA early diastolic strain rate and LA late diastolic strain rate. This was also accompanied with significant decrease in PASP (51 ± 11 vs. 41 ± 11 mmHg).

Furthermore, patients without preprocedural atrial fibrillation (AF) ($n=46$), independently from EF, exhibited a significant increase in LA systolic strain after mitralclip deployment (10.3 ± 3.9 vs. $13.1 \pm 6.5\%$) whereas patients with atrial fibrillation preprocedurally showed no significant change in LA strain values. The greatest increase in LA systolic strain was observed in the group with preserved LVEF and without preprocedural AF (11.3 ± 3.9 vs. $15.4 \pm 5.6\%$, $p < 0.001$). On multivariate logistic regression analysis neither LA volumes nor strain parameters provided to be an independent predictor of clinical outcome for patients undergoing mitralclip procedure.

Conclusions: In heart failure patients with MR LA volumes and LA systolic strain are improved after percutaneous mitral valve repair using mitralclip. Moreover, these parameters are strongly associated with MV regurgitation, PASP and NYHA class. This procedure is especially profitable, and hence should be strongly recommended, for heart failure patients with preserved left ventricular ejection fraction and with no permanent atrial fibrillation.

DEVICES / ARTIFICIAL HEART / CRT / ICD

P906

Echocardiographic parameters relations with quality of life during cardiac resynchronization therapy

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Purpose: To estimate the influence of echocardiographic parameters changes (left ventricle ejection fraction (LVEF), LV end-systolic diameter (LVESD), LV end-diastolic diameter (LVEDD) and left atrium diameter (LAD) to health-related quality of life among patients during cardiac resynchronization therapy (CRT).

Methods: 40 patients, mean age 62.0 ± 10.5 , meeting standard CRT indications were included into this study. The study lasted for 12 months. Health-related quality of life was evaluated using the Medical Outcomes Study 36-item Short Form (SF-36) questionnaire at baseline and after 12 months post - CRT. Echocardiography was performed before CRT and after 12 months. Statistical analysis was performed using SPSS version 19.0. A value of $p < 0.05$ was defined as statistically significant.

Results: Compared with baseline statistically significant improvements were observed in all health - related quality of life questionnaire subscales after 12 months: in physical functioning (PF) ($p=0.001$), role limitations due to physical health (RP) ($p=0.0001$), role limitations due to emotional problems (RE) ($p=0.0001$), energy/fatigue (VT) ($p=0.0001$), emotional well being (MH) ($p=0.001$), social functioning (SF) ($p=0.0001$), bodily pain (BP) ($p=0.0001$), general health (GH) ($p=0.0001$), physical component summary (PCS) ($p=0.0001$) and mental component summary (MCS) ($p=0.0001$). LVEF improvement did not statistically significant correlate with quality of life in patients with cardiac resynchronization therapy. The LVESD decrease ≥ 5 mm was associated with significant improvement in SF ($p=0.01$), RE ($p=0.0001$) and MCS ($p=0.002$) during 12 months after CRT. As well as LVEDD diminution ≥ 5 mm improved VT ($p=0.04$) and MCS ($p=0.036$) for this patients. LAD ≥ 45 mm was associated with significant deterioration in RP ($p=0.02$).

Conclusions: 1. CRT improves health-related quality of life, particularly in patients' physical and social functioning.

2. Patient's left ventricle EF improvement had no significant influence on health-related quality of life.

3. LVESD, LVEDD decrease are significantly associated with better improvement in MCS.

4. Smaller LAD is associated with better physical health.

P907

Parameters of intraventricular dyssynchrony predict response to CRT

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Purpose: The aim of this study was to investigate predictors of echocardiographic and functional response to cardiac resynchronization therapy (CRT) with defibrillator in patients with moderate to severe heart failure with reduced ejection fraction (HFrEF).

Methods: We retrospectively assessed baseline characteristics, functional and echocardiographic response, and outcomes of 45 patients (75.6% males, 61.0 ± 11.2 years (M ± SD), NYHA functional class II, III, IV 17.8, 62.2, 20%, respectively; median LV ejection fraction 28% (15-35), median QRS duration 161.1 ms (120-230)), who received CRT at our institution between July 2008 and July 2013. 41 patients (91.1%) had left bundle branch block (LBBB), and 4 (8.9%) had non-LBBB QRS morphology. Ischemic cardiomyopathy was diagnosed in 31 (68.9%) patients. The median of follow-up duration was 29.3 months (10.3-79.3). The clinical and echocardiographic responses to CRT were defined based on clinical improvement (≥1 NYHA class) and LV reverse remodelling (reduction in LV end-systolic volume (LVESV) ≥15%).

Results: Overall response rate was 72.1% (n=31). Significant reduction in LVESV and clinical improvement were revealed in 44.2% (n=276). Four (9.3%) and 8 (18.6%) patients showed either echocardiographic or clinical response to CRT, respectively. Two (4.4%) patients died, and 5 (11.1%) patients were lost to follow-up. Multivariable logistic analysis revealed that only pre-implant QRS duration (beta -0.36, p=0.01, odds ratio [OR] 1.05, 95% confidence interval [CI] 1.006-1.085) and standard deviation of the averaged time-to-peak strain (TPS-SD, ms) of 12 middle and basal LV segments (beta -0.29, p=0.04, OR 1.04, 95% CI 1.01-1.079) could predict echocardiographic response to CRT. A pre-implant QRS duration of 150 ms was the cut-off value that identified responders with 73.9% sensitivity and 75.0% specificity. A pre-implant TPS-SD of 57.0 ms identified responders with 85.7% sensitivity and 75.0% specificity. In this study we couldn't identify independent predictors of clinical response.

Conclusions: Besides the standard selection criteria assessment of intraventricular mechanical dyssynchrony may help identifying CRT responders.

P908

Factors associated with suboptimal response to CRT

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Purpose: In 2013 capacity for implantation of CRT and ICD devices in Russian Federation was 115 and 200 per 1,000,000 heart failure (HF) patients respectively. However, the actual number of patients meet the national criteria for ICD and CRT implantation is unknown. The main objective of this study was to estimate the needs for ICD/CRT therapy in HF population.

Methods: The present study is a cross-sectional epidemiological one center study. In 2013 838 consecutive patients with HF admitted (43.3% males, 70.4 ± 12.0 years (M ± SD), NYHA functional class I, II, III, IV 3.6, 40.3, 43.9, 12.7%, respectively) to city clinical hospital for any cause were enrolled as participants in the study. Epidemiological, clinical and laboratory data were collected for each patient. Nonischemic cardiomyopathy was reported in 289 (34.5%) patients. Mean left ventricular ejection fraction was 29.7 ± 6.3%. Intraventricular conduction disorders (left bundle branch block and right bundle branch block) were revealed in 93 (11.1%) and 34 (4.1%) patients respectively.

Results: According to national and European guidelines 7.0% (n=59) and 10.3% (n=86) of participating patients were eligible for CRT and ICD implantation respectively. Thus current capacity for implantation of CRT and ICD in Russian Federation corresponds to less than 1% coverage of the eligible population (estimated absolute unmet needs for CRT and ICD devices of 0.7 and 1.03 million individuals, respectively). In our study we also identified factors potentially contributing to suboptimal response to CRT, that included chronic kidney disease (46.0%), atrial fibrillation (39.0%), frequent premature ventricular contractions (16.0%), chronic pulmonary diseases (15%), anemia (11.0%).

Conclusions: Despite proved benefits of CRT and ICD in selected patients with HF unmet population needs in Russian Federation remain very high. The magnitude of unmet needs requires broader strategies to plan cardiovascular implantable electronic devices supply programs. Factors that potentially reduce response to CRT are present among about the half of patients with HF.

P909

Low burden of scar and left bundle branch block: low risk for ICD-therapies after cardiac resynchronization

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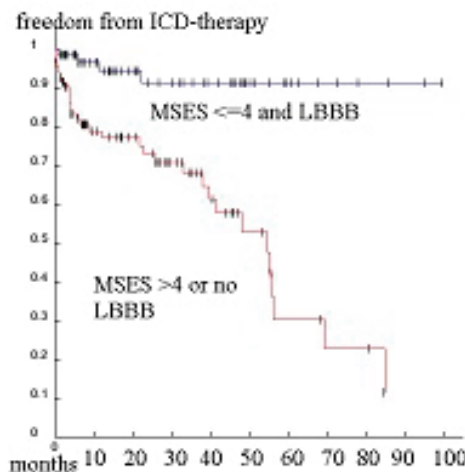
Purpose: to define patients (pts) at low risk for ICD-therapy after CRT. Burden of scar can be measured by the modified Selvester-ECG-score (MSES). It could describe pts' risk for ICD-therapy in SCD-HeFT. Benefit of CRT is more likely in pts with lower MSES (≤4) and "true" (based on a special definition by the MSES) left bundle branch block (LBBB). Combining these findings makes the MSES a promising tool to predict ICD-therapies in CRT-pts.

Methods: retrospective study of 144 pts with primary prophylactic CRT-D. MSES was calculated and occurrence of ICD-therapy and time from implantation to first ICD-therapy or to last follow up was described.

Results: Pts with MSES ≤4 and LBBB had significantly less need for an ICD-therapy. LVEF and other characteristics did not differ significantly. Hazard ratio for ICD-therapy was 7.35 (2.59 - 20.88) in pts without LBBB or a MSES >4.

Conclusion: a low MSES combined with "true" LBBB seems to be a powerful prognostic marker to identify pts at low risk for adequate ICD-therapy after cardiac resynchronization

	MSES ≤ 4 and LBBB	MSES > 4 or no LBBB	p
n	63	81	
follow up (median, days, IQR)	665 (239-1516)	551 (139-1195)	
LVEF (mean±SD)	23.8 (± 5.9)	21.4 (± 6.6)	ns
ICM (%)	48	58	ns
MSES (mean±SD)	2.5 (± 1.3)	5.4 (2.9)	
occurrence of ICD-therapy (%)	6.3	38.3	< 0.05



Kaplan Meier analysis

P910

Cardiac resynchronization therapy in the real world: mid-long term follow up

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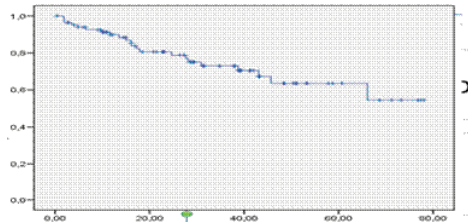
Objectives: Clinical and echocardiography evaluation of patients treated by cardiac resynchronization therapy (CRT) in our area.

Methods: Observational retrospective analysis including 110 patients treated by CRT in our hospital from 2005 to 2012. We performed clinical follow up by New York Heart Association (NYHA) evaluation and measured ejection fraction, ventricular dimensions and coexisting mitral regurgitation.

Results: 110 patients (78% male, 64.23 ± 9.4 medium age) were included. 52.4% diabetes mellitus. 80% of the devices were implantable cardioverter defibrillator (ICD). Previous ejection fraction was 24.6 ± 6.3 as well as functional class were III-IV. 91% of the patients were with optimized medical treatment. Mitral regurgitation was severe in 8.3% and atrial fibrillation was presented in 21.4%. Coronary sinus lead (CSL) implant was successful in 85% of the patients. 5.4% CSL were epicardial implant through left anterior thoracotomy. Median follow-up was 60 ± 30 months. Mortality observed was 25% of the patients. There was a clinical improvement in

96% of the remaining patients with a functional class I-II in the follow up. Diastolic ventricular dimension decreased from 66,58 (54 - 85) to 61,21 (35 - 78), moreover, systolic diameters recovered from 55.85 mm (43-74) to 48.51 (26-60). Ejection fraction in the follow up improved to achieve 37,48%(15 - 65). The other cardiac parameters measured were better in 81% of the patients.

Conclusions: CRT is an effective therapy for those patients refractory to optimized medical treatment of severe heart failure. A properly patients selection is critical in order to achieve the effectiveness of this therapy.



Kaplan Meier Mid-Long Term Survival

P911

Hemodynamic pulmonary parameters as predictors of positive response to cardiac resynchronization therapy

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Cardiac resynchronization therapy (CRT) is a well recognized form of treatment in a selected group of patients suffering from heart failure. Despite well defined indications for this form of therapy positive response to treatment might be achieved only in approximately 70% of patients. Recent data indicate the beneficial effect on morbidity, mortality and LV function maybe greater in females, patients with non-ischaemic cardiomyopathy and patients with QRS >150ms.

The aim of study was to determine whether invasively measured hemodynamic parameters of pulmonary circulation are prognostics factors of positive response of CRT in non-ischaemic dilated cardiomyopathy patients with prolonged above 140ms QRS complex and LBBB.

Study group and Methods: 39 patients (8 female) aged 50,2 ± 8,20 years old with DCM and typical indications for CRT(NYHA class≥II, LBBB, QRS: 165.63 ± 20.16ms, EF 22.2 ± 5.6%).

Before CRT implementation the invasive measurement of pulmonary hemodynamic parameters using Swan-Ganz catheter were performed. Mean pulmonary artery pressure (mPAP), pulmonary wedge pressure (PWP), right atrial pressure (RAP), transpulmonary gradient (TPG), pulmonary vascular resistance (PVR), cardiac output (CO) and stroke volume (SV) were chosen for further evaluation. The response to CRT was determined after 6 months of therapy according to two functional parameters (10% ↓ 6MWD, ↓ by one NYHA class) and six echocardiographic left ventricle parameters (EDV↓ 15%, ESV↓ 10%, ESV↓ 15%, ESV↓ 30%, LVEF↑ 5%(absolute), LVEF ↑ 15%).

Statistic - univariate logistic regression was used for statistical analysis of data. Results are presented as hazard ratio with 95% coefficient interval.

Results - Prognostic factors of improvement of NYHA class were TPG [HR:0.84(0.70-1.00)] and RAP [HR:0.74(0.60-0.94)], decrease of EDV by 15% were TPG [HR:0.77(0.63-0.94)] and RAP [HR:0.82(0.68-0.99)], decrease of ESV by 10% was TPG [HR:0.84(0.72-0.99)], decrease of ESV by 15% were PVR [HR:0.63(0.39-0.99)] and TPG [HR:0.80(0.67-0.96)], decrease ESV by 30% was TPG [HR:0.69(0.53-0.88)], increase of LVEF by 5%(absolute) were mPAP [HR:0.92(0.85-0.99)], PVR [HR: 0.54(0.32-0.90)] and TPG [HR:0.69(0.53-0.88)] and increase of LVEF by 15% were PVR [HR:0.57(0.36-0.95)] and TPG [HR:0.84(0.72-0.98)].

PWP, SV and CO were not predictors of any parameters of positive response to CRT. None of the examined parameters was an indicator of changes in 6-MW distance.

Conclusion: These results suggest the usefulness of some pulmonary hemodynamic parameters, especially PVR and TPG as predictors of positive response to CRT in six month follow-up.

P912

QRS prolongation is a determinant of residual mechanical dyssynchrony following cardiac resynchronization therapy

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Purpose: To assess if paced-QRS interval reflects residual mechanical dyssynchrony following CRT.

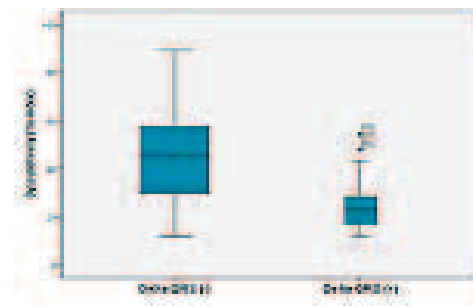
Methods: 80 patients that received CRT/CRT-D devices were included in the study. QRS intervals were recorded before and after CRT. Yu index ≥33 msec was used as a marker of mechanical dyssynchrony. Patients were divided into two groups as having dyssynchrony (N = 39) or not (N = 41) following CRT implantation.

Results: Mean age was 63 (37% female) and mean LVEF was 29%. Both groups were similar in terms of clinical and echocardiographic features (p values>0.05). Patients with residual dyssynchrony were found to have wider post-CRT QRS intervals (165 ± 22 vs. 182 ± 16, p < 0.01). Yu index was found to have a negative correlation with ΔQRS (preQRS - postQRS) (r = -0.341, p = 0.002). Patients with a positive ΔQRS (narrowed QRS) were statistically found to have less mechanical dyssynchrony than patients with a negative ΔQRS (prolonged QRS) (p < 0.01).

Conclusions: Prolonged QRS interval is related to residual mechanical dyssynchrony following cardiac resynchronization therapy.

	Dyssynchrony (-) (N = 41)	Dyssynchrony (+) (N = 39)	p value
Age (years), Gender (Male, %)	63.4 + 12.2, 41%	63.4 + 12.8, 33%	0.45
NYHA Class	2.6 + 0.7	2.6 + 0.8	0.61
QRS width before CRT (msec)	160.2 + 29.4	157.4 + 19.8	0.62
QRS width after CRT (msec)	165.4 + 22.5	182.5 + 16.2	< 0.01
LV-ESV (mL)	147 + 73	143 + 50	0.78
EF (%)	27.8 + 9.6	31.1 + 6.8	0.07

Clinical features according to the dyssynchrony index



Relation of ΔQRS with dyssynchrony

P913

Compatibility of efficiency of cardiac resynchronization therapy in patients with sinus rhythm and patients with atrial fibrillation after AV-node ablation

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Aim: to explore the effectiveness of the cardiac resynchronization therapy (CRT) in patients with chronic heart failure with NYHA functional class III or IV (III-IV FC CHF), ejection fraction <35%, QRS duration ≥ 120 ms with sinus rhythm vs. atrial fibrillation.

Methods: The study involved 30 patients who underwent CRT (group 1) and 30 patients with atrial fibrillation after CRT and AV-node ablation (group 2). Examination of patients was carried out at baseline, in 6 months after surgery and in 12 months, and included 6 minute walk test, transthoracic echocardiography and determination of myocardial dyssynchrony.

Results: The study showed a decrease of end systolic volume (ESV), end diastolic volume (EDV), the degree of mitral regurgitation (MR), an increase in ejection fraction (EF), improvement in 6 minute walk test in both groups (p < 0.05).

Presystolic aortic delay it significantly decreased by the 12 month (from 169.9 ± 5.3ms to 151.0 ± 6.3ms). The same was found in group 2 (from 175.6 ± 4.8ms to 157.8 ± 7.2ms). Interventricular delay significantly decreased in both groups in 6 months and in 12 months comparing to the baseline. Atrioventricular dyssynchrony was not measured.

Comparing parameters of haemodynamics we found improvement in both groups: EDV significantly decreased from 337.8 ± 26.3ml to 307.4 ± 23.7ml by the 6 month

and to 301.3±30.3ml by the 12 month in group 1 and. from 345.2±32.4ml to 316.5±28.7ml by the 6 month and to 312.8±34.6ml by the 12 month in group 2 ($p < 0.05$). At baseline ESV was 277.4±21.7ml in group 1 and 285.4±30.4ml in group 2. After 6 and 12 months ESV was 220.9±18.6ml and 214.6±19.4ml in patients with sinus rhythm, 243.6±28.7ml and 235.7±30.2ml in patients with atrial fibrillation respectively. EF had significantly increased from 26.0±1.5% to 32.5±1.6% by the 6 month and 32.6±2.3% by the 12 month in patients with sinus rhythm. EF had significantly increased from 24.6±2.5% to 30.1±2.4% by the 6 month and 31.2±1.8% by the 12 month in patients with atrial fibrillation. At baseline MR was 3.2±1.3 in group 1 and 3.6±1.2 in group 2. After 6 and 12 months MR was 2.8±0.7 and 2.5±0.5 in patients with sinus rhythm, 3.1±1.3 and 2.7±1.2 in patients with atrial fibrillation respectively.

We also found improvement in 6 minute walk test in both groups (from 147.6±25.8m to 283.6±31.2m in group 1 and from 142.7±23.8m to 279.9±34.4m in group 2).

Conclusion: Effectiveness of CRT in patients with III-IV FC CHF (NYHA), QRS duration ≥ 120 ms with sinus rhythm is comparable to that in patients with atrial fibrillation after CRT and AV-node ablation.

P914

Does the enhanced algorithm of intrathoracic impedance measurement reduce the frequency of alerts? A retrospective real-life-analysis

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Introduction: Patients (P) with severe congestive heart failure often fit the indication for implantation of an ICD or CRT-D. Using device-telemonitoring enables apart from continuous monitoring of technical integrity and cardiac rhythm the management of cardiac decompensation by using the Opivol-Index (OVI), which in turn measures changes in thoracic impedance and thus acts as a fluid monitor and early warning system. OptiVol (OV)-alerts which cannot be correlated to clinical symptoms remain, as false positive alerts, a problem in clinical daily routine. In order to improve the specificity of the OVI, the OptiVol 2.0 as the further development was introduced in 2010. The OVI is calculated by accumulating the difference between the daily and the reference impedance. On crossing the programmed threshold (60 ohm-days) an alert is generated. Using telemonitoring and the SQL database CareLink[®] Analytics it was possible to collect all follow-up data. A re-evaluation of the OV 1.0-data with the new OV 2.0 algorithm investigates if there would have been less alerts for the same patients, in the same situation with the same measured intrathoracic impedance.

Methodology: In this retrospective real-life-investigation 299 patients (group 1: 120 patients with OV 1.0 (182,37 patient years); group 2: 178 with OV 2.0 (121,16 patient years)) an overall observational period of 303,53 years was analyzed. The measured impedance data of the patients with OV 1.0 (group 1) were recalculated using the OV 2.0 algorithm and the frequency of the theoretical alert and real alert were compared.

Results: There is a clear difference in OV-alert (OVA) frequency: 2,46 alerts/year for OV 1.0 and 1,32 alerts/year for OV 2.0. The reevaluation of the impedance-data showed a reduction from 448 to 240 alerts means 46,43%.

OVA/year origin OVA/year recalculated OVA/year reduction

OV 1.0 2,46 1,31 1,15 (46,43%)

OV 2.0 1,32 1,32 0,0 (validation)

Conclusion: This reevaluation of the existing measured OV 1.0-data shows a significantly reduced alert frequency by using the OV 2.0 - algorithm. The calculated frequency of OVA is very similar to the frequency of the OV 2.0- algorithm in daily clinical routine. In other examinations it has been shown that the frequency of OV-alerts not correlating to patients clinic were reduced by 30-43% using the OV 2.0- algorithm. The recalculation of our own data showed a reduction in OV-alerts about 46,43%.

P915

Cardiac resynchronization therapy: left ventricular lead placement guided by coronary venous electroanatomic mapping

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Introduction: The implant of cardiac resynchronization therapy (CRT) devices driven by non-fluoroscopic navigation systems demonstrates how an electroanatomical mapping of the coronary sinus for the optimization of the left electrode placement, is feasible.

Purpose: Aim of this study was to evaluate the latest activated region in coronary sinus (CS) in patients underwent CRT devices implant.

Methods and Results: 46 consecutive CRT patients (38 males, age 72.9±7.3 years) underwent intra-procedural coronary venous EAM using EnSite NavX. A guidewire was used to map the coronary veins during intrinsic activation and right ventricular (RV) pacing. The latest activated region were reported in Table 1.

Conclusion: Coronary venous EAM can be used intra procedurally to guide LV lead placement to the latest activated region. This approach especially contributes to optimization of LV lead electrical delay in patients with multiple target veins. Conventional anatomical LV lead placement strategy does not target the vein with maximal electrical delay in many of these patients.

Delay in LAO	Latest activation during spontaneous rhythm - Number of patients	Latest activation during RV pacing - Number of patients
anterior	2	10
Antero-lateral	8	8
Lateral	27	18
Postero-lateral	8	10
Posterior	1	0
Delay in RAO		
Basal	25	16
Medium	16	15
Apical	5	15

P916

Surgical technique and feasibility of implantation of a novel pressure unloading left ventricular assist device (PULVAD)

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Purpose: The ability of the failing human heart to recover after mechanical unloading with left ventricular assist devices (LVADs) has been insufficiently exploited. Our promising results of cardiac reverse remodelling in patients with end-stage HF due to idiopathic dilated cardiomyopathy supported by an intraaortic balloon pump initiated our team to work on the development of a novel left ventricular pressure unloading device (PULVAD).

Methods: This device comprises a pneumatically-driven polyurethane pumping chamber with a valveless opening. The PULVAD is surgically implanted through a vascular graft on the ascending aorta and its function is based on counterpulsation. This device was implanted in five calves of (92±7 kg) through left lateral thoracotomy, with partial clamping of the ascending aorta without need of extracorporeal circulation. On general anaesthesia, carotid artery was catheterized for continuous monitoring of arterial pressure, a left lateral thoracotomy was performed, the pericardium was incised and suspended, ascending aorta was prepared and the PULVAD was implanted on the ascending aorta. Two pairs of piezoelectric crystals and an apical Millar catheter were placed in the left ventricle (LV) for continuous measurements of volume and pressure. Baseline and assisted LV hemodynamic parameters and afterload were compared using paired t-test analysis.

Results: During and after PULVAD implantation the hemodynamics steady state was not adversely affected. Mean heart rate, systolic and end-diastolic aortic pressure at baseline were 77±19 bpm, 101.8±19.5 mmHg and 81.7±15.9 mmHg. Left ventricular pressure unloading induced by PULVAD led to significant reduction of systolic and end-diastolic aortic pressure (from 101.8±19.5 to 87.7±20.8 mmHg, $p < 0.001$ and from 81.7±19.5 to 62.4±20.1 mmHg, $p < 0.001$, respectively). No adverse events (ventricular arrhythmias, thromboembolic events) presented during support with PULVAD.

Conclusions: Our preliminary results support the feasibility of a safe surgical implantation of this novel PULVAD with excellent hemodynamic results in terms of LV unloading.

P917

Contribution of left ventricle mechanical circulatory support implantation in patients with advanced heart failure in stage of cardiac cachexia

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Background: Patients with advanced heart failure (AHF) often develop cachexia, an important negative prognostic factor. There are no effective treatment options for this condition except mechanical circulatory support implantation. We retrospectively analyzed outcomes of pts with signs of cardiac cachexia before Heart Mate II (HM II) (Thoratec Corp) implantation in our institution.

Methods: 122 pts with AHF received the HM II in bridge to transplant indication from 02/08 to 12/13 in our institution. 30 pts (24,5%) of them were operated in the stage of cardiac cachexia, defined by the presence of significant weight loss (>6% within 6months) and by presence of abnormal biochemistry: C-reactive protein (CRP) >5 mg/l or hemoglobin (Hb) <120 g/l or albumin <32 g/l. We assessed need for right ventricular support (RVAD-Levitronix Centrimag) implantation and heart transplantation (HTx) attainment in all 122 implanted pts and in the subgroup of patients with cardiac cachexia.

Results: Mean weight loss in pts with cachexia was 13% (6-26%), 29 of them (97%) had CRP >5 mg/l, 22pts (73%) had Hb <120 g/l and 20pts (67%) had albumin <32 g/l. Mean albumin level in this group was 29,3g/l (19,6-34,6g/l).

RVAD implantation in consequence of right ventricular failure was performed in 18 pts (15%), 7 of them died in 2-42 days. In the cachectic subgroup the need for RVAD implantation was in 3 pts (10%) after HM II implantation, 1 of them died 10 days after the operation. In the whole HM II group successful heart transplantation was performed in 83 pts (68%). In the subgroup of cachectic pts we observed in 24 individuals (80%) normalization of nutritional parameters after HM II implantation, 23 of them were successfully transplanted. Normalization of albumin levels in 3 months after the HM II implantation predicted good outcome. All cause mortality in the whole group was 24,5%, in cachectic subgroup 20%.

Conclusion: In this paper we present very good results of HM II implantation in patients with advanced heart failure in the stage of cardiac cachexia. We believe that implantation of mechanical circulatory support is the only way to achieve a metabolic condition that allows a successful heart transplantation in cachectic pts.

P918

Age is a predictor of recurrent gastrointestinal bleeding in patients with left ventricular assist devices: results from an urban tertiary care center

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Background: Continuous flow left ventricular assist devices (CF-LVADs) have become a valuable therapeutic option to a growing population with end-stage systolic heart failure. Gastrointestinal bleeding (GIB) is among the most common adverse events after device implantation. The goal of this study was to determine the risk factors for GIB, timing of bleeding events and the yield of therapeutic interventions among CF-LVAD recipients.

Methods: Between September 2009 and June 2014, 53 consecutive advanced heart failure patients underwent CF-LVAD (Heartmate-II) implantation at a single tertiary care center. Electronic medical records were reviewed to identify demographic characteristics, co-morbidities and GIB episodes. Two sample t-test, chi-square test, univariate and multivariate logistic regression analyses were conducted to identify risk factors for GIB and the yield of endoscopy after device implantation.

Results: African Americans represented the majority of patients (n=28, 53%) followed by Caucasian (n=16, 30%). Seventeen of the 53 patients (32%) had at least one episode of GIB. Age, gender, BMI, presence of hypertension, diabetes, or chronic kidney disease, use of NSAIDs, and a prior history of GIB were not associated with increased risk of GIB after LVAD placement. The incidence of GIB was also not different between races (p=0.72). Of those patients with GIB, eight (47%) had recurrent bleeding. Those patients that rebled were significantly older than those patients who did not (mean age = 68 ± 10.1 years vs. 48 ± 13.8, OR=1.15, 95% CI = 1.01-1.29, p=0.03). Other variables assessed for the risk of rebleeding were not significant. Among GIB patients, 15 (88%) presented with overt bleeding and 13 (76%) underwent upper endoscopy. Esophagogastroduodenoscopy was the most commonly performed procedure (61%) followed by colonoscopy (24%). The overall diagnostic yield of endoscopy was modest, revealing a cause of bleeding in eight patients (47%). Irrespective of their location, peptic ulcers (18%) and angioectasias (18%) were the most commonly identified causes of bleeding. Similarly, the overall therapeutic yield of endoscopic procedures was only 11%. There were no complications attributed to endoscopic procedures and no deaths directly attributed to GIB.

Conclusions: GIB is a frequent cause of morbidity for patients with CF-LVAD, particularly in patients with advanced age who are at increased risk for recurrent bleeding. The most common presentation of GIB in this patient population is obscure and overt. Although safe, the diagnostic yield of endoscopy is modest and therapeutic interventions are minimal.

P919

Two different sites of berlin heart excor membrane rupture

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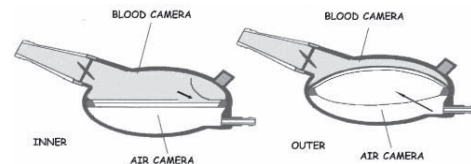
Purpose: Berlin Heart Excor (BHE) is a para-coroporeal pneumatic ventricular assist device (VAD) that creates pulsatile flow. Blood and air chambers are separated by a 3 layer membrane. Membrane rupture can occur. We present 2 cases of such complication, with two different sites and mechanisms proposed after analyzing the clinical course and explanted device.

Results: Between May 2013 and Nov 2014, 5 patients with end-stage heart failure underwent BHE implantation at our centre. Two of them had membrane rupture during support.

First case was a 62y man with bi-VAD BHE bridging to transplant. He was asymptomatic and hemodynamically stable when an irregular shadow 3cm diameter was detected during systole with fibrin filaments attached in the blood camera of right-VAD. An emergent change of right-VAD was made. After explantation, a rupture of the inner layer of the membrane was detected. Patient was successfully transplanted 57 days later.

Second case was a 65y man with bi-VAD BHE bridging to transplant. He began to feel dyspnea, malaise and cool sweating. When the physician arrived he detected a perfect rounded shadow in the blood camera of the left-VAD during systole. After few minutes the size of the shadow had enlarged and only partially disappeared during diastole. Cardiogenic shock rapidly developed. Emergent exchange was performed. After explantation, a rupture of the outer layer was detected. Patient was successfully transplanted 32 days later.

Conclusion: We present two illustrative cases of two sites of membrane rupture. Inner rupture is often well tolerated hemodynamically, the shadow is irregular (as the tear is) and thrombus can develop. Outer rupture induces a valve mechanism, the shadow is rounded, it progresses rapidly promoting VAD dysfunction and cardiogenic shock (Figure 1).



P920

Current status of application of extracorporeal membrane oxygenation (ECMO)

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Introduction: Extracorporeal membrane oxygenation (ECMO) is indicated in patients with circulatory or respiratory failure. The aim of this study is to evaluate the outcome of ECMO and compare the outcomes among certain indications of ECMO.

Methods: 65 patients have applied ECMO from May 1, 2006 until July 17, 2014 in our University hospital. Indications of ECMO included cardiogenic shock, respiratory distress and failure of weaning from cardiopulmonary bypass (CPB) during cardiac surgery.

Results: 42% of patients (27/65) have successfully been weaned from the ECMO device, and the mortality rate was 78% (51/65). Among subgroups of indications, patients who failed of weaning from CPB showed higher weaning rate (7/10, 70%) and lower mortality rate (6/10, 60%), whereas respiratory distress patients showed low weaning rate (2/12, 17%) and 100% of mortality. Patients with cardiogenic shock showed 42% of weaning rate (18/43) and 77% of mortality rate (33/43). The mean age of the survived patients tend to be younger than those who expired (mean age 54.9 vs. 61.1, p=0.18), and the mean age of the successfully weaned patients showed no significant difference with the patients who could not wean from the ECMO device (mean age 60.4 vs. 59.1, p=0.53).

Conclusion: ECMO may provide considerable survival rate in patients of cardiogenic shock or those who could not wean from CPB during cardiac surgery.

P921

Percutaneous insertion of veno-arterial extracorporeal membrane oxygenation circuit in the catheterization laboratory for refractory cardiogenic shock: first year, single center experience

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Background: Veno-arterial ExtraCorporeal Membrane Oxygenation (VA-ECMO) in the management of cardiac failure or cardiac arrest is being increasingly used.

Percutaneous insertion of the device can be performed in the catheterization laboratory (Cath Lab).

Methods: We analyzed our initial experience with percutaneous VA-ECMO reviewing the first cases treated in our institution since July 2013, when our program started, to August 2014. ECMO was percutaneously implanted at the Cath Lab by interventional cardiologists in all cases.

Results: 8 patients were supported with percutaneous VA-ECMO. The indication of circulatory support was: Acute myocardial infarction complicated with cardiogenic shock (4, 50%), severe acute decompensation of chronic heart failure (3, 37.5%), and refractory cardiac arrest secondary to anterior myocardial infarction (1, 12.5%). Mean age was 58.4 ± 6.5 years and 7 (87.5%) were men. Mean left ventricular ejection fraction prior to ECMO support was $15 \pm 7\%$ ($n=7$), while one patient presented with right ventricular infarction and preserved left ventricular ejection fraction. All ECMOs were implanted at the Cath Lab by femoral approach. Sizes of cannulae were as follows: Venous cannula 6 of 21F and 2 of 23F, Arterial cannula 6 of 19F and 2 of 17F, in 5 patients a distal perfusion sheath was inserted. Time from decision to beginning of therapy was 32.5 ± 20 minutes. Mean Lactic acid before VA-ECMO was 7.3 ± 3.4 and dropped to 1.6 ± 0.3 mmol/l after 24 hours of circulatory support. Four patients developed bleeding complications. One patient had acute arterial ischemia related to the arterial cannula, solved with subclavian artery cannulation (surgical). One patient suffered fatal accidental decannulation. Mean patient circulatory support duration was 5.1 ± 2.9 days. Weaning from ECMO was possible in five of eight patients (due to partial ventricular function recovery), one patient underwent biventricular assist device implantation (Berlin Heart Excor) as a bridge to heart transplantation successfully performed three months later. Hospital discharge was achieved in 4 patients (50%). Two patients died on VA-ECMO, one secondary to fatal decannulation and one secondary to sepsis. Two patients died during post-ECMO hospital stay due to chronic heart failure related complications.

Conclusion: This first experience shows that implantation of percutaneous VA-ECMO by the interventional cardiologist at the Cath Lab is feasible, with early beginning of support and positive results in a high risk patient group.

P922

Extracorporeal life support as a bridge to decision in acute or decompensated heart failure

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Introduction: Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) is indicated in patients with refractory cardiogenic shock who have an underlying potentially reversible heart condition, although it can also be used as a bridge to optimization prior to long term ventricular assist device implantation or cardiac transplantation.

Objectives: To determine the indication and prognosis of patients supported with VA-ECMO

Methods: Retrospective observational study including all patients who received mechanical circulatory support with VA-ECMO from June 2010 to December 2014 with the indication of severe refractory cardiogenic shock. Patients on ECMO post cardiac surgery were excluded.

Results: During the study period, 52 patients required VA ECMO. The aetiology of cardiogenic shock was acute ischaemic heart disease (with PCI) 9 patients (17.3%), chronic ischaemic heart disease with decompensated heart failure (DHF) 9 patients (17.3%), dilated cardiomyopathy with DHF 24 patients (33.3%), acute heart failure as myocarditis 7 patients (13.5%) or other 3 patients (5.8%). The mean age was 42 year old (16-66), with 75% being male. The cannulation was peripheral in 49 patients, representing the 94.2% of our population. The mean duration of support with ECMO was 7.2 days \pm 4.8 days. 19 patients were supported with IABP associated to ECMO (36.5%), with a higher incidence in the ischaemic heart disease group. In 28 patients (53.8%) was possible to undergo the ECMO weaning with total recovery of heart function in 10 patients (19.2%). 16 patients were upgraded to long term support as a bridge to transplant and 4 patients received a heart transplant during the study period. The ITU mortality was 26.9% (14 patients) and the overall mortality at hospital discharge was 44.2% (23 patients). The most common cause of death was refractory shock resulting in multiorgan failure (30.8%, 16 patients), followed by uncontrolled haemorrhage (11.5%, 6 patients). The survival rate at Hospital discharge was better for the acute myocarditis group with 100% of survival and the higher mortality observed was in the group with chronic or acute ischaemic heart disease.

Conclusions: In-hospital survival rate of patients with VA-ECMO varies from 30% to 50% according to the cause of the cardiac dysfunction. It remains difficult to determine which patients will benefit from VA-ECMO and when ECMO support will be futile. Any reversible cause of acute heart disease as myocarditis appears to have the best prognosis. The outcome for patients with ischaemic heart disease remains poor.

P923

Risk factors and clinical characteristics of in-hospital death associated with the use of IABP in acute myocardial infarction

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Background: Despite the widespread use of the IABP in AMI, there are few published data regarding the patients who are not survived in hospital with the use of IABP. Therefore, we investigate clinical characteristics and risk factors of in-hospital death with IABP support in AMI patients.

Objective: To investigate the clinical characteristics and the risk factors of in-hospital death with IABP support in AMI patients.

Methods: The clinical data of continued 572 AMI patients with the use of IABP selected from July 2005 to July 2013 were retrospectively analyzed. All patients symptom onset to admission were within 72 hours. The evolution of the risk factors of in-hospital death and clinical characteristics was compared in 81 non-survivors vs. the survivors;

Results: The non-survivors had an advanced age, more female, significantly higher heart rate, lower systolic and diastolic blood pressures, more prevalence of hypertension and diabetes mellitus, a longer time to treatment, signs of heart failure (Killip \geq 2), higher BUN and Scr and a more often an impaired left ventricular ejection fraction (LVEF) compared with the survivors. LM or LCX as culprit vessel and multivessels stenosis were more frequently observed in the non-survivors. And the non-survivors were significantly less likely to be treated with ACEI/ARB and β -blocker and more likely to get inotropic agents during hospitalization. Fewer patients were treated with emergency reperfusion therapy. Continuous renal replacement therapy was used more often. More percentage of patient's initiation IABP was post PCI. More percentage of duration of IABP support was \leq 12h and \geq 6 Days, less percentage was 12h-5 Days among the non-survivors. On the other hand, more patients' length of hospital stay was shorter than 24 hours and less patients' longer than 8 days. Multivariate Binary logistic regression showed that age $>$ 65 years, longer Time to treatment, Killip class IV, Scr at admission, and LVEF $<$ 30% were risk factors associated with higher In-hospital mortality. Killip I-II was associated with lower in-hospital mortality.

Conclusions: Advanced age, longer time to treatment, diminished LVEF, poor heart function and renal function are risk factors associated with in-hospital poor survival in AMI supported with IABP. IABP's mechanical support cannot replace a timely and effective reperfusion therapy for patients with decompensated circulation. Also, as long as the patient is enduring, longer IABP support provide time for better recovery of both myocardial and end-organ function and thus may improve the survival of AMI patients.

P924

Iron availability and expression of genes associated with iron metabolism in cardiomyocytes and myocytes and their viability when cultured either in static conditions or upon mechanical stretch

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Background: Iron is presumed to affect the functioning of cardiomyocytes and skeletal myocytes. The presence of proteins involved in intracellular iron metabolism in these cells is anticipated.

Methods: H9C2 rat adult cardiomyocytes and L6 rat adult skeletal myocytes were cultured for 24 hours in static conditions and when exposed to mechanical stretch in optimal or reduced (iron chelation using deferoxamine) or increased (supplementation of ammonium ferric citrate) iron concentrations in cultured media. We analysed the mRNA expression of HIF-1 α (hypoxia and iron depletion indicator), ferritin heavy and light chains (FTH and FTL; iron storage proteins), ferroportin type 1 (FPN1; iron exporter), transferrin receptor type 1 (TfR1; iron importer), hepcidin (HAMP; iron metabolism regulator) using qPCR, the level of respective proteins using Western Blot, and the cell viability using FACS.

Results: In static conditions, cardiomyocytes exposed to reduced iron concentrations in the medium demonstrated as compared to standard conditions an increased mRNA expression of HIF-1 α ($r=0.96$, $p<0.001$) and a decreased mRNA expression of FTH, FTL, FPN1, HAMP (all $r<0.7$, $p<0.001$), indicating depleted intracellular iron. The increased TfR1 expression ($r=0.7$, $p<0.05$) reflected a facilitated iron entrance to the cells. The inverse changes occurred in cells exposed to increased iron concentrations in the medium. The same pattern of mRNA expressions was observed in myocytes. There were strong relations between analogous genes in both cell lines (all $r>0.9$, $p<0.001$). The mRNA expression corresponded with the profile of respective proteins. When exposed to mechanical stretch, both cell lines,

when cultured in reduced iron availability, demonstrated an increased mRNA expression of TfR1 (both $r=0.96$, $p<0.001$) and a reduced mRNA expression of FPN1 (both $r=-0.96$, $p<0.001$), similarly as in static conditions. It was accompanied by an increased HAMP mRNA expression in both cell types (both $r>0.6$, $p<0.01$), suggesting HAMP to be involved in the local regulation of iron metabolism. The culture of both cell types in non-optimal iron supply decreased their viability by 20% in both static conditions and when exposed to mechanical stretch.

Conclusions: Rat cardiomyocytes and skeletal myocytes contain genes involved in intracellular iron metabolism and respond similarly to changing iron availability in static conditions. The application of mechanical stretch modulates responses to changing iron availability in these cells. Iron depletion and excess impairs the viability of the cells.

P925

Long term impact of cardiac contractility modulation on QRS duration

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Purpose: Cardiac contractility modulation (CCM) is an implantable electrical treatment for heart failure with reduced ejection fraction. CCM improves patient functional status but its effect on intra-ventricular conduction remains unknown. Prolongation of the QRS complex is a well-known prognostic factor of mortality; the purpose of this study was to analyze for the development of QRS complex duration in patients treated by CCM over a long period of time.

Methods: Between 12/2002 and 5/2013 70 consecutive patients with trivial or no ventricular paced beats received CCM at our referral center. 12-lead ECG recordings were made at baseline and final follow-up visits. QRS complex duration was evaluated automatically and reconfirmed manually at each time point. Analyses of all ECGs were made only for recordings taken when CCM therapy was OFF, to avoid the presence of CCM artefacts in the recorded complexes.

Results: Patient's baseline characteristics are shown in Table 1. Mean follow-up was 2.8 years. Mean QRS duration was unchanged from baseline (112.0msec, ranges 80 to 160msec) to last follow up (112.9msec, ranges 80 to 160msec), $p=n.s.$. Differences in QRS complex duration ranged between -15msec to +25msec. One patient (1.4%) developed new onset left bundle branch block. These results are strikingly different from comparative published data of several studies with heart failure patients without CCM, consistently indicating an increase in QRS duration (6.0-23.4msec) over a similar time period.

Conclusions: CCM appears to prevent chronic ventricular depolarization delay that is expected to develop in heart failure and that is associated with poorer outcomes. This supports the safety of long-term CCM therapy and suggests a possible long-term benefit in maintaining QRS duration. In addition, reduction in development of new LBBB means that the need for CRT-D upgrade will be lower, which should result in financial benefit to the health system.

Table 1

	Mean values (Ranges)
Age (in years)	60.7 (32-82)
Male	85.7%
Ischemic cardiomyopathy	61.4%
NYHA class	3.0 (2-4)
LVEF	22.9% (7 - 39%)

P926

Heart failure hospitalization in dual-chamber pacemaker patients with atrial fibrillation detected

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Background: Atrial fibrillation (AF) is the most common arrhythmia and is highly present in our daily clinical practice. In pacemaker patients, AF is often underdiagnosed and undertreated, and can produce adverse events like acute heart failure that require hospitalization (HFH). In this study we evaluate the relationship between the HFH and the detection of AF in our patients with dual chamber pacemakers.

Methods: We collected demographic and clinical data in patients with DDD/R pacemakers who went to the cardiology consultation (Oct'11-Oct'12). Subsequently, a follow-up period was performed, detecting the presence of AF and HFH.

Results: The sample included 349 patients with DDD/R pacemakers. Mean follow-up was 19 months. AF was detected in 100 patients (29%). The mean age of patients with AF is 76 years old (62% of them are older than 75), and 86% have

hypertension. There were 28 cases of HFH during follow-up. Related factors were: location of ventricular pacing lead (apex RV vs RVOT), history of heart disease and AF detected. Independent predictors for HFH were history of heart disease and AF detected. The complete data are available in Table n° 1.

Conclusions: The presence of AF in patients with dual-chamber pacemakers is high and can predict heart failure hospitalization.

Table n°1. Analysis of HFH predictors.

Predictor	Univariate analysis HR (95% CI)	p	Multivariate analysis HR (95% CI)	p
Atrial fibrillation	2,33 (1,07-5,09)	0,030	2,16 (1,03-4,56)	0,041
Heart disease	10,2 (1,49-83,5)	0,003	10,7 (1,46-79,2)	0,020
Ventricular pacing lead - RV apex	2,76 (1,09-7,00)	0,032	2,37 (0,96-5,87)	0,061

CI: confidence interval, RV: right ventricle.

P927

Cardiac contractility modulation: first experience in heart failure patients with reduced ejection fraction and permanent atrial fibrillation

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Purpose: Cardiac Contractility Modulation (CCM) is an electrical therapy for heart failure (HF) with reduced ejection fraction. Non-excitatory electrical signals applied during the absolute refractory period enhance the strength of left ventricular contraction without increasing myocardial oxygen consumption. Sinus rhythm is deemed necessary for effective treatment because the current CCM signal delivery algorithm requires sequential sensing of a p-wave, followed by depolarisations at each ventricular lead. In case of atrial fibrillation (AF) CCM is inhibited. The purpose of this study was to evaluate the feasibility of CCM therapy in patients with permanent AF by circumventing the requirement for sensing of a natural p-wave.

Methods: Five CCM patients with AF received a pacemaker or ICD upgrade to CRT with programmed low atrial sensitivity (4mV), which resulted in compulsory atrial stimulation followed by biventricular pacing. The CCM system recognised the atrial stimuli as p-waves, which led to CCM signal delivery.

Results: Three patients developed permanent AF after a mean follow up of 40 months of CCM therapy. Two patients had permanent AF at the time of CCM device implantation. All pacemaker or ICD devices were successfully upgraded to CRT. CRT stimulation rates of $\geq 96\%$ and CCM stimulation rates between 60 and 95% were achieved. Clinical condition of the patients improved (mean NYHA class -0.7, LVEF +2%, Minnesota living with heart failure questionnaire -15.6 points).

Conclusions: CCM signal delivery is feasible in HF patients with permanent AF by sequential atrial-ventricular pacing, so that the atrial pacing spike is interpreted as a p-wave by the CCM signal delivery algorithm. This experimental approach can be considered in individual cases. A new CCM algorithm, which does not require an atrial electrode, is desirable.

P928

Contact analysis and device leaflet interaction of a nitinol based goretex patch device in the treatment of mitral regurgitation by finite element analysis

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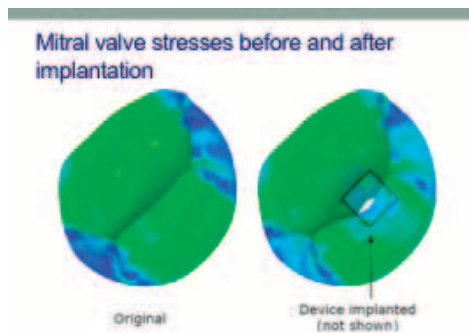
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Aims: A Nitinol based goretex patch device over a 6F screw-in pacemaker lead wire was devised and its performance was evaluated by finite element analysis.

Methods and Results: A 1.0 cm wide x 1.2 cm nitinol based device with a goretex patch sutured on its surface was designed. The device was fixed over a 6F screw-in pacemaker lead wire. The device was initially evaluated in-vitro to reduce mitral regurgitation, which was studied after cutting the chords in-vitro. The device was positioned across the mitral leaflets. Based on the 4DCT images, a patient specific model of the mitral leaflet and apparatus was generated and validated. The left ventricle was reconstructed using segmentation technique. A finite element model of the mitral valve leaflets was generated based on 3D reconstruction. The pacemaker lead was fixed at the left ventricular apex. The first contact analysis, device-leaflet interaction and the stress distribution on the mitral valves were studied after placement of device. The device-leaflet interaction of the nitinol device and the patient specific mitral valve model was analysed. A simulation was performed to observe the virtual closure behavior of the mitral valve leaflets. The analysis was performed in Abaqus. The mitral valve stress distribution was quantified before and

after implantation of the device. The mitral valve stresses were significantly lower after placement of the device across the valves.

Conclusion: The mitral valve stresses were reduced after placement of a novel Nitinol based Goretex device across mitral valves. There is potential for a novel device over endocardial pacing wire in Mitral regurgitation therapy.



P929

Reduction of readmission rate by adaptive servo-ventilation therapy in the patients with severe heart failure

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Introduction: Adaptive servo-ventilation (ASV) therapy is one of non-pharmacological therapy that was developed recently and abundant studies have reported its effectiveness for the restoring cardiac function or improving survival in the patients with severe congestive heart failure (CHF). However, it still remains unclear whether ASV treatment really reduces readmission after its commencement in severe CHF patients. Hence, we analyzed specifically the change in admission rate in patients who started ASV therapy.

Methods and Results: Admission frequencies during 12 months before and after ASV therapy (consecutive 24 months) were retrospectively analyzed and compared in consecutive 44 severe CHF patients who could continue ASV therapy at least 12 months. The admission frequency decreased from 1.9 ± 1.4 times to 1.1 ± 1.6 during 12 months before and after ASV ($p < 0.001$) and it tended to more decrease especially in the patients with more frequent hospitalization.

Conclusion: ASV therapy is effective to reduce readmission even in severe CHF patients who are already on maximum medical treatment.

P930

Efficacy and survival in patients with cardiac contractility modulation: long-term single center experience in 81 patients

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Aims: To analyze long-term efficacy and survival in patients with chronic heart failure treated with cardiac contractility modulation.

Methods: 81 patients implanted with a CCM device between 2004 and 2012 were included in this retrospective analysis. Changes in NYHA class, ejection fraction (EF), Minnesota Living with Heart Failure Questionnaire, NT-proBNP and peak VO2 were analyzed during a mean follow up of 34.2 ± 28 months (6-123 months). Observed mortality rate was compared with that predicted by the MAGGIC Score.

Results: Patients were 61 ± 12 years old with EF $23 \pm 7\%$. Heart failure was due to ischemic ($n=48$, 59.3%) or idiopathic dilated ($n=33$, 40.7%) cardiomyopathy. EF increased from 23.1 ± 7.9 to $29.4 \pm 8.6\%$ ($p < 0.05$), mean NT-proBNP decreased from 4395 ± 3818 to 2762 ± 3490 ng/l ($p < 0.05$) and mean peak VO2 increased from 13.9 ± 3.3 to 14.6 ± 3.5 ml/kg/min ($p=0.1$). The overall clinical responder rate (at least 1 class improvement of NYHA within 6 months or last follow-up) was 74.1%. 21 (25.9%) patients died during follow up, 11 (52.4%) due to cardiac conditions and 10 (47.6%) due to non-cardiac conditions. Mortality rates at 1 and 3 years were 5.2% and 29.5% compared to mortality rates estimated from the MAGGIC risk score of 18.4% ($p < 0.001$) and 40% ($p=ns$), respectively. Log-Rank analysis of all

events through 3 years of follow-up, however, was significantly less than predicted ($p=0.022$).

Conclusions: CCM therapy improved quality of life, exercise capacity, NYHA class, EF and NT-proBNP levels during long-term follow up. Mortality rates appeared to be lower than estimated from the MAGGIC score.

P931

Tracking congestion with a personalized thoracic impedance index from chest geometry and composition

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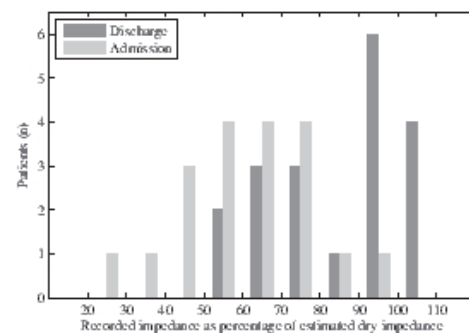
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Purpose: We investigated the effects of chest geometry and tissue composition on the measurements of thoracic impedance with a textile electrode vest to develop a personalized fluid index to track congestion.

Methods: Computational simulations of thoracic impedance for varying levels of chest circumference, fat and muscle proportion were used to derive parameters for a linear model to estimate thoracic impedance. Chest circumference, subscapular skinfold, fat free mass index (FFMI) were then selected as predictors of dry thoracic bioimpedance as provided by a wearable vest in 36 healthy volunteers. The developed model was then applied to a population of 20 HF patients to compare the outcome of the modeled fluid index based on bioimpedance, chest geometry and composition with symptoms associated with decompensation (Framingham criteria).

Results: All derived parameters affected the measured impedance for the healthy volunteers (Chest circumference $p < 0.05$, subscapular skinfold $p < 0.05$ and FFMI $p < 0.05$) and together the model predicted the measured impedance with mean absolute error below 10%. Estimated impedance correlated well with the discharge values of the HF patients ($r=0.73$, $p < 0.001$) and the fluid index followed changes in symptom levels during treatment ($p < 0.001$). However, many patients were discharged well below the model expected value.

Conclusions: Accounting for chest geometry and composition to establish a personal fluid index might help in interpreting the severity of congestion in conjunction with the more common measures of relative changes.



Percent of estimated dry impedance

P932

Cardiac contractility modulation effects on exercise capacity and quality of life - an individual patient data meta-analysis of randomised controlled trials

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Background: Although Cardiac Contractility Modulation (CCM) has emerged as a promising device treatment for heart failure (HF), the effect of CCM on functional capacity and quality of life has not been the subject of an individual patient data meta-analysis to determine its effect on measures of functional capacity and life quality. This meta-analysis aimed at systematically reviewing the latest available randomized evidence on the effectiveness of CCM on functional capacity and quality of life indexes in patients with HF.

Methods: The Cochrane Central Register of Controlled Trials, MEDLINE, and EMBASE were searched in May 2013 to identify eligible randomized controlled trials comparing CCM with sham treatment or usual care. Primary outcomes of interest were peak oxygen consumption, 6-minute walk test distance and quality of life

measured by Minnesota Living With Heart Failure Questionnaire. Mean difference and 95% confidence intervals (C.I.s) were calculated for continuous data using a fixed-effects model.

Results: Three studies enrolling 641 participants were identified and included. Pooled analysis showed that, compared to control, CCM significantly improved peak oxygen consumption (mean difference +0.71, 95% C.I. 0.20 to 1.21, mL/kg/min, $p=0.006$), 6-minute walk test distance (mean difference +13.92, 95% C.I. -0.08 to 27.91, meters, $p=0.05$) and quality of life measured by Minnesota Living With Heart Failure Questionnaire (mean difference -7.17, 95% C.I. -10.38 to -3.96, $p<0.0001$).

Conclusions: Meta-analysis of individual patient data from randomized trials suggests that CCM has significant if somewhat modest benefits in improving measures of functional capacity and quality of life, and may, therefore, following the mixed results of NECTAR-HF, ANTHEM-HF and DEFEAT-HF, be the only electrical device option for HF patients with narrow QRS with consistent RCT evidence of benefit.

P933

Enhanced external counterpulsation: an alternative in cardiological practice

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As the incidence of angina and heart failure continues to rise, enhanced external counterpulsation could be an alternative to optimal medical therapy and revascularisation.

We searched for studies in pubmed with suitable data for or against such a noninvasive modality.

Enhanced external counterpulsation (EECP) uses three sets of pneumatic cuffs that sequentially contract during the diastole, increasing aortic diastolic pressure, augmenting coronary flow and central venous return. Before the onset of systole the cuffs simultaneously deflate, thereby decreasing vascular resistance, assisting with systolic unloading and decreasing cardiac output. The direct pressure from the diastolic augmentation can cause an increase in shear stress to open or form collaterals. The angiogenesis factors, as well as nitric oxide, increase and the endothelial function is improved.

Exclusion criteria include arrhythmias, bleeding diathesis, active thrombophlebitis, severe lower extremity vaso-occlusive disease, presence of aortic aneurysm that needs surgical repair and pregnancy.

EECP has been proven (MUST-EECP) suitable for chronic angina refractory to medical therapy and reperfusion strategies. Treated patients had a significant increase in time to ST-segment depression in stress testing and significant decrease in angina episodes. The IEPR study showed a reduction in the angina class (CCS) post treatment and an improvement of the weekly anginal events and the quality of life. On the other hand, these data imply a decrease of the clinical symptoms but continued clinical events. The EECP responders had improvements in perfusion defects in radionuclide stress tests.

As regards the role of EECP in heart failure, some studies showed significant improvements in b-natriuretic peptide, uric acid, free T3/free T4 ratio levels and mitral annular E velocity. A significant increase in LVEF and reduction in the rest heart rate is also shown. In the PEECH trial the patients with ischemic and non ischemic cardiomyopathy which underwent an EECP had improvement on exercise duration and New York Association classification. In the IEPR study 81% of the patients which completed the therapy had no occurrence of congestive heart failure in the next 2 years.

To conclude, the enhanced external counterpulsation is an alternative for the treatment of chronic stable angina and could be beneficial for patients with heart failure. More investigations could shed light in the mechanisms and benefits of this noninvasive modality.

SURGERY

P934

The outcomes of surgery for heart failure in paediatric patients: the experience of a University in Turkey

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Purpose: Surgical therapy of end-stage heart failure in pediatric group (below 18 years) has some challenges such as shortage of organ donation and appropriate ventricular assist devices (VAD). Berlin Heart Excor, with its wide range of cannula and pump size, has been used in all body size and HeartWare HVAD in patients over 20 kg in weight. Herein, we present the outcomes of VAD implantation and heart transplantation performed in our center.

Methods: Between 2007 and 2014, 18 patients (5-16 years, 13 male) underwent heart transplantation and 14 patients (22 months-16 years, 10 male) underwent VAD implantation. The etiology was mainly dilated cardiomyopathy. In VAD group, Excor

was implanted in 9 patients and HeartWare in 5 patients. Batrial cuff technique has been used in all transplant patients.

Results: In hospital mortality after transplantation was 16%. All of deceased patients were bridged to transplantation. One patient was died at postoperative 6th month due to malign arrhythmia. In VAD group, in-hospital mortality was not observed. Short or long-term VAD for right ventricle was not needed. Nine VAD patients have been transplanted (64%) and three patients (21%) were expired at long-term period because of hemorrhagic stroke. Two patients are still on the waiting list while continuing their school life. In term of long-term complications, medulloblastom was observed in one patient and coronary allograft vasculopathy in another.

Conclusion: Within the structure of heart transplant program since 1998, surgical treatment of heart failure in pediatric patients was performed with satisfactory results in our center. New, small pump design and increasing organ donation are needed for better results in paediatric group.

P935

Two-dimensional speckle tracking echocardiography in heart transplant patients: two year follow up of right and left ventricular function

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Background: Evolution of left and right ventricular (LV and RV) function after heart transplantation (HT) has not been well described. Our objective was to evaluate the normal evolution of echocardiographic parameters of both ventricles along the first two years after HT.

Methods: We followed 28 HT recipients with serial echocardiograms for up to 2 years. Echocardiograms with AR $\geq 2R$ were excluded. LV global longitudinal strain (LV GLS) was analyzed by speckle tracking in 12 LV segments in 4 and 2 chamber views, and RV global longitudinal strain (RV GLS) was measured in 4 chamber view. Control group included 25 healthy volunteers.

Results: Eventhough LVEF was preserved, LV GLS was reduced in the early post-HT period ($-17.9 \pm 3.0\%$ in HT vs $-20.4 \pm 3.2\%$ in controls, $p=0.03$), improving progressively until its complete normalization two years after HT ($-19.7 \pm 3.8\%$ vs $-20.4 \pm 3.2\%$, $p=0.70$). TAPSE was impaired in the early post-HT period and increased progressively (12.3 ± 2.7 mm at baseline vs 18.7 ± 4.1 mm at 2-years, $p<0.001$). RV GLS rose during follow-up as well ($-17.2 \pm 3.8\%$ at baseline vs -23.0 ± 3.7 at 2 years, $p=0.001$), reaching normal values one year after HT.

Conclusion: In this series of HT recipients with uneventful postoperative course, LV and RV GLS values were significantly reduced early after HT and improved progressively until their complete normalization two and one year after HT, respectively. This is the first study to show a full recovery of LV and RV deformation parameters and offers "normal" ranges of strain values that could be useful for monitoring the evolution of HT recipients.

P936

Head-to head comparison of BNP/NT-proBNP and hsTnT/hsTnI after heart transplantation in the prediction of prognosis and heart function

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Purpose: Natriuretic peptides (BNP and NT-proBNP) are supposed to be of similar predictive power of heart function, whereas cardiac troponins (hsTnT and hsTnI) are the comparable biomarkers of myocardial injury. The aim of our work was to compare the prognostic power of both BNP/NT-proBNP and hsTnT/hsTnI in the early posttransplant period.

Methods: In the prospective study, a total of 115 patients after heart transplantation (HTx) was evaluated. The group consisted of 98 men and 17 women. Initial diagnoses were dilated cardiomyopathy in 60, end-stage ischemic heart disease in 45, hypertrophic cardiomyopathy in 5, restrictive cardiomyopathy in 4, congenital heart disease in 3, and other types of cardiomyopathy in 4 patients. The standard immunosuppressant therapy was used together with other medication according to the common posttransplant regimen. Blood samples were taken 30 days after HTx. 7 patients died during the first year after HTx. The left ventricular ejection fraction (LVEF, measured 12 months after HTx) and the 12-months and total survival (together with the survival interval) were selected as the main end-points. The Kruskal-Wallis test, ROC analysis, and the Kaplan-Meier survival analysis were used for statistical evaluation.

Results: Levels of BNP, hsTnI, and hsTnT (but not NT-proBNP) were significantly higher in patients with decreased LVEF (Kruskal-Wallis: $p=0.016$, $p=0.016$, and

Table 61492: Evolution of left and right ventricle

	Controls	Basal	3 months	6 months	1 year	2 years	ANOVA of the trend
LVEF	62.4±5.4	61.8 ±8.1	62.5±7.9	64.8± 8.4	63.7±7.3	63.2±6.4	0.598
LV GLS	-20.4±3.2	-17.9±3.0 **	-17.7± 3.9**	-17.8± 3.3**	-17.2± 2.1**	-19.7 ±3.8	0.180
TAPSE (mm)	23.1±4.3	12.3±2.7*	14.2 ±3.1*	16.0±3.7*	16.3±4.2*	18.7±4.1*	< 0.001
RV FAC	51.2±7.4	42.9±9.7*	45.0±8.4*	42.3±8.2*	41.4±8.2*	44.6±9.5*	0.35
RV GLS	-25.8 ± 4.3	-17.2±3.8*	-17.9±4.7*	-18.8±4.3*	-21.6±5.0	-23.0±3.7	<0.001
Free wall RVLS	- 31.4±6.3	- 18.2±4.5*	-21.1±3.5*	-23.5±5.9 *	- 26.1±9.4	- 28.2±6.3	<0.001
Septal RVLS	- 19.6±3.3	- 15.7±3.9*	-14.7±4.1 *	-15.2±2.8*	- 17.6±5.6	- 17.6±3.4	0.009

LV GLS: left ventricular global longitudinal strain. TAPSE: Tricuspid annular plane systolic excursion, RV: Right ventricle, FAC: Fractional area change, RV GLS: Right ventricular global longitudinal strain

$p=0.003$, respectively). AUC values (confidence interval, CI) for LVEF (cut-off of 50%) were: BNP 0.737 (0.636 - 0.822), NT-proBNP 0.685 (0.581 - 0.777), hsTnT 0.795 (0.700 - 0.872), and hsTnI 0.744 (0.643 - 0.828), respectively. There was no significant difference between AUCs of BNP and NT-proBNP and similarly no significant difference in AUCs of hsTnT and hsTnI. Only hsTnT was significantly higher in non-survivors (median 166.8 ng/l, interquartile range, IQR 107.0 - 275.8 ng/l) than in survivors (median 98.6 ng/l, IQR 63.0 - 137.3 ng/l) for 12-months survival (Kruskal-Wallis: $p=0.039$). Survival analysis (Kaplan-Meier) revealed significant predictive power of both hsTnI (cut-off 70 ng/l, $p<0.02$, HR 5.9, CI 1.5 - 22.7) and hsTnT (cut-off 145 ng/l, $p<0.01$, HR 6.5, CI 1.4 - 30.6), whereas the predictive power of both BNP and NT-proBNP was negligible.

Conclusions: Using the head-to-head comparison, the predictive power of BNP/NT-proBNP and hsTnT/hsTnI was similar in the prediction of heart function (assessed by EFLK at one year after HTx). However, worse outcome (survival) was predicted by troponins and not by natriuretic peptides.

P937

Pretransplant anti-HLA antibodies and clinical events after cardiac transplantation

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Introduction: Presence of antibodies against donorspecific human leukocyte antigens (DSA) has been associated with allograft rejection and coronary vasculopathy. The introduction of solid-phase Luminex techniques had facilitated antibody detection, but there is conflicting evidence between presence of DSA before cardiac transplantation (CTX) and morbidity of pts after CTX. The aim of this study was to evaluate the relationship between pretransplant antibodies against human leukocyte antigens (anti-HLA antibodies) and clinical events in CTX recipients.

Methods: Single center retrospective study included 264 from 321 CTX recipients operated since 04/2005 to 12/2012. All pts received induction therapy with ATG, initial maintenance immunosuppression consisted of CyA or tacrolimus, MMF and prednisone. FU was 19-66 (median 39) months. Cellular rejection (ACR) and antibody mediated rejection (AMR) were evaluated from endomyocardial biopsy (EMB), a total of 3270 EMB procedures was performed. ACR was graded according to Banff classification. AMR was evaluated by immunohistochemical technique using a rabbit antihuman C4d antibody (Ab). Occurrence of AMR, ACR, graft dysfunction (LVEF<40% by echo) and coronary vasculopathy (CAV-by selective CAG) were analysed since CTX until death, reTX or 12/2013. Presence of anti-HLA Abs was screened using assay against lymphocyte panel (PRA), the specificity of anti-HLA Abs was defined by LAB screen Mixed and Single antigen class I and class II beds (SAB). Univariate Cox regression models were used, the variables that were significant on univariate analysis were entered into multivariable Cox regression models.

Results: PRA during follow-up and immediately before CTX were positive in 38% resp. 19% pts. SAB demonstrated anti-HLA antibodies in 57 (22%) pts, which were in 28 (11%) DSA. Analysis of EMB specimens demonstrated AMR in 19 (7%) pts, 74 (28%) pts experienced 83 episodes of ACR grade Banff ≥ 2 , 48 (18%) pts died and 1 pt underwent retransplantation. The best predictors of AMR were the presence of DSA followed by peak PRA, both remained independent in multivariate analysis (RR 1.02, $p=0.07$ for PRA, RR 3.88, $p=0.007$ for DSA). Combination of peak PRA and pretransplant DSA provided additional predictive information. AMR was independent predictor of CAV development (RR 3.43, $p=0.004$) the strongest predictor of death or reTX was graft dysfunction (RR 3.60, $p<0.001$).

Conclusion: Pretransplant DSA and elevated peak PRA were independent predictors of AMR. Pts in high risk should be closely monitored for AMR, graft function and coronary vasculopathy development.

P938

Correlation of pre- and post-transplant factors with development of vasculopathy basing on intravascular ultrasound

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Introduction: Coronary allograft vasculopathy (CAV) remains one of the most serious complications after heart transplantation (HT) and the leading cause of death in patients, who survived more than a year after the operation. These findings suggest that coronary angiography (CAG) can be insensitive to early signs of atherosclerosis, this method is not feasible to early diagnose vasculopathy while IVUS can detect early changes in coronary arteries.

Objective: to reveal diagnostic criteria associated with early coronary lesion basing on IVUS.

Materials and Methods: The study included 40 patients, who survived more than 2 years after HT. All patients underwent transthoracic echocardiography (EchoCG), CAG and intravascular ultrasound (IVUS) of coronary vessels.

Results: In the course of CAG no signs of coronary stenosis were revealed. During IVUS we found changes in CA of various degrees. After cluster analysis of IVUS results grouped the patients basing on the combination of 2 indices: the total area of wall damage of the vessel and maximum stenosis area (table 1)

Analysis of pre- and post-transplant factors revealed that donors' age was 34.77 ± 1.03 years in group 1 and 40.00 ± 2.04 years in group 2 ($p=0.043$). The number of operations performed prior to HT was higher in group 2 - 28.5% ($p=0.008$). Donor-recipient matching frequency for HLA system was 2.36 times lower in the group 2 ($p=0.003$). In a year after HT the following echocardiographic parameters were significantly different: end systolic diameter (ESD) by 10.8% ($p=0.036$), end diastolic diameter (EDD) by 6.2% ($p=0.004$), end systolic volume (ESV) by 12.0% ($p=0.037$), end diastolic volume (EDV) by 11.3% ($p=0.012$) higher in the group with significant CA lesion.

Conclusions: IVUS-based significant CA lesion was found to be associated with the donors' age, number of operations performed prior to HT, the lower frequency matches with the HLA system. This group of patients showed significant improvement of echocardiographic parameters of left ventricular size and volume (ESD, EDD, ESV, EDV) within 12 months.

IVUS parameters in groups of patients

	group 1	group 2	p
Total area of vessel wall damage, mm ²	35.9±2.62	105.5±7.23	≤0.001
Maximum stenosis area, %	31.6±1.17	45.1±2.73	0.003

P939

Predictors of survival longer than 20 Years after heart transplantation

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Introduction and Objectives: The number of heart-transplant (HT) recipients exceeding 20 years of follow-up is steadily increasing. Identifying the predictors of prolonged survival could be of help in optimizing the selection of candidates for the low number of available donors.

Methods: Retrospective review of more than 100 variables of HT performed between 1984 and 1992. To identify predictors of 20-year survival, a logistic regression model was constructed using the covariates associated with survival ($p<0.1$) in the univariate analysis.

Results: A total of 39 patients who survived >20 years (26% of the 183 patients transplanted before 1992) were compared to 90 recipients from the same period that died between 1 and 20 years post-transplantation. In the comparison of the two groups, the following variables showed a statistically significant association with survival >20 years: lower age and lower body mass index of the recipient, dilated cardiomyopathy as pre-HT diagnosis, history of previous cardiac surgery and lower time of ischemia during HT. Other variables showed a trend but did not achieve statistical significance: weight disproportion >20% (if the donor was lighter than the recipient) and mechanical ventilation. Interestingly, variables not associated with lower survival in our series included older donor age, history of diabetes mellitus, serological risk of cytomegalovirus infection (negative recipient and positive donor) and number of rejections in the first year post-HT.

Logistic regression identified recipient age <45 years (odds ratio = 3.9; 95% confidence interval 1.6-9.7; P=.002) and idiopathic cardiomyopathy (odds ratio = 3; 95% confidence interval, 1.4-7.8; P=.012) as independent predictors for 20-year survival.

Conclusions: One fourth of all heart-transplant patients in our series survived >20 years with the same graft. Recipient age <45 years and idiopathic cardiomyopathy were associated with survival beyond 2 decades. These data may help decide donor allocation.

P940

Efficacy and safety of de novo and early use of extended-release tacrolimus (one daily dose) as compared to standard-release tacrolimus in heart transplantation

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Purpose: The aim of the present study was to evaluate the efficacy and safety of use of extended-release tacrolimus (ERT) (one daily dose) in de novo heart transplantation (HTx).

Methods: This was a multicenter, observational, retrospective study. Heart recipients aged more than 18 years who survived more than 1 week after HTx were included. We compared de novo immunosuppression with standard-release tacrolimus (SRT) (group 1; n = 42) with de novo use of ERT (group 2; n = 94) and with recipients with early conversion (< 6 months after HTx) from SRT to ERT (group 3; n = 44). One-year rejection incidence rate (IR) was the primary outcome parameter. One-year infection IR as well as safety evaluation (based on analytic and left ventricular function data) were the secondary outcome parameters. Adjusted Odds Ratios were assessed by a negative binomial model.

Results: Significant differences among groups were observed for preHTx diabetes, mechanical circulatory support, preHTx infection, donor age, CMV serology mismatch, use of statins and mean dose of prednisone. There were three deaths (1 patient in group 1 and 2 patients in group 2). The rejection IR were 0.48 (0.24-0.72) episodes per patient-years (group 1), 0.53 (0.34-0.71) episodes per patient-years (group 2) and 0.30 (0.10-0.49) episodes per patient-years (group 3). The Odds Ratio for rejection (adjusted for confounding variables) with respect to group 1 were 1.34 (0.59-3.07) for group 2 and 0.44 (0.14-1.34) for group 3 (P = 0.49 and 0.15, respectively). The infection IR were 1.42 (0.32-2.52) episodes per patient-years (group 1), 0.65 (0.44-0.86) episodes per patient-years (group 2) and 0.57 (0.35-0.79) episodes per patient-years (group 3). Adjusted Odds Ratio for infection (group 1 as reference) were 0.68 (0.34-1.37) for group 2 and 0.63 (0.27-1.45) for group 3 (p = 0.29 and 0.28, respectively). Left ventricular ejection fraction, renal function, blood cell counts, liver function tests, lipid profile and post-transplant new-onset diabetes did not show significant differences. There were not significant differences in tacrolimus trough levels over the first year after transplantation.

Conclusion: Both de novo and early use of ERT after HTx show similar efficacy and safety profiles to use of conventional SRT.

P941

Efficiency of the high sensitivity troponin to rule out acute rejection in heart transplant

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Endomyocardial biopsy (EMB) remains the technique of choice to rule out acute rejection (AR) in heart transplantation (HT). The noninvasive detection of AR remains

a challenge. A previous study analyzed the value of high-sensitivity troponin (TnT-hs) to rule out AR, observing that a concentration <17 ng/L allowed to rule out AR with a negative predictive value (NPV) 100%.

To confirm this high VPV prospectively, 71 new consecutive blood samples obtained on the day of the EMB were analyzed. Eight were excluded (EMB was not assessable for diagnosis). Four patients had AR 2R, none had levels <17 ng/L. In this study the value remains TnT-hs <17 ng/L as a cutoff to rule AR with NPV 100%.

To analyze whether the determination of TnT-hs is cost / effective the costs of analyzing the concentration of TnT-hs in the total sample (224 + 63 Current previous study) were calculated. Assuming a cost of 15 euros per determination, the total cost would be 4,305 euros.

Of the total number of 287 samples, 13% had hs-TnT values <17 ng/L, these would not be necessary for the realization of EMB to rule out AR. Assuming the price of EMB in 1028 euros, the cost of performing these 39 EMB would be 40,092 euros.

Therefore, although only it would be avoid the realization of 13% of scheduled EMB, the determination of TnT-hs routinely to all patients after heart transplantation would save 35,787 euros.

In Conclusion: 1) The high NVP for hs-TnT <17 ng/L is confirmed to rule out AR in heart transplant. 2) Despite the low percentage of patients with values <17 ng/L, the routine use of TnT-hs to rule out AR would mean better efficiency, lower cost and lower risk for posttransplant patient. 3) These results should be confirmed with a larger series of patients.

P942

CMV infection patterns in heart transplant recipients under tacrolimus therapy: is there any difference?

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Background: Cytomegalovirus (CMV) infection is associated with increased morbidity and mortality in patients undergoing heart transplantation (HT). Tacrolimus (FK) has advantages over Cyclosporine (CyA), with some benefit against rejection and no apparent increase in infections. However, in CMV infection, factors as precocity, severity and duration may be of importance and the effect of FK on these aspects is not well known.

Methods: In order to compare the pattern of CMV infections in a cohort of patients with FK vs. CyA, we included all patients undergoing HT from January 2008 to January 2014 (time period in which CyA was replaced by FK as routine IS in our center). Patients with the highest risk of CMV infection (donor serology positive, recipient negative) received prophylaxis with valganciclovir for 3 months. Elsewhere, preemptive therapy was used, based on frequent determinations of PCR against CMV. CMV infection (CMV Inf) was defined by positive PCR or histological presence of CMV. The presence of symptoms was considered disease (CMV Dis), that was severe when it required hospitalization and intravenous therapy (CMV SDis).

Results: We included 70 patients, 30 on FK and 40 on CyA, 14% of which belonged to the high risk CMV group. Thirty-nine patients showed CMV Inf (56%), with no differences between groups (53% on FK vs 58% on CyA, p = NS). However, infections in the FK group tended to be more important (CMV Dis 23% with FK vs 13% with CyA, p = 0.27 and CMV SDis 17% with FK vs. 5% with CyA, p = 0.11). If we exclude patients belonging to the high risk group that received prophylactic valganciclovir, differences were more pronounced, reaching statistical significance in the case of CMV SDis (17% in the FK group vs. 0% in the CyA group, p = 0.02).

Conclusions: Overall incidence of CMV infections was similar with CyA and FK. However, patients treated with FK showed more serious infections, especially when they received no prophylaxis. If confirmed, these findings support a universal CMV prophylaxis strategy in patients treated with FK irrespective of their serological status.

CMV infection: Tacrolimus vs ciclosporin

	Tacrolimus*	Ciclosporin*	p
Infection	55%	58%	NS
Disease	29%	9.7%	0.17
Severe disease	17%	0%	0.015

*:High risk profile group excluded

P943

The organ care system heart in high-risk transplantation with an adverse donor/recipient profile. A new standard of care?

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Purpose: A severe shortage of available donor organs has created an impetus to utilize extended criteria organs for heart transplantation. Whilst such attempts increase donor organ availability, they may result in an adverse donor-recipient risk profile. The TransMedics Organ Care System (OCS) allows preservation of the donor heart by perfusing the organ at 34°C in a beating state potentially reducing the detrimental effect of cold storage, and providing additional assessment options. We describe a single center experience with the OCS in high-risk heart transplant procedures.

Methods: Forty-eight hearts were transplanted using OCS between February 2013 and January 2015 as a method of donor heart assessment-preservation. Procedures were classified as high risk based on donor factors: transport time >2.5 hours with estimated ischemic time above 4 hours, left ventricular ejection fraction 40-50%, left ventricular hypertrophy (Interventricular septum in diastole ≥ 14 mm), donor cardiac arrest, donor death due to cocaine overdose, coronary artery disease; and/or recipient factors: mechanical circulatory support or elevated pulmonary vascular resistance.

Results: Donor and recipient age was 42 ± 11 years and 45 ± 12 years, respectively. Nine donors had reduced LVEF $\leq 50\%$, nine had LVH, two donors died due to cocaine overdoses, eleven had a previous cardiac arrest; 30 ± 9 min and six palpable coronary artery disease. N=23 recipients were bridged to transplant with a long-term ventricular assist device and another 3 with short-term ventricular support.

Allograft cold ischemic time was 83 ± 15 minutes and OCS perfusion time was 299 ± 87 minutes. The median Intensive Care Unit stay was 6,5(4;16) days. The overall 30-day survival with preserved allograft function was 89%. At follow up of 315 ± 224 days 81.2% of patients were alive with 95.4% of survival in the group of patients mechanically unsupported.

Conclusions: Use of the OCS is associated with markedly improved short term outcomes and transplant activity by allowing utilization of organs previously not considered suitable for transplantation and/or selection of higher risk recipients. Transplantation of hearts from extended criteria donors with moderate left ventricular dysfunction, prolonged donor cardiac arrest, left ventricular hypertrophy or coronary artery disease is safe and feasible with normothermic ex vivo preservation as a method of graft assessment pre-implantation and therefore should be considered for transplantation in times of donor shortage.

DISEASE MANAGEMENT PROGRAMMES

P944

Serial measurements of NT-ProBNP shorten the clinic visit time in heart failure clinics

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Purpose: Data about using serial measurements of natriuretic peptides to guide therapy in heart failure is controversial. We aimed to assess if these serial measurements could help to shorten the clinic visit time in a busy tertiary care heart failure clinic (HFC).

Methods: This study is a prospective case control study for all consecutive follow-up patients seen in the HFC in our tertiary care center between May and August 2014. Routine NT-ProBNP is requested for all patients seen in the HFC at least one day before the clinic visit. For logistic and compliance issues some patients fail to comply with this request. We compared patients who had NT-ProBNP measured (group I) to those who hadn't (group II) in terms of baseline characteristics and the duration of the visit and the interview with the physician running the clinic using stop-watch. We included follow-up visits only and new visits were excluded.

Results: We included 365 patients in our study. Group I (patients who had serial NT-ProBNP) were 260 patients and group II (patients who hadn't serial NT-ProBNP) were 105 patients. Patients in group I were younger (mean age 55 ± 11 vs 59 ± 12), more likely to be females (32% vs 27%), and more likely to be living in Riyadh city (58% vs 48%). The likelihood to have unplanned walk-in visit within the coming 1 month in group II was almost double that in group I (35% vs 18%) which could be explained by the need to have NT-ProBNP level or the need for more clinical assessment in the absence of NT-ProBNP in the current visit. The average clinic visit time was significantly lower in group I compared to group II (12 ± 8 vs 18 ± 12 minutes).

Conclusions: Serial measurements of NT-ProBNP shorten the clinic visit time and decreases significantly the need for un-planned walk-in visits in busy heart failure clinics. Serial NT-ProBNP measurements may be a cost effective and can add to the controversial benefits of BNP guided heart failure therapy.

P945

Lack of evidence based diagnosis and management strategies in those not attending heart failure specialist services in the community

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Purpose: This is an ongoing study to determine the characteristics of patients with heart failure in the primary care setting who are not undergoing active follow up with a heart failure service.

Method: A random selection of patients coded as having heart failure from GP practices in the Republic of Ireland were reviewed using a standard pro-forma by the practice nurse and GP. Patients were included if they were not currently attending a heart failure service. Data on demographics, heart failure diagnosis, self care, medications and healthcare utilization was recorded.

Results: To date 76 patients from 10 GP practices were recruited. Mean age was 78.6 years and 59% were female. 67% had an echocardiogram in the past and 51% had been reviewed by a cardiologist previously. Of those with an echocardiogram report 27% had an ejection fraction <50%. 59% were currently attending their GP only. 12% of patients monitored their own weight but only 4% were able to identify a significant weight change. 75% were NYHA class I or II. Of patient with HF-REF 76.9% were on ACE inhibitor or ARB a, 76.9% were on beta-blocker and 23.1% were on a MRA. 94.4% of patients with atrial fibrillation were on an anticoagulant. Mean BP was 130/74 and mean heart rate as 74. The average number of general practitioner visits was 12 per patient in the previous 12 months, 31 patients had 48 ED attendances 25 patients had 34 emergency hospital admissions and 11 patients had 13 emergency HF admissions

Conclusion: The majority of patients with heart failure in the community are being cared for by the general practitioner alone. There is poor self care knowledge among this group. There is underuse of echocardiography and evidence based therapies with high rates of healthcare utilization. Strategies to improve management of this patient group are required.

P946

Health literacy, treatment adherence and optimal method to teach patients with heart failure

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Purpose of the study was to assess the level of health literacy and treatment adherence in patients rehospitalized for worsening heart failure, to evaluate the effectiveness of different teaching methods in these patients.

Methods: 120 patients with heart failure (NYHA II - IV, mean age 62.8 ± 9.8) were randomized to three (the 1st, the 2nd and control) groups. In the 1st group patients were trained on the individual programs that took into account the initial level of patients' health literacy, patients from the 2nd group attended lectures, patients from the control group were not additionally trained. At study baseline and after 6 months patients' health literacy was assessed by specially created questionnaire, treatment adherence was evaluated by the Morisky - Green test.

Results: Initially groups of patients were comparable on age, sex, severity and duration of heart failure, presence of comorbidity and treatment adherence. At study baseline 52.5% patients had low level of health literacy. Treatment adherence assessed at study baseline was not sufficient. 55% patients from the 1st group, 57.5% from the 2nd group and 47.5% from control group were non-adherent. After training and 6 months follow-up period 42.5% patients from the 1st group ($p < 0.001$), 22.5% from the 2nd group ($p > 0.05$) and 5% from control group ($p > 0.05$) improved their treatment adherence. During follow-up period 17.5% patients from the 1st group, 37.5% from the 2nd group and 55% from control group sometimes forgot to take their medication ($\chi^2 = 12,13, p = 0,002$).

Conclusions: Patients rehospitalized for worsening heart failure had not sufficient level of health literacy and treatment adherence. Individual self-control and self-care skills training programs that took into account the initial level of patient health literacy in heart failure were more effective than group sessions, and could improve patient adherence to treatment.

P947

Role of depression in effectiveness of disease management programs

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Background: Congestive heart failure (CHF) is frequently associated with depression. Presence of depression leads to poorer clinical outcome and decreased adherence. Disease Management Programs (DMP) were shown to reduce hospital readmission and clinical outcomes in HF patients. However the depression influence on the patients responsiveness to the DMP and relationship between DMP and depression course are not clear yet.

Objective: To evaluate the effectiveness DMP in HF patients with depressive symptoms and impact of DMP on depression severity.

Methods: We analyzed the data from the large prospective, randomized, parallel group trial which investigate the effect of DMP on patient's outcome (Congestive Heart Failure: A multidisciplinary Non-pharmacological approach for Changing in re-hospitalisation and prognosis in patients (CHANCE)). Disease Management Program consisted on structured education and regular follow up (phone calls). Patients' assessment of depression were determined at baseline and then on 24 and 48 weeks

by the Russian version of the Hospital Anxiety and Depression Scale (HADS). Primary end-point was composite of CV mortality and HF readmission.

Results: Among 745 patients, included in the final report, evaluation of the depressive symptoms at baseline was performed in 737 patients (34,6% women, III-IV NYHA FC, average age - $62,7 \pm 10,9$) Clinically relevant depression (HADS > 10) was found in 272 (37%) of patients. Among depressed patient where were more women (45,1%, non-depressed - 28,3% $p < 0,001$). Depressed patients were older than non depressed ($64,9 \pm 10,6$ and $61,5 \pm 10,9$, $p < 0,001$) respectively. They also had more advanced NYHA FC. Patient health status and medications did not significantly differ between Active care and Control groups. DM programs had a positive impact in both non-depressed and depressed patients. In active care group number of patient with clinically relevant depression (HADS > 10) was decreased by 19,7% in comparison to control group ($p < 0,001$). During 12 months of follow-up, the primary end point (combine CV mortality and HF readmission) was decreased by 38% in overall active care group ($p < 0,001$). In non depressed patients subgroup RRR was 0,37 (95% confidence interval: 0,24 to 0,50). In patients with depression DM programs resulted in poorer outcome - RRR 0,28 (95% confidence interval: from 0,10 to 0,42).

Conclusions: DMP was shown to reduce depression severity in patient with CHF. However clinically relevant depression leads to poorer response on DMP.

P948

Long term follow up of implementation of a heart failure unit at a university hospital

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Purpose: Heart Failure (HF) prevalence shows an increasing trend towards becoming a major concern in health care systems. HF units, with specific outpatient clinics and interdisciplinary protocols, are a key component in the management of this growing problem. The present report summarise and evaluate the results of our unit after four years of implementation.

Methods: From the specific outpatient clinics, we assessed patient features, such as age, sex, follow up time, HF etiology, NYHA functional class, left ventricle ejection fraction (LVEF), and treatment to provide in the first visit and follow up, as well as mortality, and number of hospitalizations in these patients. A descriptive analysis of these variables was done.

Results: 141 patients were seen in the four first years of the outpatient clinic. Our patients had an average age of 59.6 years (CI 57.2 - 62), 75.2% male sex. Average follow up time was 856.5 days (CI 802.2 - 910.9). Diabetes Mellitus was present in 40.4% of patients, hypertension in 52.5%, and dyslipidemia in 29.1%. Current and former smokers accounted for 9.2% and 49.6% of patients respectively. Important symptoms of heart failure were found in most patients, with II or worse NYHA class in 77.3% of patients. Median LVEF was 34% (CI 31.6 - 36.5), 63.8% of patients had severe systolic dysfunction (LVEF < 35%). The most frequent etiology was ischemic dilated cardiomyopathy (36.9%), followed by idiopathic dilated cardiomyopathy (31.9%), enolic dilated cardiomyopathy (5.7%), other causes of dilated cardiomyopathy (13.5%), and other non-dilated causes (11.3%). 64.5% of the patients were in sinus rhythm and 31.2% were in atrial fibrillation. Regarding treatment, 9% received CRT. 22% received ICD. 87.2% received either an ACEI or ARB (62.4% and 24.8% respectively), 90.7% were treated with beta blockers, 13.5% with high power statins and 20.6% with low power statins, 65.2% of patients received anti-aldosterone agents. General mortality was 16.3%, mortality was higher in patients with III or IV vs I or II NYHA class (34.3% vs 10.6% $p < 0.002$), also the III or IV NYHA class patients showed a nonsignificant higher trend towards having a first readmission, after follow up start, vs I or II NYHA class patients (54.2% vs 38% $p < 0.07$).

Conclusion: Long term follow up of patients with heart failure reinforce the essential need of specific units for them, because there is room for improvement in treatment compliance according to current guidelines, as well as with participation from other medical specialties. There is a need for further investigation in specific therapies for patients at higher risk.

P949

Management of patients admitted by loss of consciousness in a central hospital

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Syncope is loss of consciousness (LC) due to transient cerebral hypoperfusion. It is characterized by rapid onset, short duration and full recovery. The differential diagnosis between other causes of LC requires clinical evaluation and diagnostic tests.

Methods: Retrospectively we analyze the management of patients admitted for LC, after initial evaluation in the emergency service (ES), during 2013 (12 months).

Results: There were admitted 168 patients, with a mean of 71 ± 16 years old and 61% were male. The mean timing of hospital stayed was 11 ± 10 days.

The majority of patients had a single episode LC (71%); 20% of patients had associated trauma and seizures in 9%.

Electrocardiogram (ECG) was performed in 96% of patients. The initial ECG was useful for diagnosis in 10% of patients (Mobitz II AV block in 20% of patients and 80% with complete AV block); 23% performed 24-Holter monitoring and having been documented additional Mobitz II AV block in 5%; 11% performed carotid sinus massage (significantly positive in 28%); 66% echocardiography (with relevant changes in 15% of the patients); 16% tilt test (positive and with LC reproduction in 54%); 8% electrophysiological study (38% with relevant changes); 11% coronary angiography (44% with changes but none for the LC); 3% exercise test (25% with changes but none for the LC). Laboratory test were performed in 99%, 60% patients performed chest X-ray, 54% brain CT (with changes in 31%); 3% brain MRI (50% with changes); 26% electroencephalogram (EEG) with changes in 24% and 17% carotid doppler (with relevant changes in 18% but none responsible for the LC).

The presence of previous syncope episodes was a predictor of performing tilt test ($p = 0.038$); and the presence of seizures for EEG ($p = 0.003$).

Reflex syncope was diagnosis in 26% (23% situational syncope; 68% vasovagal syncope; 9% carotid sinus hypersensitivity) of patients; Cardiogenic syncope in 34%; Orthostatic hypotension in 2%. Unexplained syncope causes for LC remain in 22% of patients.

Conclusion: Our study points that in addition to the initial clinical evaluation in the ES, the rational use of several exams should be based on the guidelines of the European Society of Cardiology and is essential to the best management and differential diagnostic of LC.

P950

Review of international heart failure guidelines and their use of cardiac output measurements to guide heart failure management

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Background: The control and improvement of cardiac failure can be difficult. Cardiac failure is expressed in deranged haemodynamics, yet the monitoring of circulatory parameters is uncommon. The therapeutic objective of managing the failing heart is the improvement of cardiac contractility, and therefore increasing stroke volume (SV) and cardiac output (CO) by the use of diuretics and inotropes. While arterial blood pressure is the current haemodynamic parameter of choice, it is an insensitive variable that does not directly respond to changes in SV, and sympathetically regulated changes in vascular tone. Direct measurement of SV, CO and cardiac inotropy (SMII) derived from non-invasive monitoring would improve assessment of cardiac function and enable a tailored approach to treatment of heart failure.

Methods: Five current international heart failure guidelines were reviewed. The number of pages and words in each document was determined by using the "word count" function in Microsoft word. Specific searches for words was undertaken including cardiac output, CO, cardiac index, CI stroke volume, SV and inotropy. The number of appearances in the document for the abbreviations CO, CI and SV were verified to ensure that the abbreviation correlated with the correct term.

Results: A total of 282 pages of cardiac failure guidelines from 5 different international bodies mentioned cardiac output 44 times within the guideline. Cardiac index, stroke volume and inotropy were mentioned a total of 1, 10 and 0 times respectively. No guidelines suggested using these parameters to guide treatment.

Conclusion: The use of measurement of CO, SV, or and SMII would provide physiological guidance of the treatment of heart failure and would enable the delivery of a more individualised therapy not provided by current management guidelines and may improve clinical outcomes.

P951

The first experience of using the russian version of the european heart failure self-care behaviour scale

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Background: The promotion of self-care in patients with heart failure (HF) is considered as an important strategy for preventing the deterioration of HF. The 9-item European Heart Failure Self-care Behaviour Scale (EHFScBS) is a well validated tool for the assessment of self-care in patients with HF. The 9-item EHFScBS was tested in some European countries, but not in Russia. The aim of our study was to test the Russian version of the 9-item EHFScBS in Russian patients with decompensated HF and describe relationships with clinical and demographic variables.

Methods: In preparation for this study, the 9-item EHFScBS was translated into the Russian language. Then the Russian version was back-translated into the English language. The back-translated version was checked for any differences

Table 60431.

Guideline	year of publication	Pages	Word count	Cardiac Output	CO	Cardiac Index	CI	Stroke Volume	SV	Inotropy
Australian	2011	86	41013	7	0	0	0	2	0	0
ACC	2009	41	36273	11	0	0	0	1	0	0
European	2012	61	48027	4	0	1	0	7	0	0
Latin American	2005	45	38592	17	5	0	0	0	0	0
NICE	2010	49	9262	0	0	0	0	0	0	0
Total		282	173167	39	5	1	0	10	0	0

in meaning with the original version by a professional translator and the original developers of the scale. No differences in meaning were detected. After that the 9-item EHfScBS was tested in 30 patients (mean age 57 ± 1 years, 60% male) with decompensated HF (56% of ischemic etiology), NYHA II-IV (mean 3.1 ± 0.2). All patients were evaluated by physicians using the 9-item EHfScBS at the first visit to the outpatient department and then 1 month later. In accordance with the Russian HF guidelines all patients were educated in general information about HF, symptoms, principles of self-care, diet, medical therapy and physical activity.

Results: The mean score of the 9-item EHfScBS was 22.9 ± 1.6 . There were no correlations between the total score and age, gender or etiology of HF. 1 month later the mean score of the 9-item EHfScBS was reduced to 16.8 ± 0.9 ($p < 0.01$), meaning an improved self-care behavior. The items on which patients showed most improvement were "contacts with doctor, when patient had a weight gain of more than 2 kg in a week" (-51% , $p < 0.001$), "everyday weight control" (-34% , $p < 0.001$) and "contacts with doctor or nurse in cases when edema increased" (-33% , $p < 0.001$).

Conclusions: The Russian version of the 9-item EHfScBS was found to be an easy and rapid self-administered tool to assess the self-care behavior in HF patients and did not need any training program for users.

P952

Seamless heart failure care, a dutch experience

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Purpose: Secondary and tertiary heart failure care in the Netherlands have been relatively well organized using heart failure clinics. However optimizing heart failure care, the pending rise in number of heart failure patients and the political demands to share care with primary care givers requests a different organization. Therefore a specific program has been developed in the region of Leiderdorp in the Netherlands to reach this goal.

Methods: First of all questionnaires were sent to 75 general practitioners (GP's) and 60 patients from the heart failure clinic in the Leiderdorp region. Results of these questionnaires were used by an established working group involving GP's, cardiologists and heart failure nurse practitioners from the Rijnland hospital to set up a program for seamless heart failure care across all lines of care.

Results: The working group established four protocols in total for the care of heart failure patients after evaluation of the bottlenecks in this process of care. This included protocols ranging from referral of patients being suspected of having heart failure (1), a protocol involving all diagnostic and therapeutic steps for patients being diagnosed with heart failure (2). Third, protocols for long-term patient follow-up involving either follow-up at the heart failure clinic or follow-up delivered by the GP (4). Finally a separate protocol was written involving the care for the patient with endstage heart failure (4). Tertiary heart failure care was guaranteed by including the Cardiology department of Leiden in the program. In every part of the program it is very clear for both caregivers and patients who is responsible for delivering the heart failure care at the specific stage of the disease process.

Conclusion: For the first time in the Netherlands a seamless heart failure care program has been organized constructing the care of heart failure patients across all lines of care. Goal of this program is optimal heart failure care at the right time and the right place. The program itself has been adopted by the Dutch cardiology society (NVVC) as the model to organize heart failure care across the Netherlands. Data to evaluate the results of this program will be collected and presented in the near future.

P953

Post discharge care in heart failure (PDC-HF): an analysis and comparison of workload in HFpEF and HFrEF

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Background: Disease management programmes (DMPs) are advocated to help steward patients surviving ADHF admission through the vulnerable immediate post discharge period. However, little information is available on the clinical workload of this outpatient approach to care, data that is important to units looking at how best to initiate this process. In addition patients with HFpEF form an increasing fraction of this population. Historically this population were not routinely enrolled in DMP and relative workload, when compared to those with HFrEF, is unknown. We report on the workload associated with a cardiologist-led DMP.

Methods: All patients admitted with a primary diagnosis of HF were enrolled in a comprehensive DMP encompassing in-patient & out-patient care. Workload was viewed through an assessment of post discharge clinic visits (scheduled & unscheduled), telephonic contact & medication changes as assessed by diuretic use, indicative of clinical stability in both HF groups.

Results: 1292 patients (male 58.7%;74.5yrs) surviving admission for HF were enrolled. Total clinical visit time/patient was 132 mins, with HFpEF having slightly more clinic time than HFrEF ($p > 0.05$). Total number of scheduled visits/patient over the 3 months of DMP was 3.4, with unscheduled of 0.5 visits/patient. Overall, HFpEF had a slightly decreased frequency of unscheduled visits when compared to HFrEF (0.48/patient vs. 0.5/patient, $p > 0.05$). Total telephone calls/patient over the 3 month programme was 12 (totally an average of 55mins/patient), with two inbound calls/patient and ten outbound calls/patient. There was no difference in call frequency or duration between HFrEF and HFpEF. As anticipated, there was a greater number of medication changes (ACEI/ARB and B blockers) in HFrEF patients when compared with HFpEF group (ACEI/ARB: 0.44 vs 0.64; BB: 0.39 vs 0.77; both $p < 0.05$). Finally, mean number of diuretic changes in 3 months post-discharge was 0.73, with 11.8% having two diuretic changes & 7.1% had more than two diuretic changes, again with no difference in diuretic changes between HFrEF & HFpEF. This work-intensive approach to post-discharge management likely contributes to the low event rates at 3 months, one & three years post discharge for HF readmission (7.3%, 14.3% and 25.5%) & mortality (3.8%, 15.3% and 37.7%).

Conclusion: This workload associated with post-discharge DMP care while significant, is similar for those with both HFrEF & HFpEF. Given the rapid growth in this patient population, this data should be used to inform appropriate resource organisation for establishing or evolving DMP structures.

HAEMODYNAMICS / CORONARY AND PERIPHERAL CIRCULATION

P954

Pathological orthostatic blood pressure response is a predictor of cardiac target organ damage

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Purpose: We have previously shown that prevalent orthostatic hypotension (OH) prospectively increases the risk of incident heart failure and cardiovascular disease (CVD) as well as all-cause mortality in a population-based large cohort. Left ventricular hypertrophy (LVH) is a well-established risk factor for incident CVD and all-cause mortality, whereas decreased left ventricle volume has been associated with OH in small echocardiographic surveys. In this study we aimed to investigate whether OH was prospectively associated with structural cardiac anomalies (target organ damage) as measured by echocardiography.

Methods: In a re-examination of the Malmö Preventive Project (MPP) a subset of 974 non-diabetic individuals (mean age, 67 years; 29% women) were examined with echocardiography. The association of increased left ventricular mass, pathological cardiac chamber volumes, echocardiographic parameters of systolic and diastolic dysfunction in relation to baseline OH, defined as decrease in systolic ≥ 20 mm Hg and/or diastolic blood pressure ≥ 10 mm Hg upon standing, was studied after a mean follow-up period of 23 years. Cox regression was used to adjust for covariates.

Results: Among re-examined MPP participants, 40 (4.1%) met OH criteria at baseline examination. In multivariable Cox proportional hazard models, taking conventional risk factors into account, OH was significantly associated with increased risk of developing LVH and decreased right chamber volume (hazard ratio (HR): 1.93, 1.01-3.72, and 1.75, 1.19-2.57, respectively). No significant associations were seen between OH and pathological atrial chamber volumes, left ventricular volumes or measurements indicating systolic or diastolic left ventricular dysfunction.

Conclusions: The presence of OH among middle-aged adults predicts development of structural cardiac changes such as LVH and declining right chamber volume independently of conventional risk factors. These findings might serve as a mechanistic explanation behind the previously observed epidemiological findings indicating increased risk of future CVD and death among individuals with OH.

P955

Global longitudinal two-dimensional systolic strain is associated with hemodynamic alterations in arterial hypertension

The study was supported by the Ministry of Science and Higher Education/Military Institute of Medicine, Warsaw, Poland (grant no 148/WIMP Krzesinski¹; B Uzieblo-Zyczkowska¹; G Gielerak¹; A Stanczyk¹; M Malgorzata¹; K Piotrowicz¹

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Purpose: Arterial hypertension can effect in progressive deterioration of the left ventricular (LV) performance. Global longitudinal systolic strain (GLSS) measured by echocardiography is valuable in the assessment of LV function. The aim of this study was to estimate the relation of GLSS with other echocardiographic features and central/systemic hemodynamics assessed by applanation tonometry (AT) and impedance cardiography (ICG).

Methods: This study involved 125 patients (mean age: 45.6 years) with AH, recruited to the clinical trial NCT01996085. The clinical evaluation included i.e.: 1/ echocardiographic assessment of LV ejection fraction (LVEF), indices of the LV diastolic function (E/A - mitral flow early (E) and late (A) phase ratio; e' - mitral septal annulus early diastolic velocity, E/e' ratio) and GLSS (in analysis reversed to positive values), 2/ AT (CPP - central pulse pressure; AI - augmentation index), 3/ ICG (SVRI - systemic vascular resistance index; HR - heart rate; SI - stroke index, CI - cardiac index, HI - Heather index; VI - velocity index). The statistical analysis included interquartile comparison in subgroups of GLSS <16.3% (Q1), 16.3-17.8% (Q2), 17.9-19.9% (Q3), >19.9% (Q4) and the assessment of correlation between GLSS and the above mentioned hemodynamics.

Results: The mean GLSS in the study group was 18.1 ± 2.8% (range: 10.3-25.2%). Hypertensives with more impaired GLSS (Q1 vs Q4) characterized with: 1/ worse diastolic function (e': 7.9 vs 11.2 cm/s, p < 0.00001; E/e': 8.0 vs 7.0, p = 0.014); 2/ slightly lower LVEF (64.5 vs 66.7%, p = 0.028), 3/ higher afterload (SVRI: 2459 vs. 2107 dyn*s/m²/cm⁵; p = 0.008) and 4/ lower impedance indices of LV performance (CI: 3.26 vs 3.64 l/min/m²; p = 0.007; VI: 41.5 vs 56.8 1000*Ohm/s; p = 0.0001; HI: 11.4 vs 14.8 Ohm*s²; p = 0.003). LV diastolic function was impaired in 48.4% Q1 subjects compared to none in Q4 (p = 0.00009). No relevant differences in gender, age, blood pressure, left ventricular mass index, E/A, left atrium and ventricle dimensions, SI, HR, CPP and AI were identified.

Correlation analysis revealed significant associations between GLSS and LVEF (r = 0.23; p = 0.010), e' (r = 0.44; p < 0.00001); E/e' (r = -0.19; p = 0.035); CI (r = 0.27; p = 0.002), SVRI (r = -0.30; p = 0.008), VI (r = 0.32; p = 0.003), HI (r = 0.32; p = 0.003).

Conclusions: In patients with essential hypertension impaired GLSS was strongly related to LV diastolic dysfunction, increased afterload and altered impedance indices of LV performance. ICG-derived hemodynamics revealed to be promising markers of early LV dysfunction.

P956

Thoracic fluid content is related with echocardiographic abnormalities and N-terminal pro-brain natriuretic peptide concentration in stable chronic heart failure

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Purpose: Chronic heart failure (CHF) is associated with complex hemodynamic disturbances and heart remodelling. Increased thoracic fluid content (TFC), evaluated noninvasively by impedance cardiography (ICG), revealed to be useful in the prognosis of HF deterioration. The aim of the study was to evaluate the relation between TFC, echocardiographic abnormalities and N-terminal pro-brain natriuretic peptide (NT-proBNP) in CHF patients.

Methods: In 150 stable CHF patients with left ventricular ejection fraction (LVEF) ≤ 45% (NYHA class I-III; mean LVEF 32.9%; mean age: 63.5 years) clinical assessment, including echocardiography (ECHO), rest supine ICG and NT-proBNP concentration, was performed. The analysis focused on the relation between TFC and:

LVEF, left ventricular end-systolic (LVESD) and diastolic diameter (LVEDD), left atrium diameter (LA), right ventricular end-diastolic diameter (RVEDD), right ventricular systolic pressure (RVSP), pulmonary artery diameter (PA), pulmonary valve acceleration time (PV AccT) and NT-proBNP concentration.

Results: Patients with higher TFC (>35 1/kOhm), in comparison with those with lower TFC (<35 1/kOhm), characterized with: significantly higher prevalence of NYHA class III (50% vs. 25.2%; p = 0.010), lower LVEF (30.4 vs. 33.7%; p = 0.043), higher LA (4.96 vs 4.69 cm; p = 0.041), RVEDD (3.27 vs 3.14 cm; p = 0.054), RVSP (45.7 vs 37.4 mmHg; p = 0.002), shorter PV AccT (96.3 vs. 107.2 ms; p = 0.0033) and higher NT-proBNP concentration (2010.8 vs. 1333.1 ng/ml; p = 0.016). Thoracic fluid content correlated significantly with RVEDD (r = 0.30; p = 0.0003), RVSP (r = 0.20; p = 0.023), PA (r = 0.23; p = 0.006), PV AccT (r = 0.17; p = 0.048) and NT-proBNP (r = 0.23; p = 0.006) but not with LVESD (r = 0.12; ns) and LVEDD (r = 0.11; ns).

Conclusions: In our study TFC positively related to NT-proBNP concentration and corresponded with LVEF, echocardiographic characteristics of left atrium, right ventricle and pulmonary circulation. Our results suggest that in patients with stable heart failure TFC can be useful in the evaluation of the circulatory alterations associated with chronic pulmonary congestion.

P957

Impedance diastolic to systolic wave (O/C) ratio is associated with diastolic left ventricular-atrial interaction in patients with essential hypertension

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Purpose: Impedance cardiography (ICG) revealed to be a useful tool in cardiovascular diagnostics but still little is known about the clinical meaning of diastolic to systolic wave (O/C) ratio in hypertensive patients. High O/C ratio is related to cardiac insufficiency and increased pulmonary pressure. However, big O wave in younger subjects was also observed.

The aim of this study was to estimate the relation between O/C ratio and echocardiographic features of left ventricular diastolic function in patients with essential hypertension.

Methods: This study involved 144 patients (mean age: 45.2 years) with untreated AH, recruited to the clinical trial. We analysed the correlations of clinical variables (age, SBR, DBP, BMI, HR) and mean O/C ratio, derived from 10-minute rest ICG, together with echocardiographic features of left ventricular (LV) diastolic function (E - mitral flow early phase velocity, A - mitral flow late phase velocity, E/A ratio; e' - mitral septal annulus early diastolic velocity, E/e' ratio; IVRT - isovolumic relaxation time).

Results: The mean O/C ratio in the study group was 38.0 ± 13.4% (range: 8.7-77.3%) and was significantly lower in patients with LV diastolic dysfunction (all with impaired relaxation diastolic filling pattern): 32.6 ± 14.1 vs 39.8 ± 12.7%; p = 0.001.

Correlation analysis revealed significant association of O/C ratio with: E (r = 0.40; p < 0.001), A (r = -0.22; p < 0.05), E/A (r = 0.44; p < 0.001); e' (r = 0.28; p < 0.01); IVRT (r = -0.45; p < 0.001) and insignificant with E/e' (r = 0.19, ns). The only clinical variable better correlated with echocardiographic variables was age (vs E: r = -0.39; p < 0.001; A: r = 0.43; p < 0.001; E/A: r = -0.56; p < 0.001; e': r = -0.36, p < 0.001; IVRT r = 0.45; p < 0.001 and E/e': r = -0.06, ns).

Conclusions: In patients with normal and mildly impaired LV diastolic function impedance O/C ratio is related with echocardiographic diastolic indices, especially mitral flow parameters (E, A, E/A) and isovolumic relaxation (IVRT). The distinctive association with mitral flow pattern (E, A, E/A) suggests that O/C ratio, lower in patients with impaired LV relaxation, can rise in those with more advanced grades of LVD dysfunction (pseudonormal and restrictive fillings). It should be investigated in further studies.

METABOLISM / DIABETES MELLITUS

P958

Presence of accompanying diabetes mellitus is associated with preserved right heart functions among HFREF outpatients

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Purpose: Heart failure (HF) is a complex syndrome with several dimensions. Turkish Research Team-HF (TREAT-HF) is a network which has been undertaking multicentric observational cohort studies in HF among HF centers. Diabetes mellitus (DM) is a frequent accompaniment of HF

Methods: Combined data from derivation and validation cohorts of TREAT-HF network were presented.

Results: There were 585 males and 242 females in the combined cohort (n = 827). Mean age was 61 ± 13.8 years with a mean EF of $32 \pm 9\%$. Patients with DM were older (63.6 ± 10.5 vs. 60.3 ± 14.4 years, $p = 0.001$) than patients without DM. Females were more prevalent among HFREF patients with DM compared to HFREF patients without DM (36.6% vs 27.5%, $p = 0.022$). Although, they were similar with regard to left ventricular EF and left heart chamber sizes, right ventricular and right atrial dilatation were less frequent and TAPSE was higher in patients with DM compared to patients without DM (Table 1). Of note, COPD was more prevalent among patients with DM compared to patients without DM (16.5% vs 7.7%, $p = 0.001$). Furthermore, median NTproBNP levels and creatinine levels were higher in patients with DM than in patients without DM (1275 vs 708 pg/ml, $p = 0.006$; 1.1 vs 1.05 mg/dl, $p = 0.044$ respectively).

Conclusion: In this large sample of HFREF outpatients, presence of DM was associated with relatively preserved right heart functions despite higher BNP and more frequent COPD.

Table 1

	DM(+)	DM(-)	p
Presence of right ventricular dilatation	27.6%	32.5%	0.004
Presence of right atrial dilatation	34.2%	42.5%	0.07
TAPSE (mm)	17.3 ± 5.8	12.1 ± 9.3	0.001

P959

Correlation between heart diastolic dysfunction and endothelial dysfunction in the combination of essential hypertension and type 2 diabetes

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Essential hypertension (EH) and type 2 diabetes (DM2) have a number of common mechanisms of progression, which include insulin resistance (IR). According to researchers, the link between IR and cardio-vascular diseases is endothelial dysfunction (ED). At the same time, the mechanisms of cardiac remodeling with preserved systolic function in patients with comorbidity remain still not studied enough. The aim of the study was to establish the correlation between heart diastolic dysfunction (DD) and ED in comorbid pathology - EH and DM2. We examined 120 patients with EH stage II, grade 2, heart failure I-II functional classes and DM2 moderate, subcompensated aged from 45 to 60 years old. The control group consisted of 20 healthy individuals with no EH and DM2, as they were excluded on the basis of the complex clinical and instrumental examinations.

Methods: Echocardiography evaluation of mitral diastolic blood flow and tissue Doppler spectral modes, reactive hyperemia, color Doppler mapping, enzyme immunoassay. As a result, we have established correlation indicators characterizing DD (average pulmonary artery pressure (PAP) on Kitabatake, the maximum speed of the early filling (E) of the left ventricle (LV) in the spectral Doppler mode, the maximum speed of the ring of the mitral valve during early filling LV (e) in the tissue Doppler mode, the ratio of E/e) with parameters ED (intima-media thickness (IMT) of the carotid artery (CA), pulse wave velocity in the abdominal aorta (PWV AA), endothelium-dependent brachial artery vasodilation (EDVD)), with indicators of prooxidant system - diene conjugates (DC), malondialdehyde (MDA), the factors of antioxidant protection - superoxide dismutase (SOD), catalase (Cat). PAP directly correlated with IMT CA ($r = 0.40$, $p < 0.05$), PWV AA ($r = 0.38$, $p < 0.05$), MDA ($r = 0.44$, $p < 0.01$), DC ($r = 0.41$, $p < 0.05$) and inversely correlated with EDVD ($r = -0.39$, $p < 0.05$) and Cat ($r = -0.42$, $p < 0.05$). As the average force we have established direct correlation parameters "E" and "e" with EDVD, Cat and SOD, as well as their inverse average degree of correlation with IMT CA, PWV AA, MDA and DC. Integrated indicator of E/e, characterising diastolic function, is directly correlated with an index of antioxidant protection - SOD ($r = 0.33$, $p < 0.05$), which in turn is correlated with EDVD ($r = 0.40$, $p < 0.05$).

Conclusions: The progression of diastolic and endothelial dysfunction in comorbid pathology - EH and DM2, is closely correlated, what is evident from the established correlation.

P960

Impairment of segmental contractility of the left ventricle in patients with history of coronary heart disease against a background of diabetes mellitus

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Purpose: This study establishes criteria regarding myocardial viability (MV) in patients with unstable angina (UA), against a background of postinfarction atherosclerosis by detecting changes in standard echocardiographic parameters and regional left ventricular (LV) myocardial contractility.

Methods: The study involved 27 patients with coronary heart disease (CHD) and diabetes mellitus (DM) type 2 who were hospitalized for UA. Patients were divided into 2 groups: group I - 8 (29.62%) patients with MV (hibernating) and group II - 19 (59.37%) patients with myocardial non-viability (non-hibernating).

MV was improved LV ejection fraction (EF) improvement of $\geq 5\%$ between the first observation and 14 day was observed. For a more detailed assessment of LV contractile ability, we calculated wall motion score index (WMSI) (total score segments divided by 16) and degree of local contractility (DLC) (total score segments, minus 16, divided by the number of segments with impaired contractility).

Results: In assessing the standard data LVEF were found increase in two groups of patients: the 1st group - 23% (from 32.87 ± 2.52 to 43.00 ± 3.60 , $p < 0.001$) in the 2nd group - 6.7% (from 34.31 ± 1.58 to 36.78 ± 1.46 , $p < 0.001$). However, the analysis of DLC and WMSI in the two groups of patients were found to be completely opposite to this trend. In particular, DLC in 1st group patients decreased from 1.52 ± 0.20 to 1.20 ± 0.11 , $p < 0.001$, indicating improvements in myocardial contractility by 21%. In the 2nd group-DLC increase of 1.56 ± 0.13 to 1.75 ± 0.13 , $p < 0.001$, which is a sign of worsening myocardial contractility disorders by 10.0%. WMSI in the 1st group patients decreased from 1.88 ± 0.16 to 1.42 ± 0.13 , $p < 0.001$, indicating a decrease in the total area hibernating segments by 24.0%. In the second group it increased from 1.97 ± 0.11 to 2.15 ± 0.11 , $p < 0.001$, which indicates that the increase in the area of myocardial non-viability by 8.0% due to acute ischemia.

Conclusions: Even against the backdrop of some improvement in LVEF, DLC and WMSI, which characterize the dynamics of LV regional contractility, showed diverse trends. This is especially noticeable in patients with 2nd group where DM type 2 prevails and which saw a relative improvement of LVEF, experienced decreasing of DLC, decreasing of WMSI, indicating the appearance of new lesions myocardial hibernating or an expansion of area of myocardial non-viability. Therefore, a full assessment of MV in patients with CHD and a background of DM type 2 must include not only the definition of LVEF, but must be measured in conjunction with DLC and WMSI.

P961

Patterns of cardiovascular risk factors in asymptomatic diabetics and pre-diabetics from southeast asia

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Introduction: Diabetes mellitus increases the risk of heart failure independent of coronary heart disease and hypertension. It is also associated with diabetic cardiomyopathy of which the epidemiology is not well defined. We sought to study the pattern of cardiovascular risk factors in an asymptomatic diabetic population from Malaysia.

Objectives: To assess cardiovascular risk factors in diabetic and pre-diabetic patients.

Methods: Subjects were recruited as part of a community study on cardiovascular diseases between the years 2007 to 2011. Demographic details, cardiovascular risk factors along with echocardiogram were obtained.

Results: A total of 1932 subjects with echocardiogram were analyzed. Mean age was 54.6 ± 11.6 . Majority of the subjects were male 98.3% (1899). Mean systolic ejection fraction (EF) was $64.5\% \pm 7.0$. Prevalence of heart failure with preserved ejection fraction (HFpEF) was 52.8% (1021). Of all the subjects with HFpEF, 29.9% (578) had impaired relaxation, 21.0% (406) pseudonormal and 1.9% (37) restrictive defect. Among subjects with HFpEF, 13.8% (266) were diabetic and 9.6% (185) were pre-diabetic (impaired fasting glucose). Table below summarize the cardiovascular risk factors among the subjects with diabetes and pre-diabetics. In univariate analysis only age and hypertension found to be significant predictor for diastolic dysfunction among diabetes mellitus subjects. However in multivariate analysis, age was the only the strong predictor for a diabetic patients to have HFpEF with OR 0.57 (CI:1.01-1.10).

Conclusion: The prevalence of HFpEF in diabetic and impaired glucose tolerance subjects in our population was surprisingly higher than reported. Age and hypertension remain a significant risk factor associated with risk of developing HFpEF in patients with diabetes mellitus, however after adjusted only age is the strong predictor.

Comparison of CV risk factors

CV risk factors	Impaired fasting glucose (%) N = 185	Diabetes (%) N = 266
Diastolic dysfunction	61.6	58.6
Hypertension	35.1	37.2
Dyslipidemia	55.7	57.1
Obesity	73.0	77.4

P962

Impact of diabetes on left ventricular diastolic function, heart rate variability and QT dispersion in patients with stable angina

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Purpose: Coronary patients with diabetes are at high risk of cardiovascular events. Diabetic autonomic neuropathy which first involves vagal nerves contributes to the bad prognosis of coronary patients with diabetes. The best marker of the state of activity of the autonomic nervous system is the heart rate variability (HRV), which is a predictor of cardiac mortality. Abnormally high QT dispersion has been correlated with risk of cardiac death in coronary patients.

The aim of this study was to establish the influence of diabetes mellitus on the left ventricular diastolic function, parameters of HRV and QT dispersion in patients with stable angina.

Methods: The study involved 123 patients with stable angina, in the sinus rhythm without AV blocks or branch blocks. Average age of patients was 57.8 years. 45 patients were with diabetes mellitus, and 78 were without diabetes. There was no significant difference in age or sex between two groups of patients. In all subjects 24-hour ECG recording and echocardiographic examination were performed and from standard ECG corrected QT dispersion (QTdc) was calculated. 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 stable angina and diabetes had significantly lower values of followed parameters of the heart rate variability (96.5 ± 21.4 vs 119.7 ± 25.5 ms, $p < 0.001$ for SDNN; 86.2 ± 17.8 vs 103.6 ± 20.2 ms, $p < 0.001$ for SDANN; 27.9 ± 9.4 vs 36.2 ± 11.4 ms, $p < 0.001$ for RMS-SD and 5.9 ± 4.8 vs 11.6 ± 9.4 , $p < 0.001$ for NN>50 ms), and significantly higher values of QTdc (61.2 ± 23.4 vs 48.6 ± 17.8 ms, $p < 0.005$) in comparison to those without diabetes. Patients with diabetes also had significantly higher degree of left ventricle diastolic dysfunction, in comparison to those without diabetes ($p < 0.01$ for ratio E/A and $p < 0.001$ for Dt).

Conclusions: The study demonstrated that patients with stable angina and diabetes have left ventricle diastolic dysfunction, significantly lower values of HRV parameters and significantly higher values of QTdc in comparison to those without diabetes.

P963

Lipids in heart failure: its paper in reverse epidemiology

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Objectives: Observational studies indicate that classical cardiovascular risk factors as body mass index, total cholesterol, and systolic blood pressure are associated with improved rather than impaired survival in heart failure ("reverse epidemiology"). We estimated the prognostic role of lipids in our heart failure clinics patients.

Methodology: We studied patients seen in the first four years of our heart failure specific outpatient clinic. We assessed patient features, where they were referred from, sex, age, heart failure etiology, functional class and left ventricle ejection fraction. We measured total cholesterol, HDL, LDL and triglycerides (TG) in blood analysis. The primary endpoints were major cardiovascular events (dead/readmission).

Results: 141 patients were seen in the four first years of the outpatient clinic. Our patients had an average age of 59.6 years (CI 57.2 - 62), 75.2% male sex. Average follow up time was 856.5 days (CI 802.2 - 910.9). Important symptoms of heart failure were found in most patients, with II or worse NYHA class in 77.3% of patients. Median LVEF was 34% (CI 31.6 - 36.5), 63.8% of patients had severe systolic dysfunction (LVEF < 35%). The most frequent etiology was ischemic cardiomyopathy (36.9%), followed by idiopathic dilated cardiomyopathy (31.9%), enolic dilated cardiomyopathy (5.7%), other causes of dilated cardiomyopathy (13.5%), and other non-dilated causes (11.3%). 64.5% of the patients were in sinus rhythm and 31.2% were in atrial fibrillation.

We classify our patients in groups according to their lower lipid levels (lower or higher than 150 mg/dl for total cholesterol, 35 mg/dl for HDL, 80 mg/dl for LDL and 70 mg/dl for TG). We found no statistical differences in clinical events between lower and higher levels of LDL and TG groups ($p = 0,11$ and $0,16$ respectively). We found a non significant statistical trend toward to worse clinical events in the lower total cholesterol group (58,3% vs 41,9% $p = 0,056$) as well as in the lower HDL group (64,3% vs 44,2% $p = 0,054$).

As a potential confussion factor, we measured the correlation between statine treatment and clinical events, not founding a statistical relationship ($p = 0,07$)

Conclusion: In patients with heart failure, mortality and morbidity risk seems to be increased with lower levels of HDL and total cholesterol, without any relationship founded with LDL and triglycerides.

There is a need for further and longer investigations to clarify this issue.

HEART FAILURE IMAGING

P964

Scar burden and mechanical dyssynchrony assessment with SPECT-myocardial perfusion imaging as a potential tool to predict responsiveness to cardiac resynchronization therapy

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Introduction: QRS morfology and duration on the electrocardiogram (ECG), are the best predictors of response to cardiac resynchronization therapy (CRT). A considerable number of patients (pts) who meet the criteria for CRT do not improve (~30-35%) and additional criteria for best selection are needed. Assessment of scar burden and left ventricular mechanical dyssynchrony (LVMD) by phase analysis of gated SPECT myocardial perfusion imaging (MPI), may be useful tools for improving the prediction of CRT response.

Methods: We retrospectively evaluated heart failure (HF) pts with LV ejection fraction (EF) <50% who underwent SPECT-MPI. We obtained parameters of dyssynchrony by phase analysis of SPECT-MPI: histogram bandwidth (hb - a measure of the time dispersion of the onset of systolic contraction between regional LV count changes) and standard deviation (sd) for each patient. The presence of myocardial scar (persistent perfusion defect) was defined as a "summed stress score (SSS)" >3 with a "summed difference score (SDS)" <4, and the presence of ischemia was defined as a SSS >3 with an SDS >3.

Results: Ninety-four patients (74 males; mean age 63 ± 9 years) underwent SPECT-MPI with phase analysis. Thirty-seven pts (39%) were classified as having ischemic cardiomyopathy (ICM) and 57 pts (60,6%) were classified as having non-ICM (nICM). Mean QRS duration was 139 ± 32 ms (134 ± 35 ms for ICM and 143 ± 30 ms for nICM, $p = 0,128$), and LBBB was present in 51 pts (69%) with a higher frequency in nICM (38 VS 13 pts; $p = 0,003$). Mean EF was $29,9 \pm 9,2\%$, with no significant difference between ICM VS nICM ($P = 0,06$). Mean hb and sd values were $162 \pm 77^\circ$ and $52 \pm 21^\circ$ in ICM and $99 \pm 65^\circ$ and $33 \pm 19^\circ$ in nICM (normal values of $\sim 38^\circ$ for hb and 14° for sd; $p = < 0,001$ and $p = < 0,001$ respectively). In patients SSS>3 and SDS<4 (scar), increasing values of SSS are correlated with higher hb and sd values ($r = 0,57$; $p < 0,001$), suggesting that increasing scar burden is associated with increasing mechanical dyssynchrony. Myocardial scar, was present in both populations of pts, although, as expected, was more frequent in ICM ($p = 0,004$).

Conclusions: Extensive myocardial scarring is a predictor for non-response to CRT. Although mean EF and mean QRS duration were not different between groups, LVMD assessed with SPECT-MPI phase analysis is significantly higher in patients with ICM compared to nICM, and this was related to a higher scar burden. These findings suggest that LVMD assessed with phase analysis of SPECT-MPI may be a surrogate marker of the extension of myocardial scarring and may be a useful predictor of CRT response, in addition to ECG parameters.

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Differentiation of ischemic from nonischemic cardiomyopathy in patients with exertional dyspnea utilizing technetium-99m sestamibi SPECT

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Purpose: The distinction between ischemic and non-ischemic cardiomyopathy is clinically important in terms of management of patients with exertional dyspnea. While cardiac catheterization has been the gold standard for this condition, noninvasive techniques to distinguish these groups are always favorable. This study evaluates whether Technetium-99m sestamibi SPECT can differentiate ischemic from non-ischemic cardiomyopathy in this patient subset.

Methods: This prospective study involves 87 patients who were referred to MPI with exertional dyspnea and reduced left ventricular ejection fraction (LVEF<40) documented by echocardiography. Patients were stratified into ischemic category if any of the following criteria were present: defect size is large, defect number is 2 or more, defect severity is 3+/4+. Nonischemic category was defined if none of the above criteria was present. By angiographic criteria, ischemic cardiomyopathy is defined as $\geq 70\%$ diameter stenosis at least 1 epicardial coronary artery whereas non-ischemic cardiomyopathy is defined as normal coronary arteries or less than 40% diameter stenosis in no more than 1 major epicardial coronary artery with no prior history of myocardial infarction.

Results: Segmental wall motion abnormality was more common in ischemic group (57% vs 16.6%); global dysfunction was more common in non-ischemic group (42% vs 84%). In univariate analysis, SPECT imaging variables that are most statistically significant to point ischemic group was large defect, more than one defect and 3+/4+ defect severity. Among these, severe defect has higher sensitivity (93.8%); large defect and severe defect has higher specificity (100%) for ischemic cardiomyopathy. In ischemic group, subsequent angiography demonstrated that 16 patients has 1 vessel, 28 had 2-vessel, 14 had 3-vessel, 1 had 4-vessel, 1 had left main disease, 2 had no hemodynamically significant coronary artery disease. In non-ischemic group, 3 patients had 1 vessel disease.

Discussion: Coronary artery disease is the most underlying cause of heart failure due to left ventricular systolic dysfunction. This prospective study confirms that MPI SPECT with Tc99m sestamibi can accurately differentiate ischemic from non-ischemic cardiomyopathy in patients with exertional dyspnea and documented left ventricular dysfunction. In the present study performed with Technetium-99m sestamibi SPECT, presence of any of the following 3 criteria; large defects, multiple defects or 3+/4+ defects can accurately differentiate non-ischemic from ischemic cardiomyopathy in patients with exertional dyspnea.

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Prognostic value of left ventricular dyssynchrony assessed by ECG-gated Tc-99m tetrofosmin SPECT with phase analysis in patients with chronic kidney disease and narrow QRS

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Aim: Chronic kidney disease (CKD) is reported to be associated with poor outcomes in patients with CHF. On the other hand, asynchronous myocardial contraction adversely influences Left ventricular (LV) function and is therefore associated with a poor prognosis. The aim of this study was to assess prognostic value of phase analysis of ECG gated Tc-99m tetrofosmin SPECT with phase analysis in Patients with CKD.

Materials and Methods: 85 patients (mean LVEF, 58 ± 17%, mean estimated GFR 42 ± 17ml/min, QRS width 103 ± 21msec) with CKD underwent rest and exercise 99m Tc tetrofosmin SPECT examination. Phase SD, Bandwidth (HBW) were assessed by using phase analysis of ECG-gated SPECT MPI. A cardiac event was defined as cardiac death, lethal-arrhythmia, ACS, or progression of HF.

Results: 25 cardiac events (2 cardiac death, 9 ACS, and 13 HF progression, 1 lethal arrhythmia) occurred during a follow-up period of 24 ± 13 months. There is no difference between the both group for QRS width and eGFR. (110 ± 23.9 vs 105 ± 21.1 p = 0.853, 40 ± 18 ml/min vs 43 ± 15 ml/min, p = 0.622). The patients with cardiac events were associated with significantly wider Phase SD, (33.3 ± 17 vs 18.4 ± 10.1, p = 0.0006), HBW (105.4 ± 54.5 vs 61.4 ± 29.3, p = 0.0058). The subgroup of 33 patients with ischemic group and cardiac events also had a significantly wider Phase SD and HBW (35.8 ± 16 vs 16.5 ± 7.1, p = 0.0045, 105.38 ± 48 vs 59.4 ± 28, p = 0.0042,) than did the ischemic and non cardiac events. When the patients were divided into the low (<26) and high (≥26) Phase SD groups, the hazard ratio for the low Phase HD was 0.57 (CI: 0.3515-0.9557, p = 0.035).

Conclusion: Our preliminary results indicate that LV dyssynchrony using phase analysis may provide prognostic information in patients with CKD.

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Heart failure does not change quality of visualization of coronary venous system in cardiac magnetic resonance

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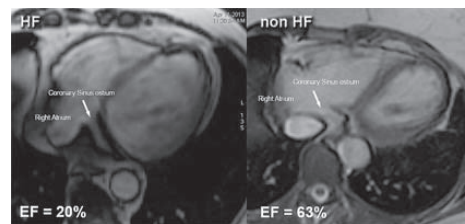
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Cardiac magnetic resonance (CMR) is a diagnostic option for patients with heart failure (HF) both for exact evaluation of cardiac function parameters including ejection fraction as well as some anatomical structures. There is no data - is it possible to visualize coronary venous system in patients with HF - this knowledge can potentially be useful before cardiac resynchronization therapy (CRT).

Methods: 93 patients aged 51.0 ± 16.9 (29W) were included into the study. 41 of them had heart failure recognized (EF ≤ 40%, clinical symptoms present) and 52 had normal EF and lack of clinical symptoms. A steady state free precession (FIESTA/45) magnetic resonance sequence was the basis for the visualization of coronary veins in CMR. All data were evaluated by CMR investigators and are given in mm, quality of visualization was evaluated by introduced scale in points (5 is max value).

Results: Similar quality of visualization of coronary veins was obtained in both groups (HF: 3.70 ± 1.0 vs. nonHF: 3.52 ± 0.9; p = 0.3765 NS. Average CS ostium diameter was smaller in the HF group (10.03 ± 4.7) if compare to the nonHF group (10.55 ± 13.6); p = 0.8171 NS. Angle of entrance coronary sinus to the right atrium were almost identical in both groups (HF: 111.07 ± 11.9 vs. nonHF: 110.24 ± 12.4; p = 0.7442 NS). We were not able to visualize distal parts of coronary venous system in steady state free precession CMR sequences.

Conclusions: Heart failure did not influence the possibility and the quality of visualization proximal parts of coronary venous system. To visualize distal parts of coronary venous system 3D whole body imaging should be incorporated.



Examples of CMR imaging HF/nonHF

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The role of SPECT/CT in revascularization of patients with congestive heart failure

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Objective: This study aimed to evaluate the role of myocardial perfusion imaging (MPI) to detect ischemic myocardial lesions and dysfunction for choice of appropriate therapy for patients with congestive heart failure (CHF).

Background: Myocardial functional capacity is an important clinical issue in patients with CHF. The availability of myocardial revascularization procedures requires specific indications for one if left ventricular failure is the most prominent feature of coronary artery disease (CAD).

Methods: SPECT/CT MPI, 2 day protocol. Stress test - Adenosine stress with low workload exercise tolerance test. 99mTc labeled tracer was used. Scanning time is 30-60 minutes after injection of radiopharmaceutical. Rest and stress ECG evaluated for ischemic changes. Left ventricle functional capacity - ejection fraction (EF), end diastolic (EDV), end systolic volume (ESV) as well as transient ischemic dilatation (TID).

Results: 50 patients (28 men and 22 women). 9 had anamnesis of MI. 5 of those had SSS>13 and 4 had scar on ECG. All 9 had diagnosis of CHF. 30 without ischemic changes in stress test also where negative on MPI. 13 with positive stress had SSS<4.

Conclusion: Patients with positive stress test and negative MPI, with both negative findings, patients with scar remain on medications. Patients with positive stress test and positive MPI (6) underwent revascularization. MPI helps to avoid unnecessary intervention.

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Inflammatory myopathies with potential heart involvement: an echocardiographic study

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Introduction: The inflammatory myopathies are extremely rare diseases, and can have a dismal prognosis. Myocardium involvement in patients with inflammatory myopathies constitutes one of the main causes of morbidity and mortality. The early identification of these patients (pts) is crucial to improve the prognosis. Strain rate analysis may allow the detection of subclinical ventricular dysfunction in this pts.

Methods: We performed an observational analysis of a sample of pts with polymyositis (PM) or dermatomyositis (DM) selected from the Rheumatology outpatient clinic. For each patient we collected laboratory data namely muscle enzymes (CK, aldolase, myoglobin and troponin) and BNP. Patients were submitted to a standard transthoracic Doppler echocardiogram, and the images were later processed using strain and strain rate analysis.

Results: Eight patients (four with PM and four with DM; all women with a median age of 60 years) were submitted to an echocardiogram. Five pts were on class I New York Heart Functional Class (NYHA) and three were on class II. The median duration of the disease since diagnosis was 2 years. Seven pts had pulmonary involvement secondary to the disease. Two pts had an overlap syndrome with another rheumatic disease (systemic sclerosis), and one pt had anti-synthetase syndrome with anti-Jo1 positivity. On echocardiogram, only one patient had a left ventricular ejection fraction below normal (at 48%). Four pts (50%) had reduced global longitudinal strain (median -9.67; normal ≤ -16). One of these 4 patients also had severe pulmonary hypertension, with a pulmonary artery systolic pressure of 70 mmHg. Other echocardiographic parameters were within the normal range (left ventricle end-diastolic diameter and mitral annular tissue doppler). BNP was slightly elevated in 2 patients

(max 210ng/L), but other cardiac biomarkers, namely troponin and CK-MB, were not elevated.

Discussion: Despite the small number of patients enrolled in the study, half of the study population had myocardial dysfunction (three patients (37,5%) had evidence of subclinical myocardial dysfunction assessed with echocardiographic strain imaging and one patient had mild systolic dysfunction assessed with volumetric measurement). Serum biomarkers may not be good surrogate markers of myocardial involvement in inflammatory myopathies since an only slightly elevated BNP value was found in two patients. We suggest that there can be a role for the routine use of strain rate analysis on echocardiography among patients with an inflammatory myopathy, as it can detect subtle dysfunction, with possible therapeutic implications.

P970

Association between left ventricular global longitudinal strain and natriuretic peptides in outpatients with chronic systolic heart failure

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Background: Both impaired left ventricular (LV) global longitudinal strain (GLS) and increased plasma concentrations of natriuretic peptides (NP) are associated with a poor outcome in heart failure (HF). However, little is known about the relationship between LV GLS and NP.

Methods: We prospectively included 149 patients with verified systolic HF at the baseline visit in an outpatient HF clinic. LV GLS was assessed by two dimension speckle tracking and plasma concentrations of N-terminal-pro-brain-natriuretic-peptide (NT-proBNP) and mid-regional-pro-atrial-natriuretic-peptide (MR-proANP) were analyzed.

Results: The patients had a median age of 70 years, 28.2% were females, 26.5% were in functional class III-IV, median left ventricular ejection fraction (LVEF) was 33% and median LV GLS was -11. LV GLS was associated with increased plasma concentrations of NT-proBNP and MR-proANP in multivariate logistic regression (NT-proBNP: Odds RatioGLS: 7.25, 95%-CI: 2.48-21.1, P < 0.001 and MR-proANP: Odds RatioGLS: 3.26, 95%-CI: 1.28-8.30, P = 0.013) and linear regression (NT-proBNP: β GLS: 1.19, 95%-CI: 0.62-1.76, P < 0.001 and MR-proANP: β GLS: 0.42, 95%-CI: 0.11-0.72, P = 0.007) models after adjustment for traditional confounders (age, gender, body-mass-index, atrial fibrillation, renal function) and left atria volume index.

Conclusion: Impaired LV GLS is associated with increased plasma concentrations of NP and our data suggest that left ventricular myocardial mechanics estimated by LV GLS reflects myocardial wall stress in chronic systolic HF. LV GLS should be used in future randomized clinical trials for risk stratification in heart failure.

P971

Prognostic value of pharmacological stress echocardiograms with dobutamine submaximal and negative to ischemia

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Introduction: The induction of ischemia in pharmacological stress echocardiograms is considered a predictor of cardiac events; their absence is associated with a favorable prognosis. The prognostic value of normal tests with maximum heart rate (MHR) reached less than 85% predicted for age (submaximal) has not been clearly defined, as the influence of beta-blockers (BB) in the last group.

Purpose: To estimate the prognostic value of pharmacological stress echocardiograms with dobutamine (EDob) and submaximal test negative for ischemia and the effect of BB in these results.

Methods: Performed a retrospective study in which 593 consecutive patients (pts) were identified submitted EDob between January 2008 and December 2012. Were excluded from the sample the pts with evidence for ischemia. The rest were divided into 2 groups (Gp) - Gp A: MHR less than 85% predicted and negative test for ischemia and Gp B: submaximal test and negative for ischemia. The pts of Gp B were divided into 2 sub-Gp, as they were treated or not BB: B1 (treated with BB) and B2 (not treated with BB). The sub-Gp were compared to group A as to their clinical characteristics, echocardiographic, the test subject and the occurrence of significant cardiac events (MACE) - death, rehospitalization or revascularization - at 12 months.

Results: Included 453 pts, average age 64 ± 11 years. 69.8% were male. 80 (17.7%) joined the sub-Gp B1 and 22 (4.8%) the sub-Gp B2. Univariate analysis comparing

the sub-Gp B1 and B2 with the Gp A, B1 pts were younger (p=0.001), had more history of dyslipidemia (p=0.005), coronary heart disease (p=0.038) and percutaneous revascularization (p=0.031). Patients in B2 were younger (p=0.001), had more history of hypertension (p=0.01), less coronary disease (p=0.005) and less segmental base changes (p=0.001). There were no significant differences in relation to the subject of the examination (known or suspected coronary artery disease). At 12 months, the pts in B1 had more MACE (p=0.034) compared to Gp A, which was not observed between B2 and A (p=0.347), mainly by re-hospitalization for cardiac causes.

Conclusions: In our sample, negative submaximal tests for ischemia in pts not treated with BB were associated with a low number of annual events, while pts treated with BB had a worse prognosis. It is possible that these results are associated with the reduction of the test sensitivity as well as a higher prevalence of coronary heart disease.

P972

Left atrio-ventricular and ventricular-arterial matching in patients with heart failure

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Objectives: This study aims to assess the left atrio-ventricular matching and the ventricular-arterial matching (VAM) in patients with heart failure (HF).

Methods: 76 patients with HF and 45 age-matched normal controls were recruited and underwent standard echocardiography. LA ejection force (LAEJF) was formulated as $1/3 \times 1.06g/cm^3 \times [mitral\ annulus\ area]^2$, where mitral annulus area = $0.85 \times D1^2$, D1 and D2 were measured from apical four-and two-chamber view; A is peak atrial velocity (sample volume at mitral annulus). After load-adjusted left atrial ejection force (aa-LAEJF) was calculated as ratio of LAEJF and septal E/E'. Arterial stiffness (Ea) was calculated as $0.9 \times SBP/SV$ (SBP is the systolic blood pressure, SV is the stroke volume). Global LV contractility index ($d\sigma^*/dtmax$) was calculated as $1.5 \times Vpeak \times ALVOT \times 1.05/LV\ mass$ where Vpeak is the peak velocity sampled at the LVOT and ALVOT is the LVOT area ($ALVOT = \pi D^2/4$ where D is the LVOT diameter). VAM was calculated as ratio of $d\sigma^*/dtmax$ and arterial stiffness Ea ($d\sigma^*/dtmax/Ea$).

Results: In patients with systolic HF (LVEF<50%), LAEJF increased and aa-LAEJF decreased significantly, $d\sigma^*/dtmax$ decreased and Ea increased significantly so that VAM significantly decreased compared with controls. In patients with diastolic HF (LVEF>50%), aa-LAEJF had no significant change but VAM significantly decreased compared with controls (Table1).

Conclusions: In patients with diastolic HF, left atrio-ventricular was still matching although LV contraction capacity decreased, but the ventricular-arterial mismatching occurs due to the artery stiffness increased. In patients with systolic HF, both left atrio-ventricular and ventricular-arterial were mismatched.

Table 1 Echo parameters in three groups

	Controls (n = 45)	Systolic HF (n = 55)	Diastolic HF (n = 21)
LVEF	71.85±6.67	53.23±5.42*	26.82±11.89*∞
$d\sigma^*/dtmax$ (s-1)	4.47±1.57	1.56±1.50*	2.45±1.01*∞
Ea (mmHg/ml)	1.76±0.42	3.55±1.29*	2.53±1.12*∞
$d\sigma^*/dtmax/Ea$ (VAM) (ml/mmHg*s)	2.73±1.36	0.52±0.55*	1.20±0.76*∞
LAEJF (kdynes)	4.55±1.42	6.55±5.33*	8.15±5.12*
E/E'	7.36±2.32	21.08±7.04*	14.75±4.25*∞
aa-LAEJF (kdynes)	0.65±0.22	0.34±0.36*	0.58±0.42∞

*: p < 0.001 compared with normal controls. ∞: p < 0.001 compared between systolic and diastolic HF groups.

P973

Left ventricular myocardial function in hemodialysis patients: a three-dimensional speckle tracking echocardiography study

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Several studies have demonstrated that uremic patients who have preserved left ventricular ejection fraction (LVEF) could still have the potential for systolic dysfunction.

The aim of this study was to evaluate the left ventricular (LV) myocardial function in hemodialysis (HD) patients based on three-dimensional (3D) speckle-tracking echocardiography (STE).

Methods: Thirty patients on maintenance HD were examined just before and after HD. All of the patients had normal left ventricular ejection fractions (50% or greater). Transthoracic 3D recordings were obtained using multi-beat reconstruction from 6 consecutive cardiac cycles. LV mass index (LVMI) was evaluated and 3D speckle tracking analysis was performed to calculate global longitudinal (GLS), circumferential (GCS), area (GAS) and radial (GRS) peak systolic strain. Serum BNP levels were also measured.

Results: The left ventricular 3D global longitudinal strain, radial strain, circumferential strain and global area strain were decreased in HD patients. LVMI was remarkably increased in our patients and decreased significantly after HD (99.13 ± 18.06 vs. 84.12 ± 13.77 g/m², $p < 0.001$). However, the three-dimensional strain increased significantly in all directions after HD [pre- vs. post-HD; GLS: -15.30 ± 3.23 vs. -17.16 ± 2.75 , GCS: -29.6 ± 3.4 vs. -22.8 ± 7.5 , GAS: -30.6 ± 5.2 vs. -34.3 ± 10.6 , GRS: 22.4 ± 6.2 vs. $26.5 \pm 9.4\%$, all $p < 0.001$].

A multivariate linear regression analysis showed that the creatinine and the BNP levels were independently associated with the values of the global longitudinal three-dimensional strain ($p = 0.02$ and $p = 0.03$, respectively). LVMI and serum BNP levels were inversely correlated with pre-HD GLS ($r = -0.777$ and $r = -0.673$ respectively, $p < 0.01$) and post-HD GLS ($r = -0.685$ and $r = -0.713$ respectively, $p < 0.01$).

Conclusion: Three-dimensional speckle-tracking echocardiography may detect myocardial dysfunction in patients with uremia on maintenance hemodialysis who have preserved LVEF.

P974

2.34% is the prevalence of congenital heart diseases in pre-employment echocardiography studies in egyptians

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Objectives: We investigate the prevalence of congenital heart diseases in pre-employment echocardiography.

Methods: The study included 469 peoples referred for pre-employment echocardiographic assessment for detection of any abnormalities in cardiac structure or function. All subjects had been subjected to the following: Informed consent, Routine medical screening, Chest X-ray, Laboratory tests and transthoracic echocardiography assessment.

Results: A total of 469 subjects were examined, comprising of 316 males (67.38%) and 153 females (32.62%). The age range of the subjects was 20-50 years (mean 27.41 ± 7.45 years). The echocardiogram was normal in 96.2% of the subjects. The commonest abnormality detected was mitral valve prolapse; accounting for 1.5% of the subjects studied. Bicuspid aortic valve was the next most common diagnosis accounting for 0.5% of our findings.

Conclusion: Normal echocardiogram was the commonest echocardiographic finding, 2.34% was the prevalence of Congenital heart diseases and mitral valve prolapse was the commonest congenital heart disease detected.

The common echocardiographic findings

Type of echocardiography abnormality	No. of subjects	Percentage of subjects
Mitral valve prolapse	7	1.5%
Bicuspid aortic valve	2	0.5%
Aortic valve prolapse	2	0.5%

P975

Echocardiographic left atrial volume index (LAVI) in a heterogenous asian population

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Introduction: The left atrium (LA) is a complex structure and involved in disease affecting the left ventricle. LA dilation is related to an increased filling pressure and is a strong predictor of cardiovascular outcome. Assessment of LAVI in asymptomatic patients may help in aggressive risk factors control and prevent further complication.

Objectives: To describe LAVI in normal and diseased states of Asian population.

Methods: Between 2007 and 2011, subjects participating in a longitudinal population study looking at cardiovascular diseases were enrolled. Demographic data, cardiovascular risk factors and echocardiograph were obtained. LA volume was calculated by the area-length method and indexed to body surface area (BSA).

Results: A total of 1932 subjects with echocardiogram were analyzed. Mean age was 54.6 ± 11.6 . Majority of the were male 98.3% (1899). Mean systolic ejection

fraction (EF) was $64.5\% \pm 7.0$. Majority was Malay ethnic 81.9% (1582), 13.8% (266) were diabetics and 9.6% (185) had impaired fasting glucose (IFG). 60.6% (1170) had high LDL level of more than 3.4mmol/L. 26.1% (505) were hypertensive and 59.1% (142) were obese. Mean left atrial volume index was 28.0 ± 9.1 ml/m². Total of 40.3% (778) had LAVI > 28 ml/m². For those with LAVI > 28 ml/m², 12.6% (98) were in the healthy subjects while the remaining 87.4% (680) had at least 1 risk factor (diabetes, hypertension, dyslipidemia or obesity). For subjects with LAVI > 28 ml/m², hypertension, and live in urban area remained the strong predictors for LAVI > 28 ml/m² after univariate and multivariate analysis with age adjusted.

Conclusion: LAVI measurement is a potential tool to be used in assessment of asymptomatic patients with cardiovascular risk factors as these subclinical patients might benefit from aggressive risk factor control to prevent further complication.

Risk factors	% LAVI > 28 ml/m ² N = 778	p value	OR	CI
No risk 1 risk or more	12.6 87.4	0.30	-	-
Diabetes mellitus Yes No	12.9 87.1	0.27	-	-
Hypertension Yes No	32.0 68.0	< 0.001	0.7	0.57-0.88
Dyslipidemia Yes No	60.2 39.8	0.50	-	-
Obese Yes No	59.4 40.6	0.85	-	-
Area Urban Rural	35.3 64.7	< 0.001	1.6	1.28-1.89

P976

Right ventricular outflow tract tissue doppler parameters in congestive heart failure (preliminary results)

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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).

Methods: We studied 125 healthy volunteers and 30 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 chamber 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 at 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), Eict1 (-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.

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Assessment of left atrial function during the acute course of myocardial infarction

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Background: The left atrium modulates left ventricular filling through three components: a phase of reservoir or expansion during systole, a conduit phase during diastole, and an active contractile component (when sinus rhythm is present) during late diastole. The aim of this study is to determine which function of the left atrium is first impaired during the acute course of STEMI

Methods: We prospectively evaluated the left atrial function in patients with a first myocardial infarction. Thirty age-matched healthy subjects served as controls. Echocardiographic assessment included left atrial sizes (diameters and surface), mitral A wave velocity and duration, pulmonary vein S, D and Ap waves.

Results: The echocardiography showed an increase in atrial dimensions in patients with STEMI compared to healthy subjects ($p = 0.04$), this increase was significantly

higher in anterior infarction than in inferior infarction. The duration of mitral A wave (138,8 vs 160; $p=0,017$) and the velocity of A wave (70,24vs 82,37, $p=0,005$), which reflects the active contractile component were significantly lower in patients with STEMI. In fact, A wave and A' velocities, were negatively correlated to the ratio E/E' ($r=-0,38$ and $P=0,004$; $r=-0,45$; $p>0,001$) and so impaired when there is increase in filling pressure. The E wave velocity and D wave on pulmonary vein, reflecting the conduit phase function were correlated to the left ventricle ejection fraction ($r=0,35$ and $P=0,009$). However, there is no significant difference regarding S wave on pulmonary vein flow (which reflect s the reservoir phase) between patients and healthy patients

Conclusion: During myocardial infarction, the reservoir function of the left atrium seems to be not affected by ischemia whereas the pump phase was affected by the elevation of filling pressure and the conduit phase affected by the impairment of the systolic function of the left ventricle.

P978

Combined circumferential and longitudinal left ventricular systolic dysfunction in patients with rheumatoid arthritis without overt cardiac disease

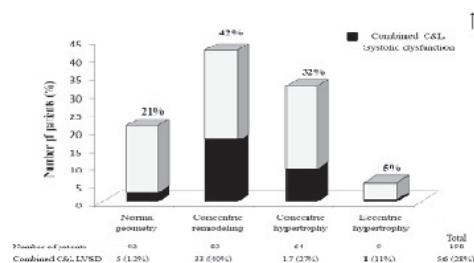
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Aim: Patients with rheumatoid arthritis (RA) have an increased risk for cardiovascular diseases (CV). Due to accelerated atherosclerosis and changes in left ventricular (LV) geometry, LV circumferential and longitudinal (C&L) shortening may be impaired in these patients despite preserved LV ejection fraction. We focused on prevalence and factors associated with combined C&L dysfunction in RA patients.

Methods and Results: 198 outpatients with RA without overt cardiac disease were analyzed during January-June 2014 and compared with 198 matched controls. C&L function were evaluated by stress-corrected midwall shortening (sc-MS) and Tissu Doppler mitral annular peak systolic velocity (S'). Combined C&L dysfunction was defined if sc-MS <86.5% and S' <0.9cm/sec, (10th percentiles of sc-MS and S' derived by 132 healthy people, respectively). Combined C&L dysfunction was detected in 56 patients (28%), and was associated with LV mass (OR 1.03 (CI 1.01-1.06), $p=0.04$) and concentric LV geometry (OR 2.76 (CI 1.07-7.15), $p=0.03$). By multiple logistic regression analysis, RA emerged as independent factor associated with combined C&L dysfunction (OR 2.57 (CI 1.06-6.25)). The rapport between sc-MS and S' was statistically significant in the subgroup of 142 patients without combined C&L dysfunction ($r=0.40$, F statistic <0.001), having the best fitting by a linear function

Conclusions: Combined LV C&L dysfunction is detectable in about one-fourth of asymptomatic RA patients. It is associated with LV concentric remodeling/hypertrophy, the presence of RA and with the loss of synergic functional relation between C&L fibers, which may explain the increased risk for CV events in these patients.



Geometry and C&L LV function in RA

P979

Prognostic value of cardiac iodine-123 metaiodobenzylguanidine imaging in patients with indications for cardiac resynchronization therapy

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Purpose: The aim of our study was to assess the predictive value of cardiac 123I-MIBG imaging for the clinical outcomes in heart failure (HF) patients with left bundle branch block (LBBB), and compare its power in different treatment groups.

Materials and methods: We have prospectively investigated 67 HF patients with the

New York Heart Association (NYHA) functional class II-IV, LBBB (>120 milliseconds), reduced left ventricular ejection fraction (LV EF) eligible for cardiac resynchronization therapy (CRT). 123I-MIBG planar and single photon emission computed tomography (SPECT) scans were performed in a supine position with calculation of early and late heart-to-mediastinum (H/M) ratios, washout ratio (WR), summed defect scores and scores difference from SPECT acquisition. All patients were then divided in two groups according to their clinical status (in general, patients assigned to CRT were clinically more severe than to OMT) - 36 patients underwent implantation of CRT, and 31 patients were continued with OMT. Initial conventional heart failure markers (left ventricular ejection fraction; B-type natriuretic peptide; left ventricular end-diastolic and end-systolic diameters) and NYHA were assessed at the time of 123I-MIBG imaging and 6 months later. Comparisons of two groups were done applying the Student's t-test, and if samples were small, the Fisher's exact test was used. NYHA groups were compared applying the ANOVA single factor analysis. ROC curve analysis was performed to establish cut off values for predictors of response.

Results: Cardiac 123I-MIBG imaging data varied insignificantly, presenting a similar cardiac adrenergic innervation status in both groups. In the CRT group, NYHA and LV EF indicated more pronounced signs of HF. For all patients, NYHA IV patients had significantly larger LV diameter, smaller EF, larger BNP levels, lower late H/M values and larger denervation score difference. Clinically responders (as ones with decreasing or stable NYHA functional class) to therapy in both groups had significantly higher early H/M ratio - 2.35 ± 0.41 than non-responders - 2.00 ± 0.44 ($p=0.004$), and late H/M ratio - 2.11 ± 0.44 for responders and 1.72 ± 0.54 for non-responders ($p=0.005$). There were no significant differences in regional cardiac 123I-MIBG data for responders and non-responders.

Conclusions: Cardiac 123I-MIBG imaging has valuable prognostic power predicting clinical outcomes of HF patients with wide QRS complexes, despite the chosen type of treatment, with better outcomes for patients with cut off value early H/M ratio above 2.00 and late H/M ratio above 1.77.

BIOMARKERS

P980

The value of the neutrophil-to-lymphocyte ratio in heart failure

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Purpose: An easily accessible hematological index, the neutrophil-to-lymphocyte ratio (NLR) is a marker of negative prognosis in patients with infectious, malignant and autoimmune disease. Our aim was to determine its utility in the assessment of patients with heart failure (HF), given the inflammatory involvement in its pathophysiology.

Methods: In this retrospective study we analyzed data from 516 HF patients admitted consecutively to our clinic. The mean age was 71.55 ± 11.73 years old and 52.84% were female. NLR was evaluated in relation to the clinical and paraclinical markers of severity: acute decompensation, NYHA class, NT-proBNP levels, ejection fraction (EF) and length of hospital stay (LOS).

Results: We observed a higher NLR in patients with acute decompensated compared to stable HF [3.34 (1.25-26.27) vs. 2.17 (0.70-17.40), $p<0.001$], patients with NYHA class IV compared to class III or less [4.07 (1.27-26.27) vs. 2.45 (0.70 - 23.26), $p<0.001$], subjects with an EF<50% compared to those with preserved EF [3.16 (0.70-23.26) vs. 2.15 (0.72-17.40), $p<0.001$], as well as patients with an EF<35% compared to those with an EF>35% [3.41 (1.26-23.26) vs. 2.40 (0.70-17.40), $p<0.001$]. NLR was correlated with NT-proBNP levels ($r=0.486$, $p<0.001$), LOS ($r=0.364$, $p<0.001$) and EF ($r=-0.307$, $p<0.001$). Using ROC curve analysis, NLR predicted NYHA class IV symptoms with an AUC of 0.759 (95%CI 0.693-0.826, $p<0.001$), acute decompensated HF with an AUC of 0.739 (95%CI 0.691-0.787, $p<0.001$), reduced ejection fraction under 50% with an AUC of 0.675 (95%CI 0.623-0.727, $p<0.001$), reduced ejection fraction under 35% with an AUC of 0.696 (95%CI 0.635-0.757, $p<0.001$) and increased NT-proBNP levels with an AUC of 0.738 (95%CI 0.693-0.783, $p<0.001$) and a Youden index associated criterion of $NLR>3.04$ with 64.7% sensitivity and 73.7% specificity. Patients with a $NLR>3$ had an OR of 6.17 (95%CI 3.18-11.96, $p<0.001$) of having NYHA class IV symptoms, an OR of 5.54 (95%CI 3.57-8.58, $p<0.001$) of having decompensated HF, an OR of 3.79 (95%CI 2.46-5.86, $p<0.001$) of having an EF<50% and an OR of 3.40 (95%CI 2.07-5.59, $p<0.001$) of having an EF<35%.

Conclusions: NLR could be a useful, cost-effective biomarker in patients with HF. We suggest a NLR above 3 to be indicative of disease severity.

P981

Plasma erythropoietin levels and its relationship with anti-apoptotic enzymes in hypertension and heart failure

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Introduction: Transmembrane reductase of ferricyanide (TMR), a voltage dependent anion channel, existing on erythrocytes and many other cells, is involved in oxidative stress, aging and apoptotic mechanisms. Protein tyrosine phosphatase (ACP1) is involved in the control at membrane level of glycolysis dependent energy production in response to growth factors like erythropoietin (EPO), connected to cell growth and energy metabolism. EPO regulates many cellular functions and, possibly, can be a biomarker for heart failure. The methemoglobin reductase (MHbR) or cytochrome-b5 reductase (NADH-dependent) maintains functional the hemoglobin for NO synthesis. These enzymes are mechanistically related to each other through a common substrate (NADH).

Objective: To relate the anti-apoptotic erythrocyte enzyme activities with EPO in patients with hypertension compared with normotensive ones.

Material and Methods: A sample of 993 subjects, aged 55.03 ± 16.47 years, 288 with stage 2 hypertension of which 75.35% presenting heart failure (CVR). There were no significant differences in the distribution of BMI between groups. The MHbR activity (mmol of oxidized NADH/min/gHb), TMR (mmol/l cell/h), ACP1 (mmol of p-nitrophenol/min/gHb) and ACE activity (U/L) were determined in the erythrocyte and serum by spectrophotometric methods. EPO (mIU/ml) was determined by ELISA. Statistical methods were the chi-square, Student's t-test and ANOVA, or its nonparametric equivalent.

Results: The TMR activity was greater in normotensive group (NT) than in cardiovascular risk one (CVR) (5.75 ± 4.06 vs. 2.44 ± 1.53 respectively, p < 0.001). The same was true with the MHbR activity (21.454 ± 5.52 vs. 17.72 ± 5.52 respectively, p < 0.001). TMR activity has been correlated with the EPO plasma levels only in NT (r = 0.461; p = 0.047). While in the NT the activity of ACP1 is correlated with the activity of MHbR (r = 0.151; p = 0.031), in CVR group that activity was correlated with the TMR (r = 0.551; p < 0.001).

Discussion and Conclusions: TMR and ACP1 directly correlated in cardiovascular risk subjects, and the greater decline erythrocyte TMR activity verified in this group, compared with normotensive one, can reflect an accelerate progressive ageing process involved in hypertension and its complications mechanisms, possibly with resistance to the action of erythropoietin. The coenzyme I reduced (NADH) can thus be channeled to the TMR activity and less for the MHbR, favoring the survival of erythrocyte to its reducing capacity of methemoglobin in this high-risk group.

P982

Galectin-3, oxidative stress and endotoxemia in patients with chronic heart failure

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Purpose: To evaluate the connection between plasma level of galectin-3 and biomarkers for oxidative stress and endotoxemia in patients with chronic heart failure (CHF).

Methods: 167 patients (age, 63.4 ± 3.2 years) with documented prior myocardial infarction were included in the study. Patients were divided into 3 basic groups according functional class (FC) NYHA. 1 group (n = 54) - patients with II FC CHF, 2 - 61 patients with III FC, and 3 group (n = 52) - IV FC. The control group (CG) - 42 healthy people (age, 54.7 ± 4.8 years). We measured the level of galectin-3, NT-proBNP, oxidized low density lipoproteins (ox-LDL), 3-nitrotyrosine (3-NT) by enzyme immunoassay. Limulus amoebocyte lysate (LAL) test was used to determine the level of endotoxemia.

Results: We found a significant increase in the level of galectin-3 in the 1st (9.8 ng/ml), 2nd (18.6 pg/ml) and 3d (37.1 ng/ml) groups in comparison with CG (5.3 ng/ml). We observed significant difference between groups (p < 0.001). We found an increase in level of 3-NT in patients (2.4, 3.3 and 4.8 nmol/ml accordingly) in comparison with CG (1.8 nmol/ml). There was a significant positive correlation between levels of galectin-3 and 3-NT in all groups of patients: r1 = 0.59, p = 0.0003; r2 = 0.64, p = 0.0001; r3 = 0.73, p = 0.00002. Plasma levels of ox-LDL were significantly elevated in all groups compared with healthy control (p < 0.01). We also demonstrated a significant positive correlation between galectin-3 and ox-LDL in groups: r1 = 0.520, p = 0.0005; r2 = 0.560, p = 0.0007; r3 = 0.61, p = 0.00002. The intensity of endotoxemia significantly increased with the severity of CHF. We observed a positive correlation between levels of galectin-3 and endotoxemia in the 2nd and 3d groups of patients (r2 = 0.38, r3 = 0.46, p < 0.05).

Conclusion: The plasma level of galectin-3 in patients with prior myocardial infarction was closely connected with indicators of oxidative stress, endotoxemia and severity of CHF.

P983

Clinical correlates of Galectin-3, ST2 and NT-proBNP: head-to-head comparison

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Galectin-3 (Gal-3) and ST-2 are biomarkers proposed for better stratifying prognosis of chronic heart failure (CHF) patients. The aim of this study was to evaluate clinical correlates of these biomarkers assessed in the same group of CHF patients.

In 99 outpatients (age 65 ± 12 yrs, 80% males, NYHA class 2.4 ± 0.6) glomerular filtration rate (GFR), NT-proBNP, Gal-3 and ST-2 serum levels were assessed. Indexed left ventricular mass (LVMi), left ventricular end-systolic volume (LVESV), left ventricular ejection fraction (LVEF), E/e', mitral (MR) and tricuspid regurgitation (TR), pulmonary artery systolic pressure (PAPs), tricuspid annulus peak of systolic excursion (TAPSE) were also evaluated by echocardiography.

As shown in the table, NT-proBNP was correlated with parameters reflecting ventricular remodelling, systolic and diastolic function, valvular and renal function. Gal-3 was correlated only with diastolic function and renal function. Finally ST-2 was only slightly correlated to PAPs and TR.

In conclusions, our findings demonstrate that Gal-3 and ST2, differently from NT-proBNP, are less correlated with parameters commonly used to stratify CHF prognosis. This is probably due to the fact that they are more influenced by acute volume overload (ST2) and inflammation/fibrosis (Gal-3) and it could also explain their additive prognostic information.

P984

Circulating levels of uric acid may predict poor prognosis of chronic heart failure in patients older than 80 years of age without advanced renal insufficiency

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Background: Several circulating neurohormones and inflammatory markers have been shown to have a prognostic significance in chronic heart failure (CHF). Elevated levels of uric acid (UA) have been reported to predict adverse cardiovascular prognosis in CHF patients. However, there were few reports describing clinical value of circulating UA levels in elderly CHF patients.

Methods: We studied consecutive 92 Japanese CHF patients older than 80 years of age (49 females, 84.1 ± 3.2 years, all serum creatinine levels were <1.0 mg/dl, NYHA II-III, LVEF < 45%). We measured circulating levels of UA, noradrenalin (NAD), brain natriuretic peptides (BNP), and interleukin-6 (IL-6). None had evidence of unstable angina, chronic inflammatory disease, collagen disease, or cancer at the time of evaluation.

Results: Patients were followed up for an average of 36.2 months, and 19 patients had death. Circulating levels of UA were correlated with circulating levels of IL-6, and BNP significantly. Patients with events had significantly higher UA, NAD, BNP, and IL-6 compared with those without events. By multivariate Cox proportional hazard analysis, UA and BNP were significant predictors for death in those patients.

Conclusions: Circulating levels of UA correlate the severity in CHF patients. The high circulating levels of UA is a significant predictor of clinical outcomes and a strong predictor of all death in those CHF patients.

P985

Low serum albumin... another prognostic marker?

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Introduction: Population-based studies have suggested an association between low serum albumin levels and coronary atherosclerosis and heart failure. The role of albumin in the context of acute coronary syndromes (ACS) remains unclear, however, seems to associate with an adverse prognosis.

Aim: The aim of the present study was to determine whether low serum albumin levels are associated with development of heart failure in ACS.

Methods: Study of patients consecutively admitted for ACS in a Coronary Unit over 6 months. Patients with infectious complications were excluded.

Results: One hundred sixty-eight patients were eligible for analysis. Males were predominant (81.5%) and the mean age was 61.7 ± 13.4 years old. Low serum albumin levels (serum albumin <3.5g/dl) were present in 44.6%. No significant differences were observed regarding demographic characteristics, except higher mean age (p < 0.001) and a higher prevalence of hypertension (p = 0.04) in the hypoalbuminemia group. This group had lower values of hemoglobin (p < 0.001) and

Table 61287

Variables	Age	NYHA class	LVMI	LVESV	LVEF	E/e'	MR
log NT-proBNP	r: 0.37 p < 0.001	r: 0.41 p < 0.001	r: 0.31 p: 0.005	r: 0.26 p: 0.01	r: -0.48 p < 0.001	r: 0.49 p < 0.001	r: 0.33 p: 0.001
Gal-3	r: 0.48 p < 0.001	r: 0.25 p: 0.015	r: 0.18 p: 0.11	r: 0.09 p: 0.36	r: -0.01 p: 0.939	r: 0.41 p < 0.001	r: 0.06 p: 0.589
ST-2	r: 0.09 p: 0.362	r: 0.10 p: 0.315	r: 0.07 p: 0.52	r: 0.18 p: 0.069	r: -0.19 p: 0.068	r: 0.02 p: 0.926	r: -0.01 p: 0.926

Variables	TAPSE	PAPs	GFR	Log NT-proBNP	Gal-3	ST2
log NT-proBNP	r: -0.38 p < 0.001	r: 0.42 p < 0.001	r: -0.54 p < 0.001	-	r: 0.44 p < 0.001	r: 0.19 p: 0.052
Gal-3	r: -0.14 p: 0.173	r: 0.19 p: 0.074	r: -0.69 p < 0.001	r: 0.44 p < 0.001	-	r: 0.06 p: 0.557
ST2	r: -0.08 p: 0.446	r: 0.23 p: 0.026	r: -0.09 p: 0.334	r: 0.19 p: 0.052	r: 0.06 p: 0.557	-

higher levels of pro-BNP (p=0.018) and C Reactive Protein (p < 0.001). In univariate analysis, hypoalbuminemia was associated with a higher prevalence of heart failure (p=0.015, OR 2.45 CI95% 1.17-5.10) and the use of intra-aortic balloon (p=0.005) during hospitalization. There were no statistically significant differences in the use of inotropic drugs and invasive ventilation as well as in-hospital mortality. At follow-up at 6 months showed a positive association between hypoalbuminemia and mortality (p < 0.05).

Conclusions: The hypoalbuminemia was associated with an increased risk of heart failure during hospitalization and death at 6 months. Although the etiology of hypoalbuminemia remain unclear, albumin assay may be useful in risk stratification of acute coronary syndromes.

P986

Cardiac biomarkers predict one year mortality beyond concurrent comorbidity in elderly patients undergoing hip fracture surgery

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Background: Long term mortality after hip fracture surgery is mainly affected by concomitant comorbidities and the additive prognostic role of cardiac biomarkers remains unclear.

Methods: In total 152 elderly patients >65 years (age 80 ± 8 years) undergoing hip fracture surgery were prospectively followed. Comorbidities were detected and preoperative serum levels of B-type natriuretic peptide (BNP), postoperative BNP and postoperative troponin I were measured. The study endpoint was mortality at 1-year follow up.

Results: Overall, at 1-year follow-up 37 patients (24%) died. Age>80 years (HR: 5.782, CI: 2.188-15.278, p<0.001) and dementia (HR: 3.071, CI: 1.158-8.140, p=0.024) were independently associated with 1-year mortality. Subsequently, a comorbidity model was created. Preoperative BNP (HR: 1.002, CI: 1.000-1.004, p=0.020), postoperative BNP (HR: 1.003, CI: 1.001-1.004, p=0.02), and postoperative troponin I >0.01 ng/mL (HR: 3.903, CI: 1.477-10.317, p=0.006) were related to the outcome independently of age> 80 years and dementia. Interestingly, when all these 3 biomarkers were introduced together in the comorbidity model only postoperative BNP was associated to 1-year mortality independently of comorbidities (HR: 1.002, CI: 1.000-1.004, p=0.049).

Conclusions: Preoperative BNP and postoperative BNP and postoperative troponin I predict 1-year mortality independently of concomitant comorbidities in elderly patients undergoing hip fracture surgery. Postoperative BNP values may have an incremental clinical role.

P987

Effect of plasma renin activity on prognosis of patients receiving renin-angiotensin system inhibitors

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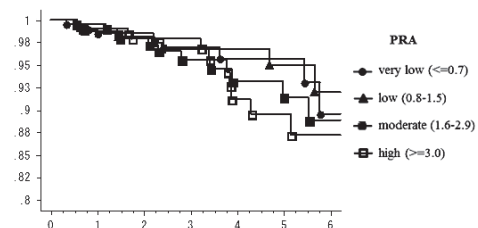
Objective: We studied the effect of increased plasma renin activity (PRA) on the prognosis of patients receiving renin-angiotensin system (RAS) inhibitors

(angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARB)).

Method: The subjects were 878 patients (average age 70.2 years old) with essential hypertension but no history of cardiovascular disease who had received RAS inhibitors for 1 year or longer (average period 6.7years). The subjects were divided into quartiles based on PRA measured during bed rest in the early morning, and the cardiovascular disease incidence of each group was examined.

Results: During the mean follow-up period of 3.9 years, 43 cardiovascular events (angina which needs intervention treatment, myocardial infarction, cardiac failure, cardiac sudden death, cerebrovascular accident) were observed. Cardiovascular events occurred in 12 of 204 subjects in the quartile with PRA at or below 0.7, 10 of 243 with values of 0.8 to 1.5, 10 of 209 with values of 1.6-2.9, and 11 of 222 with PRA of 3.0 or more. There were no significant differences among groups by the Kaplan-Meier method.

Conclusion: Increased PRA induced by RAS inhibitors does not affect the prognosis of patients with hypertension.



Kaplan-Meier

P988

Soluble CD40 ligand predicts incident heart failure in patients with preserved left ventricular function after myocardial infarction

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Introduction: Apart from its role in acute thrombotic states, soluble CD40 ligand (sCD40L) could contribute to the development of heart failure (HF) by activation of matrix-metalloproteinase complex, as well as by induction of inflammatory cytokines and chemokines which promote left ventricular remodeling, tissue inflammation, apoptosis and myocardial fibrosis.

Purpose: To investigate 1.) the correlation of sCD40L with risk factors and long-term therapy in patients with preserved left ventricular function after myocardial infarction (MI) and 2.) its influence on the occurrence of incident heart failure in the next 1-year follow-up.

Methods: We examined 99 consecutive outpatients 6 months after MI. Baseline study appointment included a medical history interview, physical examination, resting 2-D echocardiogram and fasting venous blood samples, with EDTA plasma frozen at -70°C. Soluble CD40L was measured in all patients by ELISA method according to manufacturer's advice, using new, highly-specific reagents of Bender

MedSystems-BMS293, with lower reference values, adapted for cardiovascular use. Patients were clinically followed-up for the next 1 year.

Results: The median value of sCD40L was 377 $\mu\text{g/ml}$ (IQR 299-670 $\mu\text{g/ml}$), which is higher than values in healthy population described in the literature (140, IQR 80-250 $\mu\text{g/ml}$). Among all risk factors, multiple linear regression analysis showed significant independent negative correlation of sCD40L with family history ($\beta = -0.27$; $p = 0.006$) and among long-term medications with the use of beta blockers ($\beta = -0.25$; $p = 0.011$). Soluble CD40L did not correlate with any of echo parameters. Multivariate Cox regression analysis, adjusted for age, risk factors, reperfusion therapy, ejection fraction and recurrent ischemic event showed an independent association of sCD40L and incident heart failure (HR = 2.2; 95%CI 0.98-4.8; $p = 0.04$) in the 1-year follow-up. The optimal predictive cut-off value, obtained by ROC analysis, was 380 $\mu\text{g/ml}$.

Conclusion: In our study on patients after MI, sCD40L was higher in those without family history. The use of beta blockers was associated with lower values of sCD40L. Higher values of this marker strongly predicted incident heart failure, without correlation with echo parameters, suggesting that other mechanisms than left ventricular systolic or diastolic function may play a role in this process.

P989

Hyponatremia and outcomes in Tunisian patients admitted for acute heart failure

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Purpose: The aims of this study is to characterize hyponatremic hospitalized patients with HF and to clarify the relations between hyponatremia and outcomes during hospitalization and at 6 months.

Methods: This is a retrospective study of 234 patients admitted in the cardiology department of our hospital between January 2010 and March 2011. Hyponatremia was defined as a blood value of sodium < 135 mmol/l.

Results: The mean serum sodium concentration is 138 ± 5 mmol / l. Hyponatremia ($\text{Na}^+ < 135$ mmol / l) was noted in 63 (26.9%) patients.

Hospital mortality was 7.3% (N = 17). Cardiovascular origin was observed in 58.8% of cases. This mortality was significantly higher in patients with hyponatremia, 15.87%, compared to 4.09%, in those with normonatremia ($p = 0.004$).

After their outputs, 39 patients (19.69%) required at least one re-hospitalization during the first 6 months of follow-up. The 6-month mortality was 11, 5%. The rate of readmission and mortality at 6 months was higher in patients who had hyponatremia; Respectively 32.07% vs 13.41%, $p = 0.002$ and 21.42% vs 7.78%, $p = 0.005$.

Conclusion: In our study, the presence of hyponatremia in patients hospitalized for acute heart failure is predictive of hospital mortality, readmission and mortality at 6 months.

P990

Galectin provides additional prognosis information when compared to BNP and NT-proBNP in ambulatory patients with heart failure

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Galectin-3 (Gal-3) is an emerging biomarker interesting to assess prognosis in various pathophysiological conditions including acute coronary syndromes, acute heart failure (HF) or patients admitted on hospital for HF.

The aim of this work was to investigate the prognosis interest of this marker in ambulatory patients with stable HF.

Patients

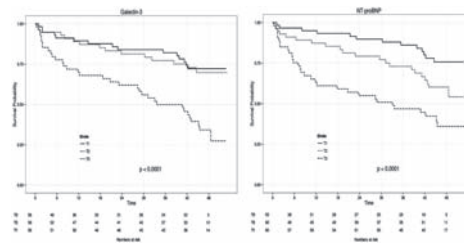
180 patients were included in 2008. All the patients gave an informed consent. Clinical characteristics were registered and biomarkers were assessed. Clinical outcomes were registered regularly on clinical follow-up or by phone by a dedicated physician.

Survival curves were built and data presented as means \pm SD when normally distributed.

Results: 180 patients (mean age 72.5y \pm 12.5y) were included. Left ventricular ejection fraction was 37.1% \pm 14.2%.

Gal-3 and NT-pro-BNP were highly correlated. Both biomarkers were able to discriminate patients' survival following the tertile of the patients. Nevertheless the gal-3 was able to discriminate more accurately the tertiles (median of survival: 6, 26, 33 months respectively for tertiles 1, 2, 3, $p < 0.01$) versus (median of survival: 10, 20, 36 months respectively for tertiles 1, 2, 3, $p < 0.01$)

Conclusion: A multimarker approach should be promising regarding the stratification of the prognosis of ambulatory patients with HF.



P991

Prognostic value of hepatic biomarkers in patients who underwent cardiac resynchronization therapy

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Purpose: To evaluate the prognostic role of hepatic biomarkers in heart failure (HF) patients with cardiac resynchronization therapy (CRT).

Methods: We enrolled 214 HF patients (83% male, mean age 69.9 \pm 8.4 yy; mean QRS length 147.2 \pm 25 ms; mean NYHA class 2.7 \pm 0.6) who underwent CRT. We measured serum levels, before the implantation of the CRT device, of aspartate aminotransferase (AST), alanine aminotransferase (ALT), γ -glutamyl transferase (GGT), alkaline phosphatase (ALP), bilirubin, hemoglobin (Hb), natriuretic peptide (BNP) and creatinine. Patients were followed-up for 29.5 \pm 21 months. Primary end-point was total mortality. We used a Cox adjusted multivariable logistic regression analysis to identify independent predictors of death for any reason.

Results: In our population mean GGT values were 54.8 \pm 54.2 UI/L. Elevation of GGT (≥ 50 UI/L) was found in 69 patients (32.2%). During follow-up 39 patients (18.2%) died from any cause. An adjusted multivariate Cox analysis showed that GGT (HR 2.05, C.I.95% 1.082-3.874, $p = 0.028$), BNP (HR 1.56, C.I.95% 1.065-2.309, $p = 0.022$), ALP (HR 1.004, C.I. 95% 1.001-1.007, $p = 0.006$), Hb (HR 2.41, C.I.95% 1.214-4.811, $p = 0.012$) and creatinine (HR 2.09, C.I. 95% 1.059-4.145, $p = 0.034$) were independent predictors of all-cause death. Kaplan-Meier curves pointed-out a statistically significant different mortality between patients with normal or elevated GGT values.

Conclusions: Prevalence of GGT increase among HF patients with CRT seems to be elevated. GGT serum levels result as independent predictors of all-cause mortality. Thus, evaluation of hepatic biomarkers may contribute to a more accurate selection of patients to candidate for CRT.

P992

Comparison of serial monitoring of multiple biomarkers in patients with acutely decompensated heart failure

the Key Projects in the National Science & Technology Pillar Program of the 12th Five-year Plan Period (No. 2011BAI11B02, project for heart failure) R Rongcheng Zhang¹; Y Zhang¹; T An¹; Y Huang¹; Q Zhou¹; J Zhang¹

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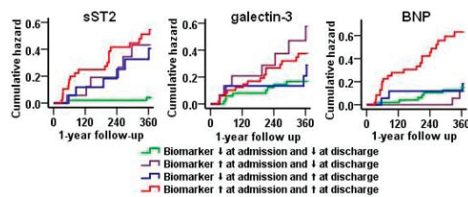
Purpose: To evaluate the prognostic value of serial measurements of soluble ST2 (sST2), galectin-3 and B type natriuretic peptide (BNP) in patients with acutely decompensated heart failure (ADHF).

Methods: We prospectively enrolled 136 patients hospitalized with ADHF, and followed up for 1 year. sST2, galectin-3 and BNP were measured at admission and discharge. The endpoint was cardiovascular (CV) events defined as CV death and hospitalization due to worsening HF.

Results: 37 patients have experienced a CV event. Only BNP significantly decreased in patients who did not have event ($P = 0.04$). Cox regression showed all biomarkers both at admission and discharge independently predicted CV events after adjustment for reference model, but only the change in sST2 and BNP were significant in univariate analysis. When biomarkers were dichotomized according to their median value at admission and discharge respectively, patients with higher sST2 concentration at both two time points had a comparable cumulative rate of CV events to patients with sST2 higher at either time point. In addition, patients with BNP concentration higher at admission and discharge had the highest risk of events. When considering changes of galectin-3, we did not observe different cumulative risk under same level of galectin-3 at baseline. The changes of biomarkers did not provide additional prognostic value to model in discrimination and reclassification analysis.

Conclusions: In patients with ADHF, serial measurements of sST2 and BNP at admission and discharge were significantly associated with 1-year CV events. In

particular, change in BNP appeared to provide more prognostic information.



K-M survival curves for CV events

P993

Inflammatory biomarkers predicting prognosis in patients with acute dyspnoea

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Objective/Purpose: The aim of this study was to identify inflammatory biomarkers that predict risk of 90-days mortality in patients presenting with acute dyspnoea at the Emergency Department (ED).

Method: Adult patients admitted to the ED with acute dyspnoea were enrolled in the study. Conventional risk assessment parameters were recorded and plasma collected immediately at admission was analysed for 25 inflammatory biomarkers using a multiplex immunoassay. The biomarkers were related to risk of 90-days mortality using multivariate Cox proportional hazard models, adjusted for age, sex, oxygen saturation, respiratory rate, C-reactive protein (CRP) and "Medical Emergency Triage and Treatment System-Adult" score (METTS-A).

Results: Of 407 enrolled patients (mean age 70 ± 18.3 years, 52.3% women), 50 (12%) patients died within 90-days from admission. Among conventional risk stratification parameters, age ($P = 0.007$) and respiratory rate ($P = 0.002$) were the strongest predictors of 90-days mortality. The strongest relationship between inflammatory biomarkers and 90-days mortality was observed for Interleukin-8 (IL-8) and Growth Differentiation Factor 15 (GDF-15). The Hazard Ratio (95% confidence interval) for 90-days mortality per 1 standard deviation (SD) increment of log-transformed IL-8 was 2.20 (1.67-2.90) ($P = 2.5 \times 10^{-8}$) and for GDF-15 3.45 (2.18-5.45) ($P = 1.3 \times 10^{-7}$) and when all nominally significant biomarkers were simultaneously entered, IL-8 and GDF-15 came out as the two independent biomarker signals. A "Biomarker Mortality Risk Score" (BMRS) summing standardized and weighted values of IL-8 and GDF-15, revealed that of patients belonging to quartile 1 (Q1) of the BMRS, only 1 patient died within 90 days, whereas 32 patients died among those belonging to quartile 4. Each 1 SD increment of the BMRS was associated with a Hazard Ratio of 3.79 (2.50-5.73) ($P = 2 \times 10^{-10}$) for 90-days mortality and the point estimate was 13 times higher in Q4 as compared to Q1 of the BMRS (Ptrend over quartiles = 2×10^{-6}). Additional adjustment for smoking, comorbidities and brain natriuretic peptide did not change the results.

Conclusion: IL-8 and GDF-15 are strongly and independently related to risk of 90-days mortality in unselected patients admitted to the ED because of acute dyspnoea, suggesting that they may guide first-line physicians at the ED in risk assessment which in turn could lead to more accurate level of care and treatment intensity.

P994

Novel biomarkers as predictors of adverse short-term prognosis in patients with acute decompensated chronic heart failure

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Purpose: Evaluation of the prognostic significance of soluble ST2-receptor (sST2), galectin-3 (Gal-3), high-sensitivity troponin-T (HSTnT) and neutrophil gelatinase-associated lipocalin (NGAL) in short-term prognosis (90 days) of patients with acute decompensated heart failure.

Methods: A prospective single center study included 113 patients hospitalized with acute decompensated chronic heart failure (CHF). Blood samples to determine the biomarkers concentrations were collected before the first dose of diuretic and in the day of discharge from hospital. The primary endpoint was defined as the combined endpoint including cardiovascular death, HF deterioration requiring intravenous diuretics and first hospitalization due to CHF.

Results: Increase concentration of the studied markers observed in all included patients. Correlation between markers were weak, both at admission and at discharge from hospital, the maximum relationship was found between sST2 and

HSTnT ($r = 0.36$, $p < 0.0001$). During the 90 days follow up period the end point was reached by 19 pts (16.8 percent). The prognostic significance of this model was assessed by calculating the area under the curve in ROC analysis. The model included clinical factors of adverse prognosis (gender, age, obesity, left ventricular ejection fraction, glomerular filtration rate, hemoglobin concentration and blood urea) at admission and at discharge from hospital, had an area under the curve of 0.75 and 0.8, respectively, $p < 0.05$. Implications for clinical model the classic markers of adverse prognosis (NT-proBNP and HSTnT) at discharge from hospital was accompanied by an increase the area under the curve from 0.8 to 0.85, $p < 0.05$. But subsequent progressive including in clinical model concentrations of sST2, Gal-3, HSTnT, NGAL at discharge from hospital was accompanied by further increasing the area under the curve to 0.93, $p < 0.05$.

Conclusion: Multimarker approach, including sST2, Gal-3, HSTnT, NGAL concentrations and clinical model at discharge from hospital is a more powerful predictor of adverse short-term prognosis in patients with acute decompensated heart failure, compared with clinical model and only NT-proBNP.

P995

Galectin-3 levels and the assessment of clinical severity in patients with ST segment elevation myocardial infarction

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Materials: 87 patients (65 -males, 22 - females; mean age - 58.9 ± 1.03 yrs), admitted with ST-segment elevation acute coronary syndrome (ACS), were examined. Galectin-3 levels were measured by ELISA on day 2 after disease onset in all patients. The studied biomarker levels were measured in 81 patients on days 10-14 after the onset of myocardial infarction. The baseline serum values of galectin-3 were 0.0-2.28 ng / ml.

Results: Galectin-3 levels, measured in MI patients on day 2 after disease onset, were elevated compared to the baseline values (9.5 [3.3, 11.9] ng/ml). On days 10-14 after MI, elevated galectin-3 levels (15.6 [9.9; 37.4] ng/ml) were observed ($p < 0.01$). A trend toward significantly higher levels of galectin-3 on days 10-14 after the disease onset was observed by the retrospective clinical record cards analysis in patients with arterial hypertension (AH) (20.1 [10.4; 38.9] ng/ml vs. 9.9 [9.1; 33.8] ng/ml, $p = 0.04$) as well as in patients with acute cerebrovascular accident (ACVA) (15.5 [9.9; 35.9] ng/ml vs 42.5 [25.4; 57.1] ng/ml, $p = 0.04$). Patients with a history of diabetes mellitus (DM) demonstrated higher galectin-3 levels on days 10-14 (38.0 [20.6; 48.4] ng/ml) compared to patients without it (13.4 [9.5, 35.8] ng/ml, $p < 0.01$). Importantly, ACS patients with a history of hypercholesterolemia demonstrated elevated biomarker levels on days 10-14 (35.6 [21.4; 40.1] ng/ml, vs. 10.9 [9.5; 33.7] ng/ml, $p < 0.01$). Patients with coronary artery disease and burdened heredity had significantly ($p = 0.02$) higher levels of galectin-3 (35.6 [15.6; 44.1] ng/ml), compared with patients without it (12.6 [9.5; 35.9] ng/ml). The assessment of instrumental findings reported that galectin-3 levels on day 2 in patients with intima-media complex (IMC) thickening were 3.3 [3.1; 9.9] ng/ml, that significantly ($p = 0.01$) differed from patients with normal IMC - 9.9 [3.7, 11.9] ng/ml. Thus, elevated galectin-3 levels were found on days 10-14 in patients with reduced ejection fraction (EF) (45.2 [32.8; 49.2] ng/ml), than in patients with normal ejection fraction (15.5 [9.9; 35.9] ng/ml, $p = 0.02$). The correlation analysis reported a weak positive correlation between galectin-3 levels on day 1 and IMC ($r = 0.2$, $p = 0.03$). A direct correlation between biomarker levels on days 10-14, the number of diseased coronary arteries ($r = 0.29$, $p = 0.01$) and door - to - balloon time (min) ($r = 0.27$, $p = 0.02$) has been defined as well as a reverse correlation between EF ($r = -0.25$, $p = 0.03$).

Conclusion: Galectin-3 levels allow evaluating clinical severity of patients with STEMI.

P996

Serial changes in serum ACE 2 and plasma ang (1-7) concentration of acute heart failure syndrome patients with standard therapy

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Background: Recently the existence of the ACE2/Ang-(1-7)/Mas receptor axis and the organ-protective effect by activating this axis have been revealed. Last year we reported at Japanese Congress that serum ACE2 concentration level is higher and plasma Ang (1-7) concentration level is lower in acute heart failure syndrome (AHFS) patients than healthy volunteers. There are no reports about its serial changes.

Aim: To evaluate the serial changes of serum ACE2 concentration and plasma Ang (1-7) concentration for hospitalized AHFS patients.

Methods: Seventy-three patients hospitalized with acute heart failure at our institute between Nov. 2012 and May 2014 who gave consent were enrolled. Plasma renin activity, serum ACE, plasma Ang II, serum ACE2, plasma Ang- (1-7), and plasma aldosterone concentrations were measured immediately after the patient were able to sit up, and then one and three months after the onset of the standard therapy then evaluated the serial changes.

Result: Average age was 63 ± 14 years old, 22% male, and the cause of acute AHFS was 29 ischemic heart disease, 43 non-ischemic heart disease. There were no serial changes in plasma renin activity, serum ACE, plasma Ang II, and plasma aldosterone concentration. Although serum ACE2 concentration significantly decreased (8.54 ± 4.72 ng/ml vs 6.87 ± 6.24 ng/ml vs 7.34 ± 3.65 ng/ml, $p < 0.05$) and plasma Ang (1-7) concentration significantly increased (2.43 ± 1.18 ng/ml vs 3.02 ± 1.98 ng/ml vs 3.35 ± 2.01 ng/ml, $p < 0.05$).

Conclusion: Serum ACE2 concentration decreased and plasma Ang (1-7) concentration increased in AHFS patients with standard therapy.

P997

Prognostic value of novel biomarkers compared to broad biochemical evaluation in heart failure patients

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Background: Adequate evaluation of patients' prognosis is crucial in clinical management of heart failure (HF). The aim of the study was to evaluate the usefulness of novel biomarkers compared to standard biochemical assessment in HF.

Methods: There were 179 subsequent inpatients with HF included in the study. All of the patients underwent standard biochemical assessment and biomarkers evaluation (N-terminal pro B-type natriuretic peptide, high sensitivity C reactive protein, growth hormone, myeloperoxidase, metalloproteinase 9, procollagen III, soluble toll like receptor-2, insulin growth factor and Neutrophil Gelatinase-Associated Lipocain). Primary end-point (PEP) included death or urgent heart transplantation, whereas secondary end-point (SEP) incorporated PEP plus adequate cardioverter-defibrillator intervention or HF hospitalization.

Results: Mean age was 52.5 years (91% were man). Most patients were in advanced HF. There were 21 PEP and 63 SEP. From univariate logistic regression both biomarkers and biochemical parameters were predictive of events (Table). However, on the multiple regression from all variables only uric acid and sodium were independent predictors of PEP. On the other hand for SEP only eGFR (estimated glomerular filtration rate) remained significant. No biomarker was significant.

Conclusions: Biomarkers do not outweigh biochemical tests. Data obtained from the standard tests revealing multiorgan involvement deliver the most prognostic information. Biochemical evaluation should remain the gold standard for HF prognosis assessment.

P998

Association of circulating MiR423-5p with heart failure in stable coronary artery disease: the heart and soul study

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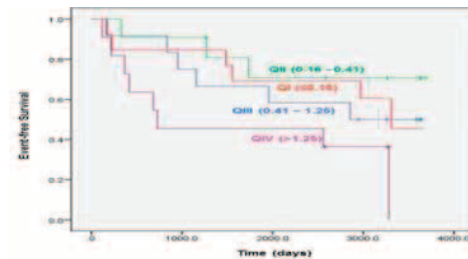
Purpose: Circulating microRNA (miR) 423-5p is elevated in patients with heart failure (HF). The aim of this study was to investigate the association of circulating miR423-5p with B-type natriuretic peptide (BNP) level, left ventricular (LV) structure and function and HF in stable coronary artery disease (CAD).

Methods: In 47 patients with stable CAD (11 with a history of HF, 23 with left ventricular hypertrophy (LVH) and 24 with neither HF nor LVH), real-time quantitative polymerase chain reaction (qPCR) was used to measure miR423-5p levels in serum

samples and echocardiography was used to determine LV mass and ejection fraction. Cox proportional hazards models were used to study the association of miR423-5p level with time to HF hospitalization.

Results: MiR423-5p levels (median 0.41, IQR 0.16, 1.25) were significantly correlated with B-type natriuretic peptide (BNP) level ($r = 0.40$; $p = 0.006$) and LV mass index ($r = 0.48$; $p = 0.001$) but not with age or LV ejection fraction. During 6.2 ± 3.6 years of follow-up, there were 23 hospitalizations for HF. Participants with the highest quartile of miR423-5p had a trend toward worse event-free survival than those in the first three quartiles ($p = 0.06$) and significantly worse event-free survival than those in the second quartile ($p = 0.03$; Kaplan-Meier plot attached). When modeled as a linear variable, miR423-5p was associated with increased risk of HF hospitalization (HR 1.45 per SD (1.20 unit) increase; 95% C.I. 1.04 - 2.02). However, this association was no longer significant when the model was adjusted either for LV mass index or for BNP level.

Conclusions: In stable CAD, circulating miR423-5p levels are correlated with LV structural change and biomarkers of elevated LV filling pressure and are associated with an increased risk of HF hospitalization.



Kaplan-Meier Plot by MiR423-5p Quartiles

P999

Exhaled breath analysis in diagnostic of heart failure

This study was supported by Russian Academy of Science AA Bykova¹; L K Malinovskaya¹; MV Kuznetsova¹; P SH Chomahidze¹; PH YU Kopylov¹; V B Betelin²; A L Syrkin¹

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Purpose: The purpose of this study was to investigate exhaled breath in patients with and without heart failure, with reduced LV EF and find out novel biomarkers of HF.

Methods: From October 2013 to December 2014 we have included 35 patients with LV EF less than 45% in heart failure group and 15 patients without HF in control group. We collected fasting exhaled breath samples of all patients in 1L Tedlar bags. Exhaled breath was analyzed using PTR-MS. **Results:** The baseline characteristics were similar in both groups. The mean EF in HF group was $36 \pm 9\%$. In compare with control group several biomarkers were significantly higher in HF group. They are: acetone, acetic acid, ethanol, propylene and xylol. The median (interquartile range) concentration of acetone in HF group when compared to control group was 683,5 ppb [343-3156] vs 316,8 ppb [230-376] ($p = 0,002$); acetic acid 35,5 [27-57] vs 23,5 [20-25] ($p = 0,001$); ethanol 18,9 [13-40] vs 10,4 [9-21] ($p = 0,018$); propylene 207,5 [90-581] vs 106 [74-138] ($p = 0,01$); xylol 1,4 [0,8-2,9] vs 0,64

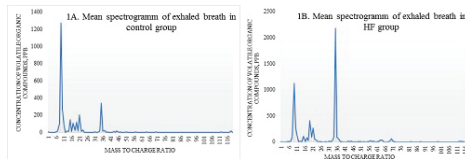
Table 60306: Predictors of outcomes

Predictors of PEP	Univariate model for PEP	Multivariate model for PEP	Predictors of SEP	Univariate model for SEP	Multivariate model for SEP	OR	p	OR	p
	p	OR		p	OR				
RDW	1.361	0.002	-	Ns	RDW	1.238	0.01	-	Ns
% of neutrophils	1.064	0.02	-	Ns	ST-2	1.013	0.04	-	Ns
Bilirubin	1.057	0.003	-	ns	NGAL	1.006	0.02	-	Ns
ST-2	1.019	0.005	-	Ns	NT-proBNP	1.000	0.04	-	Ns
Uric acid	1.006	0.001	1.006	0.002	eGFR	0.970	0.002	0.98	0.02
NT-proBNP	1.000	0.01	-	Ns	Sodium	0.86	0.0003	-	Ns
eGFR	0.963	0.008	-	Ns	Total cholesterol	0.732	0.03	-	Ns
Sodium	0.811	0.0009	0.79	0.0003	LDL-cholesterol	0.673	0.03	-	Ns
HDL cholesterol	0.144	0.01	-	Ns					

*Presented only significant variables

[0,6-1,2] ($p=0,022$) respectively. We also found a significant negative correlation between these biomarkers and ejection fraction.

Conclusion: There is a significant difference in several biomarkers in exhaled breath between patients with and without heart failure. Further investigation is necessary to determine the correlation between these biomarkers and levels of natriuretic peptides. The place of this method in diagnostic of heart failure with preserve ejection fraction is also unclear.



Mean spectrograms of exhaled breath

P1000

Association between galectin-3, renal injury and neutrophil gelatinase-associated lipocalin in heart failure patients

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Purpose: Elevated circulating levels of galectin-3, a mediator of fibrogenesis, are associated with left ventricular remodeling and adverse outcome in heart failure (HF). Renal function impairment and inflammation further deteriorates clinical outcome in HF patients. We examined the association between renal function, inflammatory status clinical parameters and galectin-3 levels in patients with ischemic HF.

Methods: We consecutive enrolled 115 subjects with stable ischemic HF of NYHA status II and III. We measured serum Galectin-3 as a fibrogenesis marker, b-type natriuretic peptide (BNP) as an index of left ventricle loading condition, neutrophil gelatinase-associated lipocalin (NGAL) as an early marker of kidney injury and tumor necrosis factor alpha (TNF α) as a well-established inflammatory index. Creatinine clearance (eCCL) was estimated using Cockcroft-Gault formula.

Results: Galectin-3 levels were associated with BNP levels ($r=0.37$, $p=0.006$), NGAL levels ($r=0.40$, $p=0.001$) and inversely associated with eCCL ($r=-0.59$, $p<0.001$) while there was no association of galectin-3 levels with left ventricle ejection fraction ($\rho=-0.03$, $p=0.77$) and TNF α ($r=0.24$, $p=0.1$). Interestingly, galectin-3 levels were also positively associated with age ($r=0.38$, $p<0.001$) and were higher in subjects with diabetes mellitus compared to normoglycemic patients [18.05 (15.42-24.85)ng/ml vs. 14.50(12.40-19.60)ng/ml, $p=0.02$]. There was no difference in galectin-3 levels between hypertensive and normotensive subjects [17.30 (14.20-21.60)ng/ml vs. 13.50(11.20-23.35)ng/ml, $p=0.22$]. Moreover, there was no difference in galectin-3 levels between subjects on mineralocorticoid receptor antagonist treatment or not ($p=0.94$) and between subjects on angiotensin converting enzyme inhibitors or angiotensin receptor blockers treatment ($p=0.77$). As many confounders exist we applied a linear regression model which revealed that only NGAL levels were independently associated with galectin-3 [b = 0.04 95%CI (0.02-0.06), $p<0.001$].

Conclusion: Galectin-3, a fibrogenesis protein, is elevated in HF patients and is strong associated with renal injury as it is expressed by NGAL levels.

P1001

Usefulness of serial measures of galectin-3 in hospitalized patients with acute heart failure

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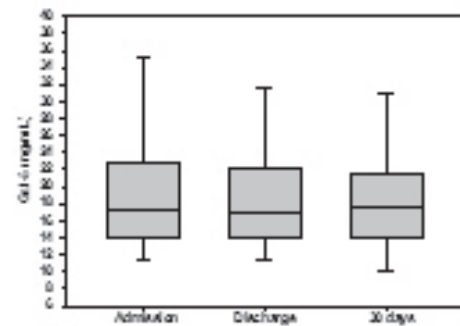
Purpose: In acute heart failure (AHF) patients, high levels of Gal-3 (>17.8 ng/mL) upon discharge are associated with higher risk for adverse events. The utility of serial measures of Gal-3 in AHF patients has not been established.

Methods: We studied 111 patients admitted with AHF (60% male, 71 \pm 11 years, LVEF 41 \pm 15%). Blood samples were obtained at the arrival to the emergency

department, at discharge (median 7 days) and 30-days after discharge. Gal-3 was measured by enzyme immunoassay using a commercial assay. Patients were followed (453 \pm 517 days) and the occurrence of death and HF readmission were registered.

Results: Levels of Gal-3 (ng/mL) were: 20.6 \pm 11.8 at admission, 19.2 \pm 8.1 at discharge and 19.9 \pm 11.7 at 30-days. Considering the threshold of 17.8 ng/mL, 46% of patients were over this level at admission, 45% at discharge and 46% at 30-days. The repeated measures analysis revealed that Gal-3 levels did not change significantly between the three time points ($p=0.726$) (Figure). A total of 25 (22.5%) patients died, 40 (36%) were readmitted with AHF and 53 (48%) had any adverse event. Cox regression analysis showed that patients with Gal-3>17.8 ng/mL at admission had a higher risk of HF readmission or death (HR 2.17, 95%CI 1.25-3.77, $p=0.006$). After the multivariable adjustment, Gal-3>17.8 ng/mL at admission remained as predictor of adverse events (HR 2.02, CI95% 1.14-3.57, $p=0.015$), but Gal-3 at discharge ($p=0.069$) or 30-days ($p=0.575$) did not reach statistical significance.

Conclusions: In patients with AHF, Gal-3 at admission identified a more adverse phenotype, with higher risk of death or HF readmission. Gal-3 levels did not change in the first month, and serial measures did not add prognostic information over a single measure at admission.



Gal-3 levels

P1002

MicroRNA related to worsening renal function in patients with acute heart failure

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Purpose: MicroRNA (miRNA) deregulation is involved in heart failure and renal disease pathogenesis. Our aim was to describe miRNA profiles related to early worsening renal function (WRF) in acute heart failure (AHF) patients.

Methods: Levels of fifteen previously selected miRNA, related with the severity of heart failure, were measured in plasma samples of 98 AHF patients. We studied the association between miRNA levels at hospital admission and WRF (increase in serum creatinine ≥ 0.3 mg/dL from admission to day 3), and absolute change in creatinine and NGAL from admission to day 3.

Results: Circulating levels of all miRNA (except for miR-128) were lower in WRF patients, with statistically significant downregulation of miRNA 199a-3p, 423-3p, let-7i-5p. Absolute creatinine increase was associated with lower levels of miRNA 199a-3p, 27a-3p, 652-3p, 423-5p, let-7i-5p (all $p<0.05$) while plasma levels of miRNA 18a-5p, 106a-5p, 223-3p, 199a-3p, 423-3p and 18b-5p were negatively correlated with NGAL levels (all $p<0.05$). MiRNA 199a-3p was the strongest predictor of WRF, with Odds Ratio of 1.48(1.061-2.065; $P=0.021$) and C-index of 0.701.

Conclusions: MiRNA levels at hospital admission are consistently lower in AHF patients who developed WRF. MiRNA 199a-3p is the best predictor of WRF.

levels of miRNA in WRF and non WRF			
miR	non WRF	WRF	P-value
18a-5p	-0.7 [-1.6-0.6]	0.3 [-0.3-0.6]	0.107
106a-5p	-3.4 [-4.5-2.4]	-2.9 [-3.3-2.2]	0.088
26b-5p	-0.5 [-1.4-0.4]	-0.3 [-0.7-1.1]	0.304
301a-3p	0.6 [0-1.4]	1.1 [0-1.7]	0.538
223-3 p	-6.2 [-7.6-5]	-5.8 [-6.9-4.9]	0.367
199a-3p	-1.4 [-3.2-0]	0 [-1-1.3]	0.012
27a-3p	-3 [-4.4-1.7]	-2.3 [-3-0.9]	0.084
652-3p	-1.1 [-2.3-0.2]	0 [-1.2-0.5]	0.064
423-5p	-3.4 [-4.7-2.6]	-2.8 [-3.4-2]	0.096
423-3p	-1.8 [-2.9-0.4]	-1 [-1.4-0.1]	0.032
16-5p	-8.7 [-9.7-7.5]	-8.4 [-9-7]	0.325
30e-5p	-3.3 [-4.4-2.1]	-2.6 [-2.9-1.7]	0.053
Let-7i-5p	-3.2 [-4-2.2]	-2.3 [-2.8-1.7]	0.034
18b-5p	-0.9 [-2-0.5]	0 [-1.1-1]	0.187

miRNA:microRNA;WRF:worsening renal function

P1003

Reverse remodelling and 4-year survival using the ST2-R2 score in patients with heart failure. A multicenter study

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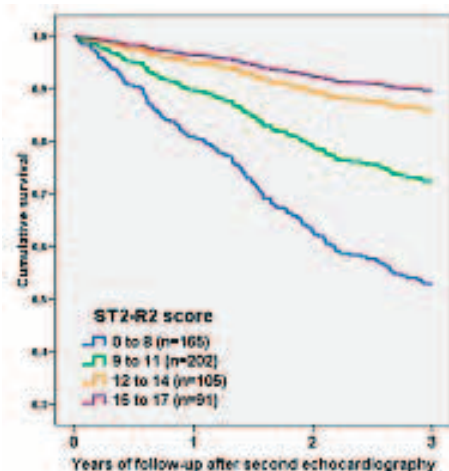
Background: Recently, the ST2-R2 score (ST2 <48 ng/mL, non-ischemic aetiology, absence of LBBB, HF duration <12 months, baseline LVEF <24%, and β -blocker treatment) was developed to predict relevant reverse remodelling (R2).

Aims: To validate the degree of LVEF improvement and LV reduction at one year according to the ST2-R2 score and its prognostic implications up to 4 years.

Methods: 569 patients with baseline LV ejection fraction (LVEF) <40% from 3 cohorts: Barcelona, TIME-CHF and PROTECT were included. For analysis patients were classified in 4 strata (0-8; 9-11; 12-14; 15-17) based upon their ST2-R2 score.

Results: A linear relationship was observed between ST2-R2 scoring and LVEF and LV size changes. Based on the specified subgroups a significant association was observed between LVEF recovery (mean +5.6, +6.7, +11.3 and +17.3 respectively; $p < 0.001$), and the reduction percentage of LVESVi (mean -6.1, -12.2, -25.6 and -32.1, respectively; $p < 0.001$) and LVESDi (mean -1.1, -3.6, -9.3 and -18.6, respectively; $p < 0.001$). A similar trend was observed with diastolic parameters. The improvement in LV function and size was accompanied by better outcome. Hazard ratios for risk of death taking the lower ST2-R2 group (0-8) as reference were 0.49 ($p < 0.001$), 0.27 ($p < 0.001$), and 0.17 ($p < 0.001$) for scores 9-11, 12-14 and 15-17, respectively. Figure 1 shows survival curves according to ST2-R2 score subgroups.

Conclusions: The ST2-R2 score, which includes the novel biomarker ST2 and five conventional risk parameters, reasonably predicts degree of R2 in HF patients and was useful to prognosticate mortality up to 4 years.



POPULATION STUDIES / EPIDEMIOLOGY

P1004

The profile of heart failure elderly patients in a romanian general hospital

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Background: Heart failure, as end stage heart disease, is more and more a public health problem with frequent hospitalization, high cost, low quality of life and decreases survival. Its incidence increases with age.

Purpose: To analyze the clinical profile of elderly heart failure patients in a Romanian general Hospital.

Methods: The study investigated 191 patients over 65 years of age, mean age 72.58 \pm 7.35 years, 56% women, hospitalized in a Romanian general Hospital. Heart failure was defined according to ESC 2012 criteria. In all patients, plasmatic NT-pro-BNP was determined using the ELISA method.

Results: 72.8% patients displayed atrial fibrillation (AF), and 27.2% were in sinus rhythm. Atrial fibrillation was present in women in a significantly lower ratio-65.4% vs. 82.1% in men ($p = 0.007$). 47.65% of the patients displayed ejection fraction (LVEF) \geq 50%, and 52.26% <50%. Of the patients in sinus rhythm, 17.3% had LVEF <50% and 82.7% preserved LVEF, $p < 0.001$. There was no statistically significant difference in the LVEF values in patients with AF: 65.5% had LVEF <50%, and 34.5% LVEF \geq 50%. Mean values of NT-pro-BNP in the entire cohort was 1934.66 \pm 1126.65 pg/ml. Irrespective of the presence or absence of sinus rhythm, all patients with LVEF <50% displayed significantly higher NT-pro-BNP values: 2601.24 \pm 691.25 vs 1853.12 \pm 1037.77 pg/ml ($p < 0.01$)- AF and 1784.66 \pm 1165.48 vs 646.39 \pm 761.69 pg/ml-sinus rhythm ($p < 0.001$). At the same time, NT-pro-BNP levels were significantly higher in patients with low LVEF and AF as compared to those in sinus rhythm: 2601.24 \pm 691.25 vs 1784.66 \pm 1165.48 pg/ml ($p = 0.032$). The same held true in case of preserved LVEF: 1853.12 \pm 1037.77 vs 646.39 \pm 761.69 pg/ml ($p < 0.001$). When taking into consideration the medication recommended by the ESC guidelines for heart failure, no significant difference was recorded in what concerned the administration of renin-angiotensin-aldosterone inhibitors, beta-blockers, and diuretics to patients with or without sinus rhythm. Obviously, digoxin was administered in a significantly higher percentage to patients with low LVEF and AF: 76.9% (EF <50%) vs 52.1% (LVEF \geq 50%)- $p = 0.005$. Only 11.1% of the sinus rhythm patients received digoxin, all having LVEF <50%. In conclusion, heart failure with preserved LVEF prevailed in elderly patients with sinus rhythm, and AF patients displayed significantly higher values of NT-pro-BNP, irrespective of LVEF values (suggesting that AF is a more powerful factor than LVEF in increasing cardiac peptides).

P1005

The cost of acute heart failure in Greece: a social security system perspective

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Aim: Heart failure management constitutes a significant economic burden for the health care systems across Europe, accounting for 1% to 3% of total health care expenditures. Usually, this cost is covered mainly by the social security systems and this is also the case for Greece. The objective of this study was to estimate the economic burden of acute heart failure (AHF) to the social security system.

Methods: Health economic data were extracted from a prospective European registry, the ESC Heart Failure Pilot Survey. A representative sample of 177 patients with AHF hospitalised in eight different secondary and tertiary cardiology departments across Greece were included in the study. The analysis was conducted from the social security system perspective with 2014 as reference year. Only direct costs have been estimated including costs of hospitalisations, medications, other relevant cardiovascular interventions, clinical and laboratory follow-up, for up to one year after the index hospitalisation.

Results: The mean annual economic burden of the social security system per patient was estimated at €4,755 \pm 3,921, more than a quarter of the national gross domestic product per capita. The mean cost of the index hospitalisation was €2,292 \pm 3,092 for a median length of stay 7 days and the mean annual cost after the index hospitalization was €3,006 \pm 2,571. About two thirds (67.5%) of the latter cost is associated with in-patient care, 16.1% with drug treatment and 12.5% with laboratory monitoring. Physicians' cost accounted for only 3.9% of the AHF outpatient management cost. Hospitalisation and total cost were significantly higher in male patients with reduced ejection fraction, renal dysfunction and atrial fibrillation ($p < 0.05$). Moreover, anemia, uncontrolled hypertension and increasing levels of TSH are significant independent predictors of total cost.

Conclusion: AHF imposes a significant economic burden for the social security system and national economy, mainly because of the often, long and costly hospitalisations. It is particularly important for the decision makers to have an estimate of the costs attributed to AHF, as they will have to plan and finance the care of the aging population.

P1006

Reasons for hospitalisation and rehospitalisation among Greek patients admitted for acute heart failure

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Aim: Heart failure is the leading cause of hospitalisation in Europe and in the United States, representing more than 1-2% of all hospitalisations. The objective of this study was to identify the reasons for hospitalisation and rehospitalisation among Greek patients admitted for acute heart failure (AHF).

Methods: Eight Greek secondary and tertiary cardiology centres from different cities have participated in a prospective, observational survey, the ESC Heart Failure Pilot Survey, from 2009 to 2011. Data from these centres concerning hospitalisations were analysed in the current study. All patients have been followed up for 12 months. Continuous variables were compared by the t-test or the Mann-Whitney U-test and categorical variables by the χ^2 test. A p-value of <0.05 indicated statistical significance.

Results: Ischemic heart disease constituted the primary aetiology of admission in about half (52.0%) of the 177 patients admitted for AHF. Dilated cardiomyopathy (22.6%), valve disease (11.9%) and hypertension (7.9%) were the other main primary aetiologies. The most common precipitating factors for AHF hospitalisation were non-compliance with the medications (28.8%) followed by uncontrolled hypertension (21.5%). Other common precipitating factors were atrial fibrillation, renal dysfunction, infection and myocardial ischemia or acute coronary syndrome. The most frequent clinical profile was decompensated HF (61.7%) followed by pulmonary oedema (28%). About one quarter of the patients were rehospitalised in the first three months after discharge and half of them in the first 6 months. In both cases, heart failure was the primary cause of rehospitalisation in more than 70% of the patients, followed by renal dysfunction.

Conclusion: This study has demonstrated that the primary aetiology and the main reasons for AHF-related admissions are due to preventable factors. Improving compliance with guidelines and adherence to medication, as well as early identification and treating cardiovascular risk factors could reduce the burden of the disease; however further research is necessary to validate these conclusions.

P1007

Dilated non-ischemic cardiomyopathy is the 1st cause of referral to tertiary care heart failure clinics in Saudi Arabia

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Purpose: Ischemic heart disease and hypertension are the 1st and 2nd cause of heart failure in western countries respectively. Data about heart failure in the Middle East is generally scarce.

We aimed to describe the contribution of dilated non-ischemic cardiomyopathy (DNICM) to the etiology of heart failure in the chronic setting in Saudi Arabia and to compare the clinical characteristics and outcome between dilated non-ischemic and ischemic cardiomyopathy (ICM) in a cohort of patients followed in a tertiary care heart failure clinic.

Methods: This study included all consecutive patients with high risk chronic heart failure referred to a tertiary care heart failure clinic in Saudi Arabia between September 2012 and December 2013. We evaluated causes, risk factors, clinical features, management, and outcomes including death and re-admission rates in dilated non-ischemic versus ischemic cardiomyopathy in this cohort. Other etiologies were excluded.

Results: We included 434 patients in our study. DNICM constituted 42.7% of the causes of high risk chronic heart failure patients followed in a tertiary care heart failure clinic. We compared the group of DNICM (186 patients 42.7% Group I) vs ICM (165 patients 37.9%, Group II). The mean age was 34.25 ± 13.4 vs 61.2 ± 12.4 years (p value 0.0001), and 71.79% vs 70.41% were men (p value 0.18). Risk factors in the 2 groups included diabetes mellitus (18.2% vs 55.4%, p value 0.0001), hypertension (16.5% vs 68.8%, p value 0.0001), and current or ex-smoking (36% vs 43% p value 0.23). Left bundle branch block on ECG in the 2 groups was present in 11.8 vs 12.5% with p value 0.12, and median NT-proBNP was 1050.49 pg/ml (IQR 911 pg/ml) vs 2934.37 pg/ml (IQR 2512 pg/ml) with P value 0.0001, and median EF was 23% vs 32% with P value 0.005. The overall 1 year mortality rate was 9% vs 14% (p value 0.005) and the 1 year re-admission rate 26% vs 37% (p value 0.008). P value of less than 0.05 was considered significant.

Conclusions: DNICM is the 1st cause of referral to tertiary care heart failure clinics in Saudi Arabia. Patients with DNICM are younger and having fewer incidences of diabetes mellitus and hypertension. Despite having lower ejection fraction at the time of referral, the group with DNICM has significantly lower NT-ProBNP level, one-year mortality and readmission rate compared to the ICM group.

P1008

Relationship between tsunami damage and incidence of acute decompensated heart failure after the 2011 northeast Japan disaster

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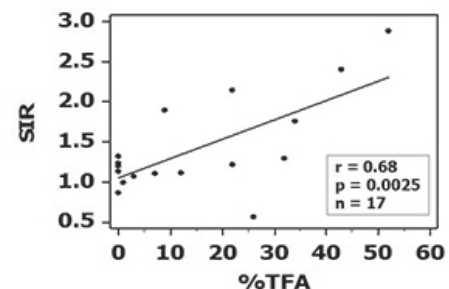
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Background: We have reported that the incidence of acute decompensated heart failure (AHF) was increased after the earthquake and tsunami disaster. However, no study have shown the impact of tsunami severity on the increased incidence of AHF in this situation.

Methods: The AHF cases 2 years before and 2 years after the disaster were registered according to the Framingham criteria in 17 municipalities attacked by various degree of tsunami impact. The severity of tsunami was evaluated by the percentage of tsunami flood area in residence area (%TFA) of each municipality. The tsunami stricken area was defined by %TFA >= 30%, and other municipalities were assigned as the control area. The age-adjusted standardized incidence ratio (SIR) for 2 years after the disaster were determined relative to pre-disaster period in each municipality.

Results: When the SIR were compared between the control area and the tsunami stricken area, SIR was significantly higher in the tsunami stricken area in the disaster year of 2011 (SIR = 1.92), and this increase was sustained even in the post disaster year of 2012 (SIR = 1.55). However, in the control area, no such increase was apparent during the disaster year (SIR = 1.03) or the post disaster year (SIR = 1.27). In fact, as shown in Figure, the SIR in 17 municipalities were significantly correlated with %TFA ($r = 0.69$, $p < 0.01$).

Conclusion: The increase in the incidence of AHF is closely correlated with severity of tsunami damage. These suggest that sudden environmental changes and psychological stress augments increase risk of AHF incidence in a sustained manner.



Relationship between SIR and %TFA

P1009

Risk factors of prevalence and progression of chronic heart failure in studied population

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Aim: To study the prevalence, progression frequency and risk factors for development of chronic heart failure (CHF).

Methods: To determine the prevalence of CHF an epidemiological cross-sectional study of adult population was conducted. The CHF diagnosis was confirmed by clinical examination. The prevalence of CHF was calculated as the ratio of the number of patients with a confirmed diagnosis of CHF to the total number of surveyed people. The assessment of CHF progression was evaluated based on clinical re-examination of patients with CHF in two years. Non-parametric methods of statistics were used including the calculation of relative risk (RR).

Results: The features of CHF were detected in 18.3% of the total surveyed population, the diagnosis of was confirmed in 71.9%. The prevalence of CHF in the surveyed population on 01.12.2014 totaled 13.2%. The following are the risk factors for CHF in the studied population: age - older than 45 years (RR = 10.0 (4.07-24.65), $p < 0.001$), history of concomitant cardiovascular disease (RR = 11.89 (5.84-24.16), $p < 0.001$), the presence of cardiovascular diseases in relatives (RR = 2.13 (1.40-3.23), $p < 0.001$). The frequency of CHF progression within

24 months after the initial survey was 10.4% of re-examined patients with CHF. The statistically significant risk factors for the progression of heart failure are: smoking (RR = 4.43 (1.27 - 27.66), $p < 0.001$), left ventricular ejection fraction $\leq 52\%$ in the initial evaluation (RR = 4.59 (1.18 - 13.70), $p = 0.024$) and the history of atrial fibrillation (RR = 3.60 (1.39-16.11), $p < 0.001$).

Conclusion: The prevalence of CHF is associated with patients' age, history of concomitant cardiovascular diseases and the same diseases in close relatives. The following risk factors are important in the progression of CHF: smoking, the presence of chronic atrial fibrillation and left ventricular ejection fraction $\leq 52\%$.

P1010

Heart failure in internal medicine departments of Italy: the SMIT study

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Purpose: In Italy most of Heart Failure (HF) patients are admitted in Internal Medicine Department (IMD). We performed an observational study in IMD of an Italian region (3,7 million inhabitants) characterized by a mean age of population higher than the mean of Italy, with the aim of recording the epidemiological and clinical data and to analyze the HF management in relation to the most recent guidelines.

Methods: Most of this region IMD (32 of 35) took part in the study. We enrolled patients who were discharged by departments in a period of 30 days (30 January-28 February 2014) with the main diagnosis of HF.

Results: We recruited 770 patients (M = 45.4%) with a mean age of 82.5 + 8.9 years. Only 16.1% had "de novo" HF, most of them were readmitted for decompensated HF. Hypertension and Ischemic disease are the prevailing etiologies. Less than 2% had "HF alone", 71,5% of patients had more than two comorbidities and 40,6% more than three. The mean hospital stay (overall 8,6 + 5,5 days) correlated with the number of comorbidity. Hospital mortality was 5,9%. About 25% of patients had a creatinine clearance < 30 ml/min. Near 50% of patients had atrial fibrillation but only half was anti-coagulated. Beta blockers, ACE-inhibitors or ARB were prescribed in about two-third of the subjects, Antialdosterone agents in half of patients. Echocardiography was performed in 64,1% of patients. BNP or NT-pro BNP was tested in 67% at the hospital admission but only in 18,3% at the discharge. At the discharge 50,1% of patients had loss of autonomy, 57% a poly-pharmacy prescription (> 8 classes of medicines) and 21,2% needed domiciliary oxygen therapy.

Conclusions: The main characteristics of patients with HF admitted in IMD are the advanced age and the presence of multiple comorbidities, like the patients of the real world. The use of echocardiography and the pharmacological therapy with ACE-I, ARB, Beta blocker and Anti-aldosterone agents is wider than that of previous surveys in similar settings. However some diagnostic, therapeutic and prognostic aspects are not still similar to that recommended by the most recent HF guidelines. This survey underlines once again the differences between "HF trials world" and "HF real world".

P1011

National trends in heart failure hospitalization rate between 2004 and 2012

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Purpose: Hospitalization rate for heart failure (HF) in Western Europe is decreasing, while little is known about trends in Central and Eastern Europe. We aimed to evaluate HF hospitalization rate trends in Slovenia.

Methods: Slovenian National Hospital Discharge Registry was searched for HF hospitalizations (coded as any or main cause) between 2004 and 2012 and annual hospitalization rate (per 100,000 person) was calculated for main, any and first HF hospitalization. First HF hospitalization was defined as the first recorded HF hospitalization of an individual that had to occur after 2008. Effects of year of admission, age and sex with HF hospitalization rate were evaluated with Poisson regression.

Results: Overall, 157,695 HF hospitalizations in 80,180 individuals (76 ± 12 years, 52% women) were recorded. A mean of 5 ± 3 comorbidities were recorded, most commonly arterial hypertension, atrial fibrillation, diabetes mellitus and ischemic heart disease (51%, 35%, 25% and 20%). Main and first HF hospitalization were recorded in in 55,740 (35%) and 40,675 (44%) of all HF hospitalizations, respectively. Over time there were 25%, 24% increase and 7% decrease in main, any and first HF hospitalization rate detected (table 1). More recent year of admission, older age and female sex were independently associated with higher HF hospitalization rates ($p < 0.001$).

Conclusions: National based study demonstrated constant and age/sex independent increase in HF hospitalization rates, mainly due to re-hospitalizations.

HF hospitalization rate per 100,000

	2004	2005	2006	2007	2008	2009	2010	2011	2012
main	271	284	296	306	302	308	322	324	338
any	745	842	832	868	852	868	913	939	927
first	na	na	na	na	409	401	403	398	381
Male									
main	259	273	280	305	290	291	321	310	340
any	712	803	781	846	825	823	897	905	910
first	na	na	na	na	377	370	384	361	358
Female									
main	282	294	312	308	315	324	322	339	337
any	776	879	881	890	878	912	928	972	943
first	na	na	na	na	439	431	422	433	405

na - not applicable

EXERCISE TESTING & TRAINING

P1012

Relationship between functional test walk in six minutes and health-related quality of life in heart failure patients

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Background: The heart failure functional limitations affect some life aspects of patients: capabilities, symptoms and psychosocial characteristics; including emotional state, social interaction, intellectual functions, economic balance and personal perception of health status. The functional capacity of patients directly affects their quality of life and prognosis.

Objective: To identify the association between indicators of functional capacity in six-minute walk and Health-Related Quality of Life (HRQL) of patients with heart failure.

Methods: Participants: 134 patients (mean age 63.61 ± 16.82 , 50.7% men) assessed by a City Cardiomyopathy Questionnaire for HRQL and walk test six minutes, which was recorded: subjective level of physical fatigue initial and final, level of effort, distance traveled and time spent.

Results: Using a Spearman correlation analysis, significant and inversely proportional correlation between HRQL and initial subjective level of physical fatigue were found ($r_s = -.294$, $p < 0.01$), final subjective level of physical fatigue ($r_s = -.495$, $p < 0.01$), level of effort ($r_s = -.528$, $p < 0.01$); and directly proportional to the distance ($r_s = .539$, $p < 0.01$) and timing ($r_s = .419$, $p < 0.01$).

Conclusions: The functional capacity is associated with HRQL: patients with better HRQL walk longer distance and spend more exercise time, in addition reporting less effort and fatigue. Multidisciplinary intervention improve the heart failure patients prognosis

P1013

Exercise training after acute coronary syndrome: impact on functional capacity and brain natriuretic peptide

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Background: Brain natriuretic peptide (BNP) is a peptide hormone released from ventricles in response to myocyte stretch. We aimed to establish the influence of exercise training on plasma BNP and whether BNP correlates with the degree of functional capacity improvement in myocardial infarction patients undergoing a cardiovascular rehabilitation program.

Methods: We conducted a retrospective study of 388 patients enrolled into a cardiac rehabilitation programme after acute coronary syndrome between 2009 and 2013. BNP levels were measured before (T1) and after (T2) a training program that included 2 exercise sessions per week during a mean of 8 weeks beside routine recommendations. Functional capacity was estimated using exercise testing duration of Bruce protocol on T1 and T2. Paired data was compared using paired sample t or wilcoxon tests according to variables distribution. Correlation between variables was determined using Spearman's correlation test.

Results: Mean age was $53,5 \pm 9,5$ years and 87,6% were male. STEMI occurred in 51% of cases. The majority of patients that underwent coronary angiogram (97,4%) had one vessel coronary disease (60,5%), with 24% having 2-vessel disease, 10,6% having a 3- vessel disease and 4,9% without significant angiographic coronary disease. Most patients had preserved left ventricular systolic function (67,3%). Both exercise capacity [T1: 08:43(2:15) versus T2: 10:11(2:10); $p < 0,001$] and BNP [T1: 80,2(P25-P75) versus T2: 58,9(P25-P75); $p < 0,001$] showed a significant response to exercise training. No correlation was found between functional capacity and BNP levels at baseline ($\rho = -0,10$, $p = 0,288$) and program completion ($\rho = -0,04$, $p = 0,634$).

Conclusions: Exercise training program in patients after myocardial infarction induced a reduction in BNP levels and an improvement of exercise capacity although in this study BNP levels were not useful as a surrogate marker of functional capacity.

P1014

Cardiopulmonary exercise test parameters in patients with coronary heart disease and chronic obstructive pulmonary disease

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Introduction: Chronic obstructive pulmonary disease (COPD) appears to be relatively frequent in coronary heart disease patients (CHD). Exercise intolerance is an integral component of CHD and COPD. Cardiopulmonary exercise test (CPET) is a gold standard for an exercise intensity assessment and prescription in patients with cardiovascular and pulmonary disease. In stable clinical conditions, when available, it is proposed to conduct functional evaluation through exercise testing prior to starting and after completed cardiopulmonary rehabilitation program.

Aim: The study aims to assess cardiopulmonary exercise test (CPET) parameters examined prior to starting rehabilitation program in patients with coronary heart disease (CHD) and chronic obstructive pulmonary disease (COPD) to evaluate the differences between these groups and improving the individual rehabilitation program.

Methods and Results: We studied 54 inpatients at the Institute for Rehabilitation in Serbia, divided in two groups. Group 1, included 30 patients after myocardial infarction (MI) (26 men, mean age $54,93 \pm 8,39$ years, ejection fraction of $41,1 \pm 8,1\%$) and group 2 included 24 patients after MI who had COPD (21 men, mean age $57,93 \pm 7,27$ years, ejection fraction $39,1 \pm 4,3\%$).

COPD was confirmed according to clinical and spirometry data (FEV1 $61,3 \pm 21\%$, and FEV1/FVC $60 \pm 9\%$).

We measured and compared CPET parameters between these two group of patients at the baseline of inpatients cardiopulmonary rehabilitations.

Peak VO₂ expressed in ml/kg/min was significantly higher in group 1 ($17,27 \pm 3,34$ vs. $14,02 \pm 4,6$; $p < 0,001$), ventilatory anaerobic threshold (VAT) was significantly higher in group 1 ($11,71 \pm 2,4$ ml/kg/min vs. $10,01 \pm 3,2$ ml/kg/min; $p < 0,05$). Slope of minute ventilation vs. carbon dioxide production (VE/VCO₂), was significantly lower in group 1, ($26,01 \pm 4,7$ vs. $28,47 \pm 7,2$; $p < 0,001$). There was no significant difference in peak heart rate (HR) ($115,77 \pm 16,94$ b.p.m. vs. $115,65 \pm 12,32$ b.p.m. $p > 0,05$). The work rate was significantly higher in group 1 ($105,35 \pm 22,03$ W vs. $88,5 \pm 12,2$ W; $p < 0,001$).

Conclusions: In patients with MI associated with COPD, the functional capacity, workload and ventilatory efficiency are significantly reduced, while the chronotropic value is not significantly affected, which should be taken into account when prescribing the rehabilitation program for these patients.

P1015

Comparison of the long-term reproducibility of the walk test and of exercise peak oxygen consumption in patients with preserved exercise capacity

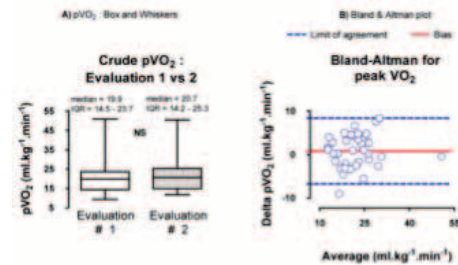
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Background: The aim of the study was to examine the long-term reproducibility of distance walked in an allotted time and to check the stability of the relationship between walked distance and exercise peak VO₂ (pVO₂).

Methods and Results: 46 subjects were studied twice by cardiopulmonary (CPX) and walking test. We performed a 12-minute walk test and the distance covered in 6 minutes was systematically taken down. Distance walked in the allotted time and pVO₂ were analysed. The time interval between the 2 evaluations was 290 ± 10 days. Minute walked distance was respectively 522 ± 83 and 527 ± 76 m in 6 minutes, 1033 ± 182 and 1041 ± 153 m in 12 minutes. pVO₂ was 21 ± 7 and 22 ± 7 ml/kg/min (all $p = NS$). The walk test was reproducible in the long-term, regardless of the modality (6 or 12-minute walk) as shown by the Bland-Altman plots and the high ICC of.89. The Spearman's rho coefficient between distance ambulated and pVO₂ was modest and remained stable over time whatever the allotted time: Spearman $r = .54$; $p = .0011$ (1st evaluation) and Spearman $r = .51$; $p = .0019$ (2nd evaluation) between 6-minute distance walked and pVO₂.

Conclusions: The walking distance in an allotted time seems highly reproducible in the long-term. Its relationship with pVO₂ remains stable over time.



Bland-Altman plot: CPX vs 6MWT

P1016

The dynamics of morphological and psychological status of the quality of life of patients

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Objective: To assess the psychological status, echocardiography and exercise tolerance in 2 years after completion of training at the School of Health for patients with cardiovascular disease (CVD).

Methods: During the 5 years we have carried out school health for patients with CVD, which trained 2,373 person. 222 patients were examined at the end of classes in the school health and again after 2 years. The average age at baseline was $59,5 \pm 7,22$ years. Psychological status was assessed by the Hospital Anxiety and Depression Scale (HADS), quality of life of patients with heart failure by questionnaire MLHFO, exercise tolerance - with the help of the six-minute walk test. Assessed by echocardiography main parameters affecting the prognosis of patients with CVD -left ventricular ejection fraction (LVEF), left ventricular mass (LVM), the size of the left atrium (LA). In order to monitor adherence to treatment once every six months, we conducted telephone counseling, after 1 and 2 years were administered the patient visits to the clinic.

Results: 2 years in regular contact with the audience school health improved psychological status of patients. Levels of anxiety and depression ($7,35 \pm 3,32$ and $6,16 \pm 3,67$ points) at the first examination was significantly reduced to no clinical manifestations ($5,02 \pm 3,04$ and $3,78 \pm 2,14$ points, $p = 0,0000$). Control over compliance with the prescribed treatment allowed to keep without any changes during the observation period indicators echocardiography: LVEF ($58,76 \pm 7,93\%$ and $59,35 \pm 7,67\%$ respectively, $p = 0,0787$), LA ($40,56 \pm 7,27$ mm and $41,32 \pm 6,57$ mm, $p = 0,434$), LVM ($250,63 \pm 72,86$ g and $244,72 \pm 80,99$ g, $p = 0,5791$). The absence of negative dynamics in morphology confirmed reduction of clinical manifestations of chronic heart failure. After 2 years, increased distance covered in the six-minute walk test with $437,02 \pm 104,08$ m significantly increased to $466,34 \pm 86,96$ m ($p = 0,0001$). Improving the physical and psychological state, led to a significant increase in patient assessment of their quality of life $31,88 \pm 16,73$ to $23,29 \pm 13,64$ points ($p = 0,0000$).

Conclusion: improving patients' adherence to compliance with CVD secondary prevention through education in the School of Health and regular monitoring by a doctor, can not only improve the psychological status of patients, but also slow the progression of the morphological and functional reorganization of the myocardium, increase exercise tolerance, achieving better quality of life.

P1017

Description of our experience with cardiopulmonary exercise test in patients with congenital heart disease

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Objectives: Cardiopulmonary exercise testing (CPET) variables provide valuable prognostic and clinical information in the patients with heart failure. The purpose of the present study is to describe this test in our congenital heart disease (CHD) population. Methodology: We have used all the consecutive patients with CHD evaluated with CPET in our center from June 2011 to July 2014. The tests were performed by the same operator. We analysed peak oxygen uptake (peak VO₂) and ventilatory efficiency parameters (end tidal carbon dioxide in anaerobic umbral [PetCO₂AU], lowest VE/VCO₂ ratio and predicted for age and gender) and their relationship with clinical cardiovascular adverse events (death, transplante or cardiovascular hospital admissions).

Results: A total of 45 subjects were analysed. Median age was 32 years (interquartile range [IQ]: 27-42 years), 48,9% males. Etiologies were simple lesions in 4(8,9%), valvular lesion in 5 (11,1%), repaired tetralogy of Fallot (TOF) in 16 (35,6%), Ebstein anomaly in 3 (6,7%), Fontan in 1 (2,2%), Eisenmenger in 1 (2,2%) and complex cyanotic disease in 15 (33,3%). New York Heart Association (NYHA) Class were I in 27 (60%), II in 12 (26,7%), III in 2 (4,4%) and IV in 1 (2,2%). Our median follow up period was 18 months (IQ: 11, 21 months). There were 6 clinical adverse events during the follow up, 1 transplantation and 5 hospital admissions (2 for decompensated HF and 3 Cardiac-related hospitalizations) and any death. Mean peak VO₂ was 18,2 ± 7,5 mL · kg⁻¹ · min⁻¹ (abnormal value < 14 mL · kg⁻¹ · min⁻¹ in 15[33,3%]). The mean of the ventilatory efficiency parameters were PetCO₂AU 37,5 ± 6,3 mmHg (abnormal value <36 mmHg in 16 [35,6%]), lowest VE/VO₂ ratio and predicted 35,2 ± 7,7 (abnormal value > 33 in 22 [48,9%]) and 137,9 ± 31,7% (abnormal value > 125% in 23[51,1%]), respectively. Clinical adverse events were distributed arbitrarily in our population, regardless of the values of aerobic capacity or ventilatory efficiency parameters.

Conclusion: The cardiopulmonary exercise testing is useful and safe to clinical evaluation of patients with congenital heart disease. The small size and stable clinical situation (few adverse events) influenced probably not find prognostic value. Further studies are mandatory to validate these results.

P1018

Impact of short-time physical training on exercise tolerance, renal and hematological parameters in elderly patients with chronic heart failure

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Back ground: The positive effects of physical training in patients with chronic heart failure (CHF) are reflected in improving exercise tolerance, reduce symptoms and less hospitalization, increasing survival and improving quality of life. Elderly patients have more advanced CHF than younger because they tend to be more sedentary and thus do not note symptoms or do not receive a diagnosis of CHF until their cardiac limitation is advanced. In elderly patients with heart failure are often present anemia and chronic renal failure, which further affect the tolerance of physical exertion.

Objective: To evaluate the effects of short-term physical training on exercise tolerance and value of renal and hematological parameters in elderly patients with CHF.

Patients and Methods: The study involved 78 patients (52 males), with coronary artery disease, mean EF 34.05 ± 3.24%, NYHA II and III, without anemia and/or chronic kidney disease. All patients were included in three-week rehabilitation program at the residential center, with individually prescribed physical training. Before and after rehabilitation, all patients underwent exercise stress test, and from the veins blood samples renal and hematological parameters were measured. In relation to age, patients were divided into three groups: A (<60 yrs: n=29), B (60-69 yrs; n=36) and C (≥70 yrs; n=13).

Results: After rehabilitation, only in group C significantly lower serum creatinine (p=0.028) was registered, compared to the value before rehabilitation. In groups A and B, there was a decreasing trend of creatinine, but without significance. Serum urea and uric acid in all groups after rehabilitation, showed no significant change. It was also shown that after rehabilitation, only in group B there was a significant reduction in the number of leukocytes (p=0.037). Other hematologic parameters did not show significant changes. Exercise tolerance improved in all groups (p<0.001 for all). After the rehabilitation in group C, heart rate at rest, was substantially lower than in the group A and B (p=0.003).

Conclusion: Residential short-term physical training led to reduction of serum creatinine in the oldest patients (≥70yrs) with heart failure. Reduction of leukocytes is more pronounced in patients aged 60-69. The largest reduction in heart rate at rest was achieved in patients older than 70 years.

P1019

Patients with heart failure who do not response to exercise training have lower interleukin 6 and galectin 3

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Background: Exercise training can improve functional capacity in patients with heart failure (HF), but the response is heterogeneous. Change in peak oxygen consumption (peak VO₂) after an exercise program is related to survival in this population. We sought to investigate if there are any differences in biomarker serum levels among patients with HF who respond to exercise training in comparison to those who do not respond.

Methods: This is a sub-study of "Interval training versus continuous training on sympathetic activity and peripheral perfusion in patients with HF: randomized study with control group." Forty patients with diagnosis of HF, left ventricle ejection fraction (LVEF) ≤ 0,40, under optimized clinical treatment and stable in the previous six weeks were randomized into three groups: interval exercise (group I), continuous exercise (group II) and control group (group III). Serum levels of adiponectin, galectin-3, interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF-alpha) were measured before and after 12 weeks of aerobic exercise, three sessions per week. For this analysis, only the patients in the groups I and II were included and classified as responders if they achieved a 6% increase in percentage predicted peak VO₂ measured by a treadmill cardiopulmonary exercise testing (CPET).

Results: Twenty six patients, 51 ± 7 years old, 53% men, LVEF 30 ± 6%, 31% ischemic were included in the analysis (responders - 12, non-responders - 14). At baseline, the CPET exercise time, (8,9 ± 1,8 vs 11,4 ± 1,8 min, p=0,001), the VO₂/work-rate relationship [9,7 (9,5-11,3) vs 11,5 (10,2-12,5) mL.min⁻¹.W⁻¹, p=0,041], the galectin-3 levels [1,0 (0,3-2,0) vs 3,2 (1,6-6,7) pg/mL, p=0,015] and the IL-6 levels (5,3 ± 1,9 vs 7,2 ± 1,8 ng/mL, p=0,015) were lower among the responders than the non-responders patients, respectively.

Conclusion: We have found that galectin-3 and IL-6 levels are lower among the patients with HF who respond to 12 weeks exercise training than those who do not respond.

P1020

Resting hemodynamic measurements by transthoracic impedance cardiography can predict outcome of cardiopulmonary exercise test

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The cardiopulmonary exercise test (CPX) with peak oxygen consumption (peakVO₂) is an unquestionable tool reliably stratifying risk in patients with stable chronic heart failure. The role of impedance cardiography in the evaluation of those subjects is still under investigation.

This study aimed to evaluate the power of impedance cardiography to predict the outcome of the cardiopulmonary exercise test as measured by peak oxygen consumption.

The study population comprised 54 individuals with stable chronic HF on individually adjusted optimal therapy (44 males, 49 ± 9.6 years; 18 with coronary artery disease, mean left ventricular ejection fraction 27 ± 6.9%, mean NYHA functional class 2.68 ± 0.66). The ICG measurements were performed during 30-minute rest in supine subjects. All participants underwent standard clinical evaluation typical of heart failure. They also underwent maximal CPX (modified Bruce's protocol: plus 3-min initial stage at 1.7 km/h and 5% inclination). The CPX variables were measured breath-by-breath. Based on the peak VO₂ measured, all subjects were arbitrarily divided into 2 following subsets: A <11 ml/kg/min (heart transplantation candidates), and B ≥11 ml/kg/min (better prognosis). The mean peak VO₂ (SD) in the subsets were 8.69 (1.73) and 18.11 (4.67) ml/kg/min, respectively. There were significant differences between the non-invasive hemodynamic measurements well discriminating the two analyzed sub-groups of subjects (shown in the Table).

The results confirm potential of the noninvasive impedance cardiography for discrimination between different risk groups of patients with stable chronic heart failure. This supports a potential use of this objective bedside modality in a clinical setting. However further clinical research is required.

Major ICG parameters	Group A n=7	Group B n=47	p value
Stroke volume	50.9 (19.1)	74.8 (23.0)	0.010
Stroke volume index	27.2 (8.4)	37.9 (10.6)	0.013
Cardiac output	4.01 (1.44)	5.33 (1.42)	0.023
Cardiac index	2.15 (0.62)	2.70 (0.65)	0.036
Systemic vascular resistance	1871.4 (670.4)	1346.3 (455.3)	0.008
Systemic vascular resistance index	3399.0 (1157.8)	2616.5 (729.5)	0.014

P1021

Comparative analysis of the impact strength and aerobic training on the biological reserves of adaptation to physical exercise in healthy people

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Purpose: To perform comparative evaluation of the impact strength and aerobic training on the biological reserves of adaptation to physical exercise (PE) in healthy people.

Methods: The study included 25 healthy people (21 men) age - 27,0+/-5,7, BMI, 25+/-2,8 kg/m². Participants were divided into two groups of 12 and 13 people. First group for the 12 weeks performed aerobic training (AT), consisting in the daily running of 40-60 minutes with heart rate not exceeding 130 bpm. Second group for the 12 weeks perform strength training (ST) of 8 major muscle groups. Cardiopulmonary testing (CPET) was performed initially and after 12 weeks of training on treadmill using equipment «Oxycon Pro». For each participant was created individual exercise protocol continuously increasing load, composed in such a way that the maximum effort reached in 12-15 min. Studied were instructed to perform maximum effort (respiratory exchange relations (RER) above 1.15, the achievement of a «plateau» in the curve of VO₂). The cubital venous catheter was inserted in all subjects before CPET. Blood samples were taken at baseline and at 1-minute intervals during test. PH, lactate and HCO₃- concentration were estimated using analyzer i-STAT, cartridge CG4 (Abbot, USA). The state of biological reserves of adaptation to the PE was determined by changes in the level of lactate, pH, and HCO₃ in venous blood and change of gas exchange.

Results: In both groups it was registered a significant increase in VO₂ after 12 weeks of training compared with the initial rates. In AT group - 32+/-3,1 ml/min/kg to 38+/-2.5 ml/min/kg, p<0.01; in ST group - 31+/-2.8 ml/min/kg to 36+/-3.0 ml/min/kg, p<0.05., there were substantial differences in change of lactate and pH at peak exercise in AT and ST groups. Lactate levels at the peak of exercise initially and after 12 weeks in AT group were 6.5+/-1,7 and 7.5+/-1,2 mmol/l, respectively, p<0.05. In ST Lactate levels at the peak of exercise group initially and after 12 weeks were 6.4 of+/-1.5 and 12.7+/-3,5 mmol/l, respectively, p<0.001. pH-levels at the peak exercise initially and after 12 weeks in AT group were 7.34+/-0.03 and 7.32+/-0.02 mmol/l, respectively, p>0.05. In ST group pH-levels at the peak exercise initially and after 12 weeks were 7.33+/-0.03 and 7.19+/-0.03 mmol/l, respectively, p<0.001.

Conclusion: The strength training have significantly more marked effect on increasing the buffer adaptation reserves to physical exercise than aerobic training. A similar effect can be observed in patients with heart failure

PROGNOSIS

P1022

Incidence, predictors and 5-year prognostic impact of new-onset atrial fibrillation in patients with left ventricular systolic dysfunction following ST-elevation myocardial infarction

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Purpose: New onset atrial fibrillation (AF) was associated with an increased risk of short- and medium term mortality in patients with ST-elevation myocardial infarction (STEMI) and in patients with left ventricular systolic dysfunction (LVSD). The aim of this study was to assess the incidence, predictors and prognostic impact of new-onset AF on 5-year mortality and major adverse cardiovascular events-MACE (cardiovascular death, reinfarction, ischemic stroke and target vessel revascularization) in patients with LVSD following STEMI.

Method: We analysed 433 consecutive STEMI patients who were treated with successful primary percutaneous coronary intervention (pPCI) and had left ventricular ejection fraction <45% (calculated using Simpson's biplane method). Echocardiographic examination was performed within the first 3 days after pPCI. Successful pPCI was defined as postprocedural flow TIMI = 3. Patients presenting with cardiogenic shock were excluded.

Results: New-onset AF occurred in 49 of 433 patients (11.3%); 17 (34.6%) patients presented with AF, and 32 (65.4%) patients developed AF after pPCI at a median time of 4h (interquartile range 1-25h). In comparison with patients without AF, patients with new-onset AF were older and presented more often with heart failure and lower systolic blood pressure; they were more likely to have reduced renal function, 3-vessel coronary disease and occluded infarct artery on initial angiogram (preprocedural flow TIMI = 0). Multivariable analysis identified (older) age (HR 1.03, 95%CI 1.00-1.06, p<0.001), systolic blood pressure <100mmHg at admission (HR 2.72, 95%CI 1.51-4.90, p=0.001) and 3-vessel coronary disease (HR 2.82, 95%CI 1.21-4.29, p=0.010) as independent predictors for the occurrence of new-onset AF. Patients with AF had significantly higher 5-year mortality and MACE rate as compared with patients with no AF (32.6% vs 8.5%, p<0.001 and 40.8% vs 19.8%, p<0.001 respectively). In Cox regression model new-onset AF was an independent predictor of 5-year mortality (HR 2.13, 95%CI 1.21-3.78, p=0.009) and MACE (HR 1.84, 95%CI 1.12-3.03, p=0.016).

Conclusion: New onset AF is an independent predictor for the occurrence of 5-year mortality and MACE in patients with LV systolic dysfunction following STEMI. Accurate prediction of AF in these patient might help deciding a more aggressive treatment strategy in order to improve their long-term prognosis.

P1023

Prevalence, prognosis and its determinant factors in patient with depressed left ventricular systolic function after acute myocardial infarction

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Purpose: Although there are many differences in baseline clinical characteristics according to left ventricular (LV) systolic function in patients with acute myocardial infarction (AMI), there has been lack of studies primarily focusing on the difference of prognostic factors in patients with AMI according to their LV systolic function. This study was performed to identify different prognostic factors in patients with depressed LV systolic function after AMI.

Methods: Total 12,988 patients with AMI were enrolled into a nationwide registry database study. Major adverse cardiovascular events (MACE) within 12 months of AMI including death, nonfatal MI and revascularization, and administration due to heart failure were assessed. Patients were stratified into 2 groups according to their LV ejection fraction (LVEF): LVEF <40% vs ≥40%, and prognostic factors for MACE were identified in each group.

Results: The 1,962 patients (15.1%) who had LVEF <40% were older and had more un-favorable cardiovascular risk factors than those with LVEF ≥40%. The rates of MACE in patients with LVEF <40% was higher than those with LVEF ≥40% (26.8% vs 11.4%, P<0.001). Independent predictors for 12-month MACE in patients with LVEF ≥40% were history of previous myocardial infarction, high Killip stage, three vessel disease, and lower renal function, which are already known risk factors. Otherwise, diabetes mellitus (hazard ratio [HR], 1.54; 95% confidence interval [CI], 1.12-2.11; P=0.008) and the nonuse of rennin-angiotensin system (RAS) blockers (HR, 0.67; 95% CI, 0.47-0.97; P=0.034) were independent risk factors for 12-month MACE in patients with LVEF <40%.

Conclusion: Prognostic factors determining 12-month MACE in patients with depressed left ventricular function after AMI are diabetes mellitus and RAS blocker, and MACE was more than two times of that without heart failure. Management for the patients with AMI should be tailored according to the presence of depressed left ventricular function.

P1024

Development of risk stratification model in a multi-ethnic asian acute heart failure cohort to predict 30-d readmission

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Purpose: The purpose of this study is to identify predictors for heart failure (HF)-related readmission within 30 days post acute HF discharge and to develop a risk stratification model for 30-day HF readmission.

Methods: Our hospital is a 1000 bed tertiary hospital caring for a multi-ethnic predominantly South East Asian community of 1.4 million people. It has an established HF program since 2007.

A retrospective cohort of 1475 HF admissions to our hospital Cardiology department by patients aged ≥21 years between 2010 and 2012 was analyzed in this study. 60% of the entire cohort was used as the derivation cohort and 40% was used as the validation cohort in the development of the predictive model. Different logistic regression models were tested to determine the best fit model for the data. Discriminatory powers of the models were evaluated using the following measures: sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and AUC. 30D HF Readmission risk was stratified into low, medium and high risk groups based on predicted readmission rates of <10%; 10% to <30%; and, ≥30% respectively.

Results: The following were found to be significantly associated with 30 D HF readmission: number of previous HF admission in the preceding year; medical social service needs, length of stay; creatinine level during admission; ECG QRS duration; serum NT-ProBNP level; and prescription of beta blocker.

The variables of the best model, (AUC: 0.76, Sensitivity: 78.3%, Specificity: 60.7%, PPV: 18.9%, NPV: 96%), were used to construct a weighted readmission risk scoring tool with scores 7-17, stratified into three risk levels: low risk score 7-9 (<10% readmission rate); medium risk score of 10-12 (10 to <30% readmission rate); and high risk score of 13-17 (≥30% readmission rate).

Conclusions: We have developed a risk stratification model using readily available clinical, social and biomarker information, to identify patients at risk of 30D HF related readmissions.

P1025

Research of 1-year prognosis status and its effect factors among discharged patients with heart failureLL Sun¹; T Liang²¹Tsinghua University, Beijing Tsinghua Changgong Hospital, Medical Center, Beijing, China, People's Republic of; ²Chinese Academy of Medical Sciences, Peking Union Medical College, School of Nursing, Beijing, China, People's Republic of**Objectives:** Describe the 1-year prognosis status among discharged heart failure patients and explore its effect factors.**Methods:** Multiple ways were used for data collection, the multivariable Cox proportional hazard regression model was used to explore the effect factors of rehospitalization and mortality in heart failure patients.**Results:** A total of 258 heart failure patients were included in the study, with mean follow-up time of 7 months. After discharged 1, 3, 6 and 12 months, cardiac caused rehospitalization were 1.9%, 10.1%, 14.3%, 17.4%, respectively; cardiac caused mortality were 2.3%, 6.6%, 8.9%, 11.6%, respectively; combined rehospitalization and mortality were 4.3%, 16.7%, 23.3%, 29.1%, respectively; the cumulative rehospitalization and mortality show by Kaplan-Meier survival function curve were 95.7%, 83.3%, 76.5%, 65.7%, respectively. The multivariable Cox proportional hazard regression analysis showed that sex, surgical treatment, hemoglobin level, serum sodium and NT-proBNP significantly impacted on 1-year prognosis among heart failure patients.**Conclusions:** The 1-year cumulative rehospitalization and mortality caused by cardiac was poor, which were 34.3%; sex, surgical treatment, hemoglobin level, serum sodium, NT-pro-BNP were still the main effect factors of 1-year prognosis among patients with heart failure, and aimed interventions should be enhanced to promote the prognosis of heart failure in the future.

P1026

The predictive value of st2 concentrations in plasma in patients with systolic heart failure, living in the north-west region of the russian federationLV Prokopova¹; MY Sitnikova¹; VV Dorofeykov¹; PA Fedotov¹; TA Lelyavina¹; BI Smirnov²; EV Shlyakhto¹¹Federal North-West Medical Research Centre, Saint Petersburg, Russian Federation; ²Saint Petersburg Electrotechnical University "LETI", Saint Petersburg, Russian Federation

In clinical practice for the clinician one of the main problems is the accurate assessment of the severity of the patient's condition and timely determination of indications for non-drug therapies. Identification of significant markers of the severity of systolic heart failure is preceded by the development of regional scales prognosis of CHF.

Objective: To assess the contribution of modern prognostic indicators in the structure of the portrait patients with systolic heart failure - a resident of the North-West region of Russia.**Materials and Methods:** A prospective study of 83 patients. Inclusion criteria: patients with chronic heart failure II - IV functional class (FC); ejection fraction less than 35% under the age of 65 years, signed a voluntary agreement to participate in the study. In a survey of 200 analyzed prognostic significance of parameters, including the concentration of NT -proBNP, ST2 in the blood plasma; cardiorespiratory performance test. Data on the actual survival of patients obtained during a telephone survey 1 year after enrollment.**Results:** 76% (n=63) of patients were men, 24% - women. Functional class of heart failure in the middle reaches 2,7±0,7, distribution of CHF FC (II: III: IV) - 34%: 53%: 13%. Ischemic etiology of heart failure was diagnosed in 55% (n=46) of patients. Indicators echocardiography: ejection fraction by Simpson 25±8,5%, the index of left ventricular EDV - 126,9±39,4 ml / m³, the index of the left ventricle CSR 91,9±39,4 ml / m³. Within one year, deaths were recorded in 10% of patients (n=8). Heart transplantation performed in 4 patients; two patients implanted system EXCOR. The group of patients who died more different frequency breathing movements (p=0,009), at a concentration of albumin (p=0,04), high NT-pro BNP (p=0,03), ST2 (p=0,005) in the blood plasma, more high myocardial mass index (p=0,02), low oxygen consumption at peak exercise (VO2 peak) (p=0,00001). ST2 correlated with the level of uric acid r=0,38 (p=0,05), creatinine (r=0,34, p=0,05), glomerular filtration rate (r=-0,3 p=0,05) albumin (r=-0,3 p=0,05); concentration of NT-proBNP (r=0,48 p=0,05); VO2 peak (r=-0,56. P=0,05).**Conclusions:** ST2 - a powerful predictor of assessing the severity of systolic heart failure in patients of the North-West region of Russia, comparable in significance to the already proven predictors: NT-proBNP concentration and the indication of the maximum oxygen consumption (VO2peak).

P1027

Pulmonary thromboembolism in the elderly- clinical presentation and therapeutic strategy influence the prognosis?A P Anne Paula Bohlen Delgado¹; S Nunes²; B Marmelo¹; L Abreu¹; J Gil¹; B Rodrigues¹; E Correia¹; O Santos¹¹Hospital Sao Teotónio, Viseu, Portugal; ²Instituto Politécnico de Castelo Branco-Escola Superior de Gestão, Castelo Branco, Portugal**Purpose:** The in-hospital mortality predictors of venous thromboembolic events in the elderly are still under study.**Aims:** To determine whether increasing age influences the clinical approach (therapeutic strategy) and their impact on in-hospital prognosis.**Methods:** Retrospective study of 107 patients (women - 60%), accepted by PE (intermediate / high risk) in UCIC (Jan. 2007 to Sep 2011). Were re-evaluated the images of CT angiography of 102 patients (MDCT 16C). The study population was divided into 2 groups according to age: GI (> 70 years;) and non-elderly GNI (<70 years). The two groups were compared regarding demographic, clinical, ECG, echocardiography, CT angiography, therapy (conservative vs. invasive) and in-hospital prognosis. Statistical analysis with SPSS 18 statistical Meaning a p < 0.05.**Results:** Study population consists of GI 47.1% (57.1% women). GI presents less frequently chest pain (p=0.002) and fever (p=0.05). There are no statistical differences in the 2 groups regarding Scores of Geneva and Wells, however GI presents lower values of shock index (p=0,04). GI presents higher D- dimer levels (p=0.019), uremia (p < 0.001) and serum creatinine (p=0.016) and lower values of eGFR MDRD (p 0.001) and PaO2 / FiO2 (P=0.006) ratio. On echocardiography, the value of the SPAP revealed no statistical difference between the 2 groups, but there was a higher dilatation of the right cavities on admission in GI (p=0.041). In CT angiography, there were no statistical differences in the two groups with respect to the diameter of the RV, ratio RV / LV diameter and the pulmonary artery (PA), whereas the ratio PA / Aorta (p=0.001) which was lower in the elderly. The reflux of inferior vena cava (p=0.005) and the overhead in the septum IV (p=0.014) was higher in the elderly.

Regarding the therapeutic strategy: conservative vs fibrinolysis, there was no statistical difference between the groups. Of patients undergoing fibrinolysis 49.2% were elderly. 45% of elderly were approached conservatively. There were no statistically significant differences in mortality between the groups (GI:6.1% vs GNI: 3.6%; p=0.5).

Conclusions: The group of older people does not seem to be less addressed in terms of fibrinolytic therapy comparatively to the younger patients

P1028

Relationship between sodium, potassium and magnesium consumption, and life prognosis in patients with heart failureM Lozada¹; DG Gonzalez¹; A Orea¹; L Castillo¹; N Vaquero¹; MF Bernal¹; O Lozano¹; E Kauffman¹¹National Institute of Medical Sciences and Nutrition Salvador Zubiran, Heart Failure Clinic, Mexico City, Mexico**Introduction:** Heart Failure (HF) is a complex clinical syndrome whose incidence and prevalence is increasing. HF is the leading cause of hospitalization in adult population, becoming a serious health problem. Prognosis of patients with HF is poor, with a high number of fatalities. Nowadays, there's no clear evidence about sodium, potassium and magnesium consumption and its effect on mortality in patients with HF.**Purpose:** To evaluate the effect of sodium, potassium and magnesium consumption in mortality in patients with HF.**Methods:** Cohort study involving patients from the HF clinic of INCMNSZ. A total of 129 patients were included. We evaluated sodium, potassium and magnesium consumption via 24 hours reminders with a 2 year follow up.**Results:** Patients who where either hospitalized and/or died had more prevalence of nephropathy (17.2 vs 33.3%, p=0.046), compared with those who didn't. Regarding sodium consumption, this was less in patients who died compared with those who didn't (837.07 mg/day vs 1748.80 mg/day, p=0.03). There was no statistically significant data relating sodium consumption with hospitalizations. Moreover, those with hospitalization and / or death had a lower intake of magnesium (200.38 mg/day vs 243.23mg/day, p=0.08) compared with those who were not hospitalized. In addition, patients who consume less than 200 mg/day of magnesium had higher risk of hospitalization and/or death [OR: 2.88, 95% CI: 1.28 to 6.49]. No statistically significant data were found about consumption of potassium.**Conclusions:** Dietary intake of sodium and magnesium is associated with an increased rate of hospitalization and/or death in patients with HF.

P1029

Cognitive impairment is an independent predictor for prognosis in Japanese heart failure patient in elderlyH Hiroshi Saito¹; Y Matsue²; Y Endo¹; Y Hasegawa¹; Y Negishi¹; M Soeda²; M Suzuki²; A Matsumura²; Y Hashimoto²¹Kameda Medical Center, Department of Rehabilitation, Kamogawa, Japan;²Kameda Medical Center, Department of Cardiology, Kamogawa, Japan**Introduction:** The Mini-Mental State Examination (MMSE) is a widely used instrument for evaluating cognitive disorder. Although cognitive impairment is common among chronic HF patients, prognostic implication of cognitive impairment is

unknown. Aim of this study is to investigate whether MMSE is an independent predictor for prognosis even in elderly Japanese HF patients.

Methods: A total of 136 HF patients equal or over 65 years old who admitted to our hospital were retrospectively included. MMSE was measured in all patients before discharge. Endpoint was combined of readmission due to HF and all-cause death. We diagnosed cognitive disorder if MMSE was below 27, and all cohorts were divided into two groups, with and without cognitive disorder.

Results: Mean age of all cohort was 81.6 ± 7.3 years old and 47.1% were male. According to MMSE, cognitive disorder was prevalent in 101 (74.3%) patients. During follow-up for median of 161 days, 33 patients (24.3%) were readmitted due to HF or died. Kaplan-Meier curve analysis showed that prognosis of Cognitive impairment group was worse compared to non-cognitive impairment group ($P = 0.019$). In multivariate Cox regression analysis, being Cognitive impairment group was independent predictor for worse prognosis in elderly HF patients even after adjusting by other prognostic factors (HR:7.56, 95%CI: 1.79-31.9).

Conclusion: Cognitive impairment is an independent predictor of worse prognosis in elderly HF patients in Japan.

P1030

Complete myocardial revascularization improves short-term clinical outcomes in STEMI patients with severe left ventricular dysfunction

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Introduction: Primary angioplasty has led to a drastic reduction in mortality in patients with ST elevation myocardial infarction (STEMI). Preventive PCI in noninfarct coronary arteries with major stenosis seems to reduce mortality and reinfarction. However, it is unknown whether this strategy could be beneficial in the subgroup of patients with severe left ventricular dysfunction (LVSD) after STEMI.

Methods: From 2006 and 2014, all patients with severe LVSD after STEMI admitted to an 8 weeks cardiac rehabilitation program in our institution were included. Preventive PCI strategy was defined when PCI was undergone in all noninfarct coronary arteries with major stenosis before discharge. Before and after the rehabilitation program, we assessed heart failure symptoms (according the NYHA scale) and exercise capacity besides a treadmill stress test using Bruce protocol (reported in terms of estimated metabolic equivalents of task or METs and time of exercise). In addition, left ventricular ejection fraction (LVEF) was assessed before and after the rehabilitation program using transthoracic echocardiography.

Results: A total of 156 patients were included, mean age 56.19 ± 12.22 years, 90.4% male. Preventive PCI was underwent in 66.2% of patients. Baseline clinical status was 46.5% class I, 43.7% class II and 9.9% class III. Baseline LVEF was $29.93 \pm 5.14\%$ and mean initial exercise capacity was 5.9 ± 2.69 minutes, 6.46 ± 2.98 METs. After 8 weeks, mean LVEF was $42.32 \pm 10.52\%$, exercise time $8.65 \pm 2.69\%$, and METs $10.04 \pm 2.98\%$. Preventive PCI strategy was significantly associated with better functional class compared to those patients with partial revascularization (figure 1). In addition, although non-significantly, there was a trend to higher improvement in LV function (10.7% vs. 12.8% LVEF) and exercise capacity (3.3 vs. 3.5 METs) in those patients with preventive PCI strategy compared with partial revascularization.

Conclusions: A complete revascularization strategy after STEMI in patients with severe LVSD improves short-term clinical outcomes.

P1031

Prevalence and prognostic significance of heart failure phenotypes: a population-based study

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Background: Although current evidence indicates that Heart Failure (HF) occurs across different left ventricular ejection fraction (LVEF) classes, the information on comparative data of HF according to LVEF are still conflicting.

Purpose: The object of our study was to characterize and compare prognosis of HF according to LVEF categories (LVEF $\leq 40\%$ - HFrEF, LVEF 41-49% - HFbEF, LVEF $\geq 50\%$ - HFpEF).

Methods: Clinical variables of study population was derived from the E-data chart for Outpatient Clinic (Cardionet[®]) collected in a regional Data Warehouse. The end-point of the study was death from any cause, HF hospitalization and all-cause hospitalization.

Results: A total of 2424 patients (mean age 78 ± 8 , 57% men) fulfilled the selection criteria. Of these 597 (25%) had HFrEF, 358 (15%) HFbEF, and 1457 (60%) HFpEF. The rate of noncardiac comorbidities was high (54% with >3 comorbidity) but no significant difference occurred across LVEF groups. The high mean age and

noncardiac comorbidities ran similarly across different HF phenotypes. The most significant clinical differences were observed between HF-REF and HF-PEF group. Patients with HFpEF were more often female, more likely to have a history of hypertension and atrial fibrillation, but less likely to have a history of coronary artery disease. The mortality rates adjusted for significant predictors (age, sex, number of comorbidities) at 1-year and mid term follow-up (28 ± 14 months) were similar in HFpEF and HFbEF group. Conversely, patients with HFrEF showed a significantly higher mortality than other HF phenotypes. These trends were maintained unchanged considering HF and all cause hospitalization.

Conclusion: In contrast to previous reports, this study found that in contemporary HF population-based cohort, advanced mean age and high frequency of noncardiac comorbidity ran similarly across all HF phenotype. Among HF phenotypes, HFrEF identified the subgroup with the worst outcome.

RIGHT VENTRICULAR FUNCTION

P1032

sST2 as a marker of right ventricular dysfunction in patients with chronic obstructive pulmonary disease and pulmonary hypertension

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Background: We evaluate the association between serum levels of soluble interleukin-1 receptor family member (sST2) and right ventricle structural and functional parameters in patients with chronic obstructive pulmonary disease and associated pulmonary hypertension presenting acutely aggravated dyspnoea.

Methods: We conducted a prospective study on forty patients with chronic obstructive pulmonary disease and forty healthy volunteers matched for age and sex (mean age 59 ± 6 years), measuring sST2 and NT-proBNP serum levels and specific echocardiographic parameters.

Results: sST2 was significantly higher in patients with chronic obstructive pulmonary disease and elevated systolic pulmonary artery pressure than in healthy volunteers and better discriminated between patients with likely and possible pulmonary hypertension when compared to NT-proBNP. In univariate analysis the sST2 levels were inversely associated with RV fractional area change ($r = -0.742$; $p < 0.001$), as well as with the RV ejection fraction ($r = -0.765$; $p < 0.001$), tricuspid annular plane systolic excursion ($r = -0.763$; $p < 0.001$). In multivariate analysis, the global model was better related to sST2 than to NT-proBNP levels ($R^2 = 0.54$ vs. 0.29, $p < 0.001$). Moreover, in contrast to NT-proBNP levels, correlations between sST2 levels and systolic and diastolic right ventricle dysfunction persisted after adjustment for cardiovascular risk factors and chronic obstructive pulmonary disease-induced inflammation.

Conclusions: sST2 levels were shown to be predictive of right ventricular dysfunction at echocardiography and better correlated than NT-proBNP to right ventricular dysfunction parameters in patients with chronic obstructive pulmonary disease-associated pulmonary hypertension presenting acutely aggravated dyspnoea.

P1033

Right ventricular dysfunction after acute myocardial infarction in the era of percutaneous coronary intervention: a substudy of the GIPS-III randomized clinical trial

The GIPS-III trial was supported by grant 95103007 from ZonMw, the Netherlands Organization for Health Research and Development. TM Gorter¹; CPH Lexis¹; E Lipsic¹; DJ Van Veldhuisen¹; JP Van Melle¹; TP Willems²; ICC Van Der Horst³; P Van Der Harst¹

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Purpose: In contrast to the left ventricle (LV), right ventricular (RV) myocardium is relatively protected against irreversible damage after myocardial infarction (MI). Yet persistent RV dysfunction after MI is associated with worse prognosis. In the era of percutaneous coronary intervention (PCI), the amount of myocardial damage after MI is increasingly limited. We hypothesized that for the relatively protected RV, permanent dysfunction after MI is virtually absent in patients receiving PCI. As a substudy of the GIPS-III trial, we investigated RV function 4 months after reperfused MI using cardiovascular magnetic resonance imaging (MRI).

Methods: GIPS-III was a prospective, randomized, controlled trial, in patients without diabetes, who underwent primary PCI for ST-segment elevation myocardial infarction (STEMI). The investigators compared the administration of metformin with placebo. The primary efficacy measure was LV ejection fraction (LVEF) 4 months after STEMI, assessed with MRI in 271 patients. The GIPS-III demonstrated no significant difference in LVEF between metformin and placebo. For this substudy,

RV ejection fraction (RVEF) and late gadolinium enhancement (LGE) of the RV was measured in GIPS-III patients with sufficient RV image quality (n=258). Baseline and cardiovascular MRI variables were correlated with RVEF using linear regression models.

Results: Four months after STEMI, mean RVEF was 64.1% (95% CI, 63.5%-64.8%) and mean LVEF was 54.3% (95% CI, 53.3%-55.3%). LGE of the RV was found in 13 patients (5%). Both LV infarct size and the presence of RV-LGE were independently associated with lower RVEF at 4 months ($p=0.001$ and 0.006 , respectively).

Conclusions: Permanent RV dysfunction after MI is absent in the vast majority of non-diabetic patients receiving primary PCI for STEMI. Any RV dysfunction still present late after reperfused MI may be due to irreversible RV myocardial damage or impaired left-to-right ventricular interaction.

P1034

Comparing the efficacy of Tadalafil versus Placebo on pulmonary artery systolic pressure and right ventricular function in patients with beta-thalassemia intermedia

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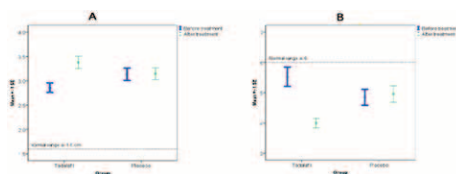
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Background & Objective: Pulmonary arterial hypertension (PAH) is the most important and the most common complication in patients with beta-thalassemia intermedia and its cardiac involvement is the main cause of death in these patients. This study was conducted to assess the effect of tadalafil on pulmonary artery pressure and right ventricular function in patients with beta-thalassemia intermedia.

Methods & Materials: 44 patients with beta-thalassemia intermedia were inducted in the study based on the maximum amount of a normal pulmonary artery systolic pressure (PASP) and the tricuspid regurgitation velocity (TRV) measured by transthoracic echocardiography (TTE), which is the threshold for the diagnosis of pulmonary hypertension. Patients with hepatic or renal insufficiency and also patients who are treated with organic nitrates or alpha-blockers were excluded. And then patients were randomly divided into two groups of 22 patients and were treated for 6 weeks with tadalafil capsules (40 mg daily) or placebo capsules (containing lactose) that were same in weight, size and shape. PASP, TRV and variables related to systolic and diastolic function of the right ventricle (TAPSE, S' and E / E') were measured by TTE before and after treatment and finally were analyzed.

Result: At the end, significant improvement in all of the variables were observed in the group who received tadalafil ($p<0.05$). Mean difference made on all of the variables studied was also significant in the tadalafil group compared to the placebo group ($p<0.05$).

Conclusion: Tadalafil has a significant reducing effect on PASP and TRV in patients with beta-thalassemia intermedia. Tadalafil also improves right ventricular systolic and diastolic function in this patients.



A) mean of TAPSE - B) Mean of E/E'

P1035

Ventricular dysfunction evaluated through gated equilibrium radionuclide ventriculography in cirrhotic patients

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Background: Cirrhotic cardiomyopathy is a hemodynamic disturbance in cirrhotic patients, characterized by an abnormal left ventricular response during physical, pharmacological, hemorrhagic or surgical stress. It is unknown if right ventricular dysfunction is associated with complications such as ascites and spontaneous bacterial peritonitis (SBP), regardless of the degree of portal hypertension, and its association with left cavity dysfunction.

Objective: To determine the prevalence of left and right ventricular dysfunction on rest and during exercise in cirrhotic patients without coronary artery disease, its correlation with the severity of cirrhosis and its complications.

Methods: In a Cross sectional study, 19 patients were included and divided based on Child-Pugh classification. Left and right ventricular function at rest and during exercise was evaluated through MUGA.

Results: Female sex predominated in our study (14, 73.7%). The etiology of cirrhosis was: primary biliar cirrhosis (PBC 36.8%), Hepatitis C virus (HCV 31.6%), cryptogenic (10.5%), autoimmune hepatitis (AIH, 10.5%), alcoholic (5.3%), nonalcoholic steato-hepatitis (NASH, 5.3%). They were classified as Child A, B and C (26.3%, 63.2%, 10.5%, respectively). Mean left and right exercise ejection fractions (EF) on rest were 38.68 +/- 13.05% and 35.97 +/- 14.01% respectively. During exercise, mean EF were 38.89 +/- 12.17% and 40.23 +/- 14.17% respectively. Left (16, 84.2%) and right (17, 89.4%) ventricular dysfunction was found; in both cases, on rest and/or during exercise. (Figure 1).

Discussion: There is a high prevalence of left (84.2%) and right (89.4%) ventricular dysfunction in cirrhotic patients, independently of Child-Pugh classification, that needs to be explored given its prognostic impact, especially in those who are in hepatic transplant protocol.

P1036

Right ventricular dysfunction predicts poor exercise tolerance in patients with heart failure with preserved ejection fraction

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Aim: to evaluate the impact of right ventricle disfunction on exercise tolerance of elderly patients with heart failure and preserved ejection fraction (HFPEF).

Methods: Data of 144 patients with coronary artery disease undergoing cardiac rehabilitation were collected. Median age 74 ± 6; Right ventricle function was evaluated at admission by echocardiography using tricuspid annular plane systolic excursion (TAPSE). All subjects attended an aerobic exercise training program at 60-70% of heart rate reserve lasting 4-weeks. Exercise tolerance was evaluated at admission and at discharge by six minute walking test (6MWT). Patients were divided into two groups according to the presence of right ventricle disfunction (TAPSE value < 16). Group 1 = TAPSE < 16; Group 2 = TAPSE > 16.

Results: Fifty-four out of 144 (37%) patients had TAPSE lower than 16. Considering the overall population, patients of group 1 were more often males (M/F = 2.1 vs 1.2, $p=0.02$) had a lower ejection fraction (42.4 ± 6 vs 51.8 ± 7 $p=0.003$), walked a lower distance at 6MWT both at admission (88.4 ± 13 m vs 111 ± 26 m) and at discharge (88.4 ± 13 m vs 111 ± 26 m) compared to group 2. The correlation between TAPSE and distance walked at 6MWT was significant for patients of group 1 ($r=0.24$; $p=0.01$) but weak in group 2 ($r=0.16$; $p=0.07$). TAPSE resulted significantly related to distance walked at 6MWT both at admission ($r=0.46$; $p=0.001$) and at discharge ($r=0.39$; $p=0.003$) in males. Conversely TAPSE was poorly related to distance walked at both 6MWTs in females.

Conclusions: TAPSE is a marker of lower exercise tolerance in elderly patients with HFPEF undergoing cardiac rehabilitation. This relation is stronger for male subjects with right ventricle disfunction.

P1037

Left ventricular systolic dysfunction may precede right ventricular systolic dysfunction in obese patients

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Purpose: It's well known how obesity is an independent cardiovascular risk factor. The increasing growth of obesity focuses on what are the initial cardiac abnormalities that occur in these patients. The aim of this study was to estimate which are the primitive alterations occur on the heart.

Methods: Fifteen consecutive patients (mean age 24 ± 5 ; mean BMI 40, 9 female and 6 male) referred to our obesity center were enrolled. All these patients were submitted to an echocardiographic evaluation. All the obtained data were compared with a population of fifteen normal individual similar in age and sex (mean age 23 ± 4 ; BMI 21; 8 female and 7 male). Throughout the population analyzed there were no cardiovascular risk factors.

Results: The left atrial anteroposterior diameter differs significantly between the two population (37 mm in obese vs 32 mm in normal individuals; $p<0.001$), left atrial area was 15.7cm^2 vs 11.5cm^2 respectively; $p<0.01$. Left ventricular E/A ratio was 1 in obese vs 1,5 in normal individuals; $p=0.001$; left ventricular systolic function evaluated with S' velocity was significantly lower in obese individuals (0,09 vs 0,15; $p=0.003$). Right atrium area was higher in obese individuals (13.2 cm^2 vs 10 cm^2 ; $p=0,01$); Right ventricular E/A ratio was 1,0 in obese and 1,44 in normal individuals, $p=0,001$. We have no statistical difference in right ventricular S' velocity and Tricuspid annular plane systolic excursion (TAPSE) between the two group.

Conclusions: From the data obtained we can conclude that the alteration of diastolic function in right and left ventricle occurs simultaneously and is related to the

enlargement of both atria; instead left ventricular systolic dysfunction may appear before right ventricular systolic dysfunction in obese individuals and is not correlated with other cardiovascular risk factors.

P1038

Hyponatremia in heart failure is associated with right ventricular dysfunction: a propensity score-matched study

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Purpose: Hyponatremia is a significant predictor of poor clinical outcome in heart failure, which is considered to be mediated by arterial underfilling and vasopressin release. However, severity of left ventricular (LV) dysfunction does not always account for hyponatremia and pivotal clinical features about hyponatremia have not been elucidated, yet. We aim to evaluate the association between right ventricular (RV) dysfunction and hyponatremia in patients hospitalized for acute heart failure syndrome (AHFS).

Methods: We prospectively enrolled consecutive patients hospitalized for AHFS in our University Hospital from March 2011 to February 2014. A total of 689 patients have been enrolled in this cohort. Among them, there were 32 patients with significant hyponatremia at admission (serum sodium (sNa) < 130 mg/dL) which persists during the hospitalization (sNa during admission < 135 mg/dl). We excluded 2 patients due to end-stage renal disease. They were matched with comparative patients without hyponatremia (n=60), based on propensity scores for hyponatremia. RV dysfunction assessed by echocardiography at admission was compared between the groups.

Results: Persistent hyponatremia during admission was related to LV ejection fraction < 40%, history of ACE inhibitor or aldosterone antagonist use, serum creatinine, and 12 other factors. Between the patients with persistent hyponatremia (n=30) and the comparative patients without hyponatremia matched by propensity score (n=60), there was significant difference in prevalence of RV dysfunction represented by RV FAC < 35%. RV dysfunction was observed in 26 of 30 patients (86.7%) with hyponatremia vs. 27 of 60 patients (45.0%) without hyponatremia ($\chi^2 = 14.34$, $p < 0.001$). Persistent hyponatremia was associated with RV dysfunction after adjustment for age, sex and propensity score (adjusted OR 8.30; 95% CI 2.53 - 27.25; $p < 0.001$). In particular, sNa level at admission showed positive correlation with RV FAC ($r = 0.51$; $p < 0.001$). In addition, persistent hyponatremia was also related to inferior vena cava plethora (adjusted OR 5.12; 95% CI 1.96 - 13.39; $p = 0.001$) and estimated pulmonary artery systolic pressure ≥ 40 mmHg (adjusted OR 3.50; 95% CI 1.08 - 11.38; $p = 0.045$).

Conclusions: In this study, hyponatremia was significantly associated with RV dysfunction independent from other risk factors for hyponatremia including LV dysfunction. This result suggests that RV dysfunction might be critical in development of hyponatremia in HF and provide new insight for pathophysiologic mechanism of hyponatremia development in HF.

P1039

Prognostic role of echocardiographic parameters in hospitalized patients with severe pulmonary hypertension and heart failure with preserved ejection fraction

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Purpose: Increased left ventricular filling pressure leads to pulmonary hypertension (PH) in patients with heart failure with preserved ejection fraction (HF-PEF). We evaluated the prognostic role of two echocardiographic parameters related to right ventricular function and PH.

Methods: We included 154 consecutive patients who were admitted for HF and had a LVEF > 50%. Patients with end-stage renal disease, high output HF, valvular prosthesis, severe mitral or aortic native valve disease were excluded. Tricuspid annular plane systolic excursion (TAPSE) was used for the diagnosis of right ventricular systolic dysfunction (RVSD, TAPSE ≤ 17 mm). An eccentricity index (EI) > 1.0 at both end systole and end diastole indicated right ventricular pressure overload. All patients were followed during one year after hospital discharge. RESULTS Mean age was 81 years (SD 9), 63% were female. History of chronic pulmonary obstructive disease was present in 35.1%, obesity in 42.8%, and obstructive sleep apnea syndrome in 11%. Severe PH (SPAP > 60 mmHg) was found in 34.5% and was associated to RVSD (RR 1.90; 1.03-3.47 CI 95%, $p = 0.038$), and to a systolic EI > 1 (RR 2.46; 1.48-4.08, $p = 0.001$). During follow up, 37 patients died (24%). There was no significant association between mortality and severe PH. However, the univariate analysis showed an association between mortality and RVSD (RR 3.35;

1.96-5.73 CI 95%, $p < 0.0001$). The best prognostic TAPSE threshold was 17 mm, Fig. 1. An EI > 1 was related to a higher in-hospital mortality (RR 6.40; 1.84-22.18, CI 95%, $p < 0.001$).

Conclusions: This study emphasizes the role played by echocardiographic parameters routinely used for the assessment of patients with right HF and PH. Both, RVSD and EI > 1 were identified as prognostic factors in hospitalized HF-PEF patients.

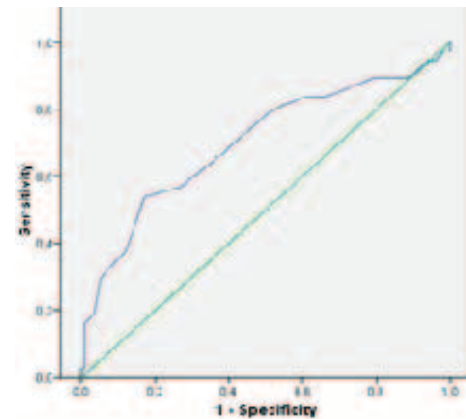


Figure 1. TAPSE ROC curve

P1040

Assessment of right ventricular function by two-dimensional strain in patients with left ventricular dysfunction and normal right ventricle by standard echocardiography

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Purpose: The measurement of tricuspid annular plane systolic excursion (TAPSE) is one of the most widely used methods for evaluation of right ventricular systolic function. The role of the interventricular septum in right ventricular function is not considered in this assessment.

The goal of this study was to analyse by two-dimensional strain (2D strain), the consequences of the functional interdependence between the two ventricles in patients with significant left ventricular dysfunction and normal right ventricular function as by the determination of TAPSE.

Methods: We compared 26 patients with left ventricular dysfunction (ejection fraction of $32 \pm 7.5\%$) and normal TAPSE, (58.8 ± 13 years) (Group A) with a control group of 10 subjects with a normal echocardiogram, (48.5 ± 9.5 years) (Group B). All the patients were imaged using a GE Vivid i Ultrasound system. Digital loops were acquired from 4-chamber view and the analyses were performed offline using EchoPac workstation (GE). We determined the following parameters: the deformation of the RV systolic strain measured at the right ventricular free wall and interventricular septum as well as the right ventricular global longitudinal strain.

Results: The average longitudinal systolic strain determined in the septum was significantly different between Group A and B, basal septum ($-7.5 \pm 4.6\%$ vs $-15.5 \pm 6.6\%$, $p < 0.05$), mid septum ($-7.4 \pm 5\%$ vs $-16.8 \pm 6.9\%$, $p < 0.05$). While the same parameter on the lateral wall of the RV was not, basal lateral (-18.5 ± 7.9 vs -23.6 ± 8.8 , NS) and mid lateral ($-17.8 \pm 7.5\%$ vs $-22.7 \pm 8.4\%$, NS). The value of a global longitudinal strain of the two groups was also significantly different ($-14.7 \pm 5.4\%$ vs $-22.9 \pm 6.8\%$, $p < 0.05$).

Conclusion: In patients with impaired left ventricular function and right ventricular systolic function considered to be normal by standard echocardiography, the global longitudinal strain is significantly reduced when compared with a control group of normal subject due to the common wall between the two ventricles. The percentage of deformation of the free wall of the RV is not significantly different from that found in the normal group. This last fact explains why the tricuspid annular plane systolic excursion remains normal despite a compromised global right ventricular function.

P1041

Radionuclide assessment of right ventricle dysfunction in pulmonary embolism patients

The study was supported by a grant from the Russian Science Foundation (14-15-00178). K Zavadovskiy¹; YUB Lihmanov²; NYU Efimova¹; VI Chernov¹; OYU Kiliina¹

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Background: Weight of a clinical current of patients with pulmonary embolism (PE) branches of a pulmonary artery is defined not only volume embolism, but also evidence of right ventricular (RV) dysfunction. In this connection, adequate diagnostics pulmonary embolism should include as presence verification PE in branches a.pulmonalis, and evaluation contractile functions RV. Works of last time testify, that gated blood pool single photon emission computer tomography (GBPS) has a more potential in an evaluation of function RV, not conceding on indicators of diagnostic accuracy cardiac magnetic resonance imaging. The echocardiography of a condition right ventricular has a number of the restrictions connected with thoracic by its localisation and the complex geometry.

Aim: To study the possible causes of the dissociation between the volume of pulmonary embolism and the degree of RV dysfunction.

Material and methods: Patients with pulmonary embolism (the main group, n = 73) and patients with coronary heart disease (comparison group, n = 15) performed equilibrium radionuclide blood pool SPECT, lung perfusion scintigraphy and determination of the concentration of stable metabolites of nitric oxide, endothelin-1 and 6-keto-prostaglandin F_{1α} in blood plasma.

Results: Radionuclide right ventricular contractility indexes in patients with PE were significantly lower than those in the comparison group. With an average volume of emboli found no correlation between the number of embolize lung segments and the degree of RV dysfunction. In patients with pulmonary embolism levels of endothelin-1, the stable metabolites of nitric oxide and prostacyclin and a stable metabolite - 6-keto-prostaglandin-F_{1α} in plasma were significantly higher, relative to those in the comparison group.

Conclusions: The most significant scintigraphic indices of RV dysfunction in patients with pulmonary embolism are: reduced ejection fraction, stroke volume, and peak ejection rate and mean filling rate. One reason for the dissociation between volume embolization and the degree of RV dysfunction may be an imbalance in the humoral regulation of the tone of the vascular bed of the lungs.

P1042

Retrospective observational study of pulmonary embolism diagnosed by CT pulmonary angiography

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Background and Objectives: Pulmonary embolism (PE) is a blockage of the main artery of the lung or one of its branches by a substance that has travelled from elsewhere in the body through the bloodstream. The obstruction of the blood flow through the lungs and the resultant pressure on the right ventricle of the heart lead to the symptoms and signs of PE.

The aim of this study was to describe the characteristics of patients from a single center with the diagnosis of PE.

Methods: We retrospectively studied 266 patients with PE who were diagnosed in our center, since January 2010 to December 2010. We analyzed the differences between them in terms of clinical presentation, demographic and laboratorial characteristics. Also, we analyzed the in-hospital mortality and during follow up of 1200 days.

Results: Were included 266 patients, 102 were men and 116 women, with a mean age of 73 +/- 16,5 years. In 50.5% of cases were screened with orange in Manchester severity index scale. The main symptoms at the presentation were dyspnea (39.9%) and chest pain (17.4%). Only 2.4% had syncope on admission. About 65% of patients were in Killip Class I and 26.6% in class II. The mean value of BNP was 286.5 pg/mL and troponin was 0.43 ng/mL.

The mortality intra Hospital was 10.6% and during the time of follow up was 13.8%.

Conclusions: In-hospital mortality still remains higher, despite improvements in diagnosis, which opens the door to new prognostic scores.

LEFT VENTRICULAR FUNCTION

P1043

Afterload induced changes on left ventricular contractility are preload independent and mediated by CaMK II- the Anrep effect revisited

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Background: The Frank-Starling mechanism describes preload dependent- (heterometric autoregulation), the Anrep effect afterload induced changes in cardiac performance (homeometric autoregulation). Aim of the study was to examine the influence of changing afterload on cardiac contractility and relaxation independent of alterations of preload and heart rate as well as to assess some aspects of mechanism.

Methods and Results: LV pressure- volume (PV) analyses of isolated working hearts were performed in C57BL/6N mice (n = 11). The end-systolic pressure-volume relationship (ESPVR) was calculated by multiple and single beat analysis. Additionally, other functional and energetic parameters were measured to characterize LV performance at two afterload levels (60 and 100 mmHg) while heart rate and preload were kept constant.

With abruptly raised afterload (100 mmHg) the ESPVR was shifted leftward in the PV relation indicating increased contractility. This effect coincided with an increase in dP/dt_{max}, stroke work and peak power index, while stroke volume initially decreased markedly (first rapid phase). The second slower phase (half time of approx. 3 seconds) was characterized by partial restoration of stroke volume and a further increase of contractility parameters. These changes were completely reversible when hearts ejected against the initial afterload of 60 mmHg. Improvement of cardiac contractility was accompanied by simultaneous changes in myocardial relaxation. The afterload induced increase in contractility was associated with a significant increase of a Ca/Calmodulin-dependent protein kinase II (CaMKII) dependent phospholamban phosphorylation at Threonine 17, which leads to elevated Serca2A activity. In agreement with these results, the afterload-induced increase in cardiac contractility and stroke volume restoration were attenuated in mice with myocyte-specific double knock out of CaMKII delta and gamma (n = 8).

Conclusion: Cardiac contractility is afterload dependent. At constant preload and heart rate an acute increase in afterload enhances LV contractility in two rapid phases within seconds. This response is reversible and illustrates homeometric autoregulation of the heart, tending to preserve stroke volume, while myocardial stretch (preload change) is not a prerequisite. The effect is at least partially mediated by CaMKII.

P1044

Influence of epicardial fat on left ventricular diastolic function in patients with abdominal obesity

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Purpose: Epicardial fat is a part of visceral adipose tissue and is an active endocrine organ. Epicardial fat may affect on cardiac structures and function. We studied the influence of epicardial fat thickness (EFT) on the left ventricle diastolic function in patients with abdominal obesity (AO).

Material and methods: We observed 97 patients with AO (IDF, 2005): 37 males and 60 females, age - 42.2 ± 0.8 years and 52 non-obese subjects (32 males and 20 females, age - 40.5 ± 1.1 years). 31.5% of obese patients were hypertensive. 30% of them had metabolic syndrome (MS). Non of obese patients had clinical symptoms of heart failure. Parameters of left ventricular diastolic dysfunction (LVDD) and EFT were evaluated by echocardiography with tissue Doppler imaging.

Results: EFT in obese patients was higher than in non-obese subjects (3.9 ± 0.1 mm and 1.9 ± 0.1 mm, p = 0.0001). EFT in obese patients with arterial hypertension (AH) was higher than EFT in obese patients without AH (4.4 ± 0.2 mm and 3.6 ± 0.1 mm, p = 0.02). EFT in patients with AO and body mass index (BMI) ≥ 30 kg/m² was higher vs EFT in patients with AO and BMI = 25.0-29.9 kg/m² (4.4 ± 0.2 mm and 3.5 ± 0.1 mm, p = 0.004). EFT in patients with MS were higher than EFT in patients with only AO (4.3 ± 0.2 mm vs 3.7 ± 0.1 mm, p = 0.03). We revealed correlations between EFT and BMI (r = 0.8, p = 0.0001), EFT and waist circumference (r = 0.8, p = 0.0001) in obese patients. EFT in patients with LVDD and without LVDD didn't differ (4.0 ± 0.1 mm vs 3.8 ± 0.1 mm, p > 0.05). But we revealed correlations between EFT and parameters of LVDD (EFT and E/A: r = - 0.4, p = 0.0001; EFT and E/E': r = 0.3, p = 0.0001; EFT and DT: r = 0.4, p = 0.0001; EFT and IVRT: r = 0.5, p = 0.0001) in patients with AO. We have used method of classification trees and obtained the following data: EFT over 3.2 mm in females and over 3.8 mm in males increase the risk of LVDD in 7 (OR = 7; 95% CI 2.7 ÷ 18.0) and 1.8 (OR = 1.88; 95% CI - 0.58 ÷ 6.2) fold, respectively.

Conclusions: Epicardial fat thickness was increased in patients with abdominal obesity and metabolic syndrome. Increase in the epicardial fat thickness augments the risk of left ventricular diastolic dysfunction.

P1045

Heart failure: does ejection fraction also perturb sleep?

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Purpose: Even though sleep-disordered breathing (SDB) is a very prevalent comorbidity amongst heart failure (HF) patients (pts), it remains underdiagnosed. Polysomnography, the gold standard diagnostic test for SDB demands specialized technicians and laboratories. The authors tested a Type III Portable sleep monitor

(PSM) on HF pts, a screening method for SDB that is easily executed, and provides an automatic interpretation. The authors aimed to analyze the prevalence and types of SDB in HF and their relationship with left ventricular ejection fraction (LVEF).

Methods: Prospective study of pts consecutively discharged from a HF Unit of a central hospital during one year. After clinical stabilization and therapeutic optimization, all pts without a previous diagnosis of SDB realized PSM. Demographic data, comorbidities, etiologic characterization of HF and LVEF were evaluated. Apnea Hypopnea Index (AHI), central apnea (CA), obstructive apnea (OA) and Cheyne-Stokes respiration (CSR) were analyzed. SDB was compared in pts with preserved and reduced ejection fraction (PEF and REF, respectively). The presence of SDB was defined as AHI > 15/hour.

Results: A total of 111 pts were included, with a mean age of 75.5 ± 10.8 years, of which 64,0% were women. The average LVEF was $54.5\% \pm 18.9\%$, with a majority of HF with PEF (62,2%). Hypertensive cardiomyopathy was the most prevalent etiology (42,3%), followed by coronary artery disease (22,5%). After hypertension (76,6%), atrial fibrillation (75,5%) and anemia (56,8%) were the most frequent comorbidities. SDB was detected in 48,6% of pts, of which OA was the most prevalent ($n=39$, 35,1%), followed by CSR ($n=35$, 31,5%). In pts with REF, 59,5% had SDB, 68% with OA, 12% with CA and 32% with CSR. In pts with PEF, 42,0% had SDB, 75,9% had OA, 10,3% had CA and 10,3% CSR.

Conclusions: Patients with HF present a high incidence of SDB. LVEF did not statistically influence the prevalence of SDB, although its prevalence tends to be higher in pts with REF, namely CSR and CA.

P1046

Affective disorders in patients with primary and recurrent myocardial infarction

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Comorbidity of depression and Acute Myocardial Infarction (AMI) is of current interest due to their potentiating interaction.

Purpose: to study affective disorders in patients with primary and recurrent AMI on the basis of the constitutional approach, the analysis of age changes and sex, EF.

Methods: The study involved 125 patients with AMI: 68 patients with primary AMI (46 men and 22 women, average age 53.4 ± 11.2 yrs)-1st group and 57 patients with recurrent MI (31 men and 26 women, average age 62.7 ± 9.3 yrs)-2nd group. For estimation of anxiety and depression Beck Depression Inventory and the Hamilton Anxiety Scale (HARS) were used. The evaluation was done on 2-3rd and 14-15th day from the onset of AMI. All patients were examined due to standards of AMI diagnostics, on 14-15th day they underwent a 6-minute walk test to assess exercise tolerance.

Results: In 1st group on 2-3rd day patients with anxiety disorders dominated. The prevalence of clinically significant anxiety (> 11 points on HARS) and mild depression (13 ± 2 points on Beck scale) was observed mostly in female. At 14-15th day in 1st group the severity of anxiety disorders had reduced. In 2nd group on 2-3rd day symptoms of moderate depression (18 ± 1 by Beck scale) in 21 patients and major depression (23 ± 3 points by Beck scale)-in 36 patients with a prevalence of women over 65 y.o.were found. At 14-15th day the ratio of moderate to severe depression in the 2nd group was 57% to 43% respectively. In 82% of patients with severe depression EF was <40%, this subgroup showed a significant decrease in exercise tolerance due to the 6-minute walk test. Among patients with severe depression in 47% of cases, there was complicated course of myocardial infarction compared with patients with mild depression-32%, and 1st group-26%. The degree of severity of affective disorders was more significant in men of asthenic body type and was independent of constitutional features in women.

Conclusions: Patients with primary AMI were suffering mainly of anxiety disorders versus patients with recurrent AMI which suffered mainly from depression. The increase of depression severity was associated with the presence of LV systolic dysfunction, reduced exercise tolerance, with elderly age and a rising up of the percentage of complicated myocardial infarction. Among men, affective disorders were more significant in men of asthenic body type. Anxious and depressive disorders are more substantial in women vs men regardless of their somatotype. The study of these aspects is important to optimize the treatment and rehabilitation of patients with AMI and improve their prognosis.

P1047

Development of left ventricular systolic function of premature infant. By use of new echocardiographic tissue doppler imaging of strain and strain rate

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Purpose: Left ventricular cardiac function of premature infant is gradually developed after birth. In this period, it is difficult to assess their cardiac function itself because of pulmonary hypertension. We assessed their cardiac function by use of new echocardiographic technique strain and strain rate.

Study design: We assessed 45 premature infant (33 to 35 weeks gestation). We performed echocardiographic assessment by use of Philips iE33 at within 7 days (early phase) and 21 to 28 days (late phase). We divided left ventricle in 6 segments.

Parameters: Mean velocity, mean strain and mean strain rate (Tissue Doppler imaging; TDI). Tei index (Doppler imaging), EF (M mode). We assessed these parameters in early and late phase.

Results: We could not find difference EF ($62 \pm 13\%$ vs $65 \pm 20\%$; early phase vs late phase), Tei index (0.53 ± 0.07 vs 0.60 ± 0.34) between early and late phase. While we could find left ventricular dysfunction in early phase of premature infant in strain ($35.9 \pm 10.9\%$ vs $43.6 \pm 9.80\%$) and strain rate ($0.58 \pm 0.065s$ vs $0.68 \pm 0.089s$) in septal segment.

Conclusion: We assessed cardiac function of premature infants by use of new TDI and conventional Doppler imaging, M mode echocardiography. We could find left ventricular dysfunction of septal segment in early phase of premature infant by use of new technique of strain and strain rate (TDI).

P1048

Long-term left ventricular reverse remodeling in dilated cardiomyopathy: current incidence and implications

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Purpose: Our goal is to describe the incidence of left ventricular reverse remodeling (LVRR) in patients with dilated cardiomyopathy (DCM), factors able to predict it and prognosis of these patients.

Methods: Retrospective analysis of a cohort of 387 consecutive outpatients. Left ventricle ejection fraction (LVEF) was classified into four categories. We considered there was LVRR when the LVEF improved at least by one level.

Results: Mean age was 64.5 ± 12.1 years and female gender 25.6%. Mean follow up was 50.4 ± 28.4 months. Reverse remodeling occurred in 57.6% of patients.

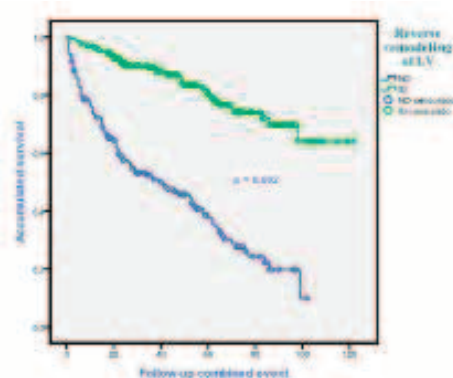
The number of coronary arteries with severe stenosis ($p=0.001$ HR 0,69 IC 95% 0.55-0.86), the NYHA-FC ($p<0.001$ HR 0.39 IC 95% 0.27-0.54), the degree of mitral regurgitation at the end of follow-up ($p<0.001$ HR 0.42 IC 95% 0.30-0.58) and the time until first event (including death, cardiac transplantation and hospitalization for heart failure) ($p<0.001$ HR 1.02 IC 95% 1.01-1.03) were independent predictors for LVRR.

LVRR was tightly related to prognosis: recovering of the cardiac function ($p<0.001$ HR 1.89 IC 95% 1.44-2.48) as well as a shorter time to achieve it ($p=0.048$ HR 1.01 IC 95% 1.01-1.01) formed part of the best model for predicting prognosis independently from final NYHA-FC ($p<0.001$ HR 2.79 IC 95% 1.92-4.07) and CKD ($p<0.001$ HR 2.90 IC 95% 1.71-4.90).

Conclusions: More than a half of patients showed LVRR during the follow-up, being prognosis in this group significantly better.

Fewer number of coronary arteries with severe stenosis, less severe NYHA class, absence of significant mitral regurgitation at the end of follow-up and longer event-free period constitute a simple model for predicting LVRR.

LVRR as well as time to achieve it are independent factors in the best model for predicting prognosis in patients with DCM.



Kaplan Meier combined event

P1049

Left ventricular dysfunction after acute myocardial infarction in young patients

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Purpose: The aim of this study was to find both predictors of new-onset left ventricular dysfunction (LVD) after Acute Myocardial Infarction (AMI) and predictors of systolic function recovery in young patients. Another objective of this study was to evaluate the influence of this LVD in long-term prognosis.

Methods: 199 young patients (males under 45 years of age and females under 55) hospitalized in our Cardiology unit between 2006 and 2011 with diagnosis of AMI were retrospectively and consecutively analyzed. They were divided into two groups: patients with new-onset LVD (LVEF<40%) after AMI and patients with preserved EF. Epidemiological, clinical, angiographic and follow-up data were collected.

Results: Of the 199 young patients, 34 had LVD after AMI (17.1%). Factors independently associated with LVD were: previous cocaine use (OR 5,36, IC 95% 1,27-22,53), anterior wall location (OR 5,1, IC 95% 1,27-22,53), multivessel disease (OR 3,05, IC 95% 1,14-8,14) and clinical presentation with Killip>1 (OR 13,86, IC 95% 2,93-65,5). 189 patients had a follow-up longer than one month, being all the events studied (AMI, HF, ICD implantation, death) except angina more frequently found in patients with LVD. However, mortality was similarly low in both groups. In patients with LVD, diabetes was independently associated with non-improvement of systolic function (6,3 vs 41,7%, p=0.02).

Conclusions:

1. In our population, cocaine consumption, multivessel disease and the presence of signs of HF were predictors of new-onset LVD after AMI.
2. Patients with LVD presented more cardiovascular events during follow-up, without an increased mortality.
3. Diabetes Mellitus was a negative predictive factor of systolic function improvement during follow-up.

P1050

Assessment of left ventricular function in systemic lupus erythematosus patients by speckle tracking echocardiography: relation to circulating endothelial progenitor cells

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Background: Systemic lupus erythematosus (SLE) is a typical systemic autoimmune disease associated with endothelial dysfunction that leads to accelerated atherosclerosis. Endothelial progenitor cells (EPCs) responsible for vascular regeneration were shown to have reduced number and impaired function in SLE.

Objective: The aim of this study was to assess left ventricular (LV) diastolic and systolic function of SLE patients using the relatively new speckle tracking echocardiography (STE) and examine whether any detected abnormalities of LV function have any relation with peripheral circulating EPCs count.

Methods: 50 SLE patients without clinical evidence of cardiac involvement or cardiovascular risk factors and 25 healthy age and sex matched controls were subjected to quantification of peripheral circulating VEGFR2+/CD133+ and VEGFR2+/CD34+ EPCs using flow cytometry technique, conventional transthoracic echocardiography (TTE), tissue Doppler imaging (TDI) and STE.

Results: SLE patients showed a significantly lower CD133+/VEGFR2+ EPCs and CD34+/VEGFR2+ EPCs counts compared to controls [5 (3-12) vs. 109(3 - 429) cells/(10⁶) lymphocytes; p=0.009 and 3.5 (2-9) vs. 63 (5 -104) cells/(10⁶) lymphocytes; p=0.0001; respectively]. TTE/TDI revealed a significantly lower LV ejection fraction (64.0±6.7 vs. 68.8±7.7%; p=0.007), and significantly higher LV end systolic dimensions (33.0±6.1 vs. 29.6±5.6 mm; p=0.02) mitral flow A filling (0.8±0.2 vs.0.6±0.1 m/sec; p=0.002), mitral flow E/lateral annulus E' ratio (11.5±5 vs. 7.6±2.2; p=0.002) in patients compared to controls. STE showed a significantly lower global longitudinal strain (GLS), global circumferential strain (GCS) and global strain rate during isovolumic relaxation (GSRiv) in patients compared to controls (14.5±2.8 vs. 19.0±1.3%; p<0.001; 19.3±6.8 vs. 26.2±6.9%; p<0.001 and 0.14±0.09 vs. 0.2±0.1 1/s; p=0.01 respectively). No correlation was detected between age of the patients, duration of disease, prednisolone dose or intake duration, use of azathioprine vs. cyclophosphamide, SLE disease activity index, LV myocardial performance index, LV ejection fraction, CD133+/VEGFR2+ or CD34+/VEGFR2+ EPCs count and GLS. By multiple logistic regression model, the independent variables affecting GCS and GSRiv were the prednisolone dose (p=0.028) and the LVEF (P=0.021) respectively. **Conclusion:** TDI and STE detected subclinical

systolic and diastolic abnormalities of LV function in SLE patients. The significantly lower EPCs count detected in patients did not however have any impact on these abnormalities of LV function.

P1051

Heart rate variability and left ventricular diastolic dysfunction in postmenopausal women

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Purpose: To assess heart rate variability (HRV) parameters in postmenopausal women depending on left ventricular (LV) filling parameters.

Methods: 203 postmenopausal women were included in the study (age 46,2±4,7 years, menopause duration 4,3±2,1 years). Control group contained 35 healthy women. ECG was recorded in the supine position for 10 min. Spectral analysis included total power (TP), low and high frequencies (LF and HF) in absolute units. All patients underwent ambulatory ECG monitoring (Cardiotens-01, Meditech, Hungary). Evaluated time-domain HRV parameters were SDNN, rMSSD and pNN50. Statistical methods such as Cruskell-Walles and Dan criteria were used.

Results: 117 (57.6%) women had LV diastolic function disturbances (1st group) and in 86 women had not (2nd group). Nobody had LV systolic function failure. TP, LF, HF, SDNN, rMSSD and pNN50 were significantly reduced in all postmenopausal women compared with healthy controls. All above indicators were significantly reduced in postmenopausal women with diastolic dysfunction in compared with those who had normal diastolic function. LF/HF ratio was 2.9 times higher in postmenopausal women of the 1st group than in healthy women and it was 54% more than in postmenopausal women of the 2nd group. This fact testifies about increased cardiac sympathetic modulation in postmenopausal women, especially in those with LV diastolic function disturbances.

Conclusions: Decreased HRV at simultaneous signs of a sympathetic overactivity can reflect increased cardiovascular risk at postmenopausal women, especially with LV diastolic function disturbances

HRV indicators in postmenopausal women

Indicator	Healthy controls (n=35)	1st group (n=117)	2nd group (n=86)
Tp, ms ²	1867 (1229; 2319)	762 *, ** (518; 966)	1048 * (619; 1465)
LF, ms ²	432 (358; 644)	152 *, ** (73; 296)	243 * (117; 371)
HF, ms ²	586 (404; 727)	86 *, ** (69; 205)	113 * (74; 255)
LF/HF, units	0.9 (0,8; 1,2)	2.7 *, ** (2,3; 3,1)	1.75 * (1,1; 2,3)
SDNN, ms	185 (154; 202)	124 *, ** (108; 135)	142* (124; 176)
pNN50, %	21 (17; 26)	3.5 *, ** (2; 6)	6 * (3; 8)
rMSSD, ms	61 (47; 73)	26 *, ** (20; 37)	30 * (21; 35)

Statistically significant: * - compared with healthy controls (P<0,01); ** - compared with postmenopausal women with normal LV diastolic function (P<0,01).

P1052

Evaluating the effectiveness of bisoprolol and carvedilol on the processes of postinfarction remodeling

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The purpose of the present research was to study on the processes of postinfarction remodeling with chronic heart failure (CHF) and assess the impact of bisoprolol and carvedilol.

Methods: The study included 217 patients with CHF between the ages of 38 and 60 (mean age 50.6±6.8 yrs). Group 1 consisted of 107 patients with CHF FC I-III, who received bisoprolol on the background of basic therapy during 6 months; Group 2 consisted of 110 patients with CHF FC I-III, who received carvedilol on the background of basic therapy during 6 months. The mean daily dose of bisoprolol was 10 mg, and carvedilol. 25-50 mg. All patients underwent clinical examination, ECG, and echocardiography.

Result: In patients with CHF FC-I wall thickening in the intact myocardium without changes in left ventricular (LV) geometry occurred in 15% of patients, which corresponded to the presence of concentric left ventricular remodeling (CLVR). Concentric left ventricular hypertrophy (CLVH) was observed in 52%, and signs of eccentric left ventricular hypertrophy (ELVH) were observed in 33% of patients. CLVH was found in 21.3% of patients with FC-I and in 50.8% of patients with FC-II. ELVH was found in 58.3% of patients with FC-III. Therapy with bisoprolol and carvedilol for 6 months had a positive impact on LV remodeling. In the group receiving bisoprolol, a statistically significant decrease in LVMI was noted, improving

LV systolic function, which resulted in a significant increase in LVEF in patients with ELVH. The type of cardiac remodeling had also undergone significant changes: at baseline, CLVH was predominant (52.3%), and ELVH accounted for 35%. At the end of observation, we noted a decrease in the proportion of patients with CLVT and ELVH; normal LV geometry was determined in 40.1% of patients. By the end of the observation in patients with baseline CLVH (n=56), CLVR and normal LV geometry was observed in 16 patients, ELVH in 4 patients, and CLVH in 36 patients; in patients with baseline ELVH (n=38), CLVR and normal LV geometry was observed in 10 patients, CLVH in 4 patients, and ELVH in 24 patients.

Conclusion: Thus, reverse remodeling and improvement in left ventricular function was observed in both groups, with a slight advantage in the bisoprolol group. There was a decrease in the number of patients with prognostically unfavorable types of remodeling (eccentric and concentric LVH) and restoration of normal LV geometry.

P1053

Improvement of functional capacity is not associated to recovery of left ventricular ejection fraction in post myocardial infarction patients after a cardiac rehabilitation program

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Background: Cardiac rehabilitation improves outcomes after Myocardial Infarction (MI). We analyzed if the improvement of functional capacity is associated to the recovery of Left Ventricular Ejection Fraction (LVEF) in post ST segment elevation MI patients with severe left ventricular systolic dysfunction after a cardiac rehabilitation program.

Methods: We retrospectively reviewed 70 patients (88.6% male) with severe left ventricular systolic dysfunction (LVEF<35%) post ST segment elevation myocardial infarction, who were referred to a cardiac rehabilitation program. The program included physical training, dietary and pharmacotherapy counseling and a specific smoking cessation follow-up when needed, lasting for about 8-10 weeks. The functional capacity was assessed with a treadmill stress test before and after the program. Exercise capacity was reported in terms of estimated metabolic equivalents of task (METs) and a significant improvement was considered if the exercise capacity before the program was ≤ 6 METs and ≥ 8 METs after. The LVEF was assessed by echocardiography before and after de program, and a significant recovery was considered if the LVEF was $>35\%$ at the end of the program.

Results: Mean age was 58.2 years (SD = 10.5), 61.4% were hypertensive, 35.7% diabetic, 72.9% dislipidaemic, 25.7% obese, 65.7% were current smokers and 12.9% had been previously diagnosed with coronary heart disease. The mean LVEF at the beginning of the program was 30.2% (SD = 5.3) and 40.6% (SD = 9.8) at the end, 37 patients (52.9%) had significant recovery in their LVEF. The functional capacity before the program was 5.7 METs (SD = 2.5) and 9.8 METs (SD = 2.6) at the end, 20 patients (28.6%) had significant improvement in their functional capacity. The functional capacity improvement was not related to the LVEF recovery ($p = 0.4$).

Conclusions: Cardiac rehabilitation program is effective improving functional capacity and LVEF in post myocardial infarction patients with severe left ventricular systolic dysfunction. There is no association between them and the improvement of the functional capacity seems to be independent of the LVEF recovery.

P1054

Left ventricular remodeling in patients with ST-elevation myocardial infarction and depressed left ventricular ejection fraction treated with primary percutaneous coronary intervention

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Purpose: To estimate the prevalence of left ventricular systolic dysfunction in patients with anterior ST-elevation myocardial infarction and to describe the mid-term evolution of left ventricular ejection fraction (LVEF) in this population.

Methods: We conducted a single-center retrospective study based on a cohort of 278 consecutive patients with anterior STEMI who underwent PPCI between 2012 and 2014. Left ventricular systolic dysfunction was defined as an LVEF <40%, as measured during the index admission. To describe the evolution of LVEF after hospital discharge, follow-up echocardiograms until August 2014 were reviewed.

Results: Mean LVEF, as measured during admission, was $48 \pm 13\%$, and mean left ventricular end-diastolic diameter (LVEDD) was 48 ± 7 mm. Overall, 78 patients presented an LVEF $\leq 40\%$ at the acute phase of STEMI. In-hospital mortality in this subgroup of patients was 15.4%, in comparison to 2.4% among those with LVEF $>40\%$. Two patients with LVEF <40% underwent CABG and one patient underwent heart transplantation during the index admission.

134 patients had a follow-up echocardiogram after discharge. Mean time elapsed since STEMI to follow-up echocardiogram was 4.5 months. Mean LVEF at this time was $50 \pm 12\%$ and mean LVEDD was 51 ± 8 mm. A follow-up LVEF $\leq 40\%$ was observed in 39 patients, 30 of whom already had a baseline LVEF $\leq 40\%$ during the acute phase of STEMI. Among patients with LVEF $\leq 40\%$ during the follow-up 1 underwent transplantation (post-STEMI day 32) and 2 underwent LV restoration surgery (post-STEMI days 89 and 185), 5 subjects (28%) had an improvement of the LVEF, 2 were asymptomatic, and another 2 had important comorbidities.

Conclusions: In our single-center cohort of patients with anterior STEMI treated with PPCI, the prevalence of LV systolic dysfunction (LVEF $\leq 40\%$) was 28% during the acute phase and 14% at mid-term follow-up.

P1055

Ischemic heart disease: models of myocardial hypertrophy

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Purpose: In the light of a modern sight, the place of the left ventricle hypertrophy (HLV) is considered to be as an immediate one to the way from arterial hypertension (AH) to the chronic heart insufficiency. The present chain of events, where there is a HLV, is described as the only one. The work, conducted by us with the patients with coronary artery disease and AH, has revealed, that the HLV not necessary and not always correlates with AH and the character of treatments.

Material and Methods: 52 patients have been examined by us (59,3+8,5 years; M+m). For estimation the peculiarities of a local contractility myocardium of the LV in conditions of standard physical activities and, accordingly - for estimation the extent of coronary insufficiency, the method of dobutamine stress echocardiography (5-10-20-40 mkg/kg\min), with ECG estimation in all leads.

Results: Carrying out the echocardiography investigation we estimated the thickness of interventricular septum, back wall, apex and left side wall (14,1+1,8; 12,3+1,5; 14+1,3; 13,5+2,6 mm). Besides the dependence of the LV myocardial thickness on ECG changes was estimated, revealed with bicycle ergometric test (BET) in DVI leads with the next correlation of indicated leads with segment's structure of revealed hypertrophy. A strong correlation tie of that sign, as «the presence of hypertension disease» ($r = 0,9$) is observing in respect to the size of ST segment change in I (inferior) lead with BET test; V4 and V6 with stress test does not influence the size of mass myocardial LV and thickness of walls. The significant criterion which influences the myocardial thickness LV was the «age». The «AH» diagnosis, the thickness change of all parts of the LV ($r = +0,9-0,96$) directly depended on the age, while a strong back correlation tie ($r = -1$) observed between the age and ST size with loading tests in IV4\V6 leads. The thickness of walls of the LV were in reverse correlation dependence ($r = -0,9$) on ST dynamics in IV4\V6 with loading, and it doesn't depend on arterial pressure (BP) size. The only index, which was in direct dependence on diastolic BP size was the thickness of a apex ($r = 0,8$); the lesser dependence was observed on systolic BP ($r = 0,53$).

Conclusions: The possible mechanism, which has influence on the HLV, with due regard for revealed peculiarities, is most probably an expression of genes, initiated by ischemia cascade in investigated segments; the AH is mainly an accompanying disease.

HFpEF – HEART FAILURE WITH PRESERVED EJECTION FRACTION

P1056

Assessment of atrial conduction times in patients with mild diastolic dysfunction and normal atrial size

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Objectives: Abnormalities in atrial electromechanical delays (EMD) is considered as independent predictors of atrial fibrillation and can reflect atrial remodeling. Main purpose in this study was to compare inter-, left and right-intra atrial EMD of patients with mild left ventricular (LV) diastolic dysfunction, without left atrial (LA) structural remodeling in absence of high filling pressure with healthy individuals.

Methods: In this prospective study, a total of 41 consecutive outpatients referred to our echocardiography laboratory with mild diastolic dysfunction (age: 60.9 ± 9.6 years) and 45 healthy control subjects referred from outpatient clinic for check up (age: 32.2 ± 10.3 years) with normal diastolic function were enrolled to this study. All subjects had normal LA volume, normal right atrial area and had not high filling pressure. Diastolic dysfunction determined as American society of echocardiography recommendation Time interval from the onset of P wave on ECG to the beginning of late diastolic wave (Am wave) on tissue Doppler trace, which is named PA, was obtained from lateral and septal mitral annulus and right ventricular

(RV) tricuspid annulus, as atrial conduction times (ACTs), so named as lateral PA, septal PA, and RV PA, respectively. The difference between lateral PA and septal, PA septal and and RV PA was defined as left and right intra-atrial EMD, respectively. The difference between lateral PA, and RV PA was defined as inter-atrial EMD.

Results: A, DT, S/D ratio and E/e' (average) were significantly lower in control group and E, D, E/A ratio, e' septal and e' lateral wall were significantly lower in patient group. Atrial conduction times were longer in patient group but in multivariate analysis there was no correlation between ACTs and diastolic dysfunction. There was no significant difference in left intra-atrial EMD (14.2 ± 9.7 ms vs 16.4 ± 11.4 ms; $p = 0.336$), right intra-atrial EMD (12.8 ± 12.2 ms vs 15.4 ± 12.1 ms; $p = 0.321$) and inter-atrial EMD (26.9 ± 13.7 ms vs 31.7 ± 13.7 ms; $p = 0.108$) between two groups. Multivariate analysis showed no correlation between inter- and atrial EMDs and diastolic dysfunction.

Conclusion: There was no significant difference in ACTs, inter-atrial and left and right intra-atrial EMD in patients with mild LV diastolic dysfunction, normal LA volume in absence high filling pressure compared with normal subjects.

P1057

Noninvasive diagnostic approach of abnormal left ventricular filling pressure during exercise in patients with preserved ejection fraction: echocardiography versus cardiac catheterization study

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Background: Latent heart failure at rest could be revealed during exercise. Doppler echocardiography derived index (E/e') has been correlated with left ventricular filling pressures (LVFP); left atrial (LA) remodeling has been reported as the reflection of the cumulative effects of LVFP over time. There are limited data on how these noninvasive indices may diagnose abnormal exercise LVFP in patients with preserved LV ejection fraction (EF).

Methods and Results: Sixty patients prospectively underwent exercise cardiac catheterization and echocardiography. E/e' was measured at rest and during exercise. LA volume was indexed to body surface area (LAVi). To investigate the relative expansion of LA over LV, the LA to LV maximal volumes ratio was calculated (LA/LV). LV end diastolic pressure (LVEDP) >16 mmHg was used to define abnormal LVFP.

34 (57%) patients had elevation of LVEDP only during exercise. Exercise septal E/e' ≥ 8 identified patients with abnormal LVEDP with 71% sensitivity and 83% specificity. Although LA size indices were not linked to LVEDP at rest, they were correlated to exercise LVEDP. LA/LV ≥ 0.5 identified patients with abnormal LVEDP with 88% sensitivity and 58% specificity. LA/LV had a better diagnostic value than LAVi. In the 26 patients with cardiac disease (CD), exercise septal E/e' ≥ 8 (sensitivity = 90%; specificity = 100%) appeared more appropriate than LA size indices; whereas in patients without CD, LA/LV ≥ 0.5 (sensitivity = 82%; specificity = 83%) appeared more appropriate than exercise E/e'.

Conclusions: In patients with preserved LVEF, exercise E/e' and LA size are valuable to predict abnormal exercise LVEDP. In patients with CD, E/e' seems the best noninvasive index, whereas LA/LV appears more accurate in patients without CD.

P1058

The hypertensive response during Treadmill exercise and left ventricular diastolic function in patients with normotension

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Background: Hypertension very often accompanies diastolic dysfunction. A high blood pressure response to exercise is future risk of developing hypertension. We investigated the association of the hypertensive response in Treadmill testing and diastolic function on echocardiographic indices in normotensive patients.

Methods and Results: Three hundred nineteen consecutive normotensive patients (mean age 54 ± 10.5 years; male: female = 163: 156) who showed negative Treadmill exercise stress echocardiography (TSE) were enrolled. TSE was performed using Bruce protocol. LV diastolic function was assessed before exercise. Systolic blood pressure (SBP) response was defined as [exercise SBP] - [resting SBP] and was corrected by the estimated metabolic equivalent (MET). SBP response corrected by MET was correlated with age ($r = 0.116$, $p = 0.038$), resting diastolic blood pressure (DBP) ($r = -0.13$, $p = 0.021$), left atrial dimension (LAD) ($r = 0.146$, $p = 0.009$) and early diastolic transmitral velocity/early diastolic tissue velocity (E/e') ($r = 0.153$, $p = 0.007$). SBP response corrected by MET was associated with E/e' ($\beta = -0.167$, $p = 0.011$, adjust R² = 0.037) after adjusting for age, DBP.

Conclusions: Hypertensive response to exercise is associated with diastolic dysfunction as reflected by echocardiographic index, E/e' in normotensive patients. It suggests that diastolic dysfunction can accompany in normotensive individuals with hypertensive response as well as in hypertensives.

P1059

Emergence of diastolic dysfunction in south east Asia

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Introduction: Heart failure with preserved ejection fraction (HFpEF) is an important independent risk factor for cardiovascular morbidity and mortality. Challenges in early diagnosis make HFpEF easily left out and remained untreated. As such, late presentation with heart failure symptoms is not uncommon and confer significant health burden in population.

Objectives: To assess prevalence of HFpEF and the predicting risk factors in south east asia population.

Methods: Subjects were recruited as part of a community study on cardiovascular diseases between the years 2007 to 2011. Demographic details, cardiovascular risk factors along with echocardiogram were obtained. An exclusion criterion is abnormal left ventricular ejection fraction less than 40%.

Results: A total of 1932 subjects with echocardiogram were analyzed. Mean age was 54.6 ± 11.6 . Majority of the subjects were male 98.3% (1899). Mean systolic ejection fraction (EF) was $64.5\% \pm 7.0$. Prevalence of HFpEF was 52.8% (1021). Of all the subjects with HFpEF, 29.9% (578) had impaired relaxation, 21.0% (406) pseudo-normal and 1.9% (37) restrictive filling. Of all 15.3% (156) had diabetes mellitus (DM), 11.2% (114) had impaired fasting glucose (IFG), 61.5% (628) had dyslipidemia of LDL level more than 3.4 mmol/L. 32.9% (336) were hypertensive and 64.0% (653) were obese. Table below summarize the univariate analysis of the cardiovascular risk factors among the subjects with HFpEF. In multivariate analysis hypertension (OR 2.0, 95% CI 1.6-2.9) and obesity (OR 1.4, 95% CI 1.12-1.64) were the independent predictor of DD.

Conclusion: The prevalence of HFpEF in our population is higher than reported with hypertension and obesity being the strong independent predictor. Early diagnosis and intensive conventional risk factor control should be implemented to prevent overt complications in the high-risk group.

CV Risk Factors in HFpEF

CV risk factors	Diastolic dysfunction (%) n=1021	No diastolic dysfunction (%) n = 911	p value	OR	95% CI
Diabetes	15.3	12.1	0.04	0.76	0.58-0.99
Hypertension	32.9	18.6	<0.001	0.45	0.38-0.57
Dyslipidemia	61.5	59.5	0.37	-	-
Obesity	64.0	57.3	<0.001	0.66	0.55-0.79

CV = Cardiovascular Heart failure with preserved ejection fraction = (HFpEF) CI Confidence interval OR = Odds ratio

P1060

Utility of the 6-minute walk test for clinical trials in patients with heart failure and preserved ejection fraction

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Background: The ability to perform a six-minute walk test (6MWT) has been used as an entry criterion and changes in 6MWT as an outcome measure for clinical trials in patients with heart failure and preserved ejection fraction (HFPEF).

Aim: we explored the utility of 6MWT as a useful entry criterion and as a measure of outcome in this population.

Results: Of 546 patients enrolled in our centre with suspected heart failure and trivial LV impairment or normal LV function on echocardiography, 425 had clinical features of HFPEF and an NT-proBNP >220 ng/l (78%), and 121 were thought not to have HFPEF (controls). A similar proportion of HFPEF patients and controls managed to complete (64 (53%) and 199 (47%), respectively), attempt (32 (26%) and 116 (27%), respectively) or were unable to attempt the test (25 (21%) and 110 (26%) respectively; $p = 0.410$). Compared to controls, those with HFPEF who completed the 6MWT performed worse (315 (IQR: 255-375) metres vs 348 (IQR: 293-377) metres, $p = 0.012$).

During a median follow-up of 2100 (IQR: 992 - 3252) days, 235 (55%) patients with HFPEF and 44 (36%) controls died. Compared to patients who completed the test, those who were unable to perform a 6MWT had a worse outcome (HR: 2.36, 95%CI: 1.75-3.20).

Conclusions: Compared to controls, patients with HFPEF have impaired 6MWT. However, a substantial proportion of patients with HFPEF cannot perform a

6MWT. The inability to perform a 6MWT is a strong measure of outcome in this population.

Variables associated with 6MWT				
Variable	Completed (N = 199)	Attempted (N = 116)	Did not attempt (N = 110)	P Value
Age- Years	76 (70-81)	76 (71-81)	78 (73-74)	0.002
Sex- Female (%)	86 (43)	73 (63)	81 (74)	<0.001
NYHA II - N (%)	173 (87)	73 (63)	59 (54)	<0.001
NYHA III- N (%)	26 (13)	42 (36)	43 (39)	<0.001
NYHA IV- N (%)	0 (0)	1 (1)	8 (7)	<0.001
Clinically congested - N (%)	17 (9)	15 (13)	24 (22)	0.004
NTproBNP (ng/l)	742 (416-1411)	559 (306-1617)	948 (448-1759)	0.016

P1061

Phosphodiesterase-5 inhibitor sildenafil decreases pulmonary and left ventricular filling pressures and improves functional capacity in patients with diastolic heart failure and reactive pulmonary hyp

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Background: Heart failure with preserved left ventricular (LV) ejection fraction (HFpEF) is frequently complicated with venous pulmonary hypertension (PH) with reactive component. PH is a strong negative prognostic factor in HFpEF patients which underscores a substantial need for new therapeutic approaches capable of reversing reactive PH as well as improving LV diastolic function.

Objective: to test the hypothesis that chronic phosphodiesterase-5 inhibitor sildenafil treatment reverses reactive PH and improves exercise capacity and LV diastolic function in patients with HFpEF and reactive PH. **Methods.** 50 patients with HFpEF (by ESC algorithm, 2007) and reactive pulmonary hypertension (systolic pulmonary artery pressure \geq 35 mm Hg at rest and Doppler-derived pulmonary vascular resistance $>$ 3.0 units Wood) receiving standard CHF therapy had been randomly assigned to sildenafil (25 mg TID for 12 weeks followed by 50 mg TID for 12 weeks; n = 30) or to control group (no sildenafil, n = 20).

Results: At 6 months sildenafil treatment mediated significant improvement in patients' exercise capacity (6-minute walk distance, $+48.4 \pm 7.5$ m; cycle ergometer exercise duration, $+78.3 \pm 15.3$ s), systolic pulmonary artery pressure (-10.5 ± 1.4 mm Hg) and right ventricular (RV) function assessed by tricuspid annular systolic excursion ($+24.2 \pm 3.0\%$). These effects may have resulted from changes within the pulmonary vasculature (acceleration time of the right ventricular outflow velocity curve, $+40.6 \pm 6.8\%$) and left-sided diastolic function (E/e' ratio, $-12.9 \pm 2.3\%$; average mitral annulus velocity, $+13.8 \pm 2.2\%$). No improvement in control group was observed.

Conclusions: The multifaceted response to phosphodiesterase-5 inhibition in HFpEF and reactive PH includes improvement in pulmonary pressure and vasomotion, RV function, LV relaxation and filling pressure. These data may provide new approaches for management of HFpEF patients.

P1062

Alternate haemodynamic response to exercise in patients with heart failure and preserved EF - diastolic 3D stress echocardiography

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Aims: To evaluate changes in non-invasively derived parameters of cardiovascular properties to provide insight into the pathophysiology of exercise-induced symptoms among patients meeting conventional criteria for HFpEF but with borderline evidence of diastolic dysfunction by Doppler echocardiography at rest.

Methods and Results: Studies were performed in 52 HFpEF patients identified on the basis of symptoms and E/E' values between 8-15. Results were compared to those obtained in 26 control patients with no evidence of cardiovascular disease. Mitral flow patterns, tissue Doppler imaging and volume analysis obtained by three-dimensional echocardiography (3DE) were performed at rest and during bicycle exercise (2 minute stages, 25W increments). Diastolic compliance was indexed as the ratio between E/E' (a correlate of LV filling pressures) and LV end-diastolic volume [(E/E')/EDV]. There were no significant differences in EDV, stroke volume (SV), EF at rest between groups. In 27/52 patients, E/E' (11.2 ± 3.7 to 16.8 ± 10.5) and diastolic pressure volume ratio [(E/E')/EDV] (0.122 ± 0.038 to 0.217 ± 0.14 ml⁻¹)

as non-invasive estimate for LV stiffness both increased significantly under stress, without changes in systolic performances indicating that an impaired diastolic reserve causes exercise intolerance in those patients (PEF-IDR). 25/52 patients, showed no further change in diastolic performance under stress, but did show a reduction in LV elastance, indicating that an impaired systolic reserve contributes most likely to their exercise-intolerance (PEF-ISR).

Conclusion: The HFpEF population includes heterogeneous pathophysiologies. Impaired systolic (PEF-ISR) or diastolic (PEF-IDR) reserve can contribute to exercise-induced symptoms. 3D stress echocardiography allows to distinguish PEF-ISR from PEF-IDR patients.

P1063

Prognostic value of ECG in HFPEF in two years follow-up

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Purpose: Prognostic importance of ECG in HFPEF has not been sufficiently researched. This study sought to evaluate the common ECG parameters and its prognostic importance in HFPEF and compare it with HFREF in two years follow-up.

Methods: We included a total of 109 patients admitted to internal department for HF within one year period (2010-2011). The follow-up was 24 months. We obtained ECG, echocardiography and laboratory parameters every 6 months. Patients were divided into two groups based on left ventricular ejection fraction; HFPEF with EF $>$ 40% (n = 63) and HFREF with EF \leq 40% (n = 46). Data were analyzed using JMP9 statistical program.

Results: Patients with HFPEF were significantly older (74.1 ± 9.8 vs 66.8 ± 12.1 , $p < 0.05$), with higher BMI (30.3 ± 6.5 vs 27.6 ± 4.3 , $p < 0.05$), higher systolic blood pressure (median 145mmHg,IQR 130-160 vs 125mmHg,IQR 110-145, $p < 0.05$), higher prevalence of arterial hypertension (90.5% vs 73.9%, $p < 0.05$) and female gender (46% vs 23%, $p < 0.05$). There was no significant difference in 2-years all-cause and CV mortality in HFPEF vs HFREF (29% vs 36%, NS and 17% vs 22%, NS, respectively). Admission pulse rate on ECG was significantly higher in HFREF vs HFPEF (98/min vs 84/min, $p < 0.05$). There was no significant difference in latter follow-up visits. The prevalence of AF on admission was significantly higher in HFPEF vs HFREF (46.0% vs 26.7%, $p < 0.05$). We observed a trend to longer QRS complex and QTc interval in HFREF compared to HFPEF (median 100ms,IQR 80-120 vs 80ms,IQR 80-115), $p = 0.066$ and (452 ± 58 ms and 435 ± 44 ms, $p = 0.066$), respectively. QTc interval was significantly longer in those that died from CV causes in HFPEF (median 462ms,IQR 428-498 vs 429ms,IQR 400-453, $p < 0.05$), but not in HFREF. Similar trend was observed in all cause mortality in HFPEF (median QTc 441ms,IQR 426-489 vs 429ms,IQR 400-454, $p = 0.058$). Paradoxically we found opposite outcome in HFREF (median QTc 423ms,IQR 396-446 vs 463ms,IQR 440-504, $p < 0.05$). There was no significant influence of QRS duration, PQ duration and heart rate on all-cause and CV mortality in HFPEF and HFREF. We found weak but significant correlation between QTc duration and QRS duration in HFPEF ($r = 0.3$, $p < 0.05$) and HFREF ($r = 0.5$, $p < 0.05$). We performed Cox model and identified QTc interval as independent predictor of all-cause mortality in HFPEF (HR 1.7 per 1mm change, 95% CI 1.1 to 2.6, $p < 0.05$).

Conclusions: We found out that the QTc interval is related to CV and all-cause mortality in HFPEF in 2 years follow-up. QTc was identified as a weak but independent predictor of all-cause mortality in patients with HFPEF.

BASIC SCIENCE: EC COUPLING AND ARRHYTHMIAS

P1065

Does leaky ryanodine receptors play any role in maladaptive remodeling after chronic mechanical stress in mice?

This work was supported by the Deutsche Forschungsgemeinschaft (DFG) through the SFB 1002 (B04)BA Mohamed¹; S Khadjeh¹; S Sossalla¹; S Neef¹; SE Lehnart¹; G Hasenfuss¹; K Toischer¹

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Rationale: Increased sarcoplasmic reticulum (SR) Ca²⁺ leak via cardiac ryanodine receptors (RyR2s) is thought to play a role in heart failure (HF) development. Inhibition of this leak has been suggested to be an emerging therapeutic strategy. Previously, we have shown that pressure overload (PO) results in an increased SR Ca²⁺ leak and maladaptive hypertrophy, whereas volume overload (VO) results in a more favorable cardiac remodeling.

Objective: We tested the hypothesis that SR Ca²⁺ leakiness aggravates HF pathogenesis and whether inhibiting this leak could avert non-ischemic HF progression.

Methods and Results: Wild-type (WT) and knock-in mouse model with a gain-of-function mutation RyR2-R2474S+/- that result in leaky channels were subjected to aorticavalvular shunt-induced VO. Despite increased diastolic SR Ca²⁺ leak in RyR2-R2474S+/- myocytes, both WT and RyR2-R2474S+/- mice had

depressed pump function to the same extent with no significant difference in survival after shunt. As different loads result in distinct phenotype differences, we examined HF development in C57BL/6J WT mice exposed to transaortic constriction (TAC)-induced PO, with or without novel RyR2 stabilizer, Rycal S36. SR Ca²⁺ leak was significantly reduced in S36-treated mice versus controls both at baseline and following TAC. However, both groups exhibited cardiac hypertrophy and systolic dysfunction equally after TAC, indicating a comparable development of heart failure. Interestingly, there was a trend toward improved survival in S36-treated mice compared with placebo (40% versus 22% 2 months post-TAC; *P* = 0.16), denoting a possible antiarrhythmic effect of the Rycal S36.

Conclusion: Our data suggest that SR Ca²⁺ leak does not appear to impact significantly the maladaptive cardiac remodeling and non-ischemic HF progression in mice following chronic mechanical stress.

P1066

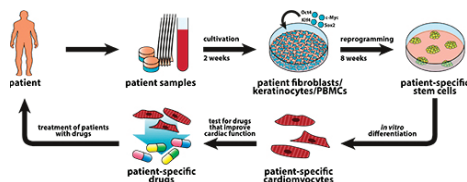
Functional analysis of distinct ryanodine receptor type 2 mutations in induced pluripotent stem cell-derived cardiomyocytes from CPVT patients

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Catecholaminergic polymorphic ventricular tachycardia (CPVT) is a cardiac ion channel disorder, which is characterized by abnormal calcium handling, ventricular arrhythmias, and sudden cardiac death. This inherited disease is predominantly caused by ryanodine receptor type 2 (RyR2) mutations, whereby most of the identified RyR2 mutations in humans are clustered into four distinct domains of the channel. Although heterologous expression systems and animal models have brought important insights in the CPVT pathogenesis, the lack of *in vitro* sources for human cardiomyocytes and the inability to model patient-specific variations of CPVT significantly impeded the deeper investigation of this disease. The goal of our study is to use patient-specific induced pluripotent stem cells (iPS cells) from CPVT patients with distinct RyR2 mutations in order to model the disease *in vitro* for a better understanding of the disease mechanism and for the investigation of novel therapeutic applications for heart failure.

Our analysis indicates that, in contrast to control cardiomyocytes, CPVT iPS cell-derived cardiomyocytes with RyR2 mutations in domain II and III show phenotypic stress-dependent arrhythmia, delayed afterdepolarizations and higher spontaneous calcium releases. However, the stress-induced effects can be robustly alleviated by treatment with different therapeutic drugs. Therefore, this study reveals the potential of modeling cardiac diseases with patient-specific iPS cells in order to investigate the disease mechanisms and to optimize drug therapies.



Disease modeling with iPS cells

P1067

Corrective action of soluble Quercetin on cardiac arrhythmias induced by peroxynitrite *in vitro*

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Has long been known that reperfusion, which develops after ischemia equally, is more terrible than the ischemia. Reperfusion dramatically increased production of nitric oxide and superoxide. A tenfold increase in the concentration of these compounds leads to a 100-fold increase in the synthesis of ONOO-. Excess of ONOO- in blood and tissues is a cause of severe reperfusion arrhythmias, including lethal ventricular arrhythmias.

In experiments on isolated papillary muscles of rats, isolated rat hearts and anesthetized animals (rats and dogs) were obtained strong evidence that laboratory synthesized ONOO- actually has the ability to trigger arrhythmias in isolated organs, and in terms of *in vivo* and *in situ*.

ONOO- harmful effects on the myocardium may be indirect (ie related to its effects on the coronary circulation), because he, like NO, has the ability to relax vascular smooth muscle.

One of the key issues of modern cardiology is how to prevent the occurrence of

cardiac arrhythmias in post ischemic reperfusion period. To this end, we used the bioflavonoid Quercetin included in liposomes were prepared from phosphatidylcholine (Lecithin).

In order to clarify the effects of ONOO- on contractile activity of cells and cardiomyocytes and study the likely effects of antioxidant quercetin in these circumstances, the next part of the research was carried out on isolated papillary muscle preparations of the heart in rats. Adding to the perfusion solution ONOO- a concentration of 10 μM caused a breach of rhythmic activity and reduce the amplitude of contractions of papillary muscles that were generated electrical stimulation. Phosphatidylcholine liposomes containing quercetin (2 mg / ml of active substance) against the backdrop of renewed applications ONOO- amplitude of contractions of papillary muscle.

Large concentrations of ONOO- (100 μM) in contrast to the low concentration (10 μM), which lead to a decrease in contractile properties of cardiomyocytes, caused a sharp increasing of contractile activity of isolated papillary muscle preparations until the development of contractures and generation of arrhythmias. Adding of phosphatidylcholine liposomes containing corvitan immediately after application of 100 μM ONOO- completely prevented the development of arrhythmias and restore the contractile function of the papillary muscle.

Thus, the results of this series of studies indicate the presence of a strong ability of Corvitan to prevent rrythmogenic effect of ONOO- in cardiomyocytes.

P1068

Myocardial NOS1AP overexpression alters QTc intervals in transgenic mice

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Background: Congenital long- or short-QT syndrome may lead to life-threatening ventricular tachycardia and sudden cardiac death. Apart from rare disease-causing mutations in ion channels, common genetic variations in the neuronal nitric oxide synthase (NOS1) regulator NOS1AP, have recently been associated with QT interval variations in a human whole-genome association study. In fact, NOS1AP SNPs have been linked to increases in QTc intervals and sudden cardiac death. We therefore speculate that myocardial NOS1AP overexpression may lead to a decrease of the QTc interval and an increased susceptibility to rhythm disorders.

Methods and Results: We generated transgenic mice (TG) with a conditional myocardial NOS1AP overexpression and focused on electrical alterations. Conditional overexpression of NOS1AP resulted in a 147% ventricular increase in TG mice compared to WT littermates. NOS1AP was mainly located at the sarcolemma where it interacted with NOS1 and the L-type Ca²⁺ channel. While HW/TL ratio, ventricular ANP expression, ventricular cross-sectional area and collagen deposition were not altered in NOS1AP mice under baseline conditions these animals showed a clear decrease of QTc intervals (33 vs. 48 ms). They were more prone to bradycardia (resting heart rate 467 bpm vs. 666 bpm). Atrial programmed stimulation repeatedly caused atrial tachycardia. Ventricular programmed stimulation caused VT in some mice with NOS1AP overexpression.

In addition we investigated the functional effect of the human rs16847548 (T/C). We found that this SNP decreased NOS1AP promoter activity in a viral NOS1AP luciferase assay, suggesting that this SNP downregulates NOS1AP expression in humans.

Conclusion: Myocardial overexpression of NOS1AP leads to a significant shortening of the QTc interval with an increased susceptibility to atrial and ventricular rhythm disorders. SNP rs16847548 in NOS1AP resulted in downregulation of NOS1AP expression which provides an explanation for elongation of QTc intervals. In summary, not only a mutation in ion channels itself but also genetic alterations in expression of ion channel modifiers, such as NOS1AP, seem to have an impact on QTc intervals.

P1069

Recurrent episodes of atrial fibrillation lead to platelets activation

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Atrial fibrillation is one of the risk factors of ischaemic stroke, which probably results from haemostatic abnormalities and platelet activation. Thromboembolic complications can occur during AF and after sinus rhythm restoration.

The aim of the study was to assess if recurrent episodes of atrial fibrillation in first month after successful cardioversion can lead to platelet activation.

Patients: Two subgroups of patients with persistent lone atrial fibrillation treated with cardioversion have been included to the study. Group A (n = 10) consisted of the patients who during the study period of one month after cardioversion have episodes of AF recurrence (confirmed by 24-hours ECG), the group B (n = 16) consisted of the patient who didn't present atrial fibrillation episodes during study period.

Methods: Repeated 24-hours ECG were performed during 1 month after cardioversion in AF patients. Peripheral blood was collected in 2 time points: during atrial fibrillation (before cardioversion- T0) and 1 month after sinus rhythm restoration (T1). In T1 the mechanical function of atrium (confirmed by transthoracic echocardiography) was restored in all patients. Platelet activation and aggregation were assessed by flow cytometric method. CD62 expression on platelets, number of platelet microparticles (PMPs) and number of platelet aggregates (PA) were analyzed. The number of microplatelets and platelets aggregates was presented as percentage of the cells in the population of platelets (cells expressing CD61).

Results: In the group B there was significant decrease of CD62 expression on platelets in T1 in comparison to baseline - T0 ($3,75 \pm 0,17$ v $5,71 \pm 0,48$ $p < 0,005$) while in the group A there was no differences in platelet activation between T1 and T0 ($6,24 \pm 0,69$ v $6,89 \pm 0,77$). The number of platelet aggregates and microplatelets significantly decreased in the group B in T1 (PA: $3,05 \pm 0,24$ v $5,21 \pm 0,44$ $p < 0,001$; PMPs: $0,7 \pm 0,08$ v $1,33 \pm 0,15$ $p < 0,001$) and in the group A there was no differences in microplatelets and platelet aggregates number during the study period (PA: $4,51 \pm 0,54$ v $4,25 \pm 0,47$; PMPs: $2,42 \pm 0,37$ v $2,18 \pm 0,36$). The platelets were significantly less activated 1 month after cardioversion in the group of patients without recurrence of AF (T1 B group vs T1 A group: $p = 0.01$). In 8 patients the recurrent episodes of AF were clinically silent.

Conclusion: Recurrent, mostly silent episodes of AF in patients after cardioversion can lead to sustaining platelet activation and hypercoagulable state and increased risk of thromboembolic complications.

P1070

Antiarrhythmic drug efficacy of omega-3 polyunsaturated fatty acids in patients with dilated cardiomyopathy

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Aim: To determine the antiarrhythmic drug efficacy of omega-3 polyunsaturated fatty acids in combination with standard therapy of chronic heart failure (CHF) at patients with dilated cardiomyopathy (DCM).

Methods: The study included 29 patients with DCM in age from 18 to 54 years old (male / female 19/12) complicated by heart failure NYHA class III with complex cardiac arrhythmias. Complex examination included a physical examination, ECG, echocardiography, Holter ECG at baseline and at the stage.

Patients were randomly assigned into two groups: I-group of 15 pts (male / female 10/05) received standard therapy (ST), of CHF (aldosterone antagonists, ACE inhibitors, β -blockers, glycosides, diuretics). II group (basic) of 14 patients who received, in addition to ST CHF - omega-3 polyunsaturated fatty acids at a dose of 2 gr. a day. Treatment in both groups was carried out for three months. The groups were matched by sex, age and duration of the disease.

Results: At baseline, both groups had various rhythm disturbance: in group I frequent, single, polytopic ventricular extrasystoles (PVCs) were detected in 73% of patients; life-threatening arrhythmias (PVCs high grade) were recorded in 33% of patients, short paroxysms of supraventricular tachycardia (PST), including atrial fibrillation at 20% of patients. In group II: 50% of patients according to Holter ECG revealed frequent, polymorphic PVCs; pair, group VE, short paroxysms of ventricular tachycardia registered in 6 patients (42%). After 3 months of treatment according to Holter ECG suppression of arrhythmias detected in both groups. In group I, 3 patients (26%) register any portion of a single, polytopic VE, VE high grade were observed in 2 patients (13%), the combination of PVCs and SVE in 6 (40%) patients, short episodes of AF was detected in 1 patient (6%). In group II, PVCs high grade, as well as episodes of AF were not recorded in any patient, frequent, polymorphic PVCs detected in 2 patients (14%).

Conclusion: The use of omega-3 polyunsaturated fatty acids in combination with standard CHF therapy leads to an additional reduction in the incidence of ventricular and supraventricular arrhythmias, which favorably improves the prognosis of life for patients with severe heart failure. In all cases, tolerability was good.

P1071

Age-related degenerative changes of intercalated disc affect impulse propagation in mouse ventricular myocardium.

This work was supported by the Polish National Science Centre (NCN) grant DEC-2011/01/B/NZ4/04862K Karol Kaminski¹; TA Bonda²; B Szyńska³; M Dziemidowicz²; M Sokolowska²; WJ Musiał⁴; MM Winnicka²

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Background: Diastolic dysfunction of the left ventricle and conduction disorders are often seen in older subjects. Inflammatory mediators like IL-6 are listed among

potential stimulators of these unfavorable age-related changes. We aimed to check if aging affects intercalated disc morphology in mice and whether lack of IL-6 may be protective against degenerative changes.

Methods: We used young (4-6 months) and old (24-28 months) male C57Bl6 mice of two genotypes - wild type and lacking IL-6 gene (IL6KO). Bipolar single lead ECG was recorded to measure width of the QRS complex which corresponds to depolarization ventricular myocardium. Hearts were harvested and samples were taken for transmission electron microscopy, fluorescence microscopy. In addition protein content of connexin 43 was estimated using western blotting.

Results: The QRS interval was short in young animals ($10,1 \pm 0,5$ ms in WT and $10,7 \pm 0,6$ ms in IL6KO) and significantly prolonged in old mice of both genotypes ($12,4 \pm 1,5$ ms in WT and $13,5 \pm 2,3$ ms in IL6KO). In old animals TEM revealed disruption of intercalated disc, especially at the fascia adherens regions with presence of myelin figures in the intercellular space, fewer gap junctions and relatively preserved desmosomes. Confocal microscopy in beta-catenin immunostained tissue shown focal doubled outline in some intercalated discs in old mice and general less structured arrangement of the intercalated discs in the myocardial syncytium. Expression of cx-43 was lower in older animals of both groups as compared with young animals, supporting the functional electrocardiographic observations.

Conclusions: Ageing affects structure of the intercalated disc in the heart, which may contribute to slowed depolarization. These changes seem to be independent of IL-6 presence and lack of this cytokine does not protect against intercalated disc injury.

P1072

Continuous angiotensin-(1-7) infusion improves myocardial calcium transient and calcium transient alternans in ischemia-induced cardiac dysfunction rats

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Purpose: The effects of angiotensin-(1-7) [Ang-(1-7)] on calcium homeostasis of dysfunctional cardiomyocytes have not been fully elucidated. The aim of the current study was to evaluate the impact of Ang-(1-7) on calcium transient in cardiomyocytes during the pathogenesis of heart failure (HF).

Methods: Cardiac dysfunction was induced by ligation of left anterior descending (LAD) coronary artery in adult Sprague Dawley rats. Randomly selected rats were ligated and treated with continuous infusion of Ang-(1-7) (HF+Ang-(1-7) group) or saline (HF+saline group) via osmotic minipumps. Sham-operated group without ligation of LAD was also included. After 28 days, hemodynamic parameters were assessed and left ventricular myocytes were isolated. The calcium transient (CaT) and the heart rate threshold of calcium transient alternans (CaT-Alt) were recorded by laser scanning confocal microscope. L-type Ca²⁺ channel current (I_{Ca,L}) was measured through whole-cell patch-clamp technique.

Results: Continuous Ang-(1-7) treatment was associated with an attenuated impairment of cardiac function following LAD ligation. Compared to the Sham-operated group, the HF+saline group showed a decreased amplitude of CaT ($p < 0.05$), and a prolonged 50% and 90% CaT recovery time ($p < 0.05$) in. However, Ang-(1-7) infusion significantly improved these abnormalities (All $p < 0.05$ vs HF+saline group). Moreover, the heart rate threshold of CaT-Alt was significantly reduced in HF+saline group as compared to the Sham-operated group ($p < 0.05$), and Ang-(1-7) partly restored it ($p < 0.05$ vs HF+saline group). Although the I_{Ca,L} in HF+saline group was reduced as compared with that in the Sham-operated group, Ang-(1-7) has no effects on I_{Ca,L} in dysfunctional myocytes.

Conclusion: Ang-(1-7) attenuates the CaT disturbance and increases the heart rate threshold of CaT-Alt during the pathogenesis of ischemia-induced HF. These effects would contribute to its benefits on improving contractile dysfunction and preventing the incidence of arrhythmia in dysfunctional myocytes

P1073

Ca²⁺/Calmodulin-dependent protein kinase II does not control mitochondrial Ca²⁺ uptake in cardiac myocytes

DGK Otto-Hess-Promotionsstipendium, DFG SFB 894, DFG Heisenberg-Programm Daniel Wilhelm¹; M Kohlhaas¹; AG Nickel¹; M Wagner¹; M Kreuzer²; J Backs²; C Maack¹

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Background: Mitochondria are the main source of ATP, but also of reactive oxygen species (ROS) in cardiac myocytes. ATP production and ROS elimination are essentially controlled by Ca²⁺ which is taken up via the Ca²⁺ uniporter (MCU). Recently, it was proposed that Ca²⁺/Calmodulin-dependent protein kinase II (CaMKII) regulates Ca²⁺ uptake by interacting with the MCU, but this is currently challenged. Further to this controversy, these studies neither used knock-out technology nor

addressed the role of CaMKII under physiological conditions in which mitochondrial Ca²⁺ uptake matches energy supply to demand of cardiac myocytes.

Methods: Experiments were performed on cardiac myocytes or isolated mitochondria from mice with a conditional and cardiomyocyte-specific CaMKII delta and gamma double KO (d/g DKO) and wildtype littermates (WT). To simulate a physiological workload increase, stimulation frequency was increased from 0.5 to 5 Hz and myocytes exposed to the β -adrenergic agonist isoproterenol (30 nM; Iso/5Hz). During this protocol, cytosolic ([Ca²⁺]_c) and mitochondrial Ca²⁺ concentrations ([Ca²⁺]_m) were measured with a patch-clamp based technique (rhod-2/indo-1; n = 11-12 per group), and the redox states of NAD(P)H/NAD(P)⁺ and FADH₂/FAD, H₂O₂ emission (DCF) and mitochondrial membrane potential ($\Delta\Psi$ m; TMRM) were determined during field-stimulation of non-patched myocytes (n = 13-30). In isolated mitochondria, Ca²⁺ uptake velocity and retention capacity was determined with Calcium green 5N, and O₂ consumption, superoxide (O_2^-) formation (spin-trap) and H₂O₂ emission (amplex red) were obtained in the absence and presence of ADP (n = 6-8).

Results: In WT myocytes, 5Hz/Iso increased cytosolic and mitochondrial Ca²⁺ transients and led to accumulation of [Ca²⁺]_m. This was accompanied by an initial oxidation and subsequent (Ca²⁺-dependent) regeneration of NAD(P)H and FAD redox states, respectively. 5Hz/Iso increased mitochondrial H₂O₂ emission, while $\Delta\Psi$ m remained constant. In myocytes from CaMKII δ /g-DKO mice, no differences in mitochondrial Ca²⁺ uptake, NAD(P)H and FAD redox states or H₂O₂ emission were detected compared to WT. Furthermore, Ca²⁺ uptake velocity and retention capacity in isolated mitochondria were unchanged. Finally, no changes in O₂ consumption, O_2^- formation or H₂O₂ emission in the absence or presence of ADP, respectively, were detected between DKO and WT myocytes.

Conclusions: Our results argue against a relevant regulation of the MCU by CaMKII in cardiac myocytes under physiological or pathological conditions.

P1074

Novel cardiac myosin activator omecamtiv mecarbil acts as a calcium-sensitizer in isolated cardiomyocytes and in diaphragmatic skeletal muscle preparations

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Omecamtiv mecarbil (OM) is considered as a cardiac specific myosin activator drug for inotropic support in systolic heart failure. The aim of this study was to characterize a hypothetical Ca²⁺-sensitizer effect of OM and to elucidate the concentration-dependencies of its mechanical effects in permeabilized left ventricular cardiomyocyte and diaphragmatic skeletal myofiber preparations of Wistar-Kyoto rats under isometric conditions (at a sarcomere length of 2.3 μ M (T: 150°C)). Ca²⁺-regulated active force production (F_{active}), its Ca²⁺-sensitivity (pCa₅₀), Ca²⁺-independent passive force (F_{passive}), and the kinetic characteristics of activations and relaxations were monitored in mechanically isolated and subsequently Triton X-100-skinned preparations in the absence and in the presence of increasing OM concentrations (3 nM-10 μ M). OM treatment resulted in significant increases (p < 0.05) of the Ca²⁺-sensitivity of force production in cardiomyocytes (Δ pCa₅₀: 0.11 and 0.57 at 0.1 μ M and 1 μ M OM concentrations, respectively; EC₅₀: 81.77 \pm 1.26 nM (mean \pm SEM)) as well as in diaphragmatic myofibers (Δ pCa₅₀: 0.24 at 1 μ M OM concentration; EC₅₀: 360 \pm 70 nM). Additionally, OM significantly increased F_{passive} at 0.3 μ M concentration and higher in isolated cardiomyocytes (F_{passive}: 1.4 \pm 0.14 kN/m² and 2.24 \pm 0.31 kN/m² at 0 μ M and 0.3 μ M OM concentrations, respectively; EC₅₀: 280 \pm 80 nM) and at 1 μ M concentration and higher in diaphragmatic skeletal muscle fibers (F_{passive}: 0.68 \pm 0.09 kN/m² and 0.93 \pm 0.08 kN/m² at 0 μ M and 1 μ M OM concentrations, respectively; EC₅₀: 1.29 \pm 0.1 μ M). The kinetics of force redevelopment (following unloaded shortening and stretch) and relaxations (following the reduction of [Ca²⁺]_i from pCa 4.75 to pCa 9) slowed progressively with increasing OM concentrations in isolated cardiomyocytes (with EC₅₀ values of 41 \pm 7 nM and 540 \pm 90 nM, respectively). OM evoked kinetic changes in the diaphragmatic preparations were similar to those observed in cardiomyocytes. Our data illustrated OM as a Ca²⁺-sensitizer positive inotropic drug with additional effects on diaphragmatic skeletal muscle fibers. The reductions in the rates of Ca²⁺-regulated myofilament activations and relaxations together with increases in F_{passive} may compromise diastolic function at relatively high OM concentrations.

BASIC SCIENCE: CHRONIC HEART FAILURE

P1075

Neutralization of pathologic autoantibodies directed against the beta-1-adrenoceptor

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Purpose: Spontaneously hypertensive rats (SHR) with advancing age present in addition to clinical signs of cardiomyopathy with autoantibodies (AABs) directed to the beta1-adrenergic receptor (beta1-AABs) and with autoantibodies directed to the muscarinic 2 receptor (m2-AABs). Patients with dilated cardiomyopathy show the same type of AABs. It has been shown that removal of AABs by immunoadsorption leads to significant reduction in mortality in these patients. Furthermore, it has been demonstrated that under in vitro conditions (cell culture) well selected and identified aptamers among these the aptamer BC007 are able to neutralize rat beta1- and m2-AABs as the aptamers neutralize also comparable AABs found in humans with cardiomyopathy. Consequently, we used the model of AAB-positive SHR to demonstrate the aptamers' potency for in vivo beta1- and m2-AAB neutralization.

Methods: For each tested aptamer, five SHR, age 30-32 weeks, with positive evidence (> 5 LU) for beta1-AABs and for m2-AAB were treated with the aptamer. Control rats (n=5) were not treated with aptamers but with 0.9% saline solution (NaCl). Treatment was performed in a biphasic mode by bolus application of 2 mg/kg body weight dissolved in 0.9% NaCl solution followed by an infusion of the same amount over 20 min. The treatment procedure was repeated five times at weekly intervals. For the application, chronic catheters (PhysioCath, DSI, St. Paul, MN, USA) were inserted under general anesthesia. The AAB titers pre and post infusion were measured by a bioassay.

Results: SHR responded to aptamer treatment with a significant reduction of the cardio-pathogenic beta1- and m2-AABs below the threshold of 2 LU. In case of the aptamer BC111 application, comparable results in AAB reduction have been seen that included also beta1 and m2-AAB reduction. The AAB reduction has already been detected two days after the second infusion of the aptamer. Rats presented the lowest AAB level following the 5th aptamer application. Despite treatment finishing, thereafter, AABs did not return within the study follow-up period of six months. No signs for aptamer toxicity have been seen.

Conclusions: The application of aptamers is a very elegant method to neutralize pathogenic AABs directed against the beta1-adrenoceptor and muscarinic-2 receptor. As immunoadsorption is a costly and non patient-friendly method, aptamers have the potential to replace AAB removal by immunoadsorption.

P1076

The TNF-alpha and ET-1 inhibition mitigates ischemia-reperfusion impact in diabetes induced heart failure

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Aim: Evaluation of TNF-alpha and ET-1 inhibition on ischemia induced myocardial contracture and quality of functional cardiac recovery after reperfusion in diabetes induced rat heart failure.

Material and methods: Diabetes mellitus induced heart failure (DHF) was reproduced by streptozotocin (5 days, 50 mg/kg). TNF- α and ET-1 inhibition has been realized by i/p administration during this period of TNF- α antagonist (2,0 mg/kg), TNF-McAb; BQ-123 (15 mg/kg), a selective antagonist of ETA receptor, and CGS 35066 (2,0 mg/kg), a selective ECE-1 inhibitor. At 6-th day isolated heart was perfused by Langendorff method during 20 min, the left ventricle end diastolic pressure (LVEDP) being adjusted on 14 mm Hg. Thereby LVEDP has been assayed the myocardial contracture level after 30 min of total ischemia as well as the cardiac recovery after 45 min of reperfusion. In a special series BQ-123 (5 μ g/g/min) or CGS 35066 (0,75 μ g/g/min) were infused in perfusate before ischemia.

Results: The ischemic myocardial contracture was in DHF almost doubly augmented: 56,3 \pm 3,6 vs 28,4 \pm 1,9 mm Hg (control). On the other hand LVEDP remained significantly higher after reperfusion: 39,2 \pm 2,5 vs 18,8 \pm 1,2 mm Hg.

The ET-1 inhibition during DHF developing showed a notable cardioprotection: ischemic LVEDP reduced by 31,97% (p=0,026) in BQ-123 action and 33,57% (p=0,024) due to CGS 35066 action. Postreperfusion recovery was improved also: LVEDP was less by 32,14% and 34,44% respectively. Remarkably, that ET-1 inhibition before ischemia perfusion was conspicuously more effective in case of ETA receptor blocking. BQ-123 action led to a significant postischemic and postreperfusion LVEDP diminution by 28,4% (40,3 \pm 3,3 mm Hg) and 27,3% (28,5 \pm 1,8 mm Hg). CGS 35066 action reduced LVEDP only by a mean range of 14-16% (p > 0,05). TNF-alpha antagonist produced a similar to ET-1 inhibition beneficial effect: postischemic and postreperfusion LVEDP by 29,3% (39,8 \pm 3,1 mm Hg) and 26,8% (28,7 \pm 2,2 mm Hg).

Conclusions: 1. ET-1 and inflammation are strongly involved in ischemia-reperfusion impact on diabetes induced heart failure, and inhibition of ECE-1 or ETA receptor and TNF- α antagonizing are associated with significant LVEDP reducing. 2. Preischemic ETA receptor blocking is more effective than ECE-1 inhibition that can suggest the possible role of ET-1 release from myocardial stock during ischemia.

P1077

Interrelation between serum rankl / osteoprotegerin complex and endothelial-derived progenitor cells in chronic heart failureA Alexander E Berezin¹; A Kremzer¹¹State Medical University, Zaporozhye, Ukraine

Background: Chronic heart failure (CHF) remains one of the major causes of mortality worldwide. Recent evidences suggest that CHF is associated with factors that may contribute to deteriorate vascular integrity and endothelial function, worse angiogenesis, modulate coagulation and inflammation. Circulating level of endothelial progenitor cells (EPCs) with proangiogenic capacities is key player in the pathogenesis of cardiac failure

The objective of this study was to assess an interrelationship serum RANKL/OPG complex with counts of circulating proangiogenic endothelial progenitor cells (EPCs) labeled as CD14+CD309+, and CD14+CD309+Tie2+ in patients with ischemic CHF.

Methods: The study retrospectively evolved 153 patients (86 males) aged 48 to 62 years with exiting angiographically proven stable coronary artery disease (CAD). One hundred nine patients (71.2%) had systolic or diastolic CHF. The control group consisted of 25 healthy volunteers with matching age, sex, and body mass index. Serum RANKL (sRANKL) and OPG were measured by high-sensitive ELISA at baseline. EPC populations were labeled by flow cytometry per High-Definition Fluorescence Activated Cell Sorter methodology.

Results: Numerous of EPCs with phenotypes of CD14+CD309+ and CD14+CD309+Tie2+ were significantly lower in CAD patients when compared with healthy subjects. There is a significant trend to decrease of EPC numerous depending presence of CHF. The sRANKL level, OPG level, and sRANKL / OPG ratio were significantly higher in CHF subjects as compared to those without CHF (P=0.001). On multivariate analysis, CHF, sRANKL/OPG ratio, OPG, and NT-pro-BNP remained as independent predictors of decreased EPCs with phenotypes of CD14+CD309+ and CD14+CD309+Tie2+. Using reclassification methods, we found that the addition of sRANKL/OPG ratio to the ABC standard model (CHF) improved the relative integrated discrimination indices by 12.5% for CD14+CD309+ depletion, by 17.3% for CD14+CD309+Tie2+depletion.

Conclusion: We found that sRANKL/OPG ratio remained statistically significant predictor for depletion of proangiogenic EPCs in CAD patients. The imbalance between free fraction of RANKL, calculated as sRANKL/OPG ratio, and circulating OPG may be responsible for the homeostatic mechanism of differentiation and apoptosis of EPCs. Probably, this effect may have a prognostic value for subjects with CHF due to ischemic reason. Further studies are needed to elucidate the potential role of free fraction of serum RANKL in the complex pathogenesis of ischemic CHF.

P1078

Estrogen attenuates cardiomyocyte injury dependent on p66Shc adapter proteinM Ming Zhang¹; RUI Yan¹¹The Second Affiliated Hospital, Xi'an Jiaotong University School of Medicine, xi'an, China, People's Republic of

Objective: To explore the role of p66shc in the cardiomyocyte apoptosis induced by AngII, and the effect of estrogen pretreatment.

Methods: Neonatal rat cardiomyocytes were randomly divided into the following groups: normal control group, 10-11M AngII group, 10-9M AngII group, 10-7M AngII group, and 10-7M AngII+estrogen group. The cell viability was measured by MTT. The level of reactive oxygen species (ROS) and cell apoptosis rate were measured by flow cytometry. Mitochondrial membrane potential (MMP) was detected using a fluorescence microplate reader, and the protein expression of phosphorylated and total p66shc was detected using western blot.

Results: With the increasing AngII concentration, cell viabilities and MMP levels were gradually decreased, and the levels of ROS in the whole cells and the cell apoptosis rates both increased (P < 0.05). Moreover, the pretreatment of estrogen could significantly attenuate the cardiomyocyte injury induced by AngII (P < 0.05). The protein expression of phosphorylated p66shc in the whole cell lysates and total p66shc in the mitochondria were both increased in a dose-dependent manner when cardiomyocytes were exposed to AngII (P < 0.05). When cardiomyocytes were exposed to 10-7M AngII, the pretreatment of estrogen could significantly down-regulate the protein expression of phosphorylated p66shc in the whole cell lysates and total p66shc in the mitochondria (P < 0.05).

Conclusion: p66shc plays an important role in the cardiomyocyte apoptosis induced by AngII, and estrogen could attenuate AngII-induced cardiomyocyte injury through down-regulating the protein expression of p66shc.

P1079

Pharmacoeconomic advantages of treatment of chronic heart failure in a hospital at homeM Marina Stolbova¹¹Orenburg State Medical Academy, Orenburg, Russian Federation

Purpose: To compare clinical and economic efficiency of treatment of patients with chronic heart failure (HF) in a hospital at home (HH) and acute hospital care (AH).

Methods: The research was done on 20 adult patients from a HH with accompanying stable stenocardia and 20 patients from the HA with similar pathology. All patients were led general-clinical trial and echocardiography (thickness of walls of the left ventricle, left ventricular mass index, left ventricular ejection fraction (LVEF)). The assessment of quality of life was carried out on the Minnesota questionnaire (1987). Treatment of patients was carried out according to Recommendations of the European society of cardiologists. Efficiency of treatment was estimated by a clinical state, by indicators of quality of life, by the frequency of repeated hospitalization and according to echocardiography findings in 3 months and in a year.

Results: The clinical state of all patients was improved. Reduction of left ventricular mass index and increase of LVEF in 3 months was observed in 10 people from a HH and 14 people from the AH. Frequency of repeated hospitalization was identical in treatment in a HH and the AH. Quality of life, was initially higher in the patients who were treated in a HH as treatment was carried out in a home, there was no isolation from relatives and friends, were excluded negative sides of hospitalization. Quality of life of all patients was improved in 3 months of treatment, but more significant improvement was in patients, who were treated in HH. In a year indicators of quality of life decreased as at the patients treated in HH and in AH. As efficiency of treatment was identical, the pharmacoeconomic analysis was carried out by means of method of cost minimization. Cost of one bed day in a HH was 4,5 times less than in AH

Conclusions: clinical efficiency and pharmacoeconomic advantages of treatment of patients in HH is confirmed because of the clinical effect is associated to AH, higher quality of life, in connection with exception of negative sides of hospitalization, considerable economic effect.

P1080

The functional importance of collagen deposition for myocardial stiffness differs between reactive and replacement fibrosis.C Constantijn Franssen¹; SH Chen¹; N Hamdani¹; WJ Paulus¹¹VU University Medical Center, Department of Physiology, Amsterdam, Netherlands

Purpose: LV remodeling is frequently accompanied by myocardial fibrosis, whose distribution varies in distinct LV remodeling phenotypes with both reactive and replacement fibrosis in eccentric remodeling and only reactive fibrosis in concentric remodeling. The functional implications for myocardial stiffness (Fpassive) of the variable distribution of LV fibrosis has not yet been assessed. In the present study we determined the relative contributions of collagen and cardiomyocyte stiffness to overall Fpassive in aortic stenosis (AS) patients with concentric LV remodeling and in dilated cardiomyopathy (DCM) patients with eccentric remodeling.

Methods: Small muscle strips were created from LV samples procured from explanted donor hearts (n=5), from AS patients during aortic valve replacement (n=5) and from biopsies of DCM patients (n=3). Muscle strips were stretched from slack length (SL) to 10%, 15%, 20% and 25% above SL and Fpassive was measured. Thereafter, strips were incubated with protein kinase G (PKG) to correct a possible phosphorylation deficit and stretches were repeated. Afterwards, strips were incubated with KCl and KI to detach thick and thin filaments and unanchor titin, the cytoskeletal protein responsible for cardiomyocyte stiffness. Finally, stretches were repeated to measure the contribution of collagen to Fpassive.

Results: The relative contribution of collagen to Fpassive was significantly higher in DCM strips, compared with donor or AS for stretches at 10%, 15% and 20% above SL. Only for a stretch at 25% above SL, was the contribution of collagen to Fpassive comparable in donor, AS and DCM.

Conclusion: The functional importance of collagen varies in accordance to remodeling phenotype with a major effect of collagen at all muscle lengths in eccentric remodeling and an effect of collagen limited to high muscle length in concentric remodeling. These findings could contribute to the unequal outcome of antifibrotic therapy with aldosterone antagonists observed in heart failure with reduced (eccentric LV remodeling) and preserved (concentric LV remodeling) ejection fraction.

BASIC SCIENCE: HFpEF

P1081

ZSF-1 obese rats as a pre-clinical model to identify a treatment for HFpEFB Brandon Ason¹; G Swaminath¹; P Battiprolu¹; A Goel¹; G Raman¹;S Mihardja¹; Y Zhang¹; V Chintalgattu¹; W-C Yeh¹; A Khakoo¹¹Amgen, Inc, South San Francisco, United States of America

Heart failure with preserved ejection fraction, HFpEF, is becoming the most prevalent form of heart failure leading to hospitalization. Currently, there are no FDA approved treatments. HFpEF is characterized by diastolic dysfunction and ventricular/arterial uncoupling driven by a stiffening of the heart and vasculature, limiting reserve capacity.

ZSF-1 obese rats were recently reported to exhibit many HFpEF associated pathophysiologicals including hemodynamic features of diastolic dysfunction and myocardial titin hypophosphorylation. We have confirmed many of these findings and show that ZSF-1 obese rats exhibit an increased E/E', IVRT, LA area, LV mass, and tau while maintaining a normal ejection fraction. In addition, we have extended previously reported findings to define other parameters of the model that may have direct, translational relevance. 1) We demonstrated that ZSF-1 obese rats exhibited impaired endothelium dependent relaxation suggesting that cardiovascular abnormalities extend beyond the heart, consistent with the global nature of cardiovascular impairment associated with HFpEF. 2) We further showed that ZSF-1 obese rats exhibited a limited exercise capacity with significantly shorter times to exhaustion, lower peak VO₂, shorter distance, vertical distance, and lower vertical work following treadmill challenge. These factors were associated with a decrease in stroke volume and end diastolic volume post-exercise. The opposite was observed for the ZSF-1 lean littermates. 3) ZSF-1 obese rats failed to significantly increase their ejection fraction, stroke work, or stroke volume following a dobutamine challenge, consistent with observations that have been reported in patients with HFpEF. Together, these data provide a compelling case that ZSF-1 obese rats exhibit many of the defining features of human HFpEF. Therapeutic approaches to improve diastolic function and reserve capacity are being explored, and an update on our efforts will be discussed.

P1082

Echocardiography and invasive haemodynamics during stress testing for diagnosis of heart failure with preserved ejection fraction: an experimental study

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Purpose: Inclusion of exercise testing in diagnostic guidelines for heart failure with preserved ejection fraction (HFpEF) has been advocated but the target population, technical challenges, and underlying pathophysiological complexity raise difficulties to implementation. Haemodynamic stress tests may be feasible alternatives. Our aim was to test Trendelenburg positioning, phenylephrine and dobutamine in the ZSF1 obese rat model in order to find echocardiographic surrogates for end-diastolic pressure (EDP) elevation and HFpEF.

Methods: Seventeen-week-old Wistar-Kyoto, ZSF1 lean and obese rats (n=7 each) randomly and sequentially underwent (cross-over) Trendelenburg (30°), 5µg.Kg⁻¹.min⁻¹ dobutamine and 7.5µg.Kg⁻¹.min⁻¹ phenylephrine with simultaneous left ventricular (LV) pressure-volume loop and echocardiography evaluation under halogenate anesthesia. Effort testing with maximum O₂ consumption (VO₂max) determination was performed 1week later.

Results: Obese ZSF1 showed lower effort tolerance and VO₂max along with higher resting EDP. Both Trendelenburg and phenylephrine increased EDP whereas dobutamine decreased it. Significant correlations were found between EDP and (i) peak early filling Doppler velocity of transmitral flow (E) to corresponding myocardial tissue Doppler velocity (E') ratio, (ii) E to E-wave deceleration time (E/DT) ratio, and (iii) left atrial area (LAA). Diagnostic efficiency of E/DT*LAA by ROC curve analysis for elevation of EDP above a cut-off of 13mmHg during haemodynamic stress was high (area under curve - AUC=0.95) but not higher than that of E/E' (AUC=0.77, P=0.15).

Conclusions: Results in ZSF1 Obese rats suggest non-invasive echocardiography after haemodynamic stress induced by phenylephrine or Trendelenburg can enhance diagnosis of stable HFpEF and constitute an alternative to effort testing.

P1083

The impact of carbonylated proteins in the progression of diastolic dysfunction

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Currently, Diastolic Heart Failure (DHF) accounts for 50% of HF cases and its prevalence is increasing due to progressive ageing of the population. DHF is the most prevalent form of HF in elderly, being more prevalent in women. Imbalance between ROS production and antioxidant protection may induce deleterious changes in contractile performance and promote adverse ventricular remodeling. Increased protein carbonylation disturbs their function and has been indicated as one of the underlying mechanism of cellular senescence and age-related diseases. We aim to evaluate the effects of ageing, particularly focusing on cardiac structure and function, elucidating the importance of protein carbonyl content that might contribute to the development of DHF.

Aged male Wistar Kyoto rats (WM, n=6) and female (WF, n=7) were echocardiographically and haemodynamically evaluated, at 20 months-old. Oral glucose

tolerance and insulin resistance tests were also performed. Protein carbonyl content was determined in plasma using a colorimetric assay kit.

At 20 months of age no significant differences were found in systolic (ejection fraction - WM: 80.60±9.24 vs WF: 81.19±10.32%); cardiac index - WM: 119.31±13.76 vs WF: 99.39±20.66 µL.min⁻¹.cm⁻²) nor in diastolic function (E/A - WM: 1.00±0.09 vs WF: 1.17±0.07; E/E' - WM: 15.97±1.36 vs WF: 13.62±1.16). WM group showed elevated insulin resistance (WM: 7155.00±474.81 vs WF: 5033.57±182.61 mg.dL⁻¹.min⁻¹, p<0.0001) and hyperglycemia (WM: 15213.75±307.63 vs WF: 12229.29±188.18 mg.dL⁻¹.min⁻¹, p<0.0001). Protein carbonyl content was higher in WF group compared to WM group (WM: 0.41±0.11 vs WF: 1.15±0.24 nmol.mL⁻¹, p=0.02).

Although there were no statistically differences in cardiac structure and function between WM and WF groups, at 20 months of age, the metabolic changes observed were different. In fact, WM group presented an increase in insulin resistance and hyperglycemia, whereas WF group exhibits higher protein carbonylation. This shows that gender clearly impacts the mechanisms behind ageing. Further studies are needed to clarify the relation between carbonylation and the hormonal profile of this animal strain.

P1084

Relationship between aldosterone level and body mass index in the patients with chronic heart failure and preserved ejection fraction

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Background: As known, aldosterone and body mass index (BMI) are predicts development and progression of chronic heart failure (CHF). However, the relationship aldosterone with BMI in patients (pts) with CHF remains debatable.

Objectives: We aimed to evaluate relationship between aldosterone and BMI in patients with chronic heart failure and preserved ejection fraction (HFpEF).

Methods: 46 pts (31 M, 15 F, mean age - 68,10±1,10 years) with CHF NYHA II-III class and preserved ejection fraction were enrolled. Pts were divided into three groups: 11 (23,9%) pts (1 group) with BMI 18,5-24,9 kg/m², 15 (32,6%) pts (2 group) with BMI 25,0-29,9 kg/m² and 20 (43,5%) pts (3 group) with BMI 30,0-39,9 kg/m². The aldosterone level was determined in the blood. BMI was calculated by formula.

Results: All patients had high aldosterone level (mean level - 627,9±31,7 ng/ml). Aldosterone level was 1,5 times higher in 2 group and 2,2 times higher in 3 group compared with 1 group (p<0,001) (tab.1). Aldosterone level is correlated to BMI and decreased ejection fraction (r=0,75; p<0,001 and r=-0,46; p<0,001 respectively).

Conclusion: Our results provide suggestive evidence that the high BMI associated with increased aldosterone levels in patients with HFpEF. Relationship between BMI and aldosterone level are powerful predictor of progression HFpEF.

	I group (BMI 18,5-24,9), n=11	II group (BMI 25,0-29,9), n=15	III group (BMI 30,0-39,9), n=20	p
Aldosterone level, ng/ml	369,6±13,2 (351,3)	554,9±20,1 (584,3)	824,7±31,7 (813,2)	<0,001

P1085

A translational approach in HFPEF pathophysiology: metabolic comorbidities drive microvascular inflammation, oxidative stress and decreased NO-bioavailability.

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Purpose: Epidemiological data show that half of all heart failure (HF) patients have a preserved ejection fraction (PEF). The majority of HFPEF patients have metabolic comorbidities, such as obesity and diabetes mellitus (DM), known to induce a chronic, low-grade inflammatory state. HFPEF is characterized by diastolic dysfunction and increased myocardial stiffness. The importance of comorbidities associated with a proinflammatory profile and reduced nitric oxide (NO) was investigated in HFPEF patients and in a ZSF1-HFPEF rat model.

Methods: Human samples were procured transvascularly in HFPEF and HFPEF patients, and during aortic valve replacement in aortic stenosis (AS) patients. Obese ZSF1-HFPEF rats on a high fat diet were sacrificed at 20 weeks of age. ZSF1-lean rats served as hypertensive controls. Hydrogen peroxide (H₂O₂), Interleukin 6 (IL 6) and tumor necrosis factor α (TNFα) were quantified in rat plasma. Myocardial nitric

oxide (NO), cyclic GMP (cGMP) concentration, and protein kinase G (PKG) activity were assessed in rat and human biopsies. Myocardial CD68, CD62, myeloperoxidase (MPO), ICAM-1 and NOX2 expression were immunohistochemically quantified in rats and human biopsies. The expression of nitrotyrosine in cardiomyocytes versus endothelium was assessed with immunogold labeled electron microscopy in rats.

Results: On the myocardial level, HFPEF patients showed a higher expression of ICAM-1 than AS and HFREF patients. Plasma levels of H₂O₂ were higher, but NO levels were lower in HFPEF patients. ZSF1-HFPEF rats developed DM and a systemic proinflammatory state with high circulating levels of H₂O₂. Myocardial expression of CD68, MPO, CD62 and ICAM-1 was elevated in ZSF1-HFPEF rats compared to lean controls. Inflammation can lead to high endothelial NOX2 expression and low NO-bioavailability, which was evident from lower nitrotyrosine expression in the endothelium. Low NO-bioavailability resulted in reduction of cGMP concentration and PKG activity in ZSF-HFPEF rats. Previous research by our group demonstrated that decreased cGMP concentration and PKG activity lead to increased myocardial passive stiffness through hypophosphorylation of the giant cytoskeletal protein titin. **Conclusion:** In HFPEF, obesity and DM contribute to systemic inflammation, inducing oxidative stress in the coronary microvascular endothelium with deficient NO-bioavailability. This causes reduced PKG activity and a titin phosphorylation deficit and thereby an increase in myocardial stiffness. These findings provide novel targets for HFPEF therapy.

P1086

Oxidative stress affects human myocardial stiffness by regulating titin elasticity

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Purpose: The diastolic stiffness of the heart depends on the stiffness of the cardiac titin springs, which is regulated, e.g., by phosphorylation of unique spring elements (N2-Bus, PEVK). However, the titin springs consist mainly of immunoglobulin-like (Ig) domains, which are also crucial for the mechanism of titin elasticity. We aimed to study whether passive stiffness-regulating mechanisms involve the Ig-domains of titin and whether oxidative stress plays a role in this regulation as we have suggested recently.

Methods: The effect of redox state on titin stiffness was studied by force measurements of isolated skinned human cardiomyocytes, single-molecule force spectroscopy of recombinant titin Ig-domains using the atomic force microscope (AFM), and redox proteomics using ICAT labeling/mass spectrometry to detect titin oxidation in ex-vivo perfused mouse hearts.

Results: AFM force measurements showed that Ig-domains from the titin spring region are weakened by oxidative modification of cryptic cysteines. These cysteines became accessible to oxidative modification in the presence of millimolar concentrations of oxidized glutathione (GSSG)-but only after mechanical unfolding of the Ig-domains. In these unfolded domains, the cysteines preferentially formed mixed disulfides with glutathione, which prevented the refolding of the domains. Importantly, GSSG needed to be exposed for several tens of seconds to inhibit domain refolding, whereas exposure for only a few seconds had no or little effect. Treatment with reduced glutathione (GSH) or removal of the cysteines in the Ig-domains by site-directed mutagenesis restored the ability of the domains to refold in the AFM experiments. In stretched human cardiomyocytes, oxidation by GSSG greatly reduced the passive tension, an effect that was fully reversible with the incubation of GSH. Exposing perfused mouse hearts to oxidative stress (0.1 mM H₂O₂) and monitoring titin oxidation by ICAT labeling/mass spectrometry revealed that Ig-domains in titin's spring segment are preferential targets of oxidation in vivo.

Conclusions: Titin elasticity in the heart is regulated by oxidative stress via S-glutathionylation of cysteines in unfolded Ig-domains. Reversible weakening of these Ig-domains likely modulates diastolic stiffness in oxidatively stressed hearts under high preload. Promoting this type of titin oxidation by pharmacological intervention could be a means to reduce pathologically high diastolic stiffness.

BASIC SCIENCE: PULMONARY HYPERTENSION

P1087

Effect of estradiol on the development of hypoxic pulmonary hypertension in the female ovariectomized rats depends on the degree of hypoxia (O₂ 13%, 10%, 6%)

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Objective: The role of sex and estrogen (E₂) in pulmonary hypertension (PAH) is not fully known. The majority of animal studies thus far have suggested a protective role of female sex and a preventive as well as therapeutic role of E₂ in PAH. But women of various ages are more subjected to PAH compared with male. This apparent contradiction between clinical epidemiology and previous animal data has given rise to the concept of the "estrogen paradox" in PAH. The aim of current research was to test the hypothesis that the level of oxygen in the inspired air can influence on the effect of estradiol on the development of experimental hPAH in female rats.

Methods and design: Female gonadectomized Wistar rats were divided into 6 groups, three from which were injected subcutaneously during 4 weeks with 1,2-proprandion (vehicle, 200mk/1rat/day, C.); and three groups with estradiol (15mg/kg/day E₂). The procedures followed the FELASA/ICLAS guide for use of laboratory animals. hPH was induced by exposure to hypobaric hypoxia in all 6 groups. 2 groups (C13, E13) had hypoxia with 13%O₂, 2 groups (C10, E10) - 10% O₂ and 2 groups (C6, E6) - 6% O₂. Rats were housed in a hypobaric chamber 10h/day, 2wk. Right ventricular systolic pressure (RVSP) was measured as indices of hPH. Uterus index (Uterus weight/rat bw) was measured as a marker of plasma estradiol. Blood hematocrit (Hmt) were measured using a blood analyser Gemalait 1280 (Dikision Russia).

Results: Chronic estradiol administration in groups with hypoxia 13% O₂ caused a decrease of RVSP as the indicator of hPAH in group E13 on 14.6% compared with C13 (p < 0.05). In groups with hypoxia 10%O₂ estradiol did not caused any change in the group of E10 vs. C10. E₂ increased degree of RVBP in group E6 vs C6; (54,8 ± 1,4 vs 46,3 ± 1,1 mm Hg; p < 0,01). The RV increased by 18% (p < 0,05). E₂ decreased Hmt in E6 group vs C6 (50,2 ± 1,47% vs 55,5 ± 2,32%, p < 0,05), in E10 groups vs. C10 (47+3% vs 53+2%), in E13 groups vs. C13 (42,6+ vs. 48,5 +2%).

Conclusions: Effect of estradiol on the development of hypoxic pulmonary hypertension in the female ovariectomized rats depends on the degree of hypoxia (O₂ 13%, 10%, 6%). Decreasing effect of estradiol on the levels of Hmt does not depend on the content of oxygen in inhaled air and does not correlate with the effect estradiol on the development of hypertension.

P1088

Neuregulin-1 improves right ventricular function and attenuates monocrotaline-induced pulmonary arterial hypertension

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Purpose: This study evaluated the effects of NRG-1 treatment in the monocrotaline (MCT)-induced model of pulmonary arterial hypertension (PAH).

Methods: Two weeks after MCT administration, animals were randomly selected to receive NRG-1 (40 ug/kg/d) or vehicle obtaining 4 groups (CTRL, CTRL+NRG, MCT, MCT+NRG). At week 4, echocardiographic and hemodynamic evaluations were performed with subsequent sample collection for further analysis. Isolated skinned cardiomyocytes, morphometrical, histological and molecular analysis were achieved in order to dissect the underlying mechanisms. Pulmonary artery (PA) endothelial function was carried out in all groups.

Results: PAH induction resulted in abnormal PA flow (decreased acceleration/ejection time -PAAT/PAET ratio), and increased right atria area (RAA). RV function was deteriorated with increased systolic and diastolic pressures, and decreased ejection fraction (EF) and cardiac output (CO). RV dilation was clear in animals with PAH. Diastolic impairment in PAH was confirmed in isolated cardiomyocytes where single cell passive tension was higher versus controls.

NRG-1 ameliorated MCT-induced changes. PAAT/PAET and RAA were reverted to control levels. RV pressure rise was attenuated, and EF and CO were improved with treatment. RV dilation was abolished and cardiomyocyte passive tension development was lowered.

Morphometric RV hypertrophy together with changes in cardiomyocyte cross sectional area were evident in the MCT group and were attenuated in MCT+NRG group.

Treating animals with NRG-1 attenuated MCT-induced endothelial dysfunction, decreased lung oedema and PA wall thickness, when compared to the MCT group. NRG-1, B-type natriuretic peptide, endothelin-1 and hypoxia inducible factor-1 α RV expression was increased in MCT group, and was attenuated or normalized with treatment. Phosphorylation of the protein titin, which was lower in MCT animals when compared to CTRL, was recovered with NRG treatment.

Conclusion: NRG-1 treatment in MCT-induced PAH leads to improved pulmonary flow, improved RV function, decreased RV and pulmonary remodeling and attenuates the expression of hypertrophy and overload-associated markers.

P1089

Urocortin-2 improves right ventricular function in pulmonary arterial hypertension

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This study aims to explore the pathophysiological and therapeutic effects of UCN-2 treatment in an animal model of RV failure secondary to PAH.

Male Wistar rats randomly received monocrotaline (MCT, 60mg/Kg) or vehicle. After 2 weeks, animals were randomly assigned to receive UCN-2 (5µg/Kg/day) or vehicle. The study resulted in 4 groups: CTRL (n=9), CTRL+UCN-2 (n=9), MCT (n=7) and MCT+UCN-2 (n=10). Hemodynamic studies and sample collection were performed 4 weeks after MCT injection. Only significant results (mean±SEM, p < 0.05) are given.

Hemodynamic studies revealed that MCT group developed PAH, as shown by increased RV end-systolic pressure (MCT vs CTRL: 60±3 vs 22±1mmHg), end-diastolic pressure (6.0±0.7 vs 3.7±0.3mmHg), RV dilation (end-diastolic volume) (280±14 vs 222±11µL) and decreased cardiac output (35±6 vs 64±3mL/min) and ejection fraction (32±4 vs 75±3%). UCN-2 treatment resulted in attenuation of these changes (48±4mmHg; 4.3±0.3mmHg; 213±12µL; 47±2mL/min and 60±3%, respectively). Moreover, the survival rate for UCN-2 treated rats was higher (76%) than for MCT rats (44%).

PAH rats presented RV hypertrophy as shown by the morphometrical analysis (RV weight/tibia length ratio, MCT vs CTRL: 0.08±0.00 vs 0.04±0.00g/cm) and by histology (cardiomyocyte cross-sectional area: 366±25 vs 255±27µm²). UCN-2 treatment attenuated RV remodeling (0.06±0.00g/cm and 288±26µm², respectively).

The MCT group presented increased UCN-2 expression (MCT vs CTRL: 2.5±0.9 vs 1.0±0.3AU) and decreased CRHR2 expression (0.5±0.1 vs 1.0±0.1AU) in the RV, that were reversed by UCN-2 treatment (0.2±0.1 and 0.9±0.1AU, respectively). The increased expression of pathology markers in MCT animals, such as BNP (15.3±2.5 vs 1.0±0.1AU), ET-1 (3.4±0.4 vs 1.0±0.2AU) and HIF-1α (1.6±0.3 vs 1.0±0.2AU), as well as markers of apoptosis including caspase-3 (3.9±0.6 vs 1.0±0.1AU) and caspase-8 (2.8±0.3 vs 1.0±0.2AU) were attenuated by UCN-2 (6.9±2.1, 1.8±0.6, 1.0±0.1, 2.0±0.4 and 1.3±0.2AU, respectively).

The protein expression of both ERK and p38 kinases was decreased in MCT animals (MCT vs CTRL: 0.5±0.1 vs 1.0±0.1 and 0.5±0.04 vs 1.0±0.1, respectively) and was reversed by UCN-2 (0.9±0.1 and 1.1±0.2, respectively).

UCN-2 treatment significantly reduced the severity of PAH and RV hypertrophy, as well as the expression of genes associated with overload, hypertrophy, hypoxia and survival. These findings suggest that the UCN-2/CRHR2 pathway has a relevant role on the pathophysiology of PAH and RV failure, representing a potential therapeutic target in these conditions.

P1090

Increased mitral annular tissue velocity during isovolumic relaxation period is a left ventricular compensatory response to decreased preload during acute moderate to severe right ventricular pressure

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Purpose: Tissue Doppler (TD)-derived mitral annular velocities have been well known parameters representative of diastolic function, independent of preload. This study was designed to evaluate the concurrent changes in left ventricular (LV) diastolic function using this parameters during the entire cardiac cycle, including the isovolumic periods. TD-derived mitral annular velocities were measured in experimentally induced, acute mild, moderate, and severe right ventricular (RV) afterload conditions.

Methods: In 14 open-chest pigs (weights 43±4 kg) with preserved pericardium, acute mild (> 35 and <50 mmHg), moderate (≥ 50 and ≤ 60 mmHg), and severe (> 60 mmHg) increases in RV systolic pressure (RVSP) were induced by constriction of the pulmonary artery. At each step, pulsed-wave mitral annular TD velocities were measured from the LV lateral and septal annulus during isovolumic contraction, ejection, isovolumic relaxation (IVR), and early and late diastole.

Results: The mean RVSPs were 31.0±4.3 mmHg at baseline and 41.1±2.7 mmHg during mild, 52.7±3.4 mmHg during moderate, and 61.7±1.6 mmHg during severe afterload conditions. The LV systolic pressures were significantly decreased in the moderate RV pressure overload condition compared with baseline (108.7±20.2, 102.9±15.4, 89.8±14.3, 98.1±18.5 mmHg in baseline, mild, moderate and severe RV pressure overload conditions respectively; P=0.024 for baseline vs. moderate overload condition). There were no significant differences in LV end-diastolic pressures, LV end-systolic and end-diastolic volumes as well as ejection fractions

among each RV pressure overload condition. TD-derived velocity during the IVR period varied among the baseline through moderate RV pressure overload conditions, but was significantly increased in the severe RV pressure overload condition as compared with mild RV pressure overload condition (3.14±0.86, 2.83±0.58, 3.15±0.69, 4.17±1.17 cm/s; P=0.018 for mild vs. severe RV pressure overload condition). There were no significant differences in mitral annular velocities during early or late diastole, and there were also no differences in mitral inflow velocity to annular tissue velocity ratio in early diastole (E/Ea) among each RV pressure overload condition.

Conclusion: Our experimental study suggests that the increase of mitral annular IVR velocity during the severe RV pressure overload condition (>60 mmHg) indicates a compensatory LV response to impaired filling even though distinct signs of decreased LV filling pressure were absent.

BASIC SCIENCE: VASCULAR BIOLOGY

P1091

The anti-inflammatory and antiatherogenic effect of nad-containing drug on early atherosclerosis in high cholesterol fed rabbits.

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Purpose: Changes in cellular bioenergetics concomitantly reprogram inflammatory and metabolic responses. The initiating proinflammatory phase of inflammation is anabolic and requires glucose as the primary fuel. The fuel switch to fatty acid oxidation depends on the sensing of AMP and NAD⁺ by which couple inflammation and metabolism by chromatin and protein reprogramming. The aim of the study was to evaluate the effect of the original NAD⁺ reduce form containing drug on the inflammatory molecule and lipid profiles in high cholesterol diet (CHD) induced atherosclerosis in rabbits.

Materials: 26 chinchilla-strain rabbits, weighing 2,1-2,6 kg were used in this study. 19 animals, weight 2,1±1,4 were fed with a normal or HCD (1% cholesterol, 10% yolk powder, 5% animal oil) with or without Nadcin (6 mg/kg/day equivalent of 0,5 mg/kg of NAD⁺) treatment. At the end of 6 weeks all the rabbits were weighted and 2,0 mL blood was taken via the marginal ear vein and centrifugated 8,000 g for 10 min. Levels of blood NAD⁺, ratio NAD⁺/NADH (by using Amplitude Fluorimetric NAD⁺/NADH Assay Kit (ABD Bioquest, Inc.), lipids, serum tumour necrosis factor-alpha (TNF) and interleukin-6 (IL-6), soluble vascular cell adhesion molecule 1 (VCAM-1) and intercellular adhesion molecule 1 (ICAM-1), superoxide dismutase (SOD) activity were determined.

Results: After feeding on HCD, the increasing of serum lipid levels including total cholesterol (TC), triglyceride (TG), high density (HDL-C) and low density lipoprotein cholesterol (LDL-C) was increased greatly (p<0.01) compared with control rabbits accompanied with the decreasing of NAD⁺/NADH redox-potential from the 1,21±0,13 in normal group to 0,85±0,09, p<0,01 without changes in total pyridine nucleotide and ATP pool. Increases or unchanged level of ATP production and NADH formation that leading to the decrease the ratios of AMP/ATP, and NAD⁺/NADH occurs during the early proinflammatory-phase response of innate and adaptive immunity effector responses. HCD induced a high inflammatory status, as indicated by increased concentrations of IL-6, TNF without deterioration in the concentrations of endothelial dysfunctional markers, such as soluble VCAM-1 and ICAM 1. Treatment of Nadcin restorates the redox-potential and AMP/ATP ratio, significantly lowered TG and LDL-C levels of rabbits in comparison to the model group (p<0.01 or p<0.05). And as a much important increased the activity of SOD.

Conclusion: Drug, containing reduced form of NAD⁺, shows antiatherosclerotic effect and decreased the reserve ability of immune system.

P1092

Asymmetric dimethylarginine (ADMA) induces endothelial dysfunction via microRNA-126 modulation

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Background: Asymmetric Dimethylarginine (ADMA), an endogenous inhibitor of nitric oxide synthase (NOS), is known to be elevated in patients with cardiovascular disease conditions and to contribute to endothelial dysfunction. The role of non-coding RNAs, especially microRNAs in the context of endothelial dysfunction has been implicated recently. In this study, the role of microRNA-126-mediated mechanism via exosomes in ADMA induced endothelial dysfunction is addressed.

Methods and Results: Plasma levels of ADMA from 39 patients with coronary artery disease (CAD) were measured by ELISA assay and correlated to circulating

miR-126 levels using qRT-PCR. ADMA levels in plasma of patients with CAD correlated inversely to circulating levels of miR-126 ($r = -0.52$; $p < 0.001$). Infusion of ADMA into healthy rats and healthy human volunteers led to a decrease in circulating levels of miR-126 in rats and significantly also in healthy humans. In vitro, stimulation of HUVECs with ADMA resulted in a decrease of extracellular miR-126 levels whereas intracellular miR-126 expression was increased. Furthermore, stimulation with another eNOS-inhibitor (L-NAME) showed a significant reduction in extracellular levels of miR-126. Immunofluorescence staining and confocal microscopy revealed an accumulation of CD-63 positive multivesicular bodies/exosomes in HUVECs after ADMA/L-NAME treatment. HUVEC-derived exosomes were further isolated from the conditioned medium of ADMA-treated HUVECs and characterized by electron microscopy and Nanoparticle tracking.

Conclusion: miR-126-mediated signalling via exosomes is impaired by Asymmetric Dimethylarginine. This represents a novel mechanism how ADMA could contribute to endothelial dysfunction.

P1093

Monoamine oxidase inhibition improves vascular function in diseased human mammary arteries

Research supported by the university grant PIII-C1-PCFI-2014/2015-04.A Sturza¹; O Duicu¹; R Lighezan²; R Balica³; A Vaduva⁴; H Feier⁵; M Gaspar⁵; C Borza¹; D Muntean¹; C Mornos⁶

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Monoamine oxidases (MAOs) with two isoforms (A and B) at the outer mitochondrial membrane catalyze the oxidative deamination of biogenic amines and neurotransmitters via a reaction that generates hydrogen peroxide (H₂O₂) as by-product. We have previously reported an increased expression of both MAO isoforms in murine models associated with vascular inflammation and hypertension responsible for subsequent endothelial dysfunction.

Purpose: We further hypothesized that MAO-derived H₂O₂ contributes to vascular oxidative stress in humans and that MAO inhibition improves endothelial NO-dependent vasodilation in mammary arteries harvested from coronary patients with and without diabetes mellitus (DM). **Methods:** Twenty consecutive patients with coronary artery disease (CAD) and preserved ejection fraction that underwent non-emergency cardiac surgery were randomized in 2 groups: without DM (CAD-nDM) and with documented DM (CAD-DM), respectively. A fragment of mammary artery was harvested during the surgical procedure, placed in Hanks buffer and immediately transferred to the laboratory. The effect of MAO inhibition on endothelium-dependent relaxation (EDR) in response to acetylcholine was studied in isolated phenylephrine-precontracted mammary arteries segments in the presence of diclofenac (10 micromol/L). MAO gene expression was assessed by qRT-PCR. **Results:** Both MAO isoforms are present in the human mammary arteries. The impairment of EDR was detected in all vascular segments and has been significantly improved in the presence of the MAO-A (clorgyline, moclobemide, 10µmol/L) and B inhibitors (selegiline, 10µmol/L). **Conclusion:** Our partial data suggest that MAO inhibition might be useful in restoring endothelial response in conditions associated with increased oxidative stress and vascular dysfunction, such as coronary artery disease in both diabetic and non-diabetic patients.

P1094

Pre-dialysis chronic kidney disease is associated with loss of aortic-brachial stiffness mismatch

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Objective: The loss of physiological stiffness mismatch between aorta and peripheral arteries contributes to development of heart failure with reduced ejection fraction and was strongly and independently associated with increased mortality in adult dialysis population. The aim of the study was to evaluate if the reversal of arterial stiffness mismatch was present in pre-dialysis patients with chronic kidney disease (CKD).

Methods: The aortic-brachial arterial stiffness mismatch (pulse wave velocity (PWV) ratio) were assessed using carotid-femoral PWV divided by carotid-radial PWV in 112 adult treated hypertensive CKD patients: 54 - with CKD IIIa (age 59,5 ± 8,4 years, male 46,3%, brachial blood pressure (BP) 149,6 ± 10,3/85,8 ± 9,8 mmHg), 35 - with CKD IIIb (age 60,2 ± 7,8 years, male 45,7%, BP 152,5 ± 12,5/86,4 ± 10,2 mmHg) and 23 with CKD IV (age 57,3 ± 10,2, male 43,4%, BP 156,1 ± 14,3/92,8 ± 12,4 mmHg). $P < 0,05$ was considered significant for group comparisons, Spearman correlation test and multivariate regression analysis.

Results: In CKD IIIa aortic PWV was 10,2 ± 2,0 m/s, brachial PWV - 12,9 ± 1,6 m/s, PWV ratio 0,82 ± 0,25. In CKD IIIb aortic PWV was 11,3 ± 2,9 m/s, brachial PWV 12,2 ± 1,8 m/s, PWV ratio 0,90 ± 0,27. In CKD IV aortic PWV was 12,7 ± 3,1 m/s ($p < 0,05$ vs CKD IIIa), brachial PWV 11,4 ± 1,6 m/s ($p < 0,05$ vs CKD IIIa), PWV ratio 1,09 ± 0,33 ($p < 0,05$ vs CKD IIIa). Increased aortic stiffness (aortic PWV > 10 m/s) was observed in 55,6%, 62,9% and 73,9%, respectively. For the whole study population ($n = 112$) multivariate analysis revealed independent significant correlation between aortic PWV and glomerular filtration rate (GFR) $\beta = -0,36$ ($p < 0,05$), PWV ratio and GFR $\beta = -0,32$ ($p < 0,05$), PWV ratio and age $\beta = 0,44$ ($p < 0,05$).

Conclusion: In the pre-dialysis hypertensive CKD patients worsening of kidney function was associated with discordant changes in aortic and brachial artery stiffness in the reversal of the physiological stiffness mismatch. The loss of this physiological mismatch may promote kidney damage through increased forward pressure wave transmission into the microcirculation. PWV ratio evaluation (in addition to traditional aortic PWV measurement) may be useful for better evaluation of arterial stiffness in pre-dialysis CKD patients.

P1095

The effect of statins in erectile dysfunction

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Introduction: The term erectile dysfunction (ED), which replaced the emotive word "impotence" is the inability to start and maintain an erection sufficient to achieve sexual intercourse. The aetiology of this condition is multifactorial but it is usually attributed to vascular lesions caused by endothelial dysfunction.

Purpose: This study aims to investigate the relationship of erectile dysfunction with dyslipidemia and the possible impact of statins on erectile dysfunction (not receiving phosphodiesterase inhibitors).

Methods: The study included 100 male patients (aged 40-70 years) with unique risk factor dyslipidemia (none of them was receiving lipid-lowering treatment) and erectile dysfunction. The diagnosis of erectile dysfunction and its extent were assessed using the international questionnaire erectile function (IIEF). The lowest prices of the international questionnaire indicate significant erectile dysfunction. Total cholesterol (CHOL), low (LDL) and high (HDL) density lipoproteins and triglycerides (TRG) were assessed in all participants. The study group was divided in two subgroups each consisting of 50 patients. In the first subgroup patients received a statin (atorvastatin) while the second subgroup received no treatment (control group). All the participants were re-examined using the same processes (completion questionnaire IIEF-determination in blood levels of CHOL, LDL, HDL, TRG) after three months.

Results: The results of the study demonstrated at the following Table 1

Conclusions: Patients receiving lipid-lowering therapy for 3 months significantly improved both lipid profiles and erectile dysfunction compared to the control group. Therefore men using statins to improve their cholesterol levels may emerge a significant improvement in erectile function. Although statins are not recommended as primary treatment for erectile dysfunction in men with normal cholesterol levels, this effect could improve compliance in hypercholesterolemic patients treated with statins.

Table 1

	STATINS	CONTROL GROUP
Before treatment	11,4*	10,8*
After treatment	16,3*	11,2*

* Mean (average) score IIEF (International Index of Erectile Dysfunction) - $p < 0,05$

P1096

Cardiovascular calcification contributes to the loss of aortic-brachial stiffness mismatch in pre-dialysis chronic kidney disease

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Objective: Chronic kidney disease (CKD) is associated with the presence and progression of vascular and cardiac valve calcification. Vascular calcification may promote the reversal of arterial stiffness mismatch and thus development and progression of heart failure with preserved ejection fraction. The aim of the study was to evaluate the relationship between cardiac valve calcification and aortic-brachial arterial stiffness mismatch in pre-dialysis hypertensive CKD patients.

Methods: The cross-sectional study included 112 adult treated hypertensive CKD patients: 54 - with CKD IIIa (age 59,5 ± 8,4 years, male 46,3%, brachial blood pressure (BP) 149,6 ± 10,3/85,8 ± 9,8 mmHg), 35 - with CKD IIIb (age 60,2 ± 7,8 years, male 45,7%, BP 152,5 ± 12,5/86,4 ± 10,2 mmHg) and 23 with CKD IV (age

57,3 ± 10,2, male 43,4%, BP 156,1 ± 14,3/92,8 ± 12,4 mmHg). The aortic-brachial arterial stiffness mismatch (pulse wave velocity (PWV ratio) were assessed using carotid-femoral PWV divided by carotid-radial PWV. Cardiac valve calcification was evaluated by 2D echocardiography. Mitral valve calcification was graded according to the Wilkins score index. Aortic valve calcification scoring was done empirically: 1 - partial calcification on single cusp; 2 - partial calcification on 2 cusps; 3 - extended calcification on 2 cusps; 4 - extended calcification on all 3 cusps. $P < 0,05$ was considered significant for group comparisons, Spearman correlation test and multivariate regression analysis.

Results: In CKD IIIa, IIIb and IV mitral valve calcification score of grade 1 was observed in 41% 28% and 22%, respectively, of grade 2 - in 50%, 60% and 65%, respectively, of grade 3 - 0, 6% and 13%, respectively. Aortic valve calcification score 1 was found in 6%, 3% and 0, respectively, score 2 - 44%, 31% and 9, respectively, score 3 - in 50%, 60% and 65%, respectively, score 4 - 0, 6% and 26%, respectively. Average cardiac valve calcification score in CKD IIIa was 2,6 ± 0,2, in CKD IIIb 2,8 ± 0,3, in CKD IV - 3,6 ± 0,2 ($p < 0,05$ vs CKD IIIa). PWV ratio in CKD IIIa was 0,82 ± 0,25, CKD IIIb - 0,90 ± 0,27, in CKD IV 1,09 ± 0,33 ($p < 0,05$ vs CKD IIIa). For the whole study population ($n = 112$) multivariate analysis revealed independent significant correlation between cardiac valve calcification score and PWV ratio $\beta = 0,38$ ($p < 0,05$).

Conclusion: In the pre-dialysis hypertensive CKD patients cardiac valve calcification score associated with loss of arterial stiffness mismatch.

P1097

Determinants of central systolic blood pressure in the very elderly hypertensive patients with acute coronary syndrome and normal ejection fraction

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Objective: The systolic blood pressure (SBP) and age are the main factors which influence arterial stiffness. Data on the interrelation of arterial stiffness with other cardiovascular risk factors is controversial. The aim of this study was to evaluate relationship of arterial stiffness, SBP and cardiovascular risk factors in very elderly subjects.

Methods: Routine investigations, aortic pulse wave velocity (PWV) measurement and central pulse wave analysis (PWA) was done in 64 subjects older than 80 years (mean age 83,4 ± 0,8 years, 34,4% male, mean brachial SBP 132,6 ± 6,96 mm Hg) with BPLab Vasotens system ("Petr Telegin", Russia). The subjects were admitted due to acute coronary syndrome. Patients with ejection fraction (EF) <40%, atrial fibrillation, aortic stenosis and severe comorbidities were not included. Kruskal-Wallis test was used for comparison PWV and PWA results in subgroups by brachial SBP tertiles (I from 94 to 127,3 mmHg, II from 127,4 to 140 mmHg and III from 140,1 to 174 mmHg). Pearson test was used for correlation analysis.

Results: By brachial SBP tertiles central SBP was 102,3 ± 5,7, 124,5 ± 3,2, 138,8 ± 8,5 mm Hg ($p < 0,0001$), respectively. There was no significant increase of augmentation index (AI) from I to III tertiles of brachial SBP: 34,6 ± 8,3, 40,9 ± 7,1, 40,1 ± 7,4% ($p = 0,43$), respectively. No significant difference in PWV was observed also: 12,0 ± 0,89, 11,1 ± 0,78, 11,1 ± 1,3 m/s ($p = 0,27$), respectively. Central SBP was associated with body mass index (BMI) ($r = 0,42$, $p < 0,05$), waist circumference ($r = 0,52$, $p < 0,005$), triglycerides level ($r = 0,45$, $p < 0,05$). Paradoxical negative correlation between central SBP and PWV $r = -0,33$ ($p < 0,001$) was observed. Moderate correlation between central SBP and EF was found ($r = 0,43$, $p < 0,05$).

Conclusion: In the very elderly central SBP is not determined by arterial stiffness (PWV) but is associated with LV contractility (ejection fraction).

P1098

Functional relevance of endothelial hypoxia-sensitive long non-coding RNAs (lncRNAs)

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Introduction: During angiogenesis, either pro- or anti-angiogenic signalling guides endothelial cells to sustain vascular integrity. Hypoxia is one of the most potent pro-angiogenic stimuli. The role of non-coding RNAs, such as microRNA (miR), has been extensively studied in the past. Here, we questioned if human long non-coding RNAs (lncRNAs) would be differentially expressed after hypoxic treatment in human umbilical vein endothelial cells (HUVECs). In addition, specific candidate lncRNAs were investigated for functional relevance in vitro and ex vivo applying human induced pluripotent stem cell (hiPSC)-derived engineered heart tissue (EHT) to analyse lncRNA-dependent impact on vascular development.

Methods and Results: HUVECs were cultured under normoxic or hypoxic (0.1% O₂, 24 h) conditions and total RNA was analyzed by microarray and RNA-sequencing analysis. We identified a set of deregulated lncRNAs after hypoxic intervention. Expression levels of hypoxia-sensitive lncRNAs were validated via qRT-PCR. With this approach, we identified the highly upregulated intergenic lncRNAs LINC00323 and MIR503HG-002. Of note, hypoxia induced all three LINC00323 isoforms. Loss of function experiments using siRNA or GapmeR technology revealed a crucial participation of LINC00323 and MIR503HG-002 in proliferation, cell cycle progression, wound healing and capillary tube formation. Interestingly, knockdown of endogenous lncRNA altered gene expression profiles related to cell cycle control and angiogenesis. More specifically, the GATA2-SIRT1 axis and ERK signalling were disturbed by transient repression of lncRNAs. Overexpression studies were also applied to study enhanced lncRNA expression in a permanent cell line in vitro. Translation of in vitro findings to a relevant ex vivo model was performed applying hiPSC-EHTs. Therefore, lncRNAs were silenced in HUVECs that were mixed to the developing hiPSC-EHT. In line with in vitro findings, knockdown of endogenous lncRNAs deteriorated the appearance of vascular structures, emphasizing the potent angiogenic function of herein identified intergenic lncRNAs LINC00323 and MIR503HG-002.

Conclusion: In summary, based on microarray and RNA sequencing of lncRNAs in endothelial cells, we here report functional relevance of specific hypoxia-sensitive intergenic lncRNAs LINC00323 and MIR503HG-002. Balanced endothelial lncRNA expression is of great importance to sustain crucial endothelial cell properties.

P1099

Mean platelet volume and prognosis of unstable angina

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Methods: A total number of 230 patients admitted to our CCU with unstable angina over a period of one year (from June 2013 till May 2014) was enrolled. Exclusion criteria were: severe anemia, thrombocytopenia, myelodysplastic syndrome, coagulopathy and recent blood transfusion. Grouping was then done according to MPV into group (I) who had a low MPV less or equal than 7.00 fl and, a group (II) with MPV equal to or higher than 9.00 fl. Demographical and clinical variables of the patients were recorded. Routine laboratory parameters and clinical manifestations were meticulously reported. Major complications as bleeding or, urgent need for percutaneous coronary intervention (PCI) are also studied.

Results: Among the 230 patients analyzed, 175 patients (76%) were found to have MPV ≤ 7.00 fl, (group-I) and 55 patients (24%) having MPV ≥ 9.00 fl, (group-II) with mean ± SD MPV (8.4 ± 1.5 fL, vs 11.7 ± 1.2 fL respectively), ($p < 0,001$). Observation of clinical course during admission period revealed, a statistically significant clinical deterioration in group-(II) than group-(I) and presence of more frequent AMI cases in group-II who having a high MPV. A high cut-off value of 9.7 fl for MPV was detected in prediction of clopidogrel nonresponsiveness (group-II) with a sensitivity of 78.2% and specificity of 66.8% and a low cut-off value for bleeding tendency in (group-I) of lower than 6.3 fL with a sensitivity of 71.4% and specificity of 62.5%

Conclusion: This study showed that MPV can be used as a simple bed-side predictor for detection of clopidogrel response in patients with unstable angina. And a cut-off value for both platelet responsiveness and risk of bleeding is now reached.

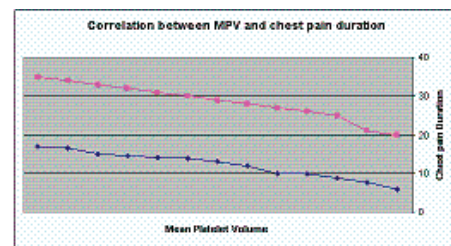


Figure 3): Correlation between MPV and chest pain duration

BASIC SCIENCE: MOLECULAR BIOLOGY AND GENETIC

P1100

Long term follow up after heart transplantation in danon disease

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Background: Danon disease is an X-linked disorder characterized by hypertrophic cardiomyopathy, myopathy, intellectual disability and results from deficiency of the lysosome-associated membrane protein-2 (LAMP-2). Men are involved more severely than women. Heart transplantation is considered the gold standard therapy for end stage cardiomyopathy. However scarce information are available about follow up of Danon disease after heart transplantation.

Methods: We report long term follow up (mean 13.2 years, range 8 - 20) of 4 patients, brother and sister, mother and son, transplanted for end stage Danon disease cardiomyopathy. LAMP2 mutations were L272P or G294A.

Results: Mean age at time of heart transplant was 32 years for men and 46.5 years for women. All patients are still alive. Mean ejection fraction of transplanted hearts is 68.7% (62% - 74%). One female had 3A rejection after 10 years treated with steroids. Immunosuppressive treatments used were cyclosporine, azathioprine, micophenolate. Myopathy remained mild in the two men affected while women do not show signs of myopathic involvement. All patients have retinitis pigmentosa but only a male developed severe reduction of visus due to macular atrophy and retinogenic cataract. Two males had intellectual disability and one developed persecutive psychosis. Cardiac NMR after 9.5 years showed normal hearts. In Fig 1 black symbols:affected subjects, Slashed symbol: deceased members, Y:years, HCM: hypertrophic cardiomyopathy, HT:heart transplantation, SD: sudden death.

Conclusions: Heart transplantation represents a life-saving therapy in Danon disease as there are no signs of late recurrence in the heart, whereas there was a slow progression of the disease in other organs, in particular eyes due to retinitis pigmentosa.

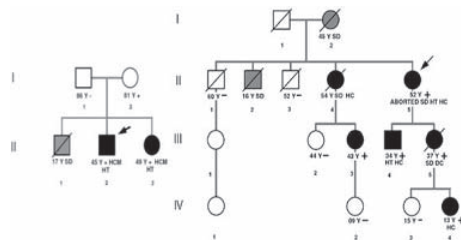


Fig. 1. Pedigree of the two families

P1101

Association of gene polymorphism T-786C NOS3 in patients with chronic heart failure

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Purpose: Study the role of gene polymorphism T-786C (rs2070744) NOS3 in CHF manifestation in Uzbek patients.

Methods: The study involved 81 CHF (ischemic genesis) male patients, Uzbeks, aged from 41 to 60 years. Group 1 consisted of 12 patients with CHF FC-I, Group 2 consisted of 30 patients with CHF FC-II, and Group 3 consisted of 39 patients with CHF FC-III. Genomic DNA was extracted from peripheral blood using the Diatomtm DNA Prep 200 Kit according to the manufacturer's protocol. Polymerase chain reaction restriction fragment length polymorphism-based (PCR-RFLP) techniques and visualization were employed and performed to determine the NOS3 T-786C (rs2070744) polymorphism. Statistical analysis was performed using a statistical software package, "GenePop". Chi square (χ^2) or Fischer's exact test (two sided) was used to compare the association between the genotypes and alleles in relation to the cases, and test for deviation of genotype distribution from Hardy-Weinberg equilibrium.

Results: In CHF patients, the observed frequency of genotypes was as follows: TT=0.556; CT=0.432; CC=0.012; the expected frequency of genotypes was as follows: TT=0.595; CT=0.352; CC=0.052 ($\chi^2=4.14$, P=0.04). Deviation from Hardy-Weinberg equilibrium was noted due to an excess of heterozygosity. The frequencies of T and C alleles were 0.772:0.228 in patients versus 0.853:0.147 in the control group (P>0.05). Comparative analysis showed a significant association between the CT genotype and CHF manifestation in Uzbek patients according to an additive model of inheritance ($\chi^2=4.20$, P=0.04; OR=1.83; 95% CI: 0.94-3.56). In patients with CHF FC-I, the observed frequency of genotypes was as follows: TT=0.667; CT=0.333; CC=0; the expected frequency of genotypes was as follows: TT=0.694; CT=0.278; CC=0.028 ($\chi^2=0.48$, P=0.49). In patients with CHF FC-II, the observed frequency of genotypes was as follows: TT=0.500; CT=0.467; CC=0.033; the expected frequency of genotypes was as follows: TT=0.538; CT=0.391; CC=0.071 ($\chi^2=1.12$, P=0.29). In patients with CHF FC-III, the

observed frequency of genotypes was as follows: TT=0.564; CT=0.436; CC=0; the expected frequency of genotypes was as follows: TT=0.612; CT=0.341; CC=0.048 ($\chi^2=3.03$, P=0.08).

Conclusions: Our findings suggest that the presence of the NOS3 gene mutant allele reduces endothelial production of NO in vessels and predisposes the post-MI patients carrying the mutant C allele to CHF.

P1102

Should sarcomere protein genes mutations be more important in risk of sudden cardiac death hypertrophic cardiomyopathy evaluation?

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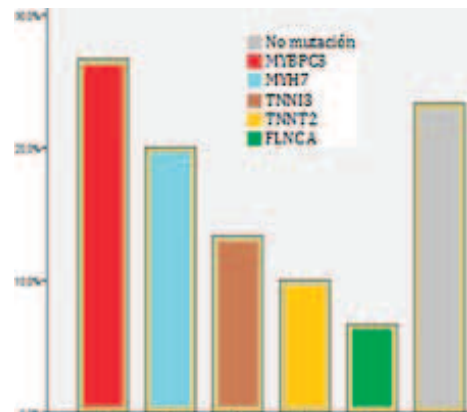
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Purpose: Genetic testing is recommended in hypertrophic cardiomyopathy (HCM) in 2014 European Society of Cardiology (ESC) Guidelines (class of recommendation IB). Mutations in sarcomere genes are found in 40-60% of HCM, being MYBPC3 and MYH7 the most commonly affected. Our study aimed to review genetic analysis in HCM patients with cardioverter-defibrillators implanted (ICDs), due to their known high risk clinical profile.

Methods: we retrospectively studied 47 consecutive patients with HCM from our hospital or referred to our center in order to receive an ICD, from 2008 to the end of 2014.

Results: Population: mean age 55.8 ±16 years. ICDs for primary prevention of sudden cardiac death (SCD) in 76.7%; 23.3% for secondary. Positive familial antecedents for HCM and/or SCD in the same patient in 72.7%; 61.4% positive for HCM and another 61.4% for SCD if considered independently. Within the genetically studied group (63.8%), mutations in cardiac sarcomere protein genes were identified in 76.7% (59.9-93.5), finding significant differences with general population (p<0.05). MYBPC3 and MYH7 were the most commonly affected genes (60.8%), followed by 17.4%TNNI3, 13% TNNT2 and 8.6% FLNC.

Conclusions: While Family History of SCD is considered a HCM Risk variable of SCD in the new formula for primary ICD from de 2014 ESC Guidelines, presence of genetic mutations is not. In our population of HCM with high SCD risk, we found significant differences in proportion of mutations in sarcomere genes, higher than expected. Troponin and filamin C mutations also deserve a special consideration. Therefore, although this small sample is insufficient to draw definitive conclusions, greater clinical relevance of these mutations in estimating risk of SCD should be evaluated in further studies.



P1103

Genome-wide association studies of heart failure

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Purpose: To investigate genome-wide association studies for HF through the current literature and genetic network databases.

Methods: A study search was performed in PubMed including the search term 'heart failure & GWAS'. Furthermore, genome networks were explored in order to outline essential genes and pathways leading to HF.

Results: A total of 97 studies were retrieved according to the search terms in PubMed. We found 15 of the studies to report on experimental animal studies, where 82 studies were based on humans. Systematic reviews were 24.

We saw a trend separating genes and pathways related to HF differentiated into Ca²⁺, metabolism, cardiomyopathy, and necrosis or apoptosis (Table 1). In humans, the ubiquitin carboxyl-terminal hydrolase 3 was significantly associated with the HF incidence ($P = 1.4 \times 10^{-8}$) established in the CHARGE consortium suggesting a role in the incidence of cardiomyopathy. Titin was equally found to be essential for the development of cardiomyopathy. In animal studies, SERCA2A was shown as a pivotal Ca²⁺ transporting ATPase. Peroxisome proliferator-activated receptors have shown to be influential for the fatty acid degradation of the cardiomyocytes. Signal transducer and activator of transcription 3, and protein kinase B were important for necrosis and apoptosis. **Conclusion:** Structural, metabolic and cellular signalling genes have been significantly associated to HF. Yet, several of these have not been unravelled in humans.

Gene or SNP	Cohort	Target protein
Cardiomyopathy		
"TTN"	312-dilated cardiomyopathy; 231 hypertrophic cardiomyopathy; 249 controls	Titin
USP3	20,926 (4 community-based prospective cohorts)	Ubiquitin
Ca ²⁺		
SERCA2A	Animal studies	Ca ²⁺ -uptake pump
Metabolism		
PPAR α & β ; Nuclear respiratory factor 1 & 2	Animal studies	PCG-1 α
Apoptosis/Necrosis		
STAT3	Animal studies	JAK-STAT signaling
Akt	Animal studies	PI(3)K-Akt signaling
Ppif	Animal studies	Cyclophilin D

Table 1. SNPs related to heart failure

P1104

Gelsolin (GSN) induces cardiomyocyte hypertrophy and BNP expression via p38 signaling and GATA-4 transcriptional factor activation

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Cardiomyocyte hypertrophy is an adaptive response of the heart to various types of stress. During the period of stress accumulation, the transition from physiological hypertrophy to pathological hypertrophy results in the promotion of heart failure.

Gelsolin (GSN) is a member of the actin-binding proteins (ABPs), which regulate dynamic actin filament organization by severing and capping. Moreover, GSN also regulates cell morphology, differentiation, movement, and apoptosis. In this study, we used H9c2 and H9c2-GSN stable clones, in an attempt to understand the mechanisms of GSN overexpression in cardiomyocytes.

This data showed that the overexpression of GSN in H9c2 induced cardiac hypertrophy and increased the pathological hypertrophy markers atrial natriuretic peptide (ANP) brain natriuretic peptide (BNP). Furthermore, we found that E-cadherin expression decreased with the overexpression of GSN in H9c2, but β -catenin expression increased. These data presume that the cytoskeleton is loose. Further, previous studies show that the mitogen-activated protein kinase (MAPK) pathway can induce cardiac hypertrophy. Our data showed that p-p38 expression increased with the overexpression of GSN in H9c2, and the transcription factor p-GATA4 expression also increased, suggesting that the overexpression of GSN in H9c2-induced cardiac hypertrophy seemed to be regulated by the p38/GATA4 pathway. Moreover, we used both the p38 inhibitor (SB203580) and GSN siRNA to confirm our conjecture. We found that both of these factors significantly suppressed gelsolin-induced cardiac hypertrophy which through p38/GATA4 signaling pathway. Therefore, we predict that the gene silencing of GSN and/or the downstream blocking of GSN along the p38 pathway could be applied to ameliorate pathological cardiac hypertrophy in the future

P1105

Intracardial hemodynamic indicators in patients with coronary artery disease depending on T-786C polymorphism of the endothelial NO-synthase gene promoter

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Purpose: Evaluation of impact of the endothelial NO-synthase (eNOS) gene promoter T-786C polymorphism on intracardiac hemodynamic parameters and clinical presentation in patients with CAD.

Methods: 120 patients with CAD were enrolled into study, with control group of 35 healthy persons. Examination included 6-minute walk test and cardiac ultrasound. eNOS gene promoter allele polymorphism was determined with PCR. **Results:** Distribution of TT, CT and CC genotypes of eNOS gene promoter C-786S polymorphism in patients with CAD was 37.5%, 40.8% and 21.7%, while in the control group - 45, 7%, 48.6% and 5.7%, respectively. Patients with CAD were divided into two groups: group I - 46 patients with TT genotype and II group - 74 patients with CT and CC genotypes. When comparing the groups, patients in group II were younger, more likely to have AH, multivessel or diffuse CAD on cardioventriculography ($p < 0,05$), had earlier onset of AH and CAD, higher heart failure functional class ($p < 0,05$). The result of 6MWT in group II patients was significantly lower ($(414,0 \pm 11,6)$ m vs. $(458,6 \pm 14,2)$ m, $p = 0,01$). Cardiac ultrasound results were also worse in group II patients: ESV of LV and LA size were significantly greater ($p < 0,05$), EF and LV relative wall thickness (RWT) index - significantly lower compared to group I ($p < 0,05$). Stepwise regression analysis shown the relationship between the eNOS gene promoter T-786S polymorphism and LV RWT index ($p = 0,01$), EDV ($p = 0,001$) and LV ESV ($p = 0,01$).

Conclusions: In patients with CAD who carry C allele of eNOS gene T - 786C polymorphism changes in LV systolic function were shown to be more severe. C allele of eNOS gene T - 786C polymorphism was independently associated with EDV and ESV. Presence of C allele of eNOS gene T - 786C polymorphism in patients with CAD was associated with decline in exercise tolerance compared to patients with the TT genotype.

P1106

Impact of single nucleotide polymorphisms upon treatment outcome in idiopathic dilated cardiomyopathy: a pilot study

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The success of drug treatment for Idiopathic Dilated Cardiomyopathy (IDC) is an important concern, since its failure can lead to Heart Transplantation (HT). In this work a panel of 80 Single Nucleotide Polymorphisms (SNPs) was designed to assess their potential influence upon treatment outcome in IDC. The chosen SNPs were related to beta-blockers, ACE inhibitors, aldosterone antagonists and angiotensin-receptor antagonists, and included SNPs associated with the control of gene expression by microRNAs. The Sequenom MassArray platform was employed for genotyping. Statistically significant correlations between single SNPs and treatment failure (need for HT) were found for three variants: patients carrying CC or CT genotypes in AGTR1 rs5182 ($p = 0.011$), AA in AGT rs7079 ($p = 0.025$), and TT in SLC01B1 rs4149056 ($p = 0.044$). The combination of these three treatment failure variants yielded even more significant p-values (up to $p = 0.003$). These results could help identify patients receiving ineffective treatment in time to guide alternative and individualized clinical decisions

P1107

Angiotensin-converting enzyme genotype polymorphism in heart failure patients

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Purpose: Angiotensin-converting enzyme (ACE) I/D gene polymorphism have been associated with the risk of various cardiovascular conditions including heart failure (HF) which remains controversial. The aim of this study was to examine the association between heart failure and the (ACE) gene.

Methods: We included all patients >20 years presenting to emergency department for acute dyspnea. Epidemiological characteristics, clinical and standard laboratory parameters were collected. According to the result of the B-type natriuretic peptide (proBNP level), patients were divided into two groups: HF group and non-HF group. DNA study was performed for all subjects and their genotypes were identified by RFLP-PCR; either II, ID or DD. A one year follow-up was performed to assess vital status.

Results: We included 192 patients. Diagnosis of HF was established in 103 patients (53.6%). Our results showed that the frequency of ACE polymorphism were similar in HF and Non HF groups. (Table)

Conclusion: The current study suggests that ACE polymorphism is not associated to the HF neither mortality.

Table			
	Non-HF group N = 89	HF group N = 103	p
Sex (M/F)	80/27	73/56	0.03
Age (mean±SD)	65 ±14	67 ±13	0.59
Hypertension n (%)	37 (41)	69 (67)	<0.01
Diabetes n (%)	20 (22)	57 (55.3)	<0.01
Smoking n (%)	65 (73)	64 (62.1)	0.218
Creatinine (mean, µmol/l)	110 ±57	144 ±108	0.001
proBNP median (IQR), pg/ml	442 (255-629)	5002 (4471-5533)	<0.01
Genotypes n (%)			
II	15 (17)	11 (11)	0.56
ID	32(36)	37 (36)	0.956
DD	42 (47)	55 (53)	0.562
Mortality at 1 year n (%)	9 (10.1)	31(30)	0.001

Clinical, biological and genetic characteristics of patients.

P1108

Genetic predictors of heart failure among 13331 healthy danish citizens: protocol

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Purpose: The aim is to outline specific genetic predictors for the incidence and prognosis of heart failure (HF) in three separate cohorts of healthy Danish citizens followed more than 10 years.

Methods: Para- and clinical data from cohorts studies called the Monica study, Inter 99 and Health 2006 were merged. Citizens included in those were without known disease and between 18 and 80 years at the respective beginnings of the studies. Diagnosis of HF, and co-morbidities such as diabetes, kidney and pulmonary disease were retrieved from the Danish national based patient registry recorded over the follow-up. Cardiomyopathies were classified according to echocardiography based on databases from hospitals in charge of the individual patient.

Genome-wide association studies (GWASs) for HF phenotypes were explored through pre-specified single nucleotide polymorphisms (SNPs). HF phenotypes were divided into etiology: dilated cardiomyopathy; necrosis or apoptosis with or without ischemia; metabolic disorders, and Ca²⁺-signalling dysfunction.

HF was defined according to the European guidelines (ESC) differentiating into reduced and preserved ejection fraction (HF-REF & -pEF) concomitantly with an increased NT-proBNP.

Statistics: The effect of the SNPs found in the GWAS on the incidence of HF was estimated only if the p-value was less than 5X10⁻⁷. It was calculated as an Odds ratio through logistic regression. The prognosis of HF was assessed as the combined outcome of the endpoints of myocardial infarction, all-cause death and hospitalisation. A time to event analysis evaluated these. Finally, a principal component analysis was used to separate the variance among the HF subsets and thereby secure homogeneity in the event analysis.

P1109

Loss of cardiac mass and function induced by 17beta-oestradiol via a beta-catenin mechanism in C57Bl/6N female mice

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High 17β-oestradiol (E2) levels are a significant predictor of poor prognosis and higher mortality in men with heart failure and E2-dependent MYLIP regulation leads to reduced contractility in male rodent hearts. In females, we recently found that E2 induced physiological hypertrophic growth in the heart of C57Bl/6J mice

but not of C57Bl/6N mice. In the present study, we aimed at the characterisation of the effects of E2 in C57Bl/6N mice hypothesising that β-catenin mediates the effects of E2. Two-month-old female C57Bl/6N wild-type and cardiac-specific β-catenin-deleted (β-catΔex2-6) mice were ovariectomised and randomised to an E2-containing or soy-free (control, CON) diet (n = 7-13/group). All mice underwent transthoracic two-dimensional echocardiography under volatile anaesthesia (isoflurane 2%) following established procedures. The three-month physiological dose of E2 led to a higher relative uterus weight compared with CON (P < 0.001) in both WT and β-catΔex2-6 mice. The heart-weight-to-tibia-length ratio was significantly reduced by E2 compared with CON in WT mice (P < 0.001), while there was no significant effect in β-catΔex2-6 mice. Cardiomyocyte cross-sectional area was also significantly decreased by E2 (n = 5-7/group; P < 0.001) compared with CON in WT mice, while E2 had no significant effect in β-catΔex2-6 mice. Echocardiographic measurements revealed a significant decrease in septum width (P < 0.001) and posterior wall thickness (P < 0.01) in E2 treated WT mice compared with CON, while there was no significant change in β-catΔex2-6 mice (n = 8/group). We further found that these structural changes in WT mice due to E2 were accompanied by a significant decrease in cardiac function, namely a 23% decrease in fractional shortening compared with CON (P < 0.05), while there was no significant effect in β-catΔex2-6 mice. Immunoblotting analysis of the ubiquitin ligase and key regulator of proteasome-dependent protein degradation muscle-specific RING finger protein 1 (MuRF1) revealed a significant increase in its levels by E2 compared with CON in WT mice (P < 0.05), while there was no significant effect in β-catΔex2-6 mice. Genetic variation interacts with biological sex, environmental and hormonal factors to modulate the development and progression of heart failure. We conclude that in C57Bl/6N mice our surprising findings indicate that E2 leads to cardiac mass and function loss, which may ultimately lead to a form of heart failure, via a β-catenin mechanism.

P1110

Cardiac-specific long noncoding RNAs associated with heart failure

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Purpose: Long noncoding RNAs (lncRNA) have shown more expression specificity than coding genes, but the role of cardiac lncRNAs is still unclear. Some functional lncRNAs have been found on chromosome close to protein-coding genes which regulate cardiac function. Here, we deployed a bioinformatics approach to identify cardiac-specific lncRNAs which may regulate the development of heart failure.

Methods: We analysed two public RNA-Seq dataset. Firstly, we used a dataset generated from the sequencing of 15 normal human tissues to identify cardiac-specific lncRNAs. Secondly, we used a dataset generated from the sequencing of cardiac biopsies obtained from 8 controls and 8 ischemic cardiomyopathy patients to identify cardiac-specific lncRNAs associated with heart failure. Candidate lncRNAs were assessed in our biopsies from 5 controls and 27 heart failure patients (11 ischemic cardiomyopathy, 11 dilated cardiomyopathy, 3 hypertrophic cardiomyopathy, 1 toxic cardiomyopathy and 1 acute decompensated cardiomyopathy).

Results: Using the first dataset of 12 human tissues, we identified 18866 highly expressed lncRNAs. K-means clustering revealed that 7524 lncRNAs (39.9%) presented tissue specificity. 415 lncRNAs were cardiac-specific and accounted for 10.3% of highly expressed lncRNAs in the heart. Among these, 328 were located less than 50kb away from coding genes known to be functionally associated with dilated cardiomyopathy, hypertrophic cardiomyopathy and muscle contraction. Then, using the second dataset obtained from 8 controls and 8 ischemic cardiomyopathy patients, we identified 8 lncRNAs which expression correlated with neighbouring genes known to regulate cardiac function (Pearson correlation coefficient > 0.7 and false discovery rate < 0.05). Finally, the associations between lncRNAs and cardiac genes were studied in an independent group of 27 heart failure patients. In this group for instance, the expression of one antisense lncRNA was correlated with its coding counterpart (r = 0.75, P < 0.001) without being co-transcribed. In addition, this lncRNA was up-regulated in failing hearts compared to control hearts (2-fold, P = 0.004).

Conclusion: Combining publicly available and in-house data, we identified cardiac-specific lncRNAs that may regulate the development or progression of heart failure. These lncRNAs constitute candidates for future translational studies.

Rapid Fire 3

Monday 25 May 2015 08:30–10:00

Location: Agora

1140

Influence of socio-economic deprivation on comorbidity in heart failure patients

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Purpose: To assess the pattern and distribution of multimorbidity (defined as presence of two or more disorders) in HF in a nationally representative population of primary care patients.

Methods: A cross-sectional analysis of anonymised, routinely collected data from 314 general practices in Scotland in 2007, including 1,424,378 adults. We extracted data on those with a recorded diagnosis of heart failure and then analysed the data according to the number and type of comorbidities, sex, age and socioeconomic status (Carstairs score from postcodes).

Results: 18,899 HF patients were identified giving an overall prevalence of 1.3%. The mean age of HF patients was 73.6 years and prevalence increased with age to 10.3% in those over 85 years. HF was slightly more common in males (1.4% in men vs. 1.2% in females). Patients with HF had a mean of 5.2 conditions and comorbidity was present in 97.4% of HF patients, compared to 27.3% of those without HF ($p < 0.001$). Comorbidity was more common among the most deprived HF patients (98.8%, vs. 87.9% for most and least deprived deciles, respectively; $p < 0.001$). HF patients in the most deprived decile were also more likely to have five or more conditions compared to the least deprived (61.4% vs. 42.6%; $p < 0.001$) and to have at least one physical condition (excluding HF) and one mental health condition (93.1% vs. 76.4%; $p < 0.001$). The most common comorbidities in HF were: CHD 59.4% (most deprived decile 67.2% vs. least deprived decile 43.7%; $p < 0.001$), Hypertension 57% (most deprived 54.7% vs. least deprived 48.6%; $p < 0.001$), Atrial Fibrillation 26% (most deprived 24.4% vs. least deprived 20.8%; $p < 0.001$), Diabetes 23.3% (most deprived 25.1% vs. least deprived 15.9%; $p < 0.001$), and Depression 16.9% (most deprived 18.3% vs. least deprived 12.2%; $p < 0.001$).

Conclusions: Comorbidity is the norm in HF, with most patients having 5 or more chronic conditions suggesting that the use of disease specific clinical guidelines are insufficient to support provision of optimal, comprehensive care for HF patients, especially those from socioeconomically deprived backgrounds.

1141

Weight loss in obese patients with heart failure

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Background: A paradoxical association between body mass index (BMI) and mortality has been described in patients with heart failure (HF) and obesity was linked to lower mortality during follow-up. The impact of weight loss (WL) in overweight or obese patients with HF is incompletely understood.

Objective: To analyse the effect of WL during one year on mortality rates in the following 2 years in a wide outpatient population with HF, with special attention to obese patients.

Patients and Method: Weight at first visit and at one-year follow-up and vital status at 3 years of follow-up were available in 1000 patients (72.7% men; mean age 65.8 ± 12.1 years, range 28-96 years). Aetiology of HF was mainly ischemic heart disease (55.7%), followed by dilated cardiomyopathy (11.1%), hypertensive cardiopathy (8.8%) and valvular disease (8.6%). Mean LVEF was $32\% \pm 13$. Most patients were in NYHA functional class II (64.9%) and III (28.3%). Significant WL was defined as a loss $\geq 5\%$ of the initial weight. Obesity was defined as BMI ≥ 30 kg/m² (N=272).

Results: One-hundred seventy patients (17%) showed significant WL during the first year of follow-up, and 174 patients (17.4%) died during follow-up. Mortality in WL patients was significantly higher than in the patients without WL (27.6% vs 15.3%, $p < 0.001$). In Cox regression analysis adjusted by baseline BMI, WL had two-fold mortality (HR 2.01 [95%CI 1.43-2.83], $p < 0.001$). In a multivariable model adjusted by and age, sex, BMI, NYHA functional class, LVEF, HF duration, ischemic aetiology, diabetes, and treatment with beta-blockers, ACEI-ARB and MRA, WL remained highly and independently associated with higher mortality (HR 1.89 [95%CI 1.32-2.68], $p < 0.001$). Among obese patients, WL was associated to higher risk of death (adjusted HR 2.38 [95%CI 1.31-4.32], $p = 0.004$) than that observed in non-obese patients (adjusted HR 1.83 [95%CI 1.16-2.89], $p = 0.01$).

Conclusion: Weight loss $\geq 5\%$ during one year in HF patients is associated with ominous prognosis in subsequent years. This effect was even more apparent in obese patients.

1142

Clinical correlates and prognostic impact of isolated impaired iron storage in cohort of 1821 patients with chronic heart failure: should we review the FAIR-HF definition of iron deficiency?

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Background: Iron deficiency (ID) is associated with worse clinical profile and prognosis in patients with chronic heart failure (CHF). The most widely used definition of ID in patients with CHF includes: ferritin $< 100\mu\text{g/L}$ or ferritin $100\text{--}299\mu\text{g/L}$ with TSAT $< 20\%$. However, there is little information about clinical profile and outcomes of CHF patients with iron status biomarkers indicating impaired iron storage (IIS, ferritin $< 100\mu\text{g/L}$), impaired iron transport (IIT, TSAT $< 20\%$) either alone or in combination compared to patients with normal iron status (NIS).

Methods: We evaluated the clinical impact of abnormalities in iron status biomarkers indicating isolated IIS (ferritin $< 100\mu\text{g/L}$ and TSAT $\geq 20\%$), isolated IIT (TSAT $< 20\%$ and ferritin $\geq 100\mu\text{g/L}$) or their coexistence (IIS+IIT, ferritin $< 100\mu\text{g/L}$ and [MC1] TSAT $< 20\%$) compared to patients with normal iron status (NIS), on the profile of disease severity and the occurrence of events in an international cohort of 1821 patients with CHF.

Results: Baseline characteristics were mean age 66 ± 13 , 1298 (71%) were male and ejection fraction was $35\% \pm 15$. Isolated IIS was observed in 219 patients (12%), IIT alone in 454 (25%) and coexistence of both conditions (IIS+IIT) were seen in 389 (21%). In adjusted multivariable logistic regression analyses compared to the NIS group we found that, patients with IIS+IIT and patients with isolated IIT had worse quality of life (OR 1.7 [1.1-2.5] and OR 1.6 [1.1-2.4] respectively), lower LVEF (OR 1.4 [1.0-2.0] and OR 1.3 [1.0-1.8] respectively), NT-proBNP levels $>$ median (OR 2.0 [1.4-2.8] and OR 2.0 [1.4-2.8] respectively) and increased risk of all-cause death (OR 1.6 [1.1-2.4] and OR 1.5 [1.1-2.3] respectively) with all p -values < 0.05 . On the other hand patients with isolated IIS did not differ from NIS patients in terms of patient-reported outcomes, LVEF, NT-proBNP levels or all-cause mortality (all p -values > 0.05). Biomarkers indicating IIT (TSAT $< 20\%$ with either normal or low ferritin) was associated independently with all-cause mortality (OR 1.6; 95% CI [1.1-2.2]; p -value: 0.009) whereas IIS (ferritin $< 100\mu\text{g/L}$ with either normal or low TSAT) was not ($p > 0.05$).

Conclusions: IIT alone or in combination with IIS is associated with a worse clinical profile and increased risk of mortality. Patients with biomarkers suggestive of impaired iron storage but normal iron transport did not differ from patients with normal iron status in terms of clinical profile and events. Whether isolated IIS informs about a milder form of ID or does not accurately represent truly depleted iron stores needs to be elucidated.

1143

Vascular disease as a risk factor of stroke or death in heart failure patients in sinus rhythm: a nationwide cohort studyL Melgaard¹; A Gorst-Rasmussen¹; TB Larsen¹; G Lip²¹Aalborg University Hospital, Thrombosis Research Unit, Aalborg, Denmark;²University of Birmingham, Centre for cardiovascular sciences, city hospital, Birmingham, United Kingdom

Purpose: The association between different manifestations of vascular disease and risk of stroke or death among heart failure patients is poorly described. We conducted an observational study to evaluate the risk of 'stroke or death' among heart failure patients in sinus rhythm with peripheral artery disease (PAD) or prior myocardial infarction (MI).

Methods: Population-based cohort study of patients diagnosed with incident heart failure and not in therapy with a vitamin K antagonist during 2000-2012, identified by record linkage between nationwide registries in Denmark. We calculated relative risks of 'stroke or death' after 1 and 5 years follow-up to compare patients with either PAD, prior MI or no vascular disease.

Results: 39,018 heart failure patients were included, among which 73.9% had no vascular disease, 6.7% had PAD only, and 16.9% had prior MI only (2.5% had both). When comparing heart failure patients with either PAD or prior MI to patients without vascular disease, we found PAD to be associated with a significantly higher risk of 'stroke or death' both at short- and long-term follow-up (1- and 5-year adjusted relative risk [RR]: 1.42 and 1.24). Findings for the comparison of patients with PAD to patients with prior MI showed that PAD was associated with a significant higher risk (1- and 5-year adjusted RR: 1.24 and 1.21). The increased risk associated with PAD was predominantly driven by events of death.

Conclusion: Among incident heart failure patients in sinus rhythm, a previous diagnosis of PAD was associated with a higher risk of 'stroke or death' compared to a prior diagnosis of MI and no vascular disease. This finding was consistent with the observation of a more aggressive medical treatment of MI.

Relative risk of 'stroke or death'

Stroke or death - 1 year after HF diagnosis	Crude RR (95% CI)	Adjusted RR (95% CI)
PAD vs. no vascular disease	1.37 (1.29-1.46)	1.33 (1.26-1.41)
Prior MI vs. no vascular disease	0.87 (0.83-0.92)	1.16 (1.11-1.23)
PAD vs. prior MI	1.58 (1.46-1.70)	1.14 (1.06-1.23)
Stroke or death - 5 years after HF diagnosis	Crude RR (95% CI)	Adjusted RR (95% CI)
PAD vs. no vascular disease	1.29 (1.25-1.33)	1.23 (1.20-1.27)
Prior MI vs. no vascular disease	0.88 (0.85-0.91)	1.04 (1.02-1.07)
PAD vs. prior MI	1.46 (1.41-1.53)	1.18 (1.14-1.22)

Relative risk of 'stroke or death' after 1 and 5 years follow-up and according to manifestation of vascular disease.

1144

Absence of obesity paradox in type-2 diabetic patients with heart failureE Zamora¹; J Lupon¹; M De Antonio¹; N Alonso¹; J Santemas¹; M Troya¹; C Diez-Quevedo¹; A Altimir¹; M Boldo¹; A Bayes-Genis¹¹Germans Trias i Pujol University Hospital, Badalona, Spain

Background: Obesity is often paradoxically associated with survival in heart failure (HF). In HF patients of ischemic aetiology previous reports did not find such paradox; the effect of type-2 diabetes mellitus (T2D) is uncertain.

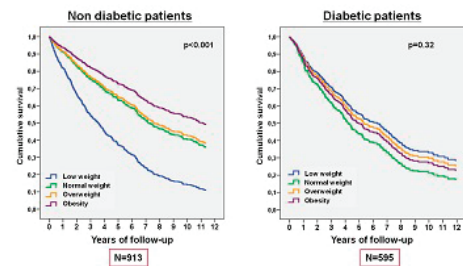
Objective: To assess the relationship between body mass index (BMI) and long-term mortality in an ambulatory HF cohort relative to T2D presence or absence.

Patients and Method: Initial BMI and survival status after a mean follow-up of 6.1 ± 2.1 years (up to 12 years) were available in 1508 ambulatory patients (73% men; mean age 68 ± 2.1 years). T2D was present in 595 (39.4%) patients. Aetiology of HF was ischemic heart disease in 53% of patients. Mean LVEF was 33.5 ± 17%. Patients were divided in 4 groups according to BMI (WHO 1999 classification): low weight (BMI <20.5 kg/m²), normal weight (BMI 20.5 to <25.5 kg/m²), overweight (BMI 25.5 to <30 kg/m²) and obesity (BMI ≥30 kg/m²).

Results: Mortality differed significantly across BMI strata in non-T2D patients but not in T2D patients (figure). Taking as reference normal weight patients, hazard ratios (HR) for low-weight, overweight and obesity were: 2.16 [1.54-3.04] p < 0.001; 0.94 [0.75-1.18], p = 0.60; and 0.66 [0.50-0.88], p = 0.004; respectively for non-T2D patients; and 0.76 [0.37-1.56] p = 0.46; 0.79 [0.60-1.02], p = 0.07; and 0.80 [0.61-1.05], p = 0.1, respectively for T2D patients. After adjustment for age, sex, HF aetiology, NYHA class, LVEF, and hypertension, BMI remained an independent predictor of survival in non-T2D (p < 0.001) but not in T2D (p = 0.76) patients.

Conclusion: The obesity paradox was only found in non-T2D HF patients after a

long-term follow-up. BMI was not independently associated with survival in T2D HF patients.



1145

Increased sympathetic activity may partially explain iron homeostasis dysregulation and iron deficiency observed in patients with chronic heart failureP Moliner-Borja¹; C Enjuanes¹; N Farre¹; S Ruiz-Bustillo¹; JM Verdu-Rotellar²; O Meroño-Duenas³; R Olivero³; I Rodriguez-Costoya³; J Bruguera³; J Comin-Colet¹¹Hospital del Mar, Heart Failure Section, Barcelona, Spain; ²Hospital del Mar Medical Research Institute (IMIM), Barcelona, Spain; ³Hospital del Mar, Barcelona, Spain

Background: The mechanisms underlying dysregulation of iron homeostasis in patients with chronic heart failure (CHF) are not well established. In cardiomyocyte models norepinephrine ([NE]) leads to intracellular iron depletion. Although this may suggest a role of sympathetic activation in the development of impaired iron status, the potential association between [NE] and iron metabolism biomarkers has not been evaluated in CHF patients so far.

Aims and Methods

We studied the association between plasma [NE] levels and serum iron status biomarkers indicating iron availability (ferritin and iron), iron supply (saturation of transferrin, TSAT), iron demand (soluble transferrin receptor, sTfR) in a prospective cohort of 742 patients with CHF. Iron deficiency (ID) was defined as ferritin <100 µg/L or %TSAT <20%.

Results: Baseline characteristics were: mean age 72 ± 11, 56% were male, in 56% LVEF was <45%, 44% NYHA class III-IV. ID was observed in 69% of patients. In unadjusted analyses we found significant correlations between [NE] and serum iron (r = -0.12; p-value = 0.001), TSAT (r = -0.15; p-value < 0.001), sTfR (r = 0.12; p-value = 0.007) but not with ferritin (r = 0.02; p-value = 0.695) nor haemoglobin (-0.04; p-value = 0.326).

In multivariable adjusted linear regression analyses, [NE] remained a significant predictor of increased iron demand (sTfR, standardized β coefficient = 0.12; p-value = 0.004), TSAT (standardized β coefficient = -0.11; p-value = 0.002). [NE] was not associated with iron or ferritin (p > 0.05). In multivariate logistic regression models greater levels of [NE] were significantly associated with ID (OR = 2.1; 95%CI [1.1-4.1]; p-value = 0.027), impaired iron transport (TSAT <20%, OR = 2.6; 95%CI [1.3-5.2]; p-value = 0.005) but not with impaired iron storage (ferritin <100 µg/L, OR = 0.93; 95%CI [0.5-1.8]; p-value = 0.831).

Adjusted marginal means and 95% confidence intervals of [NE] were significantly higher in ID compared to non-ID patients (527 pg/mL [502-553] vs. 481 pg/mL [447-518] respectively, p-value = 0.04). Interestingly, in all multivariable models, the associations between [NE] and iron status were independent of LVEF and haemoglobin concentration.

Conclusions: In CHF patients, increased sympathetic activation estimated with [NE] levels is associated with ID and particularly dysregulation of biomarkers suggesting impaired iron supply and increased iron demand independently from LVEF and haemoglobin. Whether the relationship between [NE] and iron metabolism is bidirectional and entails causality needs to be elucidated in future research.

1146

Primary care patients with heart failure with and without chronic obstructive pulmonary diseaseMJ Valk¹; BD Broekhuizen¹; A Mosterd¹; NP Zuithoff¹; AW Hoes¹; F H Frans Hendrik Rutten¹¹University Medical Center Utrecht, Julius Centre for Health Sciences and Primary Care, Utrecht, Netherlands

Heart failure and chronic obstructive pulmonary disease (COPD) are often concurrently present in elderly individuals. Previous studies suggest underuse of beta-blockers in patients with heart failure and a diagnosis of COPD.

Purpose: To compare patient characteristics and drug management of patients with heart failure and reduced ejection fraction (HFrEF) and preserved ejection fraction (HFpEF) with and without a diagnosis of COPD.

Methods Data was obtained from 30 general practices in the Netherlands. 683 patients had a general practitioner's (GP's) diagnosis of heart failure. A panel of cardiologists could confirm the diagnosis in 434 (63.5%) patients. We gathered information on comorbidities and drug prescription in these patients from the electronic medical files of the participating GPs.

Results Of the 434 patients with definite heart failure, the mean age was 77.2 (SD 10.9) years, 46.8% were male, and 55.1% received cooperative care from a cardiologist. Of the 222 patients with HFREF, 46 (20.7%) had COPD, and 39 (18.8%) of the 207 patients with HFpEF. Patients with HFREF+COPD had a tendency of more comorbidities (prior MI, angina pectoris, atrial fibrillation, diabetes, and renal insufficiency), with the exception of diabetes than HFREF patients without COPD. Both groups received similar amounts of heart failure drugs, however, with a tendency of less beta-blockers in HFREF with COPD (47.8 vs. 61.9%, $p=0.08$). Patients with HFpEF+COPD had a tendency of less comorbidities, including diabetes, than HFpEF patients without COPD. Patients with HFpEF+COPD were prescribed non-significantly less HF drugs, notably ACE-inhibitors/ARBs (41.0 vs. 56.5%, $p=0.08$) and beta-blockers (41.0 vs. 55.4%, $p=0.11$).

Conclusions Patients with heart failure and COPD tend to be under-prescribed beta-blockers in primary care. Special attention should be paid to those with HFREF and concurrent COPD.

1147

Up-regulations of xanthine pathway in chronic heart failure patients with concomitant chronic kidney disease

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Aim: To evaluate the impact of concomitant chronic kidney disease (CKD) on xanthine metabolism in chronic heart failure (CHF) patients.

Methods: The study included 112 CHF patients (51 men, 61 women) aged 72.5 ± 0.98 years, who were divided into 2 groups: within CKD ($n=72$) and non-CKD ($n=40$) participants. To evaluate serum uric acid levels we used enzymatic colorimetric test, PAP - method with antilipid factor. Asymptomatic hyperuricemia was defined as serum uric acid levels > 7.0 mg/dL in men and > 6.0 mg/dL in women. Xanthine oxidase (XO) activity was determined by a coupled enzyme assay, which results in a colorimetric (570 nm)/fluorometric ($\lambda_{exc} = 535$ nm/ $\lambda_{em} = 587$ nm) product, proportional to the hydrogen peroxide generated. XO activity was reported as nmole/min/mL = milliunit/mL. The glomerular filtration rate (GFR) values were calculated by the Modification of Diet in Renal Disease (MDRD) equation.

Results: Of the total cohort of CHF patients, 62.5% had asymptomatic hyperuricemia. The prevalence of hyperuricemia in patients with and without CKD was 65.3% and 57.5% respectively. CHF patients with CKD had higher XO activity compared to non-CKD patients: (7.51 ± 0.77) mU/mL and (4.69 ± 0.77) mU/mL respectively ($p=0.01$). The mean serum uric acid levels were not significantly different: (7.63 ± 0.27) mg/dL and (7.46 ± 0.39) mg/dL respectively ($p=0.73$). The greatest amount of patients with CKD had XO activity levels from 4.7 to 8.1 mU/mL, while most of non-CKD patients had these levels less than 3.3 mU/mL. The mean values of estimated glomerular filtration rate (eGFR) in participants with asymptomatic hyperuricemia and without hyperuricemia were (59.9 ± 2.95) and (76.6 ± 6.05) mL/min per 1.73 m^2 respectively ($p=0.007$). Patients with $eGFR \leq 60$ mL/min/ 1.73 m^2 have significantly higher serum uric acid levels and XO activity, compared to those with $eGFR > 60$ mL/min/ 1.73 m^2 ($p < 0.001$). Data showed a significant inverse correlations between eGFR and serum uric acid levels ($r = -0.3$, $p < 0.05$), XO activity ($r = -0.5$, $p < 0.05$) in CHF patients with CKD. Among patients without CKD significant correlation was observed only between eGFR and XO activity ($r = -0.4$, $p < 0.05$).

Conclusion: Patients with concomitant CKD had higher XO activity levels. Reduced GFR was associated with switching of xanthine metabolism towards oxidase pathway and increased xanthine oxidase activity.

1148

Degree of impairment of lung function parameters in patients with chronic congestive heart failure

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Purpose: Impairment of static and dynamic lung function parameters, as well as impaired diffusion capacity, is of denotative relevance for patients with chronic congestive heart failure (CHF). Recent literature discusses whether decrease in inspiratory muscle power may be involved. This study investigated the relationship of lung function parameters in a well characterized heart failure population with reduced left ventricular ejection fraction (HF-REF).

Methods: 434 patients with CHF (mean age 69 ± 11 years, 88 % male), New York Heart Association functional class 2.5 ± 0.5 , left ventricular ejection fraction (LVEF) 34 ± 8 %, NT-pro-BNP 3088 ± 11770 pg/ml, 48 % ischemic etiology underwent bodyplethysmography, CO-diffusion capacity examination and measurement of inspiratory muscle power.

Results: In the investigated population impairments of lung function parameters have been found, itemized by gender: FEV1 2.5 ± 0.7 l: 82 % of target volume, IVC 3.3 ± 0.9 l: 84 % of target, ERV 0.7 ± 0.4 l: 71 % of target, PEF 5.3 ± 1.8 l/s: 68 % of target, TLco(Hb) 6.5 ± 2.0 mmol/kPa/min: 76 % of target, Kco(Hb) 1.2 ± 0.3 mmol/kPa/min/l: 91 % of target; women: FEV1 1.8 ± 0.5 l: 82 % of target volume, IVC 2.4 ± 0.6 l: 92 % of target, ERV 0.5 ± 0.2 l: 74 % of target, PEF 3.6 ± 0.9 l/s: 62 % of target, TLco(Hb) 5.0 ± 1.7 mmol/kPa/min: 70 % of target, Kco(Hb) 1.2 ± 0.3 mmol/kPa/min/l: 84 % of target). Regarding inspiratory muscle power, only a marginal decrease in airway pressure at 0.1s (P01) was found in the investigated population: men: $p01 0.3 \pm 0.2$ kPa, women: $p01 0.3 \pm 0.2$ kPa.

Conclusions: In conclusion, in the investigated population of HF-REF patients mild to moderate impairments of static and dynamic lung function parameters have been identified. In particular cases, even severe impairments of these parameters have been found. Further studies to investigate this relationship are needed and ongoing.

1149

Hypercapnic ventilatory response to CO₂ in heart failure patients is highest in those with nocturnal cheyne-stokes respiration

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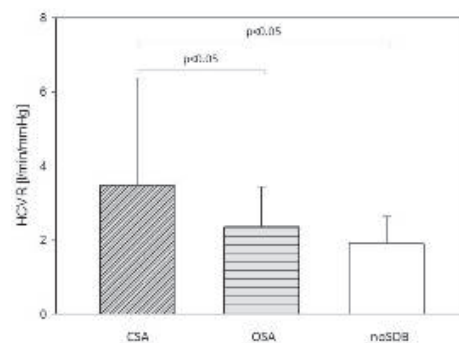
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Purpose: A supposed key element in the development of Cheyne-Stokes respiration (CSR) and respiratory instability in heart failure (HF) patients might be an altered sensitivity of central chemoreceptors to CO₂. The present study aimed to investigate the sensitivity of central CO₂ receptors in a cohort of well described HF patients without sleep-disordered breathing (SDB), with obstructive (OSA) and central sleep apnea with CSR.

Methods: A total of 153 consecutive HF (NYHA \geq II, LV-EF \leq 45%) patients undergoing simultaneous left- and right heart catheterization were screened for SDB using cardiorespiratory polygraphy. Within 24 hours, central CO₂ receptor sensitivity was analyzed using standardized rebreathing test [hypercapnic ventilator response, HCVR] according to Read.

Results: Of all 153 HF patients, CSR (apnea-hypopnea-index, AHI: 39.3 ± 18 /h) was diagnosed in 80 patients and OSA (AHI: 25.0 ± 17 /h) in 60 patients, only 13 patients had noSDB (AHI: 2.5 ± 1.4 /h). HCVR was significantly higher in HF patients with CSR (3.47 ± 2.9 l/min/mmHg) compared to OSA (2.36 ± 1.8 l/min/mmHg) and those without SDB (1.91 ± 0.7 l/min/mmHg, $p < 0.05$; figure). As compared to patients without SDB, those with OSA tended to have a higher HCVR, without being statistically significant.

Conclusions: Inappropriate sensitivity of central chemoreceptors to CO₂ can be seen in HF patients with CSA as compared to those with OSA or noSDB. This inappropriate sensitivity might be responsible for the crescendo-ventilation (hyper-ventilation) after central apneas or hypopneas. Moreover, an increased respiratory drive with chronic hyperventilation in HF patients with CSR might demand a therapy, which does not aggravate (hyper-) ventilation further.



1150

Metrics of sleep-disordered breathing in heart failure: moderate association of apnoea-hypopnoea index and hypoxemia

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A Buchholz²; K Wegscheider²; D Horstkotte¹

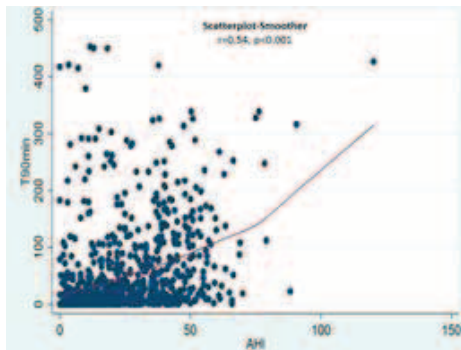
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Purpose: Sleep-disordered breathing (SDB) represents a highly prevalent co-morbidity in heart failure (HF) patients and is independently associated with an impaired prognosis. The underlying pathophysiology and the correct metric for the severity of SDB are discussed controversially: It might be the apnoeic and hypopnoeic events (apnoea-hyponoea-index, AHI) or the resulting oxygen desaturations (hypoxemia). The current study investigates the relationship of these parameters in a large and well-defined cohort of HF patients.

Methods: A total of 1249 patients (234 female; BMI 27.0 ± 4.1 ; LV-EF $30.0 \pm 7.7\%$; NYHA classes 2 (34%), 3 (58%) and 4 (8%)) were screened for the presence and severity of SDB using multichannel cardiorespiratory polygraphy (PG). AHI was scored according to current recommendations by two independent specialists. As a special metric, the total time the patient spent with an oxygen saturation below 90% ($T < 90$; available in 963 patients) was determined and the relationship between AHA and $T < 90$ was analysed.

Results: Of 1249 patients prospectively screened, a total of 1012 (81%) of patients were identified to have SDB of any severity ($AHI \geq 5/h$): mean AHI was $22.5 \pm 18/h$ and $T < 90\%$ 45.6 ± 76 min. Both parameters correlate moderately (Spearman correlation: $r = 0.54$, $p < 0.001$; figure).

Conclusion: SDB was highly prevalent in our cohort of well-defined HF patients. As an additional metric of SDB severity, we present $T < 90\%$ as an additional parameter of SDB severity in HF patients, which shows a moderate association to the established metric AHI. Which metric is best in terms of a prognostic marker needs to be determined.



1151

Heart failure in autoimmune diseases, relationship between type of antiphospholipid antibody and acute decompensated heart failure in patients with primary and secondary antiphospholipid syndrome

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Introduction: Antiphospholipid syndrome (APS) patients suffer from various cardiovascular manifestations with the presence of antiphospholipid antibodies (aPL). APS may manifest itself as a primary disease (PAPS) or as a secondary disease, most commonly in the context of Systemic Lupus Erythematosus (SLE). Data regarding influence of specific aPL presence and heart failure development (HF) are scarce.

Purpose: The aim of our study was to establish prevalence and type of HF in PAPS and SAPS patients with analysis of possible relationship between type of aPL present and HF occurrence.

Methods: We analyzed 181 APS patients (101 PAPS and 80 SAPS patients) 159 female (87.8%) and 22 male (12.2%), average age 48.7 ± 13.1 years. aPL analysis included analysis of aCL (IgG/IgM), β_2 GPI (IgG/IgM) and LA. In all patients echocardiography study was performed (revealing diameters of left ventricle chambers, left ventricle ejection fraction (LVEF) determined by the Simpson method and the presence of diastolic dysfunction (DD)). The data regarding acute decompensated HF occurrence were collected.

Results: In our cross sectional study, the prevalence of acute decompensated HF was 4.0% in PAPS and 3.8% in SAPS group ($p = 1.000$), most commonly in the context of coronary artery disease presence. PAPS developing HF had significantly lower values of LVEF ($p = 0.001$), while in SAPS group HF occurred in patients with preserved EF (HFpEF) (LVEF average value $60.53 \pm 16.37\%$), in the presence of DD ($p = 0.067$). There was significant relationship between aCL IgG positivity and HF in PAPS group ($p = 0.040$). In SAPS group no significant relationship regarding specific aPL presence was found. Titer of aCL IgG antibodies present has not been related to HF occurrence ($p = 0.444$ in PAPS, $p = 0.308$ in SAPS).

Conclusion: In our study group, PAPS patients developed HF with low EF, while SAPS patients had HFpEF. Presence of aCL IgG antibodies even in low titers was strongly related to acute decompensated HF development in PAPS, suggesting special cardiac vigilance in this subset of patients.

1152

Anemia etiology in heart failure: role of renal dysfunction and red blood cell distribution width

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Purpose: Anemia frequently occurs in chronic heart failure (CHF) and it is associated with a poor prognosis. However its etiology remains poorly defined. For these reasons the aims of this study were: 1) identification and prevalence of different anemia typologies 2) evaluation of red blood cell distribution width (RDW) and renal dysfunction 3) impact detection of different pattern of anemia on outcome during 6 months follow-up period.

Methods: The study included 297 patients with heart failure divided into 2 main groups, according to the presence or absence of anemia. Patients with anemia were divided into 3 subgroups based on the type of anemia: normocytic and normochromic anemia, microcytic anemia and macrocytic anemia; Through the evaluation of the causes were defined five types of anemia: 1-Patients with iron-deficiency anemia; 2-Patients with anemia of chronic inflammatory disease; 3-Patients with anemia secondary to IRC; 4-Patients with anemia due to deficiency of the factors of the vitamin B complex; 5-Patients with multifactorial anemia.

Results: of the 155 subjects affected to anemia, 34 had iron-deficiency anemia, 31 anemia of chronic inflammatory disease, 41 renal anemia, 29 Vit-B deficiency anemia and 20 have multifactorial anemia. The morphological analysis showed microcytic anemia in 30 subjects, macrocytic anemia in 29 subjects, and normocytic anemia in 96 subjects. During a follow up of 180 days non anemic patients had a better prognosis than anemic patients ($p < 0.01$). Patients with cardio-renal-anemia had a worse survival curve respected to patients with anemia and heart failure and to non anemic patients ($p < 0.01$). According to the aethiology, the mortality rate appeared higher in the group with renal anemia, followed by the group with iron deficiency anemia. Patients with Vit-B deficiency anemia revealed less adverse events respect to all the other subgroups ($p < 0.001$). The morphological analysis showed that subjects with microcytic anemia had the worse prognosis in comparison with patients with megaloblastic form revealing less adverse events ($p = 0.003$). Patients with $RDW > 16\%$ had a worse prognosis respect to subject with $RDW < 16\%$ ($p = 0.03$). High values of RDW were more frequently found as in sideropenic as in microcytic anemia.

Conclusions: HF patients demonstrated that different typologies of anemia had a different clinical impact. The cardio renal anemia syndrome revealed the worse outcome. Most of patients with HF associated anemia had a normocytic anemia. Finally RDW, confirmed its diagnostic and prognostic role independently of the underlying types of anemia.

1153

Nutritional deficiencies in a heart failure unit - beyond anemia

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Anormal level of hemoglobin is maintained for as long as possible after the iron stores are depleted. On a deficient diet, while vitamin B12 deficiency develops in the course of 2-3 years, it takes about four months to folate deficiency take place. In fact, even older patients with multiple comorbidities and many dietary defaults may have low levels of these hematinic factors in the absence of anemia. It is known that iron deficiency (ID) even without anemia worsens Heart Failure (HF) prognosis. Little is known about other nutritional deficiencies.

Objective: To evaluate the prevalence of hematinic factors nutritional deficits in an HF Unit.

Methods: Prospective study of patients admitted consecutively admitted in a HF Unit over a period of one year. ID was considered when ferritin < 100 ng/ml (absolute ID) or $100-299$ ng/ml and transferrin saturation $< 20\%$ (relative ID). Vitamin B12 and folate deficit when its levels were below 200 pmol/L and 6.25 nmol/L, respectively. Anemia was diagnosed according to World Health's Organization criteria.

Results: 202 hospital admissions were analyzed; mean age was 75 ± 11.8 years, 30.2% were male, preserved ejection fraction 57.9%. Prevalence of hematinic deficiencies are presented in Table 1, as well as its association to anemia.

Conclusion: Hematinic deficiencies have important clinical consequences, anemia being just one of them. Because of the various possible clinical implications, hematinic factor deficits should be evaluated in all HF patients, regardless of hemoglobin value.

Hematinic deficiencies in heart failure				
	Total	Anemia	Without anemia	Mean Cell Volume
Absolute ID	49.2% (n=88)	72.7% (n=64)	27.3% (n=24)	87.0 ± 7.5 fl
Relative ID	19.1% (n=34)	67.6% (n=23)	32.4% (n=11)	90.2 ± 6.8 fl
Vitamin B12 deficiency	14.5% (n=27)	81.5% (n=22)	18.5% (n=5)	88.0 ± 12.7 fl
Folate deficiency	2.7% (n=5)	100% (n=5)	0	94.9 ± 9.2 fl

ID - iron deficiency

1154

Sleep quality in patients with stable congestive heart failure and cheyne-stokes respiration under treatment with adaptive servoventilation

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Purpose: Adaptive servoventilation (ASV) is well established in the treatment of Cheyne-Stokes-Respiration (CSR) in patients with chronic heart failure, normalizing respiratory parameters during sleep time. This study aimed to investigate the sleep quality in patients treated with ASV.

Methods: Retrospectively we analyzed multichannel polysomnographic data of 101 heart failure patients (NYHA ≥ II, LV-EF ≤ 45%) with nocturnal CSR (Apnoea-Hypopnoea Index, AHI ≥ 15) before and under treatment with ASV (AutoSet CSTM, ResMed).

Results: 97 male and 4 female patients were included (mean age: 68.8 ± 9.8 years, BMI 29.0 ± 4.6 kg/m²). Left ventricular ejection fraction was 33.5 ± 6.9% and NT-proBNP 3794 ± 10647 pg/ml. The compliance of ASV therapy was good: ASV was used with an average of 363 ± 347 min per night, 68 ± 29% used their device more than 4 hours per night.

Results of sleep architecture und quality are presented in the following table. Remarkable findings are a normal sleep efficacy, independent of treatment with ASV and a change in distribution of sleep stages - related to total sleep time - in favor of REM-sleep.

In conclusion we found that long-term ASV therapy in patients with stable congestive heart failure and CSR leads to a normalization of respiratory parameters and a significant improvement in REM-sleep Duration.

	Baseline	Follow-up	p-value
AHI (/h)	36.0±14.8	6.2±5.8	<0.001
Oxygen Saturation (%)	92.4±2.0	93.7±2.0	<0.001
Time in bed (TIB, min)	451±54	430±55	0.008
Total sleep time (TST, min)	375±57	354±56	0.009
Sleep efficacy (SE, %)	82±17	84±12	n.s.
Light sleep (% TST)	64.2±18.3	58.1±19.1	0.08
Slow wave sleep (SWS, % TST)	25.8±15.8	28.2±17.3	n.s.
REM sleep (REM, % TST)	11.0±6.4	14.0±8.1	0.003

1155

Estimated glomerular filtration rate and mortality in implantable cardioverter defibrillator recipients. Which formula to use?

K Karin Kraaier¹; MF Scholten¹

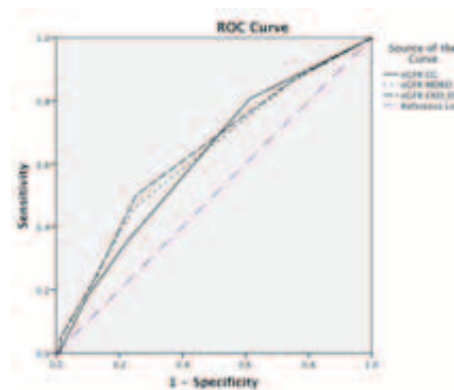
¹Medical Spectrum Twente, Enschede, Netherlands

Introduction: Renal dysfunction is an important risk factor for mortality in patients with implantable cardioverter defibrillators (ICD). There are several formulas to estimate glomerular renal function (eGFR). In this study, we compared the predictive value of the different formulas.

Methods: A total of 377 ICD recipients (mean age 63.8 ± 9.4 years, 80% male, 62% ischemic cardiomyopathy) were studied. eGFR was estimated by the use of the formulas of Cockcroft Gault (CG), the Modification of Diet in Renal Disease (MDRD) and the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI). Receiver operator characteristic (ROC) curves and area under the ROC curves were calculated.

Results: During a median follow up of 40 (range 0-71) months, mortality occurred in 72 patients (19%). For every formula, lower eGFR was significantly related to higher mortality. There were small differences in ROC curves. The CKD-EPI formula was the best predictor of mortality (ROC 0.64), closely followed by MDRD (ROC 0.63) and CG (ROC 0.62).

Conclusion: Renal dysfunction is a significant predictor of mortality. All formulas can be used and differences between those formulas are small.



Moderated Poster Session 5 – Basic mechanisms in heart failure

10:00–11:00

Location: Poster Area

1156

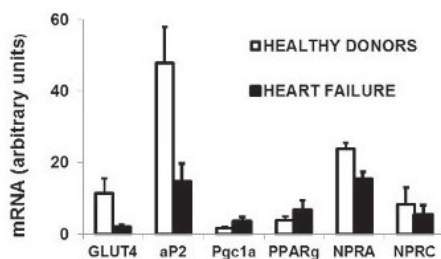
Metabolic pathways are altered in skeletal muscle satellite cells (SC) in heart failure (HF)VL Galenko¹; P Tikanova²; MA Bortsova¹; TA Lelyavina¹; MYU Sitnikova¹; R Dmitrieva²¹ Federal Almazov Medical Research Centre, Research Department for Heart Failure, St Petersburg, Russian Federation; ² Federal Almazov Medical Research Centre, Institute of Molecular Biology and Genetics, St Petersburg, Russian Federation

Background and Aim: Chronic activation of natriuretic peptides (NP) system in combination with mitochondrial dysfunction and/or defects in fatty acids (FA) oxidation are proposed as the possible mechanisms of the progression of systemic metabolic disorders in cardiovascular patients. Systemic metabolic derangements in HF were demonstrated for many tissues; however, how these alterations affect SC remains largely unknown. Our work was aimed to study the functional alterations in SC from HF patients using cellular in vitro models.

Methods: soleus muscle samples were obtained from 3 healthy donors (HD) and 7 HF patients (NYHA III; age 49+11; LVEF 31+5%); SCs were purified from muscle tissue, and myogenesis of SC was stimulated in vitro to confirm differentiation potential. Immunostaining for MHC was performed to confirm differentiation. Dynamics of gene expression for myogenic markers (Pax7, Pax3, MyoG, Myf5, Mrf4, Six4) and metabolic regulators (PPAR α , aP2, Pgc1 α , NP system genes) during differentiation was determined by Q-PCR.

Results: The most important observations are demonstrated on figure. We have found that genes involved in FA utilization (aP2), and insulin-sensitive glucose transporter (GLUT4) were downregulated in SC from HF patients. We have found that genes involved in FA utilization (aP2), and insulin-sensitive glucose transporter (GLUT4) were downregulated in SC from HF patients. Moreover, the downregulation of NPs system at mRNA level was demonstrated for HF-derived SC, while expression of PPAR α and Pgc1 α was increased. Finally, the dynamics of markers of myogenesis was altered in HF SC.

Conclusion: The systemic metabolic derangements in HF affect SC functions that may result in muscular disorders including failure of regeneration, muscle wasting and cachexia.



1157

Electrical microcurrent increases mitochondrial respiration and ATP-synthesis in cardiomyocytesJ Mueller¹; A Holly²; K Macfeldt²¹Berlin Heals, Research, Berlin, Germany; ²Medical University of Vienna, Vienna, Austria

Introduction: Zhao M. has published that PI(3)K γ enhances and PTEN decreases wound healing by endogenous physiologically induced electrical fields. We have published that electrical microcurrent applied by patch electrodes to the epicardium of rats with heart failure leads to a significant improvement of heart function, a down regulation of pro-inflammatory cytokines and normalization for extracellular matrix components. We hypothesize that one of the multifactorial reasons for this alteration induced by electrical microcurrent might be an increase in mitochondrial energy synthesis.

Methods: Cardiomyocytes of spontaneous hypertensive rats (SHR; N=5; 11 weeks old) were stimulated electrically by use of a direct current (DC) power generator via two electrodes. The electrodes were integrated into the top cover of the culture plate and connected to the microcurrent generator. The cells were either left

unstimulated (= control) or stimulated with low or high microcurrent over a period of 72h.

Mitochondrial respiration of DC treated cells was measured via the Oxygraph 2K (Oroboros, Innsbruck, Austria). This instrument allows the continuous measurement of oxygen consumption of intact cells. A sequence of the inhibitors oligomycin, carbonyl cyanide-4-(trifluoromethoxy)phenyl- hydrazone and rotenone was added to analyze the impact of different mitochondrial complexes on respiration. ATP of microcurrent treated and non-treated SHR cardiomyocytes was isolated by an ATP-assay (Abcam, ab83355) and quantified fluorometrically.

Results: Our data shows that there is an up-regulation of mitochondrial respiration in low (+28.6% +/- 3.5%, p=0.093) and a significant up-regulation in high (+45.4% +/- 5.7%, p=0.0045) microcurrent treated cells as compared to the control group. A non-significant up-regulation of ATPase efficiency was observed with low (+8.5% +/- 2.0%, p=0.750) and high (+16.7% +/- 1.9%, p=0.474) microcurrent stimulation as well. The result of ATP analysis indicates a significantly increase in ATP by 98.4% +/- 26.7%, (p=0.036) in low microcurrent and 172.3% +/- 41.7% (p=0.0047) in high microcurrent treated cells compared to the control group.

Conclusion: The data obtained in this experiment suggests that high microcurrent application increases cell respiration and ATP-synthesis significantly. The increase of energy synthesis just by microcurrent application throws additional light on the questions raised on the biological mechanism of microcurrent application.

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Tachyphylaxis to the anti-inflammatory effects of BNP in acute heart failure: potential response to therapyS Liu¹; DT Ngo²; CR Chong¹; WP Chan²; JD Horowitz²; YY Chirkov²¹University of Adelaide, Cardiology Unit, Adelaide, Australia; ²Queen Elizabeth Hospital, Cardiology Unit, Adelaide, Australia

Purpose: B-type natriuretic peptide (BNP) exerts natriuretic, diuretic and vasodilator effects. A number of clinical studies using synthetic BNP for the treatment of heart failure (HF) (high circulating BNP environment) have suggested that BNP-based restoration of homeostasis is inadequate, which raises the possibility of attenuated BNP response in such patients. Recently, we demonstrated that BNP partially suppresses superoxide (O₂⁻) release in the neutrophil "burst". The aims of the current study were to (1) quantitate the anti-inflammatory response of BNP in acute HF; (2) evaluate effect of treatment of HF on this BNP effect; (3) determine whether this effect of BNP is retained in takotsubo cardiomyopathy (TTC), an intense inflammatory myocardial disorder characterized by marked BNP release.

Methods: HF patients were studied both at acute presentation (n=45) and after at least 3 weeks' treatment (n=25). TTC patients (n=20) were studied at the time of diagnosis. Neutrophils were isolated from the peripheral blood of participants. O₂-generation in response to PMA (0.1 μ M) or fMLP (1 μ M) with or without BNP (1 μ M) was quantitated by electron paramagnetic resonance spectroscopy using cyclic hydroxylamine (CMH, 0.2mM) as the spin probe. In order to evaluate the determinants of the change in BNP response in HF patients, we correlated duration of treatment and Δ plasma NT-proBNP levels with the improvement of BNP response in HF patients after treatment.

Results: We previously demonstrated that BNP inhibited both fMLP- and PMA-associated O₂- production in control subjects (n=20) by 29 \pm 5% and 38 \pm 7% respectively (P < 0.01 for both). In the current study, plasma NT-proBNP levels were markedly elevated in both acute HF and acute TTC patients, and there was significant attenuation of BNP effects (P < 0.05 for both) on O₂- release in these patients. With treatment, NT-proBNP plasma levels had not decreased significantly (median values: 3613 to 2409 pg/mL). Paired evaluation of BNP responses before and after HF treatment revealed partial restoration (P = 0.032) of inhibition of O₂-generation. Decrease in NT-proBNP level was not predictive of this progressive re-sensitization, but re-sensitization tended to occur predominantly in younger HF patients (r = -0.388; P = 0.055). However, no relationship was found between incremental BNP effect on neutrophils and duration of treatment.

Conclusions: In both acute HF and TTC, marked increases in BNP release are associated with attenuation of the anti-inflammatory effects of BNP. Restoration of this process may be important to recovery of myocardial function.

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A novel implantable counterpulsation assist device, the PULVAD, induced superior left ventricular pressure unloading compared to the intra-aortic balloon pump in a bovine model of acute heart failure

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Purpose: We have developed a novel implantable counterpulsation left ventricular assist device, the Pressure-Unloading Left Ventricular Assist Device (PULVAD), designed to provide left ventricular pressure unloading and diastolic aortic augmentation. In the present study we aimed to compare the acute hemodynamic effects of PULVAD support to those of the intra-aortic balloon pump (IABP) in a large animal model of acute heart failure (HF).

Methods: The PULVAD comprises a pneumatically-driven polyurethane pumping chamber with a valveless opening, which is implanted in the thoracic cavity and is connected to the ascending aorta. The pump is synchronized on the basis of the ECG and operates through inflation of the device air space during diastole (injecting blood into the aorta), and deflation just prior and during systole (sucking blood from the aorta into the device blood sac).

Five calves (92 ± 7kgs) underwent left lateral thoracotomy and HF induced by left anterior descending coronary artery ligations. The PULVAD was implanted in the thoracic cavity and connected to the ascending aorta using a vascular graft via partial clamping of the aorta (without extracorporeal circulation). The IABP (balloon volume of 40ml) was inserted in the descending aorta via the femoral artery. Both devices PULVAD and IABP were driven by the Arrow Autocot 2 wave iabp system console. The devices were synchronized on the basis of the ECG to provide pressure unloading of the LV along with aortic diastolic pressure augmentation. Calves were instrumented with a Millar pressure catheter for aortic pressure measurement. Systolic and end-diastolic aortic pressures (indices of LV afterload) were measured without LV support, after 30 seconds of PULVAD support and after 30 seconds of IABP support.

Results: The PULVAD provided significantly greater unloading of the LV compared to the IABP. The systolic aortic pressure decreased by 15 ± 8% with PULVAD support compared to 4 ± 2% with IABP support (p = 0.002). End diastolic aortic pressure decreased by 18 ± 12% with PULVAD support compared to 9 ± 7% with IABP support (p = 0.021).

Conclusions: The PULVAD, a novel implantable counterpulsation LVAD, provides profound pressure unloading of the LV, significantly greater compared to that of the conventional IABP, in a large animal model of acute ischemic HF

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Evaluation of the immunomodulatory properties of cardiac adipose tissue progenitor cells: a step towards their use in cell-based cardiac regeneration

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Purpose: Cell-based strategies to regenerate injured myocardial tissue have emerged over the past decade, but the optimum cell type is still under scrutiny. In this context, human adult epicardial fat surrounding the heart has been characterized as a reservoir of mesenchymal-like progenitor cells (cardiac ATDPs) with potential benefits on cardiac function. However, additional data on the possibility that these cells could trigger a deleterious immune response following implantation are needed. Thus, in the presented study, we took advantage of the well-established low immunogenicity of umbilical cord blood-derived mesenchymal stem cells (UCBMSCs) to comparatively assess the immunomodulatory properties of cardiac ATDPs

Methods: T cell alloproliferation was determined in an in vitro allostimulatory assay using allogeneic mature monocyte-derived dendritic cells (MDDCs) co-cultured with either cardiac ATDPs or UCBMSCs. Cytokines present in supernatants collected from alloproliferation assays were measured using the CBA human Th1/Th2 Cytokine kit II.

Results: Similar to UCBMSCs, increasing amounts of seeded cardiac ATDPs suppressed the alloproliferation of T cells in a dose-dependent manner. Secretion of pro-inflammatory cytokines (IL6, TNF α and IFN γ) was also specifically modulated by the different numbers of cardiac ATDPs co-cultured (Figure 1).

Conclusions: In summary, we show that cardiac ATDPs abrogate T cell alloproliferation upon stimulation with allogeneic mature MDDCs. This suggests that these cells could further regulate a possible harmful immune response in vivo, being valid for future use in cell therapy to regenerate injured myocardium.

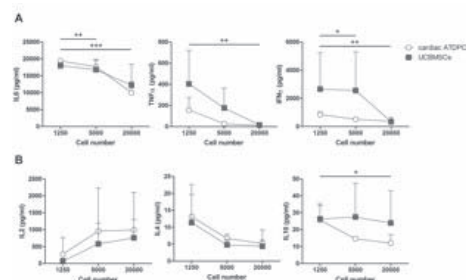


Figure 1. Cytokine production levels

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Ranolazine at the end of Trastuzumab therapy prevents left ventricular dysfunction

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Purpose: Trastuzumab (TRAS), an anti-ErbB2 inhibitor, has revolutionized the prognosis of HER2-positive breast cancer patients. However, it can produce asymptomatic left ventricular dysfunction and heart failure, whose mechanism has not been fully elucidated and can include changes in Ca²⁺ regulation related to blockade of ErbB2. Here, we aim at assessing whether Ranolazine (RAN), an inhibitor of the late sodium current, that reduces [Na⁺]_i-dependent calcium overload, administered after TRAS treatment, blunts TRAS cardiotoxicity in vivo and in vitro.

Methods: In vitro, rat H9C2 cardiomyoblasts were treated with TRAS (0.2 μ M) for 3 days and then treated with or without RAN (1 μ M or 10 μ M) for 3 days. We have evaluated tissue expression of BNP (brain natriuretic peptide) by PCR analysis. In vivo, fractional shortening (FS) and ejection fraction (EF) were measured by M/B mode echocardiography and radial and longitudinal strain (RS and LS) were measured using 2D speckle-tracking echocardiography, in C57/BL6 mice, at 0, 2 and after 7 days of daily administration of TRAS (2.25 mg/kg/day, ip). These measurements were repeated after 5 days of RAN treatment (305 mg/Kg/day, gavage, dose comparable with that used in humans of 750 mg twice, that is the maximum dose used in Italy) initiated at the end of TRAS treatment. We have divided mice in 2 groups. The first group (G1) was treated with TRAS for 7 days. The second group (G2) was treated with TRAS for 7 days and then treated with RAN for 5 days. We have 2 control groups: CG1 (sham) and CG2 (no RAN).

Results: RAN reduced TRAS toxicity in H9C2 cardiomyoblasts as evidenced by higher viability rate of cells treated with TRAS+ RAN than cells treated with TRAS alone (p < 0.01). RAN prevents the increased expression of BNP (p < 0.05) on heart tissue. In vivo, after 7 days with TRAS, FS decreased to 48.7 ± 4.1%, p < 0.01 vs 62.3 ± 0.8% (sham), EF to 81.8 ± 3.5%, p < 0.01 vs 91.7 ± 0.5% (sham), RS to 21 ± 8.1%, p < 0.01 vs 43.2 ± 4% (sham), and LS to -11 ± 3.7%, p < 0.01 vs -38.8 ± 6% (sham). In mice treated with RAN for 5 days after TRAS treatment, the indices of cardiac function recovered: FS was 61 ± 1.2%, EF was 91 ± 0.7%, p < 0.01; RS was 35 ± 1.8%, p < 0.05 vs TRAS. However the alteration of LS persists after treatment with RAN (-15.4 ± 5.1%, p = 0.3 vs TRAS).

Conclusions: RAN post-treatment blunts cardiotoxic effects due to TRAS, as demonstrated by the normalization of the values of FS, EF and RS. LS is the first to impair and may be the last to recover. We plan to test RAN as a cardioprotective agent with other antineoplastic cardiotoxic drugs in our experimental models.

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Cardioprotective effects of Ecklonia cava polyphenol on doxorubicin-induced cardiomyopathy in rats

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Purpose: Long-term therapy with doxorubicin is associated with a high incidence of a cumulative and irreversible dilated cardiomyopathy, despite of its broad anti-neoplastic effectiveness. The goal of this study was to evaluate the cardioprotective effects and safety of seapolyphenol (polyphenol purified from Ecklonia cava) against doxorubicin-induced cardiotoxicity in an animal rat model.

Methods: Of total 42 rats, we divided 21 rats into Group 1 (low-dose seapolyphenol plus doxorubicin, n=7), Group 2 (high-dose seapolyphenol plus doxorubicin, n=7), and Group 3 (single doxorubicin, no seapolyphenol, n=7) for cardioprotective efficacy of seapolyphenol. We administered seapolyphenol (32/64 mg/kg, daily, oral) one week before doxorubicin

(2.5mg/kg, weekly, intraperitoneal) was injected for 6 weeks. For safety of seapolynol, the other 21 rats were divided into Group 4 (low-dose seapolynol only, n=7), Group 5 (high-dose seapolynol only, n=7), and Group 6 (neither seapolynol nor doxorubicin, n=7). We performed transthoracic echocardiography (15MHz linear array) was before (baseline) and after (6-week) injection of doxorubicin and analyzed cardiac function and examined heart specimen by electron microscope after 6week. **Results:** Left ventricular ejection fraction significantly decreased and the left ventricular end diastolic/systolic dimension and LV mass index significantly increased in single doxorubicin group compared to high dose seapolynol plus doxorubicin group. Also, electron microscopic finding showed less impaired myofiber and mitochondria in high dose seapolynol plus doxorubicin group than in single doxorubicin group. **Conclusions:** Our data showed that high dose seapolynol had cardioprotective effects against doxorubicin-induced cardiotoxicity in an animal rat model with the evidence of electron microscopic finding in addition to echocardiographic results.

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Altered mechanical parameters and rearranged Kv4.x ion channel expression at the plasma membrane of cardiomyocytes influenced by ophiobolins

This work was supported by a grant.

TÁMOP-4.2.2.A-11/1/KONV-2012-0035.V Viktoria Szuts¹; O Bencsik²; ZS Szegeletes³; L Toth⁴; M Szuts⁴; JG Kiss⁵; L Rovo⁶; A Szekeres²; CS Vagvolgyi²; K Halasy⁷

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Ophiobolins are a major member of the ophiobolin complex of phytotoxic metabolites, and they possess with antitumor, antibacterial, antifungal activities. Increasing evidence points to a role of MAGUK proteins as an underlying factor, i.e. synapse-associated protein 97 (SAP97), related to inflammation. The SAP97 is associated with Kv4 type channels in complex modulating their kinetic properties. Our hypothesis was that the SAP97 mainly localises in the intercalated discs of the cardiac muscle therefore the altered expression of ion channels are presumably involved in the inhibition of normal mechanical parameters and physiological function of transient outward current (ITO). Our aim was to use purified ophiobolins as an effective molecular tool in the study of cardiomyocyte inflammation. In this swot we have investigated the mechanical factors by atomic force microscope technique (AFM) and the surface expression of Kv4.x ion channels on the cardiomyocytes using electron microscope and immunofluorescence methods. Atomic force microscope study showed that the elasticity of the cell surface, the Young modulus is moderately changed in the presence of low ophiobolin A concentration. The cell volume and the highest of the cells showed a moderate alteration after OA treatment. The K4.3 channels associate with synapse-associated protein 97 (SAP97) anchoring protein in the healthy myocytes. However, after treatment of OA the SAP97 binding to Kv4.3 channels and distribution of their complexes are changed in the cardiomyocytes in the intercalated discs and membranes. A growing body of research using these new reductionist models of inflammation on cardiomyocytes are demonstrating a role of SAP97 in specific ion channel stability important for cardiac functions. These results are suggested that SAP97 deactivation or reduction can (directly or indirectly) lead to changes in the functional cell surface expression of Kv4.x channels with mechanical parameters, with biophysical and biochemical properties of cardiac ITO current.

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Cardioprotective effects of matrine against apoptosis in rats with diabetic cardiomyopathy

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Objective: To investigate the cardioprotective effect of matrine against apoptosis and related possible mechanism in diabetic cardiomyopathy (DbCM).

Methods: Both of in vivo and in vitro studies were implemented in this study. In the in vivo study, diabetes in rats was induced by intraperitoneal injection of STZ.

Rats were divided into control group (Ctrl), DbCM group (DbCM), matrine treated group (Mat) and 5-HD pretreated group (5-HD+Mat). 5-HD+Mat group received pretreatment of 5-HD intraperitoneally before matrine administration. Ventricular intubation hemodynamic examination was performed to determine LVSP and LVEDP. In vitro study, isolated primary myocytes were divided into control group (Ctrl), high-glucose incubated group (HG), matrine treated group (Mat) and 5-HD pretreated group (5-HD+Mat). Cells in Mat received matrine incubation, 5-HD+Mat received pretreatment of 5-HD before matrine incubation. Mitochondrial membrane potential and apoptosis were detected by flow cytometry.

Results: In in vivo study, compared with Ctrl, in DbCM, LVSP decreased while LVEDP increased significantly ($P < 0.05$); matrine treatment in Mat improved LVEDP significantly ($P < 0.05$), which was then impaired by 5-HD pretreatment in 5-HD+Mat group significantly ($P < 0.05$). In vitro study, compared with Ctrl, mitochondrial membrane potential decreased while apoptosis rate significantly in HG ($P < 0.05$); matrine incubation improved mitochondrial membrane potential and thus reduced apoptosis compared with Ctrl ($P < 0.05$); 5-HD pretreatment reversed the effects of matrine on membrane potential and apoptosis significantly ($P < 0.05$).

Conclusions: Matrine improve cardiac function of DbCM by inducing elevation of mitochondrial membrane potential via mitoKATP opening to inhibit myocyte apoptosis.

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Combined gene therapy by VEGF165 and HGF: dynamic duo and its pleiotropy in myocardial angiogenesis

12-04-92005-HHC_aP Pavel Makarevich¹; E Gluhanuk²; Z Tsokolaeva¹; M Boldyreva¹; K Dergilev¹; A Gavrilov³; J Gallinger²; P Rodina²; K Kerova²; YE Parfyonova¹

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Number of studies focus on combined growth factor (GF) gene therapy for myocardial infarction (MI) and heart failure (HF). Still, amplifying beneficial effects is not the only property of combined administration of GF. The latter are capable to regulate inflammation, cell invasion etc., thus, we investigated whether pleiotropic action of GFs may influence their angiogenic efficacy. VEGF and HGF render additive angiogenic effects in ischemic tissue, yet deeper insights in their action in heart suggest, that pleiotropy of action should not be neglected.

In a rat MI model, we used plasmid transfection by empty vector, VEGF, HGF or VEGF/HGF combination (n=6/group). At Day 14 CD31+ capillary density in peri-infarction area was increased in VEGF or HGF group compared to empty vector with maximum increase after combined delivery. However, density of larger blood vessels with mural smooth-muscle cell was increased only in VEGF group, but not in HGF and VEGF+HGF group as well as a reduction of MI size was significant only in VEGF group. As far as both growth factors are known to influence inflammation, which affect vessel growth and tissue repair, we investigated their effects on monocyte accumulation in peri-infarct region and production of cytokines, which mediate interaction between inflammatory cells and endothelium.

Using BioPlex we found, that in HUVEC and TIME cells recombinant VEGF and HGF modulate level of chemokines - MCP-1 and IL-8. VEGF treatment increase MCP-1 secretion, while effect of HGF was opposite. Moreover, production of MCP-1 correlated with NF- κ B profile: VEGF was stimulating and HGF - suppressing. These changes were consistent with histology findings, which showed that at Day 3 after MI CD68+ monocyte density in myocardium increased in VEGF group, and did not change in HGF and VEGF/HGF groups compared to control. This data suggests that HGF alleviates VEGF-induced monocyte invasion, which is of crucial role for myocardial collateral formation. As for IL-8 we found stimulating response to both GFs with the highest level in VEGF/HGF samples, which correlated with capillary density and IL-8 known angiogenic properties. Using Luciferase reporters we showed, that VEGF and HGF induced promoter of IL-8, which was consistent with HIF-family activity. Moreover, HIF-2 plays a crucial role in maximizing IL-8 production after combined stimulation.

We conclude, that combined delivery of VEGF/HGF is effective for stimulation of myocardial angiogenesis. However, their pleiotropic action and opposite influence on inflammatory response may be an important determinant of efficacy to be taken into account.

Clinical Case Corner 4 – Extracardiac problems affecting the heart

Monday 25 May 2015 10:00–11:00

Location: Poster Area

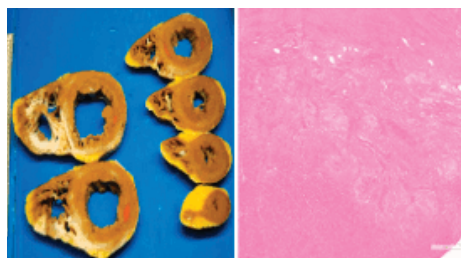
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Right ventricular tachycardia: clinical onset in a case of sarcoidosis underwent to heart transplantation.

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We report a rare case of a man of 42 years old with episodes of sustained ventricular tachycardia (SVT) and torsades de pointes in a context of dilated and hypokinetic cardiomyopathy known since 2008, initially framed as arrhythmogenic cardiomyopathy, for which he was subjected to ICD implantation. EKG during sinus rhythm showed right bundle branch block, negative T waves in right precordial, small incisions in the initial part of the ST segment and T wave. SVT had left bundle branch block morphology type, with normal electrical axis. The echocardiogram showed a slightly dilated left ventricle with moderately depressed left ventricular ejection fraction (EF 38%); altered diastolic relaxation with normal left ventricular filling pressure; minimum mitral regurgitation; dilated right ventricle with normal function; mild tricuspidal regurgitation. The coronary angiography appeared unharmed and MRI showed a suggestive picture of pulmonary sarcoidosis with cardiac involvement without major criteria for dysplasia. The patient was hospitalized several times for daily ATP and numerous DC shock so he underwent transcatheter ablation procedure (ATC) of right TV with endocardial approach in 2010; in that occasion endomyocardial biopsy was performed confirming the diagnosis of sarcoidosis, so he began immunosuppressive therapy. After further admissions to frequent recurrences of TVS with appropriate ICD interventions despite optimization of therapy (immunosuppressive, antiarrhythmic and specific for heart failure), the patient underwent two other ATC procedures, with epicardial approach too, with only temporary benefit. We placed on the waiting list for cardiac transplantation since March 2014. Clinically stable at cardiac controls (NYHA class III), cardiac catheterization (always normal filling values) and pneumological controls (pulmonary sarcoidosis stage III), without alterations of other organs. He underwent heart transplant in November 2014, complicated by embolic multi-infarct stroke with residual left hemiparesis. At macroscopic analysis of the explanted heart presence of whitish-gray areas, involving the anterior and intermediate septum and right ventricle in which we highlight, histologically, multiple granulomas in chain, non-necrotizing epithelioid type with giant cells (Fig 1).



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Speckle-tracking strain analysis accuracy in a case of cardiac sarcoidosis

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¹Mediterranean Institute for Transplantation and High Specialization Therapies (IsMeTT), Palermo, Italy; ²University of Palermo, cardiology, Palermo, Italy

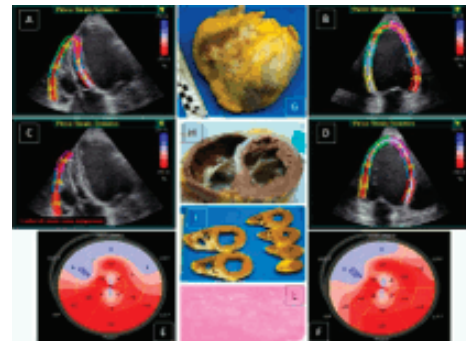
Cardiac sarcoidosis (CS) is a potentially fatal condition that presents with a wide range of clinical manifestations. Proximal part of the anterior interventricular septum

and also the involvement of the right ventricle (RV) is frequently affected by granulomatous lesions and/or scarring. Purpose: to demonstrate the accuracy of speckle tracking echocardiography (STE) in the identification of sarcoidotic areas.

Methods: We report a rare case of a 42 year old man with CS. Echocardiography showed a mild left ventricle (LV) dilatation with normal wall thickness, ejection fraction 38%, diastolic dysfunction and dilated RV with normal function. We assessed global longitudinal strain (GLS) of the LV, longitudinal strain of the RV and strain of the only free wall of the RV by STE.

Results: GLS of the LV was reduced (-10.1%), presenting dyskinesia (+ 5%) in basal-medium posterior septum (Fig B,D,F), basal (+ 4%) and apical (+ 3%) anterior septum and posterolateral apex (+ 3%). Global longitudinal strain of the RV was more reduced (-13.6%) compared to the strain of the only free wall of the RV(-14.3%) (Fig A,C,E), probably due to the greater involvement of the interventricular septum. In 2014 he underwent orthotopic heart transplant. Macroscopic analysis of the explanted heart showed in the areas with dyskinesia and reduced peak systolic of strain (anterior and middle septum and the right ventricle) the presence of whitish-gray areas with the presence at histology of multiple chain granulomas non-necrotizing epithelioid type with giant cells (Fig.G,H,I,L).

Conclusions: STE seems to be accurate in identifying the areas affected by sarcoidotic process, there is a good correlation between speckle tracking analysis and histology and in the future strain could be relate to outcomes in these patients



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'Speeding towards heart failure' - amphetamine associated cardiomyopathy

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Introduction and case report description: We report two patients with dilated cardiomyopathy secondary to amphetamine use - the diagnosis was not initially recognised and treatment was delayed.

A 45 year old male was initially diagnosed with pneumonia. He presented with dyspnoea, chest discomfort and cough, his electrocardiogram (ECG) showed T-wave inversion throughout the precordial leads, and high-sensitivity Troponin T (HS-TnT) 34. After treatment with antibiotics he remained tachycardic, hypertensive and breathless. Cardiology review demonstrated signs of acute heart failure. A focused history revealed chronic amphetamine use for the past 10-years. His echocardiogram showed a dilated cardiomyopathy with severe left ventricular systolic dysfunction (LVSD) and ejection fraction (EF) of 11%. He was diagnosed with amphetamine associated cardiomyopathy and commenced on standard heart failure treatment. The second patient was a 49 year old male presenting with exertional dyspnoea. His ECG showed T-wave inversion in the anterolateral leads and sinus tachycardia. His HS-TnT 39. General physician diagnosed and treated him for acute coronary

syndrome. Cardiology review revealed a 2 month history of paroxysmal nocturnal dyspnoea. Examination demonstrated signs of acute heart failure. In a focused drug history he disclosed amphetamine use since age 18. An echocardiogram demonstrated a dilated cardiomyopathy with severe LVSD and EF 15%. He was treated for acute heart failure.

Description of the problem: Amphetamine use is common. In the UK it is now the second most common drug of abuse and cardiomyopathy resulting from its use may become more frequent although the true prevalence is unknown. Physicians and medical doctors need to be able to recognise the clinical signs of heart failure in younger patients and be able to take a focused history to identify at risk behaviour that may lead to cardio-toxicity and subsequent cardiomyopathy.

Questions

- (1) How is this condition recognised?
- (2) How should our patients be treated and managed?
- (3) What is the likelihood of recovery of left ventricular function?
- (4) What is the underlying pathophysiology?

Answers and discussion: In young patients presenting with heart failure a high index of suspicion of substance abuse is warranted. Both patients remained abstinent from amphetamine use following diagnosis. Our first patient had a repeat echocardiogram six weeks later which showed marked improvement in left ventricular systolic function. Recovery of ventricular function is well described throughout previous case reports if managed with strict drug abstinence and standard heart failure medications. The proposed mechanism of cardiomyopathy is persistent adrenergic stimulation leading to sub-endocardial ischaemia, possibly related to coronary artery spasm, and myocarditis secondary to catecholamine toxicity.

Conclusions and learning points:

- A high index of suspicion for substance abuse is necessary for younger patients presenting with heart failure
- Drug abstinence is essential in the management of amphetamine associated cardiomyopathy
- Increased awareness is required by general physicians to identify patients on initial presentation

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A case of ventricular tachycardia and heart failure

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A55-year old Caucasian male was admitted to our hospital with complaints of palpitations and heart failure symptoms due to severe left ventricular dysfunction. He developed recurrent heart failure and ventricular tachycardia requiring several admissions to hospital and was finally referred to our institution with the clinical diagnosis of dilated cardiomyopathy. Echocardiography revealed a severely reduced left ventricular function (EF 25%).

Coronary angiography demonstrated unobstructed coronary arteries. On chest X-ray no bilateral hilar lymphadenopathy was seen.

A left-ventricular endomyocardial biopsy (EMB) was performed showing immunohistochemically increased intramyocardial inflammation and subendocardial enhanced fibrosis without proof of viral genomes. Due to the differential diagnoses we determined a gene expression profile in one EMB using a set of 10-15 of 27 altered genes. Here, we could predict the presence of multinuclear giant cells and specifically the diagnosis of cardiac sarcoidosis in the EMB, even without a direct histological proof of sarcoid granulomas or multinuclear giant cells.

The patient was immediately treated with oral high dose corticosteroids. In a 2-month follow-up EMB the diagnosis was verified showing noncaseating granulomas consistent with cardiac sarcoidosis. Intramyocardial inflammation was already decreased significantly. Follow-up echocardiogram showed a significant improvement in left ventricle function (EF of 42%), and the arrhythmias terminated.

Cardiac sarcoidosis often presents with sudden death or life-threatening arrhythmias, as well as heart failure. However, both multinuclear giant cells and granulomas are often missed by conventional histological evaluation due to the wide sampling error in focal processes. This case highlights a new method for improved differential diagnosis and tailored differential therapy by myocardial gene expression profiling in EMBs in fulminant heart failure.

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Pulmonary oedema, think beyond the heart even in the presence of severe left ventricular systolic dysfunction

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Case Report: We submit a case of a 48-year-old male with idiopathic dilated cardiomyopathy (DCM) that presented with recurrent flash pulmonary oedema (FPO). Two years prior, at the time of diagnosis, the CMR illustrated a myopathic process with the absence of scar/fibrosis or inducible ischaemia, and an ejection

fraction (EF) of 15%. Full DCM screen at that time identified no secondary cause. As he remained NYHA class III despite optimal treatment, and the ECG demonstrated LBBB with QRS duration of 153ms, he underwent CRT-d implantation. He remained stable for 1 year, following which he started to present weekly to hospital with sudden onset shortness of breath over minutes to hours suggestive of FPO, that at times required high dependency care. There were concerns with compliance to medication and fluid restriction. In view of this, referral for transplantation was not approached. CRT interrogation demonstrated adequate biventricular pacing with an AF burden of 9.6% that was managed with beta-blocker therapy. His CHA2DS2-VASc score was 1 and he was reluctant to commence on anticoagulation. Up-to-date transthoracic echocardiogram showed dilated left ventricular (LV) cavity with severe systolic impairment (EF visually estimated 15-20%). There was no significant valvular abnormality. Despite extensive education and heart failure optimisation, the presentations remained frequent.

Possible Differential Diagnosis: No identifiable triggers beyond questionable compliance and severe LV dysfunction were identified as potential causes for the admissions. Due to the presence of severe LV impairment an alternative diagnosis was not sought. It was not until renal function worsened, followed by discrepancy in renal size on ultrasound that renal artery stenosis (RAS) was suspected. Atherosclerotic disease is the most common cause of RAS and thereby an unusual diagnosis in our patient that had no vascular risk factors or ischaemic heart disease. **PROBLEMS AND ANSWERS-** MR renal angiography is used widely for the diagnosis of RAS as it avoid contrast exposure and enables anatomical and functional renal assessment. In view of the implanted MR incompatible CRT-d device this could not be performed. Therefore multiple imaging modalities including MAG-3 renogram and CT renal angiogram were used to confirm the diagnosis of significant bilateral RAS secondary to an aorta-iliac thrombus. **DISCUSSION-** The reported prevalence of FPO in RAS is around 15.3%. Revascularization in RAS has shown mixed outcomes and thereby it should be considered in a case specific basis. At the time of our patient's diagnosis it was felt that rescue of renal function with revascularization was not feasible, and thus the patient was commenced on anti-coagulation with planned initiation of peritoneal dialysis. Had a prompt diagnosis been available, perhaps medical staff would have been able to see past the severe LV impairment and consider a wider differential, altering this patient's outcome. **CONCLUSION-** This case highlights that even in severe LV dysfunction, recurrent presentations of FPO despite therapy prompts further evaluation and warrants a high index of suspicion for alternative diagnoses such as RAS. It is also important to consider thromboembolic causes for RAS particularly in the presence of AF. It is important to identify alternative diagnosis tests when certain modalities are not feasible and understand the limitation of each tool. MRI, MAG-3 renogram and CT renal angiogram can be used in different combinations to provide sensitive and specific complementary information in the diagnosis of RAS.

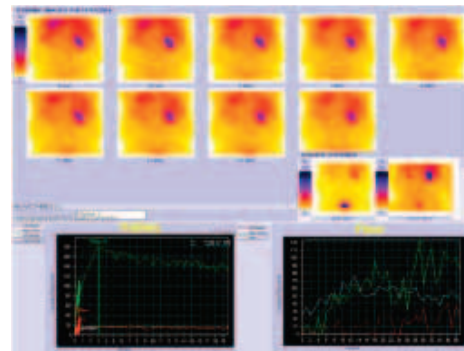


Figure 1- MAG3 renogram images

1171

An uncommon cause of reversible dilated cardiomyopathy

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Introduction: Dilated cardiomyopathy (DCM) is a heart muscle disorder defined by the presence of a dilated and poorly functioning left ventricle in the absence of abnormal loading conditions or ischemic heart disease sufficient to cause global systolic impairment. It may be idiopathic or be caused by many potentially treatable conditions.

Case report: We report a 31 years old man without any relevant previous medical history, who was admitted for orthopnea and dyspnea on routine activities, with two weeks evolution, gradually progressive. On clinical examination the patient had normal blood pressure, pale and dry skin with infiltrated edema, mainly of both lower

limbs; tachycardia and no murmur at cardiac auscultation. Chest X-ray showed cardiomegaly, with a cardiothoracic ratio of 0.63. Transthoracic Echocardiogram (TTE) revealed a pattern of DCM with marked increase in the left ventricle diameter (71/64 mm), a severe left dysfunction (ejection fraction of 22%), diffuse hypocontractility and a mild pericardial effusion. In this clinical case it is important in terms of prognosis to identify potentially treatable causes. The electrolyte imbalances and bacterial and viral infection were excluded. The ferritin was significantly elevated, with serum iron near normal; liver ultrasound imaging evidenced hepatomegaly with increased density, nevertheless genetic study was negative to hemochromatosis. Decrease of free thyroxine level ($T_4 = 0.00$ pmol/L) and an elevation of thyroid stimulating hormone (TSH = 86.22 μ U/L) supporting hypothyroidism; the anti-thyroglobulin and anti-microsomal antibodies were positive and the diagnosis of Hashimoto thyroiditis was considered as a secondary cause of DCM. Replacement hormonal treatment with L-thyroxin was initiated. Progressively, during one year, patient recovery to euthyroidism and left ventricle systolic ejection fraction improved to 47% on TTE. **Conclusion:** DCM is frequently an idiopathic disease with progressive and irreversible poor prognosis outcome. The finding of clinically reversible entities such as hypothyroidism and hormonal treatment with L-thyroxin can significantly improve myocardial function. Hence, thyroid function tests should be systematically access in all patients with DCM.

1172

Predictors of left ventricular recovery in recent onset cardiomyopathy: does size matter?

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A 44-year old male presented to a peripheral hospital complaining of progressive dyspnea, orthopnea and lower limb edema of three weeks duration. He was diagnosed with de novo acute heart failure with severely dilated LV, LVEDD 83mm and LVEF 15%. He is obese with a BMI 37 kg/m² and hypertensive. Investigations including iron profile returned normal results except for a mildly elevated bilirubin and a pro-BNP of 3127 pg/ml. Coronary angiography showed normal coronaries. CMR LGE imaging revealed no myocardial enhancement. Due to sub-optimal medical therapy and no evidence of scarring on CMR, a decision was taken to place patient on optimal medical therapy and postpone ICD implantation till further reassessment. Follow up in the outpatient heart failure clinic showed gradual improvement in LVEDD and LVEF and complete resolution at one year.

This case poses the following therapeutic challenges: Is there a potential for LV recovery? When is the right time for ICD placement or early referral for LVAD/transplant evaluation? How much time can we afford to wait?

Should we rely solely on severity of LVEDD?

As seen in the IMAC-2 study (Intervention in Myocarditis and Acute Cardiomyopathy - 2), LVEDD severity was shown to be the strongest predictor of LVEF at 6 months in patients with recent onset non-ischemic cardiomyopathy (ROCM). An LVEDD greater than 70mm had the worst outcome.

What is the right time to wait before taking a decision to refer the patient for an ICD implantation?

A sub-analysis of the IMAC-2 trial revealed that the risk of sudden cardiac death in patients with new onset ROCM was low at 1% per year additionally, early ICD placement in this subgroup did not impact survival as such, ICD implantation can be deferred while assessing potential for myocardial recovery.

What is the role of MRI in risk stratification? Scarred or fibrotic myocardium harbors an adequate medium for the generation and maintenance of lethal arrhythmias. Cardiac Magnetic Resonance Late Gadolinium Enhancement (CMR LGE) is able to detect such changes and has been shown to predict cardiac adverse outcomes. The presence of CMR LGE in a population of patients with ROCM showed an eight-fold higher risk of an index composite outcome of heart failure hospitalization, appropriate ICD firings and cardiac death, compared to patients without LGE. CMR is also used in determining degree of myocardial fibrosis which is independently associated with lack of response to medical therapy in ROCM patients making CMR useful in risk stratification concerning prediction of lethal arrhythmias and response to treatment.

Conclusion: ROCM patients have a good potential for recovery on optimal heart failure therapy with a low incidence of sudden cardiac death at one year. Searching for reversible etiologies, optimizing medical treatment, assessing a variety of prognostic markers, and observing the early clinical course may allow the clinician to better determine the degree of recovery and consequently, formulate an appropriate plan of action.

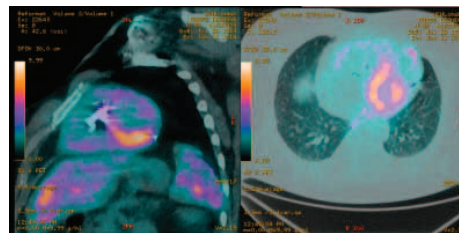
1173

Undiagnosed cardiac sarcoidosis presenting as complete heart block and ventricular arrhythmia

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Case report: A 49 year old Afro-Caribbean man presented with one week history of dizziness. His ECG on admission revealed complete heart block (CHB). Initial investigations including blood tests and transthoracic echocardiogram (TTE) were unremarkable with normal biventricular systolic function and cavity size and valvular structure. He received a permanent dual chamber pacemaker (PPM). 18 months later he presented acutely unwell with dizziness and shortness of breath. He collapsed due to pulseless ventricular tachycardia (VT) and was electrically cardioverted back into sinus rhythm with good circulatory and neurological effect. His creatinine was abnormal at 171 and he had raised serial troponins. Chest X-ray was unremarkable. The TTE showed impaired left ventricular systolic function with an ejection fraction visually estimated at 40-45% secondary to regional wall motion abnormality. The right ventricle was also impaired and dilated. Coronary angiogram revealed unobstructed coronary arteries. Problem- The first line imaging modality for detailed assessment of suspected cardiomyopathy is cardiac MRI (CMR). This was not feasible due to a PPM incompatibility. 18F- fluorodeoxyglucose positron emission tomography with CT (18F-FDG PET-CT) was used as an alternative. It showed increased uptake in multiple viscera including the myocardium, with especially high metabolic activity in the inferolateral wall in a non-perivascular distribution. History and distribution of disease was highly suspicious for systemic sarcoidosis but a tissue diagnosis was lacking. 18F-FDG PET-CT provided a good hepatic target for biopsy and this confirmed a histological diagnosis of sarcoidosis. He was commenced on prednisolone and methotrexate. As the patient was pacing dependent he was at risk of progressive cardiomyopathy in addition to further ventricular arrhythmias. For these reasons his PPM was upgraded to cardiac resynchronisation therapy device with defibrillator (CRT-d). Discussion- Sarcoidosis is a rare multi-system granulomatous condition with three times higher incidence in the Afro-Caribbean population. Cardiac sarcoidosis infers a poorer prognosis and more recent imaging led studies and meta-analysis report a prevalence of cardiac sarcoidosis in the sarcoid population between 37-50%. Cardiac sarcoid most commonly affects the inter ventricular septum causing atrioventricular blocks and secondly the myocardium, causing an infiltrative cardiomyopathy and arrhythmias. Cardiac sarcoidosis should be suspected in any patient under 55 years old who presents with CHB. In the diagnosis of cardiac sarcoidosis, 18F-FDG PET-CT has pooled sensitivities (89%) and specificities (78%) comparable to that of CMR, but is not constrained by limitation with pacemakers of metallic implants. In addition, the degree of activity on 18F-FDG PET-CT correlates with disease activity and prognosis, acting as visual representation of inflammation. As it detects active areas of disease it can guide tissue biopsy and initiation of immunotherapy. Conclusion- The case reminds us of the need to fully investigate patients under 55 years who presents with CHB. It highlights the expanding diagnostic and prognostic usefulness of 18F-FDG PET-CT in cardiac sarcoidosis; as an adjunct or alternative to CMR; in the monitoring of disease progression or response to treatment; guiding initiation of immunotherapy; and in guiding biopsy.



18F-FDG PET-CT imaging in Sarcoidosis

1174

Hypocalcemia as a reversible cause of acute heart failure

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The identification of a reversible aetiology of Heart Failure (HF) can have significant clinical implications.

We present a 23-years-old male, with a past history of Hodgkin's lymphoma in 1994 (treated with chemotherapy and cervical/thoracic radiotherapy until 1995) and a papillary thyroid carcinoma diagnosed in 2004, submitted to total thyroidectomy and radioiodine. He suffered from hypoparathyroidism and hoarseness due to recurrent laryngeal nerve lesion as early complications of the surgery. Since 2007 there was evidence of pulmonary hypertension with mild right systolic dysfunction due to lung metastasis of thyroid carcinoma (a total of 8 sessions of radioiodine were performed). He came to our attention in February 2014, when he was admitted due to dyspnea at rest, orthopnea and facial oedema with a couple of months' evolution. His routine blood tests were unremarkable, except for high type-B natriuretic peptide with normal renal function. An echocardiogram showed an elevated pulmonary artery systolic pressure (55 mmHg) and severe left ventricle

dysfunction. He performed an evaluation of cardiac pressures, showing equalization of cardiac chambers' pressure and high pulmonary vascular resistance index. A cardiac magnetic resonance confirmed the severe compromise of global systolic function but showed no morphologic changes or pericardial effusion or thickening. It was made an adjustment to his daily diuretic dosis and he was discharged. A week later he was again hospitalized complaining of worsening dyspnea, muscle cramps and diplopia. There were rales audible in both lungs and Trousseau's sign was elicited by blood pressure measuring. Blood tests revealed an ionized calcium of 0.57 mEq/L (normal range: 2.32 - 2.64 mEq/L). He began calcium therapy, with

excellent clinical, analytical and echocardiographic evolution, with ionized calcium of 2.12 mEq/L and systolic function significantly improved (ejection fraction from 16 to 42%). However, our patient maintained significant pulmonary hypertension (thoracic CT showed no thromboembolic signs or parenchyma disease) and in whole body scintigraphy high iodo uptake was observed. Sildenafil was began. One week later the patient died after mild effort.

This case illustrates a rare cause of pulmonary hypertension and HF, hypocalcemia. The recognition of reversible causes of HF is crucial, as its correction can be associated with improvement in cardiac function.

Rapid Fire 4

Monday 25 May 2015 11:00–12:30

Location: Agora

1203

Usefulness of the POP-HF score to predict acute myocardial infarction expression in patients with heart failure after coronary artery bypass surgery: a substudy of the POP-HF studyP Predrag Mitrovic¹; B Stefanovic¹; M Radovanovic¹; N Radovanovic¹; D Rajic¹; G Matic¹; T Jozic¹; A Novakovic¹; N Mijic¹; Z Vasiljevic¹¹University Institute for Cardiovascular Diseases, CCS, School of Medicine, University of Belgrade, Belgrade, Serbia

It is well known that patients with coronary artery bypass surgery (CABS) have physiological changes in coronary artery structure. In these patients, presentation of heart failure (HF) has different influence of new coronary events expression, than in patients without CABS. Acute myocardial infarction (AMI) is one of the most important major adverse cardiovascular events (MACE) in patients after previous CABS. This substudy aimed at evaluating the usefulness of the POP-HF score (PostOperative Prognosis-HeartFailure score), originally developed for the prediction of 60-day, 1-year, 5-year, 10-year, 15-year and 20-year MACE, after CABS in patients with HF.

From April 1988, we analyzed 1866 consecutive patients with HF who underwent CABS. Expression of AMI was the predefined end point. Models discrimination and calibration to predict AMI was tested using receiver-operating characteristics curves and the goodness-of-fit (GoF) test. Sensitivity analyses and 1000-resample bootstrapping were used to evaluate the model's performance. The rate of AMI was 46.2 %, respectively. Compared with controls, the cumulative AMI group was associated with much higher rates of adverse clinical outcomes at 60-day follow-up (adjusted odds ratio (OR) for death 7.18), at 1-year follow-up (adjusted OR for death 7.26), at 5-year follow-up (adjusted OR for death 7.48), at 10-year follow-up (adjusted OR for death 7.90), at 15-year follow-up (adjusted OR for death 8.12) and at 20-year follow-up (adjusted OR for death 8.29). Internal validation confirmed a reasonably good discrimination and calibration of the POP-HF score for the prediction of AMI (area under the curve (AUC) 0.70, GoF 0.32), after CABS in patients with HF.

Conclusion: The risk of AIM in patients with HF, after previous CABS, could be accurately assessed using the POP-HF score, which might help in deciding upon measures aimed at preventing adverse prognosis.

1204

Soluble neprilysin vs. NTproBNP for heart failure risk stratificationA Bayes-Genis¹; J Barallat¹; A Galan¹; J Penafiel²; J Vila²; M De Antonio¹; M Domingo¹; E Zamora¹; J Santemas¹; J Lupon¹¹Germans Trias i Pujol University Hospital, Badalona, Spain; ²Hospital del Mar Medical Research Institute (IMIM), Barcelona, Spain

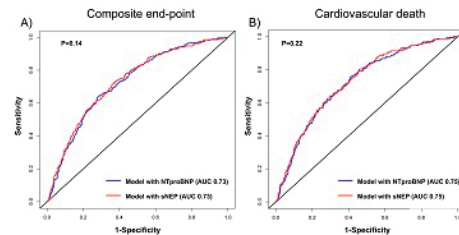
Background: Neprilysin (NEP) breaks down a plethora of vasoactive peptides. NEP has been focused as a therapeutic target and its inhibition has proven to improve outcomes in patients with chronic heart failure (HF). The soluble form of NEP (sNEP), recently identified in heart failure (HF), is associated with cardiovascular (CV) outcomes.

Objective: We directly compared sNEP and NTproBNP as risk stratifiers.

Methods: sNEP and NTproBNP levels were measured in 1030 consecutive ambulatory HF patients from May 2006 to May 2013. Patients were followed for 4.2 years. Comprehensive multivariable analyses and head-to-head assessments of performance were performed. The composite endpoint of CV death or HF hospitalization and CV death alone were explored.

Results: Median sNEP and NTproBNP concentrations were 0.64 ng/mL and 1302 ng/L, respectively. Both biomarkers significantly correlated with age (both $p < 0.001$), but only NTproBNP significantly correlated with eGFR and BMI. In multivariable Cox regression analyses, both sNEP and NTproBNP were significantly associated with the composite endpoint (hazard ratio [HR] 1.18, 95% confidence interval [CI] 1.07 to 1.30, $p = 0.001$; HR 1.30, 95% CI 1.15 to 1.48, $p < 0.001$) and CV death (HR 1.17, 95% CI 1.05 to 1.32, $p = 0.007$; HR 1.41, 95% CI 1.21 to 1.65, $p < 0.001$). Only sNEP remained independently associated with the composite endpoint and CV death when hs-TnT and ST2 were incorporated in the analysis. The head-to-head sNEP vs. NTproBNP comparison showed good calibration and similar discrimination (figure) and reclassification for both endpoints in all models.

Conclusions: sNEP performed similarly to NTproBNP as a risk stratifier in ambulatory patients with HF, though it was less influenced by comorbidities and retained its prognostic value in multimarker analysis.



1205

C-terminal fragment of endothelin-1 precursor (ET-1) strongly predicts heart failure in an elderly population without history of coronary artery diseaseEuropean Research Council (StG-282255), the Swedish Heart and Lung Foundation, Swedish Research Council, the Novo Nordisk FoundationK Klas Gransbo¹; M Persson¹; P Nilsson¹; O Melander¹¹Skåne University Hospital, Malmö, Department of Internal Medicine, Malmö, Sweden

Purpose: Our aim was to examine if plasma concentration of a C-terminal fragment of the Endothelin-1 precursor (ET-1) predicts future heart failure (HF) among elderly patients without history of coronary artery disease (CAD) on top of established risk factors.

Methods: Between 2002-2006, 4819 subjects (mean age 69.4 ± 6.2 years) without history of HF as well as CAD underwent a health screening within the community-based study "Malmö Preventive Project Rescreening Programme" (MPP-RP). We related plasma concentration of ET-1 at the baseline exam to incidence of a first HF event in models adjusted for age, sex, current smoking, LDL, HDL, systolic blood pressure, anti-hypertensive treatment and diabetes mellitus using multivariate Cox proportional hazard models.

Results: During a mean follow up time of 5.6 years, 121 subjects were diagnosed with heart failure. Each standard deviation increment of log-transformed ET-1 was associated with a hazard ratio (95% Confidence Interval) of 1.77 (1.56-2.00) ($P < 0.0001$). There was a gradual increase of the risk of HF over ET-1 quartiles, with a relative risk of 13 in the top vs the bottom quartile (Table 1). Addition of ET-1 to established risk factors improved the C-statistic from 72% to 79%. The continuous Net Reclassification Improvement (NRI) with ET-1 on top of established risk factors was 56 % ($P < 0.0001$). Further addition of Mid-Regional Atrial Natriuretic Peptide (MR-ANP) to the model only marginally attenuated the magnitude of the association between ET-1 and HF and did not lead to further improvement of the C-statistic and NRI.

Conclusion: ET-1 strongly and independently predicts heart failure in the future in an older population free of CAD. Subjects with high ET-1 may benefit from aggressive antihypertensive treatment and regular controls including echocardiography.

Table 1

	HR	p-value		
Lower 95% CI limit	Upper 95% CI limit			
ET-1, 1st quartile	REF (1.0)	-	-	-
ET-1, 2nd quartile	3.89	1.31	11.58	0.015
ET-1, 3rd quartile	6.22	6.22	2.17	0.001
ET-1, 4th quartile	13.23	4.71	37.17	<0.0001

Risk of incident heart failure over quartiles of ET-1 (quartile 1 as the reference).

1206

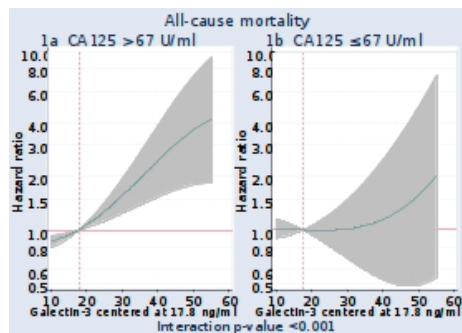
Differential mortality effect galectin-3 in patients with acute heart failure according serum antigen carbohydrate 125P Palau¹; GA Rabinovich²; E Santas³; MP Villanueva⁴; G Minana⁵; A Mollar³; J Sanchis³; J Nunez³¹Hospital La Plana, Cardiology Department, Vila-Real, Spain; ²University of Buenos Aires, Buenos Aires, Argentina; ³Cardiology Department, Hospital Clinic Universitari de Valencia, Valencia, Spain; ⁴University Hospital Clinic of Valencia, Valencia, Spain; ⁵Hospital de Manises, Cardiology Department, Valencia, Spain**Aims:** Galectin-3 (Gal-3) and carbohydrate antigen 125 (CA125) have emerged as robust prognostic biomarkers in heart failure. Experimental data have also suggested a potential molecular interaction between CA125 and Gal-3; however, the biological and clinical relevance of this interaction is still uncertain. We sought to evaluate, in patients admitted for acute heart failure, the association between plasma Gal-3 with all-cause mortality among high and low levels of CA125.**Methods:** We included 264 consecutive patients admitted for acute heart failure to the Cardiology Department in a third-level center. Both biomarkers were measured on admission. Cox regression model was used to evaluate the prognostic effect of the interaction between Gal-3 and CA125 (dichotomized by its median) all-cause mortality.**Results:** During a median follow-up of 2 years (IQR=1-2.8), 108 (40.9%) patients deaths were registered. In a multivariable setting, the effect of Gal-3 on mortality was differentially mediated by CA125 (p for interaction<0.001). Indeed, in patients with CA125 above median (>67 U/ml), values across the continuum of Gal-3 showed a positive and almost linear relationship with the risk of death (Figure 1a). Conversely, when CA125 was below median (\leq 67 U/ml), Gal-3 lacked any prognostic effect (Figure 1b).**Conclusion:** In patients with acute heart failure, Gal-3 was strongly associated with higher risk of long-term mortality but only in those patients exhibiting higher values of CA125.

Figure 1a and 1b

1207

Optimizing clinical use of biomarkers in acute heart failureB Biniyam Demissei¹; MAE Valente²; JG Cleland³; G Cotter⁴; B Davison⁴; MM Givertz⁵; P Van Der Meer²; DJ Van Veldhuisen²; HL Hillege¹; AA Voors²¹University Medical Center Groningen, Epidemiology/Cardiology, Groningen, Netherlands; ²University Medical Center Groningen, Cardiology, Groningen, Netherlands; ³Imperial College London, London, United Kingdom; ⁴Momentum Research, Durham, NC, United States of America; ⁵Brigham and Women's Hospital, Boston, United States of America**Purpose:** The clinical value of single biomarkers at single time-points to predict outcomes in patients with acute heart failure (AHF) is limited. Effective clinical use of biomarkers requires identification of the optimal combination at the optimal time-points.**Objectives:** We performed a multimarker, multi-time-point analysis of biomarkers for the prediction of post-discharge clinical outcomes.**Methods:** A set of 48 circulating biomarkers were measured in the PROTECT trial which enrolled 2033 patients with AHF. Relationships between baseline levels of biomarkers and outcomes - 30-day all-cause mortality, 30-day death or rehospitalization for renal/cardiovascular causes and 180-day all-cause mortality - were evaluated. Prognostic accuracies of baseline, day 3, 7 and 14 biomarker measurements were estimated and compared utilizing a time-dependent AUC analysis.**Results:** 46 biomarkers were significantly associated with outcomes, but 44 had limited prognostic value (C-index <0.70). However, multimarker models combining biomarkers from different clusters had a much stronger prognostic value. Combining BUN, chloride, IL-6, cTnI, sST-2 and VEGFR-1 to a clinical model yielded a 9% increase in C-index to 0.84 and 0.78 for 30-day and 180-day all-cause mortality, respectively, and net reclassification improvement of 0.90 [0.51-1.12] and 0.68

[0.58-0.86]. Time-dependent AUC analysis showed that the predictive value of most biomarkers reduced over time and late measurements provided superior accuracy for the prediction of all-cause mortality over 180 days.

Conclusion: Multimarker models significantly improve risk prediction. The predictive value of many biomarkers declines over time and subsequent measurements, beyond admission, are needed to maximize the prognostic value of biomarkers.

1208

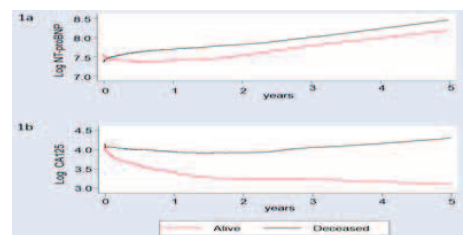
Mortality prediction following an admission for acute heart failure: a longitudinal comparison between N-terminal brain natriuretic peptide and carbohydrate antigen 125Instituto de Salud Carlos III, Red de Investigación Cardiovascular, Programa 7 (RD12/0042/0010), FEDERJ Nunez¹; E Nunez¹; G Minana²; J Sanchis¹; E Santas¹; D Escribano¹; S Garcia-Blas¹; C Bonanad¹; A Mollar¹; FJ Chorro¹
¹Hospital Clinic Universitari, Valencia, Spain; ²Hospital de Manises, cardiology, Valencia, Spain**Purpose:** Baseline values of N-terminal brain natriuretic peptide (NT-proBNP) and carbohydrate antigen 125 (CA125) predict mortality in patients with acute heart failure (AHF). However, information relative to the prognostic effect of their longitudinal trajectories is scarce. We aimed to characterize the NT-proBNP and CA125 trajectories over time and to determine their influence on the risk of all-cause mortality.**Methods:** A cohort of 946 patients attended in a HF-unit after an admission for AHF were included. The number of visits were 3402 (mean per patient 3.6) ranging from 2 to 32. Joint modeling of longitudinal and survival data was used to characterize the relationship of longitudinal measurements of NT-proBNP and CA125 with all-cause mortality.**Results:** At a median follow-up of 2.64 years (range: 0.05-11.20), 409 patients died (43.2%). Patients who died had sustained higher values of both markers all the time. However, for lnNT-proBNP both curves (died and alive) had an ascending trajectory while running in parallel (Figure 1a). A similar ascending trajectory is observed for lnCA125 but only in those who died; whereas those alive had a flat curve (Figure 1b). In multivariate scenario, lnNT-proBNP and lnCA125 longitudinally-updated values were highly predictive of mortality [HR=1.38; 95% CI: 1.16-1.69; $P < 0.001$ and HR=1.34; 95% CI: 1.16-1.58; $P < 0.001$, respectively] after being adjusted by each other and well-established risk factors.**Conclusions:** Following an admission for AHF, the lnNT-proBNP and lnCA125 trajectories were highly predictive of long-term mortality. These results endorse the role of both biomarkers for monitoring the course of the disease.

Figure 1

1209

Prognostic value of acute-on-chronic kidney injury in patients with decompensated heart failureA Klimenko¹; S Villevalde¹; Z Kobalava¹¹Peoples Friendship University of Russia (RPFU), Moscow, Russian Federation**Objective:** Acute kidney injury (AKI) is an independent risk factor for adverse outcomes in acute decompensated heart failure (ADHF), occurs as a consequence of new onset kidney injury (AKI de novo) or acute deterioration of pre-existed chronic kidney disease (CKD) (AKI on CKD). The aim of the study was to determine the prevalence of different variants of AKI in ADHF patients and to evaluate the impact on short-term (30-days mortality) and long-term (6 months rate of ADHF rehospitalizations) outcomes.**Methods:** In 183 patients admitted with ADHF (125 male, 69±9 years (M±SD), arterial hypertension (AH) 87%, ischemic heart disease (IHD) 56%, myocardial infarction (MI) 53%, atrial fibrillation 51%, diabetes mellitus (DM) 36%, known CKD 40%, ejection fraction (EF) 44±15%) the prevalence of different variants of AKI was assessed. AKI was defined using 2012 KDIGO Guidelines. Depending on the presence of known CKD AKI was divided into «AKI de novo» and «AKI on CKD». Mann-Whitney and multiple logistic regression analysis were performed $P < 0.05$ was considered statistically significant.**Results:** 41% of patients developed AKI and in 63% AKI developed among patients with pre-existed CKD. Patients with «AKI on CKD» versus patients «AKI

de novo» had greater duration of CHF (4.2 ± 1.7 vs 2.3 ± 1.5 , $p < 0.01$), higher prevalence of IHD (64 vs 29%, $p < 0.01$), AH (100 vs 71%, $p < 0.01$), MI (53 vs 29%, $p < 0.01$), DM (55 vs 15%, $p < 0.01$), anemia (53 vs 0%, $p < 0.001$), higher rate of prior HF hospitalizations (100 vs 57%, $p < 0.001$). «AKI on CKD» versus «AKI de novo» tended to develop in the later periods of hospitalization (4.2 ± 3.8 vs 3.0 ± 2.3 days, $p > 0.05$), less often was transient (45 vs 71%, $p < 0.01$), had lower risk of 30-days mortality (11 vs 29%, $p < 0.05$) and higher 6 months rate of ADHF rehospitalizations (60 vs 29%, $p < 0.01$).

Conclusions: «AKI on CKD» was more frequent in ADHF patients and developed in 63%. Patients with «AKI on CKD» were at greatest risk of adverse long-term outcomes in ADHF. Development of «AKI on CKD» was not associated with higher risk of 30-days mortality.

1210

Potential to improve drisk stratification by combining heart rate and systolic blood pressure in patients with acute heart failure: findings from the RICA Registry

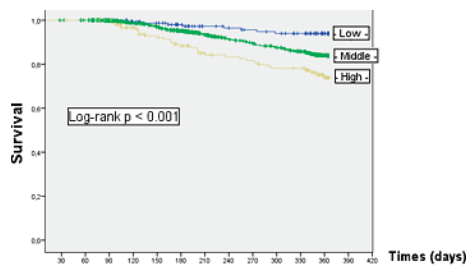
M Montero Perez Barquero¹; J Sanchez Gil¹; L Manzano²; F Formiga³; A Conde Martel⁴; A Muela Molinero⁵; R Quiros Lopez⁶; J Arias Jimenez⁷; P Llacer Iborra⁸; M Flather⁹

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Purpose: Heart rate (HR) and systolic blood pressure (SBP) are independent prognostic variables in heart failure (HF). Combining HR and SBP could be used to assess risk and may be better than using single variables in HF.

Methods and Results: We evaluated 1128 patients 1 month after discharge for acute HF patients (mean age, 82 years, 56% women) in the Spanish RICA Registry. There were 191 deaths (12%) during the median follow-up of 356 days. Using HR strata of <70, 70-80 and >80 bpm we found mortality rates of 9.7, 15.0 and 13.0% respectively (HR for low, medium and high risk were 1.0, 1.48 and 1.27). For SBP <120, 120-140 and >140mmHg, mortality rates were 20.0, 11.0 and 8.1% respectively (HR for low, medium and high risk were 1.0, 1.34 and 2.76). Using combined strata of HR <70 beats/min and SBP \geq 140 mmHg (n=122), HR 70 - 80 and SBP 120 - 140 (n=891) and HR \geq 80 and SBP < 120 (n=115) we found mortality rates of 4.5%, 12.0% and 21.0% respectively (Figure 1 shows Kaplan Meier curves for these strata). Multivariate Cox regression shows that the hazard ratio of all-cause death for low-risk, middle-risk and high-risk groups were 1 (reference), 2.32 (95% CI: 1.13 - 4.77, $p = 0.022$) and 4.45 (95% CI: 2.02 - 9.83, $p < 0.001$). Body mass index, NYHA, MDRD, hypertension and sodium were also independent prognostic factors.

Conclusions: These results suggest that an approach of combining HR and SBP may provide a better tool for risk assessment in HF than using these separately.



Curve Kaplan-Meier to level of mortality

1211

Prognostic impact of serum uric acid in patients with acute heart failure: interaction with renal dysfunction

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Purpose: Many studies evaluated the relationship between Uric Acid (UA) and adverse outcomes in chronic Heart Failure (HF) but the prognostic role of serum UA in acute HF has not been extensively studied. The aims of this study were: 1- to evaluate the impact of elevated serum UA levels on outcome in patients with acute

HF; 2- to investigate the relationship between UA and renal dysfunction, worsening renal function (WRF) and blood urea nitrogen (BUN).

Methods: We measured admission serum UA, B-type Natriuretic Peptide (BNP) and Left Ventricular Ejection fraction (LVEF) in 239 patients affected to acute HF; all patients were submitted to daily BUN and creatinine, measurement to identify in-hospital WRF defined as creatinine increase \geq 0,3 mg/dL. We also evaluated the relationship among admission renal dysfunction (defined as creatinine > 1,2 mg/dL), WRF, elevated serum UA and death or HF rehospitalization during a 6-months follow-up period.

Results: In our population, mean UA levels were $6,4 \pm 2,5$ mg/dL, with 112 patients who showed elevated serum levels of UA (defined as serum UA > 7 mg/dL in male and serum UA > 6 mg/dL in female). UA values were significantly increased in patient with baseline renal dysfunction respect to patients with preserved renal function ($6,8 \pm 2,7$ mg/dL vs $6,1 \pm 2,2$ mg/dL; $p = 0,03$). The same trend was observed in patients with admission BUN levels upper than 50 mg/dL respect to patients with admission BUN lower than 50 mg/dL ($6,7 \pm 2,6$ mg/dL vs $5,9 \pm 1,9$ mg/dL; $p = 0,01$). There were not significant variations of UA levels in patients with systolic dysfunction (LVEF < 50%) respect to patients with preserved ejection fraction. In the same way, UA was not significantly increased in patients who developed WRF and in patients with BNP values upper than 400 pg/mL. Hyperuricaemia was associated with higher risk of death or HF rehospitalization (HR: 1.54, 95% CI 1.04-2.30; $p = 0.03$). After adjustment for potential confounders factors and renal dysfunction, hyperuricaemia remains an independent risk factor for adverse outcome (HR: 1.79, 95% CI 1.19-2.68; $p = 0.005$).

Conclusions: In hospitalized patients with acute HF, elevated serum levels of UA were associated to poor outcome after discharge independently from renal dysfunction, LVEF and BNP. Hyperuricaemia is associated with the presence of renal dysfunction but not with WRF.

1212

Venous total carbon dioxide predicts readmission and death in patients with acute dyspnea at the emergency department

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Purpose: Patients presenting with dyspnea at the emergency department (ED) is a large and heterogeneous group where it can be difficult to assess the severity of the condition. The purpose of this study was to investigate if easily accessible venous blood gas parameters predict one-year risk of readmission or death in patients admitted to the ED due to acute dyspnea.

Methods: We studied 297 patients presenting with acute dyspnea at the ED and followed them for one year regarding incidence of a first readmission or death (readmission/death). In venous blood obtained immediately upon admission to the ED, we measured total carbon dioxide (TCO₂), Base Excess (BE), pH (vpH) and carbon dioxide pressure (vPCO₂). In multivariate Cox proportional hazards models, hazard ratios and 95% confidence intervals (HR, 95% CI) for one-year readmission/death were assessed in patients belonging to the top and bottom quartiles of TCO₂, BE, vpH and vPCO₂ as compared to patients belonging to the two central quartiles (reference).

Results: After adjustment for age, sex, Medical Emergency Triage and Treatment System in Adults (METTS-A) score, respiratory rate (RR) and oxygen saturation (SaO₂) both top (HR 1.576, 95% CI 1.159-2.145; $P = 0.004$) and bottom (HR 1.503, 95% CI 1.063-2.124; $P = 0.021$) quartiles of BE were associated with increased risk of readmission/death, but the strongest predictor was top quartile of TCO₂ (HR 1.831, 95% CI 1.332-2.517; $P < 0.001$). When TCO₂ and BE were entered simultaneously in the model, top quartile of TCO₂ remained significantly related to the risk of readmission/death (HR 1.714, 95% CI 1.127-2.608; $P = 0.012$) whereas BE became non-significant. Neither vPCO₂ nor vpH predicted the endpoint. Prevalence of Chronic Obstructive Pulmonary Disease (COPD) did not explain the association between high TCO₂ and readmission/death.

Conclusions: A high value of TCO₂ appears as an easily accessible marker for one-year readmission or death in patients with acute dyspnea and may thus add clinically important information for risk stratification and follow-up strategies.

1213

Prognostic impact of preexisting hypertension in hospitalized patient with established systolic heart failure: hypertension paradox

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Background: Hypertension is the most common risk factor and co-morbidity of heart failure (HF). However the prognostic value of the hypertension in established heart failure has not been well evaluated. The aim of present study was to investigate the prognostic impact of preexisting hypertension in patients hospitalized with systolic heart failure.

Methods and Results: We performed a pooled analysis of data from three observational studies performed in Korea. We selected the patients, hospitalized with systolic heart failure (Ejection fraction $\leq 45\%$) and ≥ 18 years old. We categorized the enrolled patients into 2 groups by presence of preexisting hypertension history and compared 1 year incidence of all cause mortality between two groups. Total 3538 patients were enrolled. The prevalence of hypertension was 51.6% (n=1825). Patients with hypertension presented more often diabetes (43.9% vs. 23.0%, $P < 0.001$), previous myocardial infarction (18.8% vs. 12.2%, $p < 0.001$), stroke (16.1% vs. 8.2%, $p < 0.001$) and chronic kidney disease (14.1% vs. 5.7%, $p < 0.001$). More HF medications were given to patients with hypertension (ACE inhibitor or ARB: 80.6% vs. 76.4%, $p = 0.002$; beta blocker: 58.4% vs. 49.8%, $p < 0.001$). During 1 year follow-up, patients with and those without hypertension showed similar cumulative incidence of all cause death (8.3% vs. 8.4%, $p = 0.900$). In multivariate conditional backward Cox regression model, the hypertension was associated with lower risk of all cause death (Hazard ratio = 0.712, 95% confidence interval = 0.507-0.999, $p = 0.049$).

Conclusions: In a pooled analysis of 3 observational registries, preexisting hypertension was associated with lower risk of 1 year all cause mortality in systolic heart failure.

1214

The morbidity burden of heart failure in the community

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Purpose: The rapid access clinic for possible heart failure in our University Hospital had provided the primary care physicians access to diagnosis of heart failure in the community and enrollment to disease management programme post heart failure diagnosis. We wish to report the morbidity burden of heart failure patient in the community in which were enrolled in a disease management programme early on the onset of their heart failure diagnosis.

Method: Consecutive patients attending the rapid access clinic for possible heart failure in our University Hospital, from 2002 to 2012 were recruited in this report, including both confirmed heart failure and non-heart failure group. The period of post review follow-up is up to August 2014. The hospital admission details from the tertiary hospital attached to the catchment area for the population were obtained via the hospital records and validated. Primary end points were heart failure admission, non-heart failure cardiovascular admission and non-cardiovascular admission, including elective admission.

Result: 733 patients were included in this study. There are 2581 admissions to hospital, in which 294 (11.4%) were cardiac and 2287 (88.6%) were of non-cardiac cause. Among 287 confirmed heart failure patients (median age 79.4 years, 140 [48.8%] female), 1048 hospitalisations occurred over mean follow-up of 6.4 years. Within 3 years of heart failure diagnosis; 63 (21.9%) and 27 (9.4%) of confirmed heart failure patients had 1 and ≥ 2 all types of cardiovascular admission respectively. 15 (5.2%) and 5 (1.7%) of heart failure patients had 1 and 2 acute decompensated heart failure admissions respectively. 3 (0.7%) of non-heart failure patients had subsequently developed heart failure requiring admission. The Kaplan-Meier curve showed that the heart failure with reduced ejection fraction group had more heart failure and non-heart failure cardiovascular admission compared to other groups.

Conclusion: Heart failure patients in the community still are at risk of hospital admission. Most admission was due to non-cardiac causes, reflecting co-morbidity in heart failure patients. Despite enrollment into disease management programme, a significant proportion of heart patients still had decompensated heart failure admissions. The progression of non-heart failure patients who subsequently developed heart failure provides an insight to the natural history of heart failure in the community and could create opportunity of early intervention in at risk population.

1215

A study on the association between vitamin d and pth levels with new onset heart failure in the general population

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Purpose: To study the association between plasma inactive vitamin D (25(OH)D=25-D), and active vitamin D (1,25(OH)₂D=1,25-D), as well as parathyroid hormone (PTH) with new onset heart failure (HF) in the general population.

Methods: We studied 8137 HF-free individuals, aged 28 to 75 years participating in the Prevention of Renal and Vascular End-stage Disease (PREVEND) cohort in the Netherlands. Plasma 25-D and 1,25-D were determined by liquid chromatography-tandem mass spectrometry. Plasma PTH was measured with immunoassay. HF was adjudicated by an expert panel. Cox proportional hazards regression models were built to study the association between 25-D, 1,25-D, and PTH with new onset HF. Cause-specific hazards analyses were performed to study the association of these biomarkers with HF with reduced ejection fraction (HFrEF; LVEF $\geq 50\%$) and HF with preserved ejection fraction (HFpEF LVEF $\leq 40\%$). Subjects with use of vitamin D analogues and/or non-Caucasian origin were excluded from analysis (n=432).

Results: In total 7825 subjects were included. Mean 25-D level was 59 ± 23 nmol/L, mean 1,25-D level was 145 ± 48 pmol/L, and PTH level was 3.9 ± 1.6 pmol/L. During a median follow-up time of 12.5 years (range, 12.2-12.9), 359 (4.2%) subjects were diagnosed with new onset HF, of which 231 (66%) had HFrEF and 121 (34%) had HFpEF. After correction for age, sex and season of blood withdrawal, we found that each incremental reduction by 1 standard deviation (SD) 25-D and 1,25-D levels significantly increased risk on new onset HF: hazard ratio (HR) 0.80 [95% confidence interval (CI), 0.67-0.959], and HR 0.82 [0.68-0.99], respectively. Each incremental elevation of 1-SD PTH level was associated with increased risk on new onset HF: HR 1.14 [1.01-1.29]. However, adjustment of established risk factors for HF (e.g. smoking, body mass index, hypertension, history of cardiovascular disease) and vitamin D biology (kidney function) to this model strongly attenuated the association: 25-D: HR 0.90 [0.75-1.09]; 1,25-D: HR 0.87 [0.72-1.06]; PTH: HR 1.07 [0.91-1.26]. Furthermore, we found that these biomarkers were unable to distinguish between the different types of heart failure (HFpEF versus HFrEF: 25-D: Pcr = 0.53; 1,25-D: Pcr = 0.38; PTH: Pcr = 0.43).

Conclusion: In this general population study, plasma levels of 25-D, 1,25-D, and PTH were associated with a higher risk for new onset HF when adjusted for age and sex and season, but after full adjustment this was lost. Therefore, screening for vitamin D and PTH levels to identify subjects at risk for HF cannot be advocated.

1216

Disturbances of collagen type 1 metabolism predict long-term mortality in systolic heart failure

Karolinska Institutet research foundations J Lofsjogard¹; H Persson¹; J Diez²; B Lopez²; A Gonzalez²; M Mejhert¹; M Edner³; T Kahan¹

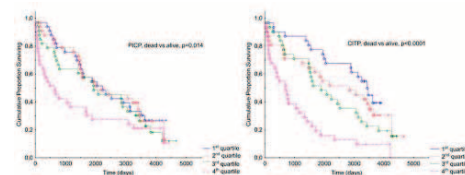
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Purpose: Disturbances of collagen metabolism leading to alterations in the myocardial collagen network may be involved in cardiac remodelling and the prognosis in heart failure (HF). Myocardial collagen I synthesis and degradation can be assessed indirectly by the circulating biomarkers carboxy-terminal propeptide (PICP) and carboxy-terminal telopeptide (CITP), respectively. We examined the associations between PICP and CITP and long-term all-cause and cardiovascular (CV) mortality in HF patients.

Method: The Optimizing congestive heart failure outpatient clinic project (OPTIMAL) studied patients aged >60 years with NYHA class II-IV and left ventricular systolic dysfunction hospitalised with acute HF during 1996-99. Mean age was 75 years, blood pressure 134/80 mm Hg, ejection fraction 34%, BNP 312 pg/ml; 55 % were in atrial fibrillation. Date and cause of death were collected from administrative databases and medical records up to 2008 (inclusive).

Results: Follow-up was 9-13 years in all 132 patients and mean survival time was 5.5 ± 4.0 years. Baseline PICP tended to be higher (84 ± 42 vs 72 ± 29 $\mu\text{g/l}$), CITP was higher (9.1 ± 6.1 vs 5.6 ± 4.2 $\mu\text{g/l}$), and PICP/CITP lower (19 ± 17 vs 12 ± 8 $\mu\text{g/l}$) ($p = 0.102$, < 0.001 , and 0.001 , respectively, log transformed data) in the 101 deceased, compared to the 31 patients alive. When quartiles of PICP, CITP, and PICP/CITP were assessed by Kaplan-Meier analyses, PICP, CITP, and PICP/CITP predicted all-cause ($p = 0.014$, < 0.001 , and 0.131), CV ($p = 0.012$, < 0.001 , and 0.338), and non-CV mortality ($p = 0.400$, 0.003 , and 0.026).

Conclusion: Thus, disturbances of collagen type I metabolism may be involved in cardiac structural and functional remodelling and have prognostic implications in HF. In particular, an increased turnover of collagen type I appears to be related to CV mortality.



Kaplan-Meier curves for PICP and CITP

1217

Lymphopenia is associated with adverse outcomes in children hospitalized with acute heart failure

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Purpose: Lymphopenia is associated with adverse outcomes in adult heart failure (HF) patients, but these data are lacking in children with HF. In patients with advanced heart failure, neurohormonal activation may lead to decreased levels of circulating lymphocytes. We hypothesized that children admitted for acute HF with lymphopenia are at higher risk of death or mechanical circulatory support (MCS).

Methods: Retrospective review was performed for patients hospitalized with acute HF from 2007-2012 at our institution. We required that HF be attributable to ventricular dysfunction and excluded patients admitted for acute graft rejection, HF due to intracardiac shunts, and patients less than 4 months of age. All potential enrollees were adjudicated by a pediatric HF specialist. Lymphopenia was examined by both lymphocyte percentage (%LC) and absolute lymphocyte count (ALC), as both have

been associated with poor outcomes in adults with HF. Given the normal decrease in lymphocyte counts as children age, lymphopenia (both %LC and ALC) was defined by age-specific norms. Multivariate analysis was used to control for anemia and renal failure.

Results: We identified 172 hospital admissions for acute HF in 130 patients. Patient ages ranged from 4 months to 23 years, with a median of 7.5 years. Etiologies of HF included: dilated cardiomyopathy (n=95), restrictive cardiomyopathy (n=14), transplant coronary artery disease (n=12), ischemic cardiomyopathy (n=3), and HF after history of congenital heart disease (n=6). Of 172 hospital admissions, 98 included first hospitalization for HF. Lymphopenia was found during 89 admissions (52%) by ALC and 85 admissions (49%) by %LC. Lymphopenia (by %LC) at time of admission was associated with increased risk of death or MCS (adjusted odds ratio [AOR]=2.58, 95% confidence interval [CI]=1.23-5.38, p=0.012). Lymphopenia at time of admission by ALC did not reach statistical significance (AOR=1.32, 95% CI=0.60-2.95, p=0.483). The presence of lymphopenia before outcome was associated with increased risk of death or MCS by both %LC (AOR=3.01, 95% CI=1.41-6.41, p=0.004) and ALC (AOR=2.33, 95% CI=1.17-4.65, p=0.016).

Conclusions: Lymphopenia occurs commonly in children hospitalized for acute HF and is associated with increased incidence of MCS and in-hospital mortality.

Rapid Fire 5 – Chronic heart failure

Monday 25 May 2015 14:15–15:45

Location: Agora

1279

Estimated lifetime benefit of LCZ696 in heart failure: the PARADIGM-HF trial

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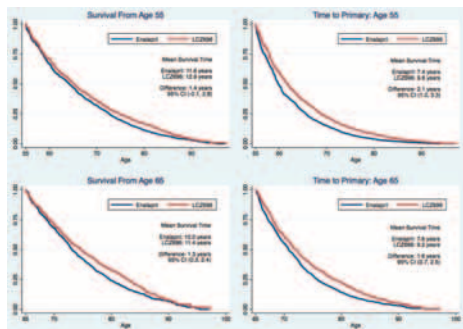
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Background: In PARADIGM-HF, the angiotensin receptor neprilysin inhibitor LCZ696 resulted in a 20% reduction in cardiovascular death or heart failure hospitalization, a 20% reduction in CV death and a 16% reduction in overall mortality relative to enalapril, estimated from Cox proportional hazards models over a median patient follow-up period of 27 months. We utilized a novel life-table analysis to non-parametrically estimate the potential long-term treatment benefits of LCZ696.

Methods: We utilized survival analysis methods using patient age, rather than time from randomization, as the underlying time scale and estimated age-specific event rates across the full range of patient ages for patients in each treatment arm. These were then combined to construct estimated survival curves over the patients' remaining lifetime. This method was validated using long-term data from the SOLVD trial.

Results: LCZ was estimated to produce an increased duration of HF-free survival of 2.1 years (95% CI: 1.0, 3.3), and an increase in overall survival of 1.4 years (95% CI: -0.1, 2.8) for an average 55-year old patient; for an average 65 year old patient, we estimated an increase in HF-free survival of 1.6 years (95% CI: 0.7, 2.5) and an increase in overall survival of 1.3 years (95% CI: 0.3, 2.4). The magnitude of long-term benefits were qualitatively similar across the age spectrum, with smaller effects seen in those >80 years old.

Conclusion: Applying life-table analyses, we estimate that lifetime therapy with LCZ696 would be associated with substantial increase in survival free of heart failure and overall survival.



Figure

1280

Sleep disordered breathing in heart failure: nocturnal desaturation as a novel prognostic marker. A prospective cohort study on 376 patients

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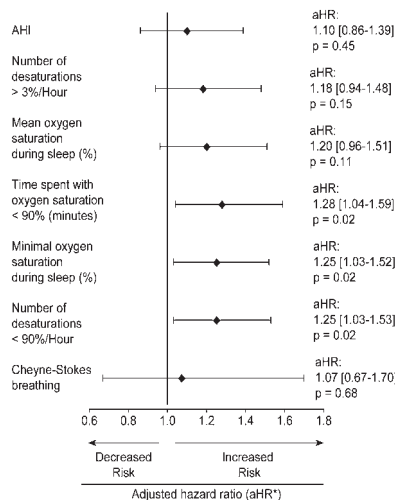
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Sleep disordered breathing (SDB) is common in patients with HF with reduced ejection fraction (HFrEF). Increased apnoea-hypopnoea index (AHI) is predictive of poor outcome. Nocturnal desaturation (ND) is associated with increase in NT-proBNP. Prognostic value of ND in addition to AHI is still unknown.

376 consecutive patients with stable HFrEF were prospectively screened for SDB between 2005 and 2010 by polygraphy. SDB was defined by an AHI ≥ 5 and sleep apnea (SA) by an AHI ≥ 15 . Mean age was 59 ± 13 y, LVEF $30\% \pm 6\%$, and AHI 18 ± 10 ; 310 patients (82%) had SDB. The composite end-point of death, transplantation and LV assistance occurred in 98 patients (26%) within 3y. Minimal oxygen saturation (MOS), number of desaturations <90%/hour and time spent with oxygen saturation <90% were significantly associated with adverse events after adjustment for confounders, whereas AHI was not (Figure). Best MOS cut-off for poor outcome was $\leq 88\%$. Patients with MOS $\leq 88\%$ without SA had similar event rates than those with MOS $\leq 88\%$ with SA. Patients with MOS $\leq 88\%$ had a significantly higher event rate than those with MOS >88% ($p < 0.01$). Risk assessment using MOS of $\leq 88\%$ in top of established prognostic markers of HFrEF yielded a net reclassification index (NRI) of 6%.

In HFrEF, ND $\leq 88\%$ is a stronger predictor of events than AHI, independently of the presence of SA. This suggests that risk assessment in HFrEF should include MOS, and that SDB treatment may also focus on patients without SA presenting ND.



Polygraphy parameters and events at 3y

1281

Effect of baseline ACEI/ARB use on the safety and tolerability of up-titrating LCZ696 over 3 vs. 6 weeks: results from the TITRATION study

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Background: LCZ696 has demonstrated significant clinical benefit vs enalapril for the treatment of systolic heart failure.

Methods: TITRATION assessed the safety/tolerability of up-titrating LCZ696 from 50mg bid to 200mg bid (target dose) over 3- (Condensed) vs. 6-weeks (Conservative) in patients naïve to or receiving varying doses of ACEI/ARB (RASi). Patients were stratified as those receiving low RASi dose (≤ 10 mg enalapril daily, or equivalent) or high dose (> 10 mg enalapril daily, or equivalent) at screening. Primary safety variables were the incidence of pre-specified adverse events (AEs, Table 1) or laboratory values related to these AEs. Secondary objectives included the number of patients achieving LCZ696 200mg bid without down-titration/dose interruption over 12 weeks (defined as treatment success).

Results: Overall, 498/540 (92%) patients enrolled in the run-in were randomized and 429 (86.1%) completed the study. Table 1 summarizes the incidence of pre-specified AEs and the rate of treatment success by RASi stratum. For laboratory values, the incidence of SBP < 95 mmHg was higher in the Condensed/low dose vs. Condensed/high dose RASi (14.3% vs 4.9%, $p = 0.016$). Few patients had serum potassium ≥ 6.0 mmol/L or notable changes in serum creatinine. Rates of primary safety variables for 33 ACEI/ARB-naïve patients were comparable between regimens and to other low dose patients. Only two cases of angioedema were reported, neither of which involved airway compromise. The rate of treatment success in the high dose stratum was similar regardless of regimen ($p = 0.783$) while the corresponding rate for low dose stratum was higher in the Conservative vs. Condensed regimen ($p = 0.030$).

Conclusion: LCZ696 had an acceptable safety profile regardless of up-titration regimen or RASi stratum. Hypotension, hyperkalemia and renal dysfunction were observed more often for the low- vs. high RASi stratum, irrespective of regimen. In the low dose stratum, the rate of treatment success was higher when LCZ696 was up-titrated more gradually.

Table 61075.

Regimen	RASi dose	Hypotension (%)	Renal dysfunction (%)	Hyperkalemia (%)	Angioedema (%)	Treatment success (%) (N=466)
Condensed (3-week)	High (n=120)	4.2	4.2	6.7	0.0	82.6
	Low (n=127)	15.0	10.2	8.7	0.0	73.6
Conservative (6-week)	High (n=127)	5.5	7.1	3.9	0.8	83.8
	Low (n=124)	11.3	8.1	4.8	0.8	84.9

1282

Temporal trends in sudden death in patients with heart failure and reduced ejection fraction: an analysis of the RALES and EMPHASIS-HF trials.

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Purpose - Patients with heart failure with reduced ejection fraction (HF-REF) are at high risk of experiencing sudden death (SD). How this risk has changed over time with the introduction of new therapies has not been described. We assessed the annual rate of SD in each arm of the Randomized Aldactone Evaluation Study (RALES), and the Eplerenone in Mild Patients Hospitalization and Survival Study in Heart Failure (EMPHASIS-HF). Patients enrolled in the different arms of these trials received incrementally greater evidence-based treatment over the period 1995-2010.

Methods: The rates of SD in each arm of each trial were calculated per 100 patient-years. A Cox regression models was used to calculate the hazard of SCD in each trial arm after adjusting for age, sex, ejection fraction (EF) and ischemic etiology.

Results: In RALES and EMPHASIS-HF the mean age was 65 and 69 years respectively ($P < 0.0001$). Patients in RALES were more often female (27%) and had a lower mean EF (25%), compared with those in EMPHASIS-HF (22% and 26%), $P = 0.001$ for difference in sex and $P < 0.0001$ for difference in EF. Patients in RALES were mainly in NYHA class III/IV (71/29%) whereas all patients in EMPHASIS-HF were in NYHA class II, $P < 0.0001$. The proportion with an ischaemic etiology was higher in EMPHASIS-HF (69%), compared with RALES (55%), $P < 0.001$. Rates of SD were lower in the more contemporary EMPHASIS-HF and in the treatment arms receiving most disease-modifying therapies (Figure). After adjustment a similar pattern was observed (Figure).

Conclusions: Rates of SD have fallen over time in patients with HF-REF enrolled in trials, consistent with a cumulative benefit of evidence-based pharmacotherapies on this mode of death.

Trial	Background medication	Treatment group	SD no./no. of patients	Annual rate per 100 patient years (95% CI)	Adjusted hazard ratio (95% CI)	P-value
RALES	ACEI/ARB	placebo	110/861	7.6 (3.3-9.5)	reference	-
RALES	ACEI/ARB	spironolactone	80/802	5.4 (3.4-6.7)	0.71 (0.53,0.94)	0.018
EMPHASIS-HF	ACEI/ARB/ARNI/BBB/BB/CC	placebo	76/737	3.2 (2.3-4.5)	0.40 (0.30,0.54)	<0.001
EMPHASIS-HF	ACEI/ARB/ARNI/BBB/BB/CC	eplerenone	60/784	2.4 (1.9-3.1)	0.30 (0.21,0.44)	<0.001

1283

Effect of comorbidities on outcomes and ivabradine effects in patients with chronic systolic heart failure in the SHIFT trial

The SHIFT study is sponsored by ServierM Bohm¹; JS Borer²; I Ford³; M Lainscak⁴; M Komajda⁵; M Robertson⁶; L Tavazzoli⁷; K Swedberg⁷
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Background: A wide range of cardiovascular (CV) and non-CV concomitant disorders may complicate heart failure (HF), thus increasing morbidity and mortality risk. Despite a high prevalence of comorbidities, there is limited evidence regarding the effects of multiple comorbidities on treatment outcomes in patients with HF. The SHIFT study showed that ivabradine significantly improves major HF outcomes in patients with HF with sinus rhythm, heart rate ≥ 70 bpm receiving guidelines-based

background HF treatment. The current analysis explored the relative impact of multiple comorbidities on outcomes as well as their potential impact on ivabradine's effect in HF patients from the SHIFT trial.

Methods and Results: The most frequent preexisting comorbidities among the 6505 patients (3241 on ivabradine; 3264 on placebo) included history of hypertension (66%), MI (56%), diabetes mellitus (30%), renal dysfunction (estimated GFR < 60 mL/min/1.73 m²; 26%), COPD (11%), anemia (hemoglobin ≤ 11.5 g/dL; 6%), history of stroke (7%), and peripheral artery disease (6%). Only 10% of patients did not have any of these comorbidities, 53% had at least two, and 37% had three and more.

Multimorbidity was associated with higher risk of outcomes: patients with three and more comorbidities had higher rate of HF hospitalization or CV death rate (HR of 1.31, $p = 0.043$), HF hospitalization (1.51, $p = 0.0083$), total hospitalization (1.65, $p < 0.0001$) than patients without co-morbidities. With ivabradine there was a reduction in the primary outcome of cardiovascular death or hospitalization for HF and in other HF-related outcomes in all groups (Table).

Conclusion: Comorbidities increased events in patients with chronic HF, but did not interfere with the effects of ivabradine.

1284

Heart rate reduction during hospitalization and its relation to outcomes of heart failure patients: results from the polish part of the heart failure pilot survey of the european society of cardiology

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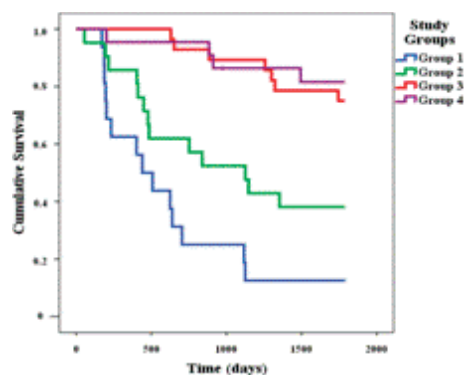
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Purpose: The aim of the study was to evaluate the impact of heart rate HR reduction during hospitalization on one-year outcome in patients (pts) hospitalized for heart failure HF.

Methods: The study included Polish participants of the Heart Failure Pilot Survey of the European Society of Cardiology. Pts with paced heart rhythm and pts with

Table 61338. Treatment effects

	0 comorbidities n=685 Adjusted hazard ratio (95% CI), P-value	1-2 comorbidities n=3442	3+ comorbidities n=2378	P interaction trend; heterogeneity test
Primary end point	0.74 (0.54, 1.01), 0.055	0.81 (0.70, 0.93), 0.0027	0.88 (0.76, 1.02), 0.082	0.31; 0.61
Heart failure hospitalization	0.64 (0.44, 0.94), 0.022	0.72 (0.61, 0.86), 0.0002	0.81 (0.69, 0.96), 0.017	0.30; 0.29
Cardiovascular death	0.76 (0.50, 1.16), 0.20	0.94 (0.78, 1.14), 0.54	0.93 (0.77, 1.14), 0.49	0.47; 0.88
Heart failure mortality	0.75 (0.37, 1.52), 0.42	0.86 (0.60, 1.24), 0.43	0.67 (0.46, 0.98), 0.038	0.73; 0.71
Cardiovascular hospitalization	0.76 (0.57, 1.01), 0.061	0.82 (0.72, 0.93), 0.0022	0.92 (0.81, 1.04), 0.18	0.11; 0.59
Total hospitalizations	0.79 (0.60, 1.04), 0.086	0.87 (0.77, 0.97), 0.013	0.95 (0.85, 1.06), 0.37	0.11; 0.88



paroxysmal or persistent atrial fibrillation (AF) were excluded from the study. Heart rate reduction was defined as any reduction in HR at hospital discharge compared to HR at hospital admission. The primary endpoint was one-year mortality. The secondary endpoint was a composite of all-cause death and hospital readmissions for cardiac causes at 12 months.

Results: A total of 468 pts hospitalized for HF were included in the analysis. During hospitalization, an increase in HR was observed in 104 pts (22.2%), no change in HR - in 93 pts (19.9%), and HR reduction - in 271 pts (57.9%). In the subgroup with HR reduction during hospitalization, medium HR decrease was 16 bpm (IQR: 8-30 bpm). Compared to pts without HR reduction, pts with HR reduction during hospitalization were more often male, and had higher serum creatinine concentration, higher HR at admission (90 [80-110] vs 72 [66-82] bpm; $p < 0.001$) and lower HR at discharge (70 [64-79] vs 80 [70-90] bpm; $p < 0.001$). In the group with HR reduction, we observed a trend towards a less frequent use of beta-blockers before hospital admission (66.1% vs 74.7%; $p = 0.058$) and a more frequent use of beta-blockers at hospital discharge (90.0% vs 84.7%; $p = 0.087$) than in pts without HR reduction. No data on the use of ivabradine were available in the registry. In the whole studied group, prevalence of the primary and the secondary endpoint in pts with HR reduction was similar as in pts without HR reduction (11.8% vs 12.2%; $p = 1.0$; 35.2% vs 36.5%; $p = 0.8$, respectively). Furthermore, no differences in the prevalence of the primary and the secondary endpoints were observed between pts with and without HR reduction in a subgroup of pts with sinus rhythm during index hospitalization nor in a subgroup of pts with permanent AF.

Conclusions: In the population of real-life HF pts, HR reduction achieved during hospitalization seems too modest to improve their prognosis. This might be due to inadequate dosing of beta-blockers and sparse use of other HR-lowering drugs, such as ivabradine in HF pts.

1285

Prognostic role of combined platelet count and neutrophil-to-lymphocyte ratio in predicting outcome in patients with chronic heart failure

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Background: Inflammatory cytokines such as interleukin-6 (IL-6) have been implicated in chronic heart failure (CHF) progression, mediating adverse cardiac remodelling. Neutrophil-to-lymphocyte ratio (NLR) and reactive thrombocytosis are cellular components of systemic inflammation that are regulated by cytokines especially IL-6. In this study, we investigated the prognostic significance of a novel inflammation-based system for CHF, collectively named the CPNR (combination of platelet count and NLR), in predicting outcome in CHF patients.

Methods: A total of 1,557 patients with CHF (mean age 76 ± 11 y, 34% females, 65% IHD; 57% in NYHA III/IV) were recruited as part of the BIOSTAT-CHF Scotland study. Routine laboratory measurements including full blood count was performed at baseline from which NLR and platelet count was determined. The cut-off values of NLR and platelet count were chosen at 3 and 275 respectively so as to maximise model fit, backed up by receiver operating characteristic curve analysis. A patient with both elevated NLR (>3) and platelet count (>275) was allocated a score of 2 (CPNR 2), and a patient shown one or neither was allocated a score of 1 (CPNR 1) or 0 (CPNR 0), respectively. Cox proportional hazard models were used to assess the prognostic impact of CPNR, adjusting for significant covariates.

Results: During a median follow-up period of 1.4 years (IQR 0.6,2.2), there were 23% all-cause deaths, 10% CHF deaths and 12% CVD deaths. Mortality rates (95% CI) were higher in CPNR 2 (all-cause: 251, CHF: 129, & CVD: 116 deaths per 1000 person years) as compared to CPNR 1 (all-cause: 189, CHF: 86, & CVD: 99 deaths per 1000 person years) and CPNR 0 (all-cause: 76, CHF: 28 & CVD: 42 deaths per 1000 person years). A Cox proportional hazard model, adjusted for relevant covariates, showed that CPNR was a significant risk factor for mortality [all-cause, HR=1.5 CI=1.3-1.8; CHF, HR=1.65 CI=1.3-2.2; CVD, HR=1.5 CI=1.2-1.9] and CHF hospitalization (HR=1.3 CI=1.1-1.5).

Conclusion: CPNR is a novel and readily available biomarker of inflammation that could potentially help in risk stratification of CHF patients.

1286

Increase of furosemide dose has detrimental effects on chronic heart failure patients prognosis independently of the change in pulmonary capillary wedge pressure

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Objective: Congestion in chronic heart failure is traditionally treated with diuretics. However, overtime changes of diuretics dosage and intracardiac pressures and their effect on HF outcome has not been systematically investigated

Methods: We retrospectively studied the 1- and 5-year survival of 122 consecutive chronic HF patients (age 53.5 ± 13 years), who underwent two right-sided heart catheterizations (RHC) within a six month interval. The cohort was divided into 4 groups according to the changes in pulmonary capillary wedge pressure (PCWP) and furosemide dose between the two RHCs as follows: Group 1: increase in PCWP/furosemide, Group 2: decrease in PCWP/increase in furosemide, Group 3: decrease in PCWP/ furosemide, Group 4: increase in PCWP/decrease in furosemide.

Results: Patients baseline left ventricular ejection fraction was $29.5 \pm 10.7\%$, New York Heart Association class 2 ± 0.7 , PCWP 17.1 ± 9.1 mmHg and initial daily furosemide dose 130 ± 149 mg. They were followed for 5.1 ± 4 years (total of 622 patient-years). The respective 1- and 5-year survival rates were in Groups 1 (↑PCWP/↑furosemide) 90.5% and 12.5%, in Group 2 (↓ PCWP/↑ furosemide) 89.7%, 3 and 38.1%, in Group 3(↓PCWP/ ↓furosemide) 100% and75.0% and in Group 4 (↑PCWP/↓ furosemide) 96.9% and 81.8% respectively. (Figure) Furosemide increase between the two RHC, showed to have a small tendency but statistically significant to increase the risk of death. (HR: 1.003; 95% CI: 1.002-1.005, $P < 0.001$ for 1-year, and HR: 1.004; 95% CI: 1.003-1.005, $P < 0.001$ for 5-year follow up).

Conclusions: Overtime increase of furosemide dosage poses a significant deleterious effect on mid- and long-term survival of patients with chronic HF reversing the potential salutary effect of intracardiac filling pressures decrease.

1287

Survival benefit of statins in patients with heart failure due to non-ischemic etiology (SUBSTANCE)

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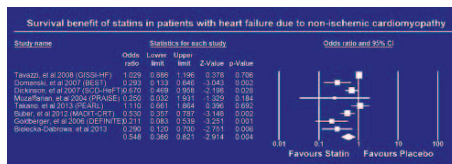
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Purpose: Results from recent randomized placebo-controlled trials on the effects of statins on survival in patients with heart failure (HF) have been conflicting. Furthermore, there is scant data on the subject in patients whose HF is due to non-ischemic etiology, for whom statins are prescribed less frequently. The purpose of this study was to see if statin therapy in patients with heart failure (HF) due to non-ischemic cardiomyopathy leads to an improvement in survival.

Methods: MEDLINE, EMBASE, Scopus, CENTRAL and ClinicalTrials.gov were searched for eligible studies that prospectively randomized patients with HF due to a non-ischemic etiology to statins or placebo and reported survival in both groups, or selectively reported survival data in the non-ischemic cardiomyopathy sub-group of HF patients. Ad-hoc analyses of previously published randomized control trials were also eligible for inclusion. The primary end point was all-cause mortality. Pooling was performed according to the random effect model with summary effect estimates (95% confidence intervals).

Results: Eight studies (7,157 patients) with duration of follow-up ranging from 1.3 years to 5 years were included. Statin therapy was found to significantly improve long-term survival in patients with HF due to non-ischemic etiology {Hazard ratio for mortality 0.55 (0.37-0.82); $p=0.004$; $I^2=13.4\%$ }.

Conclusions: This meta-analysis of randomized controlled trials demonstrated that statins improve survival in patients with HF due to non-ischemic cardiomyopathy.



1288

Adaptive servoventilation (ASV) decreases unplanned hospitalisations in chronic heart failure (CHF) patients with central sleep apnoea (CSA): the french multicentre, prospective FACE cohort study

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Purpose: CSA ± Cheyne-Stokes Respiration (CSR) is common in CHF pts and is associated with a bad prognosis. ASV is more effective than continuous positive airway pressure for treating CSA-CSR and may improve cardiac function and quality of life (QOL) in CHF pts. The FACE study is investigating ASV use over 2 years' follow-up (FU) in CHF pts eligible for this treatment. Baseline characteristics and interim 3-month FU data are presented.

Methods: Pts were included if they had CSA-CSR eligible for ASV therapy, and were divided into 2 groups depending on whether the patient accepted ASV therapy or not (controls). Baseline cardiac function, respiratory/sleep data, Epworth Sleepiness Scale (ESS) score and QOL (Minnesota Living with HF questionnaire) were assessed. Combined primary endpoints are all-cause or cardiovascular-related death, and all-cause unplanned hospitalisation or hospitalisation for worsening HF. Secondary endpoints were individual assessment of each of the above outcomes.

Results: 311 CHF pts with CSA-CSR have been enrolled. Baseline characteristics were: age 70.1 ± 11.4 y, 87% male, body mass index 28.0 ± 5.2 kg/m² (32% obese), ischaemic aetiology 53%. Left ventricular ejection fraction (LVEF) was normal, moderately or severely reduced in 31%, 52% and 17% of pts, respectively. 69% had predominantly CSA, and 31% had coexisting CSA and obstructive apnoea. Mean apnoea-hypopnoea index (AHI) was 42.7 ± 17.4 /h and 78% of pts had severe sleep apnoea (AHI >30/h). ESS score was 7.5 ± 5.0 (75% had no sleepiness). Major comorbidities were hypertension (73%), dyslipidaemia (59%), atrial fibrillation (43%), diabetes (37%) or cerebrovascular event (29%); 9% and 46% of pts, respectively, had severe or moderate renal failure (RF). Drug treatment included β -blockers (72%), ACE inhibitors (56%), diuretics (72%), angiotensin II receptor blockers (24%) and aldosterone antagonists (28%); non-drug therapy was a cardiac resynchronisation device (12%) or implantable cardioverter defibrillator (17%). 71% of pts agreed to receive ASV treatment. Patients agreeing to ASV had a higher AHI and more severe RF. At 3-month FU, AHI was 6 ± 7 /h in the ASV group vs 27 ± 16 /h in controls ($p < 0.001$). Mean ASV use was 5.5 h/night. Only 5% of pts stopped ASV

therapy prematurely. Three-month event rates for all primary endpoints were similar in both groups. All-cause unplanned hospitalisation rate was lower in the ASV group compared with the control group (15% vs 32%, $p=0.014$).

Discussion: Although CHF patients with CSA have severe multiple cardio-metabolic comorbidities, ASV treatment appears to improve health status at 3 months.

1289

Circulating neuregulin in HFpEF and HFrEF

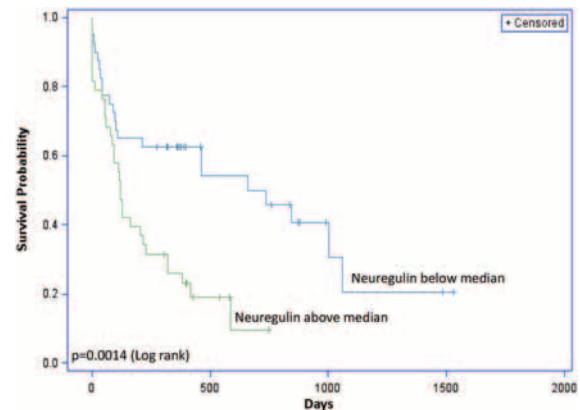
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Purpose: Heart failure (HF) with reduced ejection fraction (HFrEF) is associated with alteration of the neuregulin/ ErbB signaling system. The circulating peptide plasma neuregulin-1 β is increased in HFrEF, associated with worse functional status and poor outcome. We hypothesized that neuregulin-1 β is elevated and associated with worse prognosis also in HF with preserved ejection fraction (HFpEF), and that left ventricular assist device (LVAD) therapy and heart transplantation (HTx) in HFrEF are associated with lower levels. **Materials and Methods:** We measured neuregulin-1 β in patients with HFpEF (n=86) and advanced HFrEF (n=78), one year post-treatment with either left ventricular assist device (LVAD; n=21) and/or post-heart transplantation (HTx; n=28) and the correlation with functional status. We assessed the prognostic role of neuregulin-1 β with Kaplan-Meier analysis.

Results: In HFpEF neuregulin-1 β was median (interquartile range) 6.5 (2.2-11.3) nmol/L, in HFrEF 3.6 (2.1-7.6) nmol/L ($p=0.09$), after LVAD 1.4 (0.8-43.5) nmol/L and after HTx 2.2 (1.4-3.6) pmol/L (overall $p=0.0008$). After intervention (HTx/LVAD) neuregulin-1 β was lower compared to HFrEF (0.002). In HFrEF neuregulin-1 β correlated with NYHA class ($r=0.26$; $p=0.02$) and in HFpEF with hemoglobin ($r=0.26$; $p=0.01$). In HFrEF neuregulin-1 β above median was a prognostic predictor (Figure 1; $p=0.0014$ log rank) but not in HFpEF ($p=0.308$ log rank).

Conclusion: This study confirms that neuregulin-1 β is correlated to NYHA class and is a predictor of outcome in HFrEF. Interestingly, levels of neuregulin-1 β in HFrEF do not differ from levels in HFpEF, and are significantly lower after Htx and LVAD.



Neuregulin-1 β above and below median.

1290

Effects of up-titration of the beta-blocker dose on glomerular filtration rate in chronic heart failure

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Introduction: Beta blockers (BB) improve survival in patients with chronic heart failure (CHF) however they are frequently underdosed, especially in the elderly. Alpha-1- and beta-2-adrenergic receptors in the kidney mediate vasoconstriction, renin secretion and vasodilatation. Blockade of beta-receptors may therefore be expected to influence renal blood flow and possibly glomerular filtration rate (GFR) by intrarenal effects as well as by reducing cardiac output and blood pressure. Beta-blockers differ in the degree to which they block beta-2-receptors (cardioselectivity), so it would be expected that they have different effects on renal function. The acute administration of BB usually results in a reduction in effective renal plasma flow and GFR.

Objectives: The aim of our study was to determine whether non- or cardioselective BB (carvedilol and bisoprolol) cause significant decline in GFR during the dose up-titration in CHF.

Methods: We included patients from the CIBIS ELD study: 297 patients from Germany (age 74 years, 46% male, 37% with systolic CHF) and 579 from Southeastern Europe (age 72 years, 71% male, 89% with systolic CHF). Prior to randomization participants had to clinically stable and be beta-blocker naive or on < or =25% of the guideline-recommended target or equivalent dose. We then up-titrated the beta blocker - either bisoprolol or carvedilol -up to maximum tolerated dose over three months. At the beginning and at the end of the study the estimated glomerular filtration rate (eGFR) was calculated using Cockcroft-Gault formula, and left ventricular ejection fraction (LVEF) was determined using Simpson's biplane method.

Results: The paired sample T-test showed that mean eGFR was insignificantly lower at the end of the study (66.08 ± 36.84 vs. 64.57 ± 30.37 mL/min; p = 0.288), while LVEF significantly increased at the end of the study (41.69 ± 13.49 vs. 44.55 ± 12.72; p < 0.001). In bisoprolol group results were similar (eGFR: 66.30 ± 24.01 vs. 66.80 ± 37.56 mL/min, p = 0.779; LVEF: 42.04 ± 13.37 vs. 45.23 ± 12.71, p < 0.001) with those in carvedilol group (eGFR: 65.86 ± 46.00 vs. 62.42 ± 21.06 mL/min, p = 0.115; LVEF 41.35 ± 13.25 vs. 43.88 ± 12.72, p < 0.001).

Conclusion: Up-titration of BB (non- or cardioselective) in the elderly CHF patients with mildly reduced renal function significantly increased LVEF but did not decrease GFR. Cardioselectivity of BB, beside age and pre-existing renal impairment should not withheld adequate BB dosing in CHF.

1291

European experience with baroreflex activation therapy (BAT) in heart failure with reduced ejection fraction

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Purpose: Large-scale trials of autonomic modulation therapies including spinal cord and vagal nerve stimulation have failed to demonstrate benefit in patients with heart failure and reduced ejection fraction (HFrEF). Conversely, a first-in-man study of baroreflex activation therapy (BAT) in HFrEF demonstrated reduced sympathetic tone and hospital resource utilization. Also improved were ejection fraction (EF), 6-minute hall walk distance (6MHWd), NYHA Class and quality of life (QOL) as assessed by the Minnesota Living with Heart Failure questionnaire. The purpose of this report is to ascertain if benefits of BAT can be repeated in a multicenter European population.

Methods: European patients enrolled in one of two phases of the BAT in HFrEF program, either an open-label evaluation or a global trial in which patients were randomized 1:1 to medical management (MM) or BAT+MM. Major inclusion criteria comprised NYHA Class III, EF ≤ 40%, 6MHWd of 150-450 m and stable MM for ≥ 4 weeks before baseline assessment. A blinded core laboratory analyzed echocardiograms. Treatment effect was defined as the 6-month change with p < 0.05 as the threshold for statistical significance.

Results: 57 patients were enrolled at centers in Germany, Italy and France from April 2012 to April 2014. Unlike typical HFrEF device trials, medical history indicated atrial fibrillation and resynchronization therapy for 39% and 19% of patients, respectively. NYHA Class, QOL, 6MHWd improved significantly, HF medications and renal function were stable (table). System safety profile was similar to a pacemaker.

Conclusions: BAT improves clinical presentation and biomarker status of a diverse group of European HFrEF patients over 6 months. First-in-man results were successfully translated to centers throughout the continent.

	Baseline	Δ6 Months	N available
NYHA Class	3.0 ± 0.0	-0.9 ± 0.1§	50
Quality of Life	44.1 ± 22.1	-14.4 ± 3.1§	49
6MHWd (m)	301.2 ± 81.2	+85.2 ± 15.2§	43
No. HF Medications	5.2 ± 1.7	+0.1 ± 0.1	50
eGFR (mL/min/1.73m ²)	60.1 ± 24.2	+1.5 ± 2.4	36

Baseline: Mean ± SD. Change: Mean ± SE. §p ≤ 0.001

1292

The predictive role of different phenotypes of circulating microparticles in patients with chronic heart failure

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Background: Chronic heart failure (CHF) remains a leading cause of cardiovascular morbidity and mortality. Although the endothelium is considered an important target for traditional risk factors and endothelial dysfunction remained independently associated with mortality from CHF, the innate molecular mechanisms affected forming of endothelial dysfunction are being became not fully clear. Endothelial dysfunction is suggested an early event in the development and progression of CHF.

The study aim was to evaluate whether circulating microparticles with apoptotic or none-apoptotic phenotypes are useful for risk assessment of three-year cumulative fatal and non-fatal cardiovascular events in CHF patients.

Methods: It was studied prospectively the incidence of fatal and non-fatal cardiovascular events, as well as the frequency of occurrence of death from any cause in a cohort of 388 patients with CHF during 3 years of observation. Circulating levels of NT-pro brain natriuretic peptide (NT-pro-BNP), high-sensitivity C-reactive protein (hs-CRP), endothelial apoptotic microparticles (EMPs) were measured at baseline.

Results: Median follow-up was of 2.32 years (IQR=1.8-3.1). During follow-up, 110 cardiovascular events (including 43 fatal cases) were determined. Additionally, 74 subjects were hospitalized repetitively due to worsening CHF and also 16 subjects were readmitted in the hospital due to other cardiovascular reasons. In the univariate logistic regression analysis, the main factors independently related with cumulative end-points were creatinine, fasting glucose, HbA1c, total cholesterol, uric acid various types of EPMs, NT-pro-BNP, hs-CRP, NYHA class, decreased left ventricular ejection fraction (LVEF) less 45%, and type 2 diabetes mellitus. In multivariate model NYHA class, decreased LVEF (less 45%), NT-pro-BNP, hs-CRP, CD144+/CD31+/annexin V+ EMPs, and CD31+/annexin V+ EMPs remained statistically significant for cumulative end-point. Adding of CD144+/CD31+/annexin V+ EMPs and CD31+/annexin V+ EMPs to the standard ABC model may improve the relative IDI for cumulative end-point by 11.4% and 10.5% respectively.

Conclusion: Apoptotic phenotype of circulating microparticles may relate three-year combined clinical outcomes in CHF patients. Finally, identification of the pattern of circulating EMPs may help to determine patients at high risk and reclassify it for possible biomarker-guided therapy of CHF.

1293

Hyporesponsiveness to darbepoetin alfa in patients with heart failure and anemia in the RED-HF study: clinical and prognostic associations

RED-HF Trial was sponsored by Amgen D J Dirk Van Veldhuisen¹; MA Pfeffer²; P Van Der Meer¹; K Olson³; SD Solomon²

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Background: A poor initial hematopoietic response to erythropoietin stimulating agents such as Darbepoetin alfa (DA) has been associated with poor outcome in patients with anemia and chronic kidney disease and diabetes, but this has not been examined in heart failure.

Methods: We examined the relationship between the initial haemoglobin (Hb) response to DA after 4 weeks, and outcome, in 1136 patients with systolic heart failure and mild to moderate anemia (Hb level 9.0-12.0 g/dl) who were enrolled in the Reduction of Events by Darbepoetin alfa in Heart Failure (RED-HF) trial. Patients in the DA group received a starting dose of 0.75 mg/kg body weight once every 2 weeks until a Hb level of 13.0 g/dl was reached. Thereafter, patients received monthly injections, and the dose was adjusted. Patients in the lowest quartile of Hb change after 4 weeks were operationally considered to have a poor response. Primary outcome was a composite of all-cause death and heart failure hospitalization during a follow-up of 28 months.

Results: Patients with a poor initial Hb response (median -0.25 g/dl; n=252) were remarkably similar regarding clinical and laboratory variables to those with a better Hb response (median +1.00 g/dl; n=756). Patients with a poor initial response had lower Hb levels at week 12 (11.9 vs 12.8 g/dl), although they had received higher DA doses (both p < 0.001). Regarding outcome, patients with a poor initial Hb response had a higher rate of the composite primary endpoint (Hazard ratio [HR] 1.27; 95% CI 1.04-1.55) and a higher all-cause mortality (HR 1.29; 95% CI 1.04-1.61).

Conclusion: A poor initial Hb response to DA is associated with an adverse outcome in heart failure patients with anemia, which confirms findings in patients with chronic kidney disease and diabetes, who have anemia.

1294

Cheyne-stokes respiration occurring both at night-and daytime in patients with systolic heart failure holds an additive prognostic value

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Purpose: Cheyne-Stokes respiration (CSR) characterized by periodic central apnea/hyperpneas has been described both during night- and daytime in heart failure (HF) patients, but their relative contribution to prognosis, when simultaneously assessed, has not yet been established.

Methods: 525 consecutive HF patients were recruited (aged 66 ± 12 , 77% males; 34% NYHA class III-IV, left ventricular ejection fraction, LVEF: $33 \pm 9\%$, mean \pm SD) on guideline recommended medical therapy. All patients underwent neurohormonal evaluation, cardiorespiratory and ECG monitoring, cardiopulmonary exercise testing (CPET) and 24-hour continuous polygraphic recording of ECG and respiratory activity (nasal flow plus chest and abdomen respirograms) and were followed-up (median 33 months; interquartile range 16-54), using cardiac mortality

or appropriate implantable cardioverter-defibrillator (ICD) shocks as composite endpoint.

Results: Three groups were identified according to severity and time of occurrence of CSR (40%: no CSR; 32%: nighttime CSR, with apnea/hypopnea index -AHI- >15 events/h, 26 ± 10 , mean \pm SD); 28%: CSR with AHI >15 both at night- and daytime, nighttime AHI 38 ± 13 , daytime AHI 26 ± 11 , mean \pm SD). Patients with combined CSR were ($p < 0.01$) older, male, more symptomatic; they showed more frequently atrial fibrillation, non-sustained ventricular arrhythmias at Holter recordings, severe diastolic and systolic dysfunction, higher plasma level of N-terminal fragment of proBNP and norepinephrine, higher VE/VCO₂ at CPET. Eighty events occurred at follow-up (69 cardiac deaths, 21 ICD shocks); at Kaplan-Meier analysis, patients with night-/daytime CSR showed a worse prognosis (log rank 12.1, $p = 0.002$ vs. those with no or only nocturnal CSR)

Conclusions: CSR occurring throughout the 24-hour period is associated with greater neurohormonal activation, increased arrhythmic burden and worse prognosis. Diagnosis, risk stratification and therapeutic approaches should consider also daytime CSR in patients with systolic HF.

Moderated Poster Session 6 – Advanced heart failure

Monday 25 May 2015 15:45–16:30

Location: Poster Area

1295

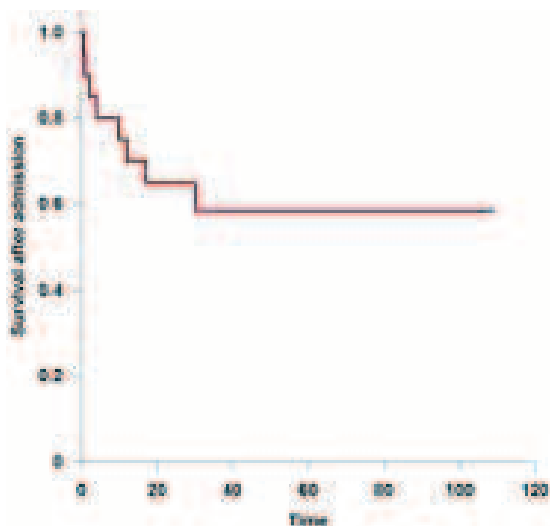
Effectiveness of extracorporeal life support for patients with cardiogenic shock due to intractable arrhythmic stormS Le Pennec-Prigent¹; RP Raphael Martins¹; C Chabanne¹; B Lelong¹; JC Daubert¹; C Leclercq¹; P Mabo¹; E Flecher¹¹University Hospital of Rennes - Hospital Pontchaillou, Department of Cardiology and Vascular Disease, Rennes, France

Purpose: Extracorporeal life support (ECLS) provides mechanical cardiopulmonary support and has been used for intractable heart failure as a bridge to heart transplantation or to recovery. Intractable arrhythmic storm is associated with high mortality. Little is known about the effectiveness of ECLS to treat refractory ventricular arrhythmias responsible for cardiogenic shock in patients non eligible for an urgent ablation.

Methods: Patients with intractable refractory ventricular arrhythmias and cardiogenic shock despite optimal medical therapy, and treated by ECLS implantation were retrospectively included. Patients' characteristics and outcome were analyzed.

Results: 20 patients (53 ± 10 yo) were included. The underlying etiology to the refractory ventricular storm was ischemic cardiomyopathy (75%), short coupled Torsades de Pointes (10%), dilated cardiomyopathy (5%), myocarditis (5%) or unknown (5%). Mean LVEF was 33 ± 17%. An average of 2.3 ± 1.2 anti-arrhythmic drugs was tried before implantation. Arrhythmic storm stopped after a median time of 15 min after ECLS implantation. 8 patients (40%) eventually died, none of them because of a complication of ECLS implantation. The remaining 12 patients (60%) had ECLS withdrawn after a median time of 5.3 days, and were discharged after a median time of 29 days after admission (survival curve in the figure).

Conclusions: This is the largest database of patients temporary implanted with ECLS for refractory ventricular arrhythmia responsible for cardiogenic shock and non eligible for ablation. It provides efficient hemodynamic support to these critically ill patients, and survival rate after the implantation is 60%.



Survival curve after ECLS implantation

1296

Infarct-related cardiogenic shock - comparison of percutaneous left ventricular assist devices versus intra-aortic balloon counterpulsationT Tobias Loehn¹; T Schweigler¹; S Kolschmann¹; S Wenning¹; S Quick¹; A Youssef¹; C Pfluecke¹; M Guenther¹; R Strasser¹; K Ibrahim¹¹Dresden University of Technology, Heart Center Dresden, Dresden, Germany

Purpose: The leading cause of death in patients with acute myocardial infarction (AMI) is cardiogenic shock (CS) although early reperfusion strategies. But even after the initial hemodynamic stabilization many patients suffer from secondary complications like systemic inflammatory response syndrome (SIRS) and a multi-organ dysfunction syndrome (MODS).

Only small studies compared percutaneous left ventricular assist devices (pLVAD) with intraaortic balloon counterpulsation (IABP) in CS, showing better hemodynamic support with pLVAD. The Impella CP is a new pLVAD system, which provides sufficient hemodynamic support in patients suffering from CS.

In the present study, we sought to evaluate the current use of the Impella CP in patients with CS complicating an AMI compared to the use of IABP.

Methods: The Dresden Shock Registry (DSR) of the University Heart Center Dresden is an ongoing monocentric registry, which includes patients with cardiogenic shock and implanted assist devices such as pLVAD and IABP. Actually, a total of 56 patients are included, whereas 42 patients were identified with infarct-related cardiogenic shock, with 16 patients supported by an Impella CP device and 26 patients by an IABP. All patients received revascularization by percutaneous coronary intervention with implantation of a coronary stent. By means of the registry, the intrahospital and 30-day-mortality, rates of MODS, the use of catecholamines, the course of hemodynamic and laboratory parameters etc. as well as complications were recorded.

Results: One hour after admission the mean arterial pressure was significantly higher in the pLVAD group compared to the IABP group (74 ± 7,6mmHg vs. 57,13 ± 10,8 mmHg, p=0,012) with a simultaneous reduction of administered norepinephrine within 24h (pLVAD: 0,38 ± 0,18 µg/kg/min to 0,17 ± 0,13µg/kg/min, p=0,034; IABP: 0,41 ± 0,17 µg/kg/min to 0,44 ± 0,38µg/kg/min, ns). The elevated serum lactate levels at admission in both groups could be lowered much more effectively in the pLVAD group compared to the IABP group (pLVAD: 7,5 ± 5,28mmol/l to 1,92 ± 1,05mmol/l; IABP: 7,56 ± 3,07 mmol/l to 5,29 ± 3,02 mmol/l, p=0,04). Intrahospital mortality rates did not differ significantly between both groups at that time.

Conclusions: The implantation of a pLVAD compared to IABP in infarct-related cardiogenic shock leads to improved hemodynamic stabilization with concomitant reduction of catecholamine doses and an increased serum lactate clearance as a sign for improved microcirculation. If intrahospital and long-term mortality could be improved has to be addressed in larger cohorts.

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Adaptive servoventilation therapy for cheyne-stokes respiration in chronic heart failure: time course of apnoea-hypopnoea index and NT-proBNP concentrationO Oldenburg¹; B Wellmann¹; T Bitter¹; H Fox¹; A Tueroff¹; J Spiesshoefer¹; D Horstkotte¹¹Department of Cardiology, Heart and Diabetes Centre North Rhine-Westphalia, Ruhr University Bochum, Bad Oeynhausen, Germany

Purpose: Cheyne-Stokes respiration (CSR) represents a highly prevalent co-morbidity in heart failure (HF) patients and is associated with impaired prognosis. Adaptive servoventilation (ASV) therapy represents the gold standard to treat this special type of sleep-disordered breathing. Purpose of the present study was to prospectively monitor changes in the severity of CSR (apnoea-hypopnoea index, AHI) and HF (NT-proBNP) with long-term ASV treatment.

Methods: Patients with chronic stable HF due to reduced left ventricular ejection fraction (HF-REF; NYHA 2, LVEF ≤ 45%) and moderate to severe CSR (apnoea-hypopnoea-index, AHI ≥ 15/h) were prospectively enrolled in our local

ASV registry (NCT01657188) and follow-ups were scheduled at 3, 6, and 12 months after therapy initiation.

Results: So far a total of 231 patients were enrolled (67.4±10.6 years; BMI 28.4±4.7; NYHA 2.6±0.5). CSR was immediately and effectively treated by ASV and NT-proBNP concentrations, as a surrogate for HF severity, improved during follow-up (table; *p < 0.05).

Conclusion: ASV is able to immediately treat CSR with a sustained effect. Long-term ASV therapy leads to an improvement in NT-proBNP concentrations, a surrogate for cardiac function.

	Baseline	1st night on ASV	3 months ASV	6 months ASV	12 months ASV
AHI (/h)	37.6±13.5	7.9±8.4*	7.5±10.5*	6.71±8.8*	6.99±7.9*
NT-proBNP (pg/ml)	3350±7856	N/D	2741±7672	2613±7941	1987±2717*

1298

Carvedilol compared to metoprolol succinate in the treatment and prognosis of patients with stable chronic heart failure. The Carvedilol or Metoprolol Evaluation Study (COMES)

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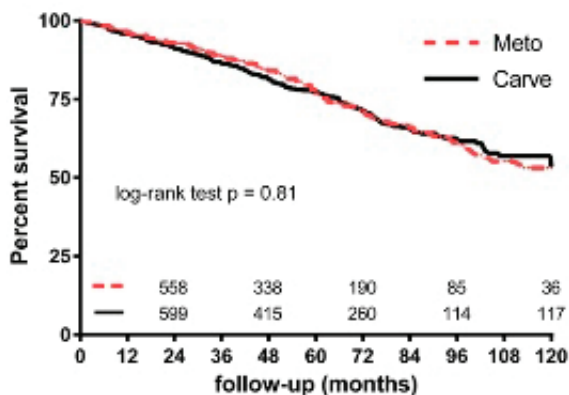
¹University Hospital of Heidelberg, Heidelberg, Germany; ²Innlandet Hospital, Lillehammer, Norway; ³Norwegian University of Science and Technology, Trondheim, Norway; ⁴Oslo University Hospital, Oslo, Norway

Purpose: Beta blockers exert a prognostic benefit in chronic heart failure (CHF). Their pharmacological properties vary. The only substantial comparative trial to date - COMET (carvedilol vs. metoprolol) - was criticized for methodical reasons. We addressed the relative efficacy of equal doses of carvedilol and metoprolol succinate on survival in multi-centre hospital CHF outpatients.

Methods: 4,016 Patients with stable systolic CHF using either carvedilol or metoprolol succinate were identified in two European heart failure registries. Patients were individually matched on both dose-equivalent and the respective propensity scores for beta blocker treatment.

Results: During a follow-up of 17,672 patient-years, 304 (27.2%) patients died in the carvedilol group and 1,066 (36.8%) in the metoprolol group. In univariable analysis of the general sample, metoprolol therapy was associated with increased mortality compared with carvedilol (HR 1.49; 95% CI 1.31-1.69; p < 0.001). However, in multivariable (HR 0.93; 95% CI 0.57-1.50; p = 0.75) and propensity score adjusted (HR 1.17; 95% CI 1.00-1.37; p = 0.06) models as well as in the propensity matched sample (HR 1.00; 95% CI 0.82-1.23; p = 0.99), this difference did not persist. These results were essentially unchanged for all pre-specified subgroups with respect to age, sex, aetiology, NYHA class, left ventricular ejection fraction, renal function, chronic obstructive pulmonary disease, diabetes, heart rate, and rhythm.

Conclusions: In CHF hospital outpatients, no conclusive association was observed in all-cause mortality between the treatment with carvedilol and metoprolol succinate.



Kaplan-Meier curve (matched cohort)

1299

The detrimental effect of excessive afterload reduction on the survival of patients with heart failure complicated by pulmonary hypertension

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Purpose: It has been demonstrated that in patients with pulmonary hypertension (PH), the right coronary artery flow and pattern is impaired due to changes in right ventricle (RV) pressures. The present study investigates the prognostic implications of changes in RV myocardial perfusion pressure due reduction of systemic pressure as a measure of afterload, in patients with chronic left heart failure (LHF) complicated by PH.

Methods and Results: Of 393 patients with chronic LHF who underwent right heart catheterization, 264 presented with PH. Myocardial perfusion pressure was defined as the gradient between the aortic pressure and the RV intra-cavitary pressure, in systole (SPP), and diastole (DPP).

The SPP was 87.3±32 mmHg in the PH group as compared to 107.1±24.8 in the no-PH group (p=0001). The DPP was similar in both groups, 62.9±17.2 vs 62.9±12.9 mmHg, respectively (p=0.97). During the follow-up (median 33.9 months), no difference in the mortality event rate according to SPP quartiles was observed (p=0.33). An analysis of the DPP as continuous variable, detected a threshold of 60 mmHg below which there is a progressive increase of the unadjusted probability of death, and confirmed by the DPP quartile analysis, with the death rate in the two lower quartiles being significantly increased, 37.4% and 28.6%, as compared with 16.5% and 17.6% in the higher quartiles (p=0.002). In a multivariate analysis, the adjusted hazard ratio (HR) for all-cause mortality was 3.27 (95% Confidence Interval (CI) 1.31-8.18, p=0.01), 2.76 (95% CI 1.10-6.86, p=0.029) and 0.81 (95% CI 0.42-1.56, p=0.53) for the first, second and third DPP quartile, respectively, as compared with the highest quartile. Nested models including both DPP and SPP had not demonstrated better data fitting.

Conclusion: The results of our study suggest that the diastolic, and not systolic, RV myocardial perfusion pressure is a strong predictor for all-cause mortality in patients with chronic LHF and PH. An excessive reduction of this pressure gradient by systemic pressure lowering may have detrimental effect on the outcome.

1300

C34T AMP deaminase 1 gene polymorphism is associated with permanent atrial fibrillation in patients with chronic heart failure

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Background: AMP deaminase (AMPD)-1 accounts for 30% of nucleotide catabolism in the heart and regulates the energetic metabolism in cardiomyocytes. The common C34T variant in the AMPD-1 gene induces a truncated protein (Glu12Stop), and a decrease in AMP catabolism, with adenosine accumulation and a potential to disrupt the energy equilibrium in cardiomyocytes. Adenosine (through action potential shortening) and impaired energetics are potential promoters of atrial fibrillation (AF).

Objectives: In patients with chronic heart failure (CHF), we assessed the association between the C34T variant and the presence of permanent AF (perm-AF).

Methods: We included 197 patients with CHF. Blood was withdrawn upon HF stabilization and the C34T variant determined by direct gene sequencing. Chi-squared and t-test were used to assess differences between patients with and without perm-AF. The independent association between perm-AF and C34T was assessed by binary logistic regression analysis adjusted for pertinent variables.

Results: Of the 197 patients (61% men, mean age 69±10), 72.6% had hypertension, 51% diabetes and 56% were prior/current smokers. CHF was of ischemic origin in 49%. Left-ventricular ejection fraction (EF) was 37.8±16% and mean NYHA functional class 2.5±0.8. Eighty-four percent of patients were treated with ACEI/RAA and 85% with betablockers. Thirty-one patients (15.7%) had perm-AF. The C34T variant was present in 54 patients (27.4%). Patients with and without perm-AF did not differ except for a greater prevalence of ischemic etiology and higher tobacco use in patients without perm-AF. The prevalence of C34T was significantly higher in patients with perm-AF (45.2% vs 24.1% in no perm-AF patients, p=0.016). Multivariable logistic regression analysis adjusting for age, sex, EF, treatment and classical factors associated with a worse outcome in CHF and AF confirmed that age (HR 1.05 [1.01-1.10]) and C34T (HR 2.62 [1.14-6.02]) were the only variables independently associated with perm-AF.

Conclusions: C34T variant in AMPD1 was independently associated with the presence of perm-AF in a population of HF-patients. Impaired cardiomyocyte energetics and adenosine accumulation could be involved in AF promotion in patients with the C34T variant.

1301

Ventricular arrhythmias in patients supported with ventricular assist devices and the role of implantable cardioverter defibrillators

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Purpose: Ventricular assist device (VAD) use is a justifiable strategy for patients with end-stage heart failure (HF) as bridges to transplantation (BTT), as temporary support to allow myocardial recovery and as destination therapy for transplant ineligible patients. Complications remain common for those patients and the optimal use of other pharmacological and non-pharmacological therapies remains uncertain. Ventricular tachyarrhythmia (VA) events while on VAD support, range from 22-52% while the majority of events seem to occur in the early post-operative period, after implantation. Implantable cardioverter-defibrillators (ICDs) are known to improve survival in patients with both ischemic and non-ischemic HF etiologies by reducing the incidence of sudden cardiac death. Given the possible survival benefit of ICDs in VAD-supported HF patients, we sought to confirm the efficacy of ICDs in a large transplant referral center of VAD-supported HF patients to improve clinical outcomes in this patient population that will surely expand in the coming years.

Methods: We reviewed data for consecutive adult HF patients receiving VAD as a bridge to transplantation from 2003 to 2013. The primary outcome was survival to transplantation.

Results: A total of 97 VADs were implanted [34 left ventricular (LVAD), 63 biventricular (BIVAD), mean age 40 ± 12 years, 90% male, left ventricular ejection fraction 18 ± 9%, 74% dilated cardiomyopathy]. Mean length of support was 740 days (range 30-1460); 53 patients survived to transplantation. Sixty patients had an ICD (22 LVAD, 38 BIVAD). More LVAD patients had an appropriate ICD shock before implantation than after (16 vs 7; P = .02). There was a trend toward higher shock frequency before LVAD implant than after (3.3 ± 5.2 vs 1.1 ± 3.8 shocks/y; P = .06). Mean time to first shock after VAD implant was 129 ± 109 days. LVAD-supported patients with an ICD were significantly more likely to survive to transplantation [1-y actuarial survival to transplantation: LVAD: 91% with ICD vs 57% without ICD; BIVAD: 54% vs 47%. ICD shocks on VAD support when appropriate and frequent predicted adverse outcomes and hospitalizations such as aortic regurgitation or right heart failure when on LVAD support.

Conclusions: Shock frequency decreases after VAD implantation, likely owing to ventricular unloading, but appropriate ICD shocks still occur in VAD patients. An ICD is associated with improved survival in LVAD-supported HF patients.

1302

Comparative evaluation of four risk scores for predicting mortality in patients with implantable cardioverter-defibrillator for primary prevention of sudden cardiac death

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¹University Clinical Hospital of Santiago de Compostela, Department of Cardiology, Santiago de Compostela, Spain; ²University Clinical Hospital, Valencia, Spain; ³Hospital Universitario y Politécnico La Fe, Valencia, Spain; ⁴Hospital of Meixoeiro, Vigo, Spain; ⁵Hospital de Basurto, Bilbao, Spain; ⁶University Hospital Marques de Valdecilla, Santander, Spain; ⁷Hospital Universitario Virgen de las Nieves, Granada, Spain; ⁸University Hospital of Virgen Macarena, Seville, Spain; ⁹Hospital Virgen de la Salud, Toledo, Spain

Objective: Several clinical risk scores (RS) have been developed for the identification of patients at high risk of all-cause mortality despite implantable cardioverter defibrillator (ICD). We aimed to examine and compare the predictive capacity of four simple scoring systems (MADIT, FADES, PACE and SHOCKED) for predicting mortality after ICD implantation for primary prevention of sudden cardiac death in a Mediterranean country.

Methods: Multicentre retrospective study performed in 15 Spanish hospitals. Consecutive patients referred for primary prevention ICD implantation between January 2010 till December 2011 were included.

Results: 916 patients with ischemic (IHD) and non-ischemic heart disease (NIHD) were included (age 62 ± 11, 81.4% male). During 33.4 ± 12.9 months, 113 (12.3%) patients died (cardiovascular origin in 86 (9.4%) patients). At 12, 24, 36 and 48 months, mortality rates were 4.5%; 7.6%; 10.8% and 12.3% respectively. All the RS showed stepwise increasing in the risk of death throughout the scoring system of each of the scores. They were significantly associated with all-cause mortality throughout the follow up period. PACE displayed the lowest c-index value regardless whether the population had IHD (c = 0,611) or NIHD (c = 0,609), whereas MADIT (c = 0,661 and 0,673 in IHD in NIHD respectively), SHOCKED (c = 0,637 and 0,681), and FADES (c = 0,637 and 0,664) provided similar c statistic values (p ≥ 0.09).

Conclusions: In this large, non trial-based cohort of Mediterranean patients with primary prevention ICD implantation, the 4RSs evaluated showed a significant stepwise increasing in the risk of death. Moreover, among the currently available RSs for predicting all-cause death, MADIT, FADES, and SHOCKED scores provide better performance than PACE scores, and might be more suitable to guide clinicians in the decision-making process for optimizing ICD use.

RISK SCORE	HR	95% CI	p	c-statistic	95% CI	SE	p	G-B p-value
Overall								
MADIT	1.48	1.30-1.68	< 0.0001	0.661	0.60-0.72	0.028	< 0.0001	0.469
SHOCKED	1.01	1.01-1.02	< 0.0001	0.637	0.58-0.69	0.028	< 0.0001	0.894
FADES	1.58	1.33-1.87	< 0.0001	0.634	0.58-0.68	0.027	< 0.0001	0.389
PACE	1.52	1.27-1.82	< 0.0001	0.611	0.55-0.67	0.029	< 0.0001	0.663

Clinical Case Corner 5 – Cancer and heart failure as an ominous combination: a new challenge for the heart failure specialist

Monday 25 May 2015 15:45–16:30

Location: Poster Area

1303

When the remedy is worse than the disease

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Introduction: With the development of new and more effective chemotherapy agents, the oncologic prognosis of patients who not so long ago had a very ominous outcome is now improving. Sometimes however this prognosis is affected by some serious cardiovascular side effects than can compromise quality of life and survival. A new field of work is being developed called cardio-oncology to deal with this patients in an integrally fashion. We present the case of a 46-year-old woman, who 8 months before admission was diagnosed with a non-Hodgkin diffuse large B-cell lymphoma and who presented with dyspnea to the emergency room.

Clinical Case Presentation: She was diagnosed on September 2013 with lymphoma after a cervical adenopathy biopsy was examined. She had no cardiovascular risk factors or family history of cardiovascular events and before chemotherapy was started a transthoracic echocardiography (TTE) was performed. It showed normal chamber dimensions and normal left ventricular ejection fraction (LVEF = 68%) and a double orifice mitral valve with normal function. On October 15th 2013 she received the first chemotherapy cycle consisting in cyclophosphamide 2740 mg, doxorubicin 120 mg, vincristine 2 mg and prednisone. A total of 8 cycles were administered finishing on March 2014 and being considered on remission.

After that she presented twice to the emergency room complaining from dyspnea on exertion. An urgent TTE was performed on the first admission, showing a dilated and dysfunctional LV. She was discharged adding to her usual treatment ramipril 2.5 mg q.d. and a diuretic. Later she returned to the emergency room complaining from non-productive cough, hoarseness, occasional orthopnea and some episodes of paroxysmal nocturnal dyspnea. Brain scans were this time performed to rule out causes of paralysis of the vocal chord finding lesions compatible with encephalomalacia due to an ischemic stroke of possibly embolic origin. A new TTE confirmed LV dilation and a LVEF = 20% with global hypokinesia. It also showed findings suggestive of LV mural thrombus and left atrial thrombi. The right ventricle (RV) was also dilated and dysfunctional. A cardiac magnetic resonance imaging confirmed these findings. Anticoagulation was started with warfarin, also adding to her treatment bisoprolol 1.25 mg q.d., spironolactone 25 mg q.d. and furosemide. Seven months after admission a new TTE was performed showing improvement in LVEF = 38% and RV systolic function recovery. LV diameters did not improve (EDD = 60mm). The intracardiac masses were not found.

Discussion: This patient underwent an aggressive plan of chemotherapy composed by an alkylating agent (cyclophosphamide) and an anthracycline (doxorubicin), both of which are associated with type I cardiotoxicity, which classically has been defined as non-reversible. She received a cumulative doxorubicin dose of 545 mg/m², which is depending on the authors closely within the recommended maximum lifetime cumulative dose or even a little above the threshold. This patient being a female, with this amount of cumulative dose and having received another type I agent, were factors that conveyed a high risk for cardiotoxicity. Fortunately, she was started promptly with specific heart failure treatment within two months from the end of chemotherapy, as some evidence suggests that rapid initiation of therapy is associated with recovery.

Conclusion: We intend to highlight the importance of the development of protocols to treat with patients with the highest risk profile to avoid unfavourable outcomes. These protocols should participate in the risk stratification, initial evaluation, follow-up during and after chemotherapy and research areas of uncertainty.

1304

Eosinophilic myocarditis as the first presentation of a hypereosinophilic multisystem disorder

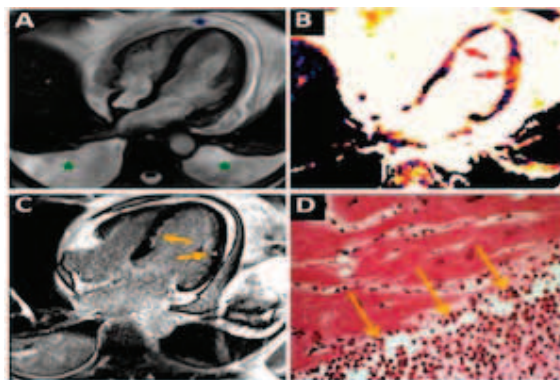
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Introduction: Eosinophilic myocarditis (EM) is a rare, potentially fatal disease if left untreated and may be part of a systemic hypereosinophilic disorder.

Case report: A 59-year-old male presented with progressive heart failure (HF) symptoms and rapidly conducted atrial flutter requiring electrical cardioversion. Initial blood work revealed an elevated Troponin T at 651 ng/L (normal value < 14); eosinophil count was normal. Echocardiography showed globally reduced left ventricular (LV) systolic function (ejection fraction (EF) 30%) and a moderate pericardial effusion. The patient had recurrent Torsades de Pointes requiring electrical cardioversion. Coronary angiography revealed minor plaque disease. Cardiac magnetic resonance identified widespread oedema on T2-weighted imaging, consistent with an inflammatory process, and patchy mid-wall (non-ischaemic) late gadolinium enhancement (A, B, C). Eosinophils increased to 1.8 10⁹/L (normal value < 0.4) on day 3 of admission. Endomyocardial biopsy demonstrated changes of EM with inflammatory cell infiltrates, a large quantity of which were eosinophils (D). Steroids and HF medication were initiated and the patient improved rapidly. LV EF was 50% prior to discharge. He represented 4 months later, whilst on a tapering steroid regimen, with malaise, wheeze and dyspnoea. Eosinophil count was markedly raised (14.7 10⁹/L). Echocardiography was unchanged from previous. Computed tomography of thorax revealed multiple pulmonary infiltrates, consistent with a systemic hypereosinophilic syndrome. He was re-established on high-dose steroid with rapid resolution of symptoms and profound reduction in eosinophil count (0.7 10⁹/L).

Conclusion: EM may be the initial presentation of a hypereosinophilic multisystem disorder. Prompt diagnosis and treatment can prevent irreversible myocardial injury.



EM CMR (A,B,C) and pathology (D) images

1305

Heart failure decompensation due to severe, multifactorial tricuspid valve regurgitation; multidisciplinary diagnosis, unconventional pharmacological treatment and innovative interventional approach

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Introduction and case report description: A 77-year-old woman was admitted to the hospital due to heart failure (HF) decompensation (NYHA class IV, NT-proBNP 6724 pg/ml). On the admission she presented dyspnoea and chest tightness. Examination revealed lower-extremity oedema, lung decrepitations, hepatomegaly, oliguria, arterial normotension and sinus rhythm. She had a history of ST segment elevation myocardial infarction (in 2005), left anterior descending coronary artery angioplasty (in 2006), chronic kidney disease, thymoma resection with adjuvant radiotherapy, rheumatoid arthritis, hypothyroidism, paroxysmal atrial fibrillation, partial right lobectomy due to bronchiectasis and tuberculous cirrhosis.

Description of the problem, procedures, techniques and equipment used.

The patient presented many co-morbidities so that it was crucial to define exact mechanism of HF decompensation in order to provide appropriate treatment. Application of various diagnostic methods included: blood and urine examination, transthoracic echocardiography (TTE), right heart catheterisation, chest X-ray, lung perfusion scintigraphy and renal ultrasonography (USG).

Questions, problems and differential diagnosis: Diagnosis focused on circulatory, pulmonary and urinary abnormalities, which were suspected to trigger multifactorial HF decompensation. Moreover, it was important to determine the etiopathology of severe renal failure.

Answers and discussion: Despite significant decrease in glomerular filtration rate (GFR 19 mL/min/1.73 m²), USG did not visualised any structural pathology; electrolyte balance and urinalysis were correct. TTE revealed right heart volumetric overload, symptoms of pulmonary hypertension and non-rheumatic tricuspid regurgitation (peak gradient of 26 mmHg). Catheterisation confirmed increased pulmonary resistance and right heart insufficiency. Scintigraphy excluded thromboembolism. HF decompensation was triggered by severe tricuspid regurgitation aggravated by pulmonary hypertension. We suspect that valve degeneration was caused by ischaemic and post-radiation factors. Right heart insufficiency led to chronic venous stasis effecting in severe prerenal failure.

High doses of oral torasemide as a bridging therapy to intravenous furosemide enabled oral therapy. After 2 months patient was discharged with decreased HF symptoms (NYHA class II, NT-proBNP 2900 pg/ml) and improved renal function (GFR 27,5 mL/min/1.73 m²).

Conclusions and implications for clinical practice: Multidisciplinary approach to HF decompensation in patient with many co-existing diseases resulted in appropriate diagnosis and provided relevant treatment options. As innovative way of interventional approach (alternative to contraindicated cardiac surgery) transcatheter tricuspid annuloplasty was taken under consideration. Currently, patient is waiting for the procedure in a stable condition.

1306

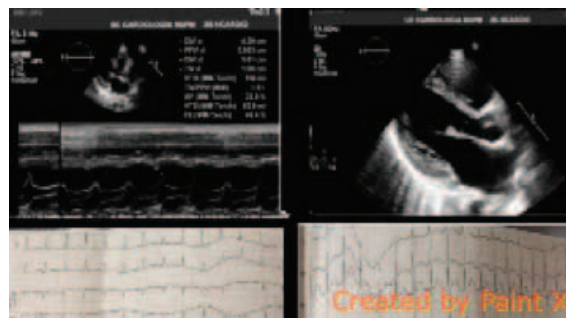
Fever, dyspnoea and pericardial rub in hematologic patient

EM Eva Maria Chueca Gonzalez¹; JL Lopez Benitez¹; C Sevillano Ruiz-Mateos²; R Arana Granados¹; MV Martin Reina²; MS Herruzo Rojas¹; R Del Pozo Contreras¹; MS Fernandez Garcia¹; P Cabeza Lainez¹; RE Vazquez Garcia¹

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A 21-year-old man was admitted to our hospital due to acute leukosis (22 January 2015). He was physically active and did not have a history of hypertension, diabetes, hospitalizations, surgical procedures, or allergic reactions to drugs. He was taking no medications at the time of the admission and there was no evidence of recent acute viral syndrome. The patient had been well until approximately 5-7 days earlier, when he presented a big ecchymosis due to a contusión behind the right thigh and spontaneous self-limited gingivorrhagies. He was attended for this reason at the emergency department where blood tests shown changes suggesting acute leukosis (white blood cell count, 103.0 × 10³/l (93% blasts with smooth granulation and 6% with pink granulation and stiks) and fibrinogenolysis. Based on peripheral and bone marrow picture, immunophenotype, and detection of PML-RAR alpha rearrangement associated with t(15;17) (fluorescent in situ hybridization), the diagnosis of hypogranular acute promyelocytic leukemia was made. Induction treatment with all-trans retinoic acid and idarubicin schedule [all-trans retinoic acid (ATRA) 45 mg/m² per day os, till complete remission or 90 days; idarubicin, 12 mg/m² per day iv, four consecutive days] was started. Supportive therapy with dexametasuna 2,5mg/m²/12h for 12 days; tranexamic acid, and plasma transfusion was also initiated. On day 7 of ATRA treatment, a routinely echocardiography showed a left ventricle without dilatation (end-diastolic diameter of 51mm; end-systolic diameter of 30mm; end-diastolic volume 112ml, normal range: 84-128ml; indexed

end-diastolic volume 63ml/m², normal range: 44-64ml/m²) and normal ejection fraction (69%). Diastolic function was normal but with elongated TDE. On day 21 of ATRA treatment, the patient started with dysthermia (37.2°C), sinus tachycardia (140 bpm) and dyspnoea. The physical examination of the lungs was pathological with crackles in both lung basis and right pleural effusion semiology; a pericardial rub was heard and slight hepatomegaly and and peripheral edema was present. A portable chest x-ray showed cardiac enlargement, bilateral peripheral edema and bilateral pleural effusion, mainly right. Electrocardiographic changes as sinus tachycardia at 140 bpm, 1mm concave-upward ST-segment elevation in right leads and plane T waves in inferolateral leads were appreciated. Principal laboratory test alterations were increased C-reactive protein (CRP) 225mg/L, and increased ultra sensitive troponin T (us-cTnT) 920 pg/ml and 455 pg/mL. An urgent transthoracic echocardiogram was performed. Slight left ventricular enlargement was detected (end-diastolic diameter 55mm; volume 138 ml, 76.6 ml/m²) with diffuse hypokinesia and reduced ejection fraction (40%, normal range: ≥55% and S' wave in lateral mitral annulus 7.79cm/s). With the diagnosis of ATRA syndrome and myopericardial involvement, treatment with diuretics and full-dose dexametasuna was started (10mg/12h) while ATRA was discontinued. Heart failure treatment was progressively introduced (low dose beta-blockers, angiotensin converting inhibitors and aldosterone antagonists). In the following two days, fever, dyspnoea and congestion symptoms stopped with the improvement of laboratory parameters. One week later, an echocardiography showed the reduction of left ventricular size (end-diastolic diameter of 45mm; volume, 100 ml; 55.5ml/m²) with normalization of ejection fraction (61%). ATRA will be reintroduced in the following cycles of consolidation chemotherapy. The patient achieved molecular complete remission after induction therapy.



1307

Rare case of constrictive pericarditis; echocardiographic diagnosis using annulus reversus technique

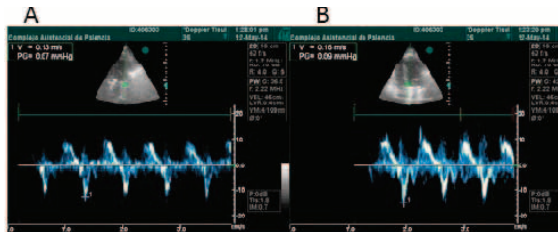
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We present a 62-year-old-man with history of aortic coarctation surgical intervention at the age of 35 years. He was being followed up by our department due to aneurismatic dilatation of the ascendant aorta and a degenerative aortic valve disease with mild aortic stenosis with an effective area of 1.1 cm². Seven years before, he had been treated with chemotherapy with R-CHOP due to a diffuse B-cell lymphoma without signs of reactivation in the present. Also he received chemotherapy with capecitabine and surgical treatment for a rectal adenocarcinoma six years before the current event. He is admitted in our cardiology department with pleuropericardic effusion and paroxysmal atrial fibrillation. Mediastinal adenopathies were found in thoracic CT. Mediastinoscopy and biopsy of the adenopathies show no proof of tumoral cells. PET was performed with no evidence of recidiva tumoral. Pleural effusion was persistent with respiratory failure. Echocardiographic finding at this moment did not show any changes from previous examination. Constrictive physiology could not be assessed. Biochemical markers were normal, including BNP (levels of). The patient had to be readmitted in multiple occasions due to signs of right ventricular heart failure. He needed at least 5 paracentesis because of ascites. NYHA Functional class was III. A right ventricular and pulmonary artery catheterization showed absence of constrictive physiology, restrictive physiology instead, with postcapillary pulmonary hypertension. Despite these results, constrictive pericarditis was still suspected to be the aetiology of the right ventricular failure and symptoms of the patient. With all the clinical data, and the suspected diagnosis we performed again echocardiographic, using tissular Doppler at the mitral annulus. In normal subjects mitral lateral e' velocity is higher than the medial e' velocity. In constrictive pericarditis e' velocity is lower than the medial one ("annulus reversus"). It can be

found in patients with constrictive pericarditis despite normal e' velocities. Differential diagnosis with restrictive cardiomyopathy can be done, as these patients did not exhibit annulus reversus. In the image we can notice how lateral e' velocity in our patient (13 cm/s) was lower than the medial one (15 cm/s). With these findings we diagnosed the patient of constrictive pericarditis. Pericardiectomy, aortic valve replacement and aortic substitution with a Dacron tube was performed. Clinical improvement was assessed immediately after discharge from the cardiac surgery department. 6 months after the surgery the patient still remains asymptomatic, with no signs of congestion and has no need of diuretics.

This case shows difficulty in diagnosing constrictive pericarditis. Using tissue doppler imaging and its practical applications as the annulus reversus may be useful in evaluation of constrictive pericarditis.



ANNULUS REVERSUS

1309

Acute left ventricular dysfunction as an paraneoplastic syndrome

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A 34-year-old man was in his usual state of health until he began experiencing fatigue, shortness of breath on exertion, cough and fever. At the emergency department was noted to have a white blood cell count of 25 000 cells/mm³, with 15 % blasts, a hemoglobin of 8.7 g/dL, and a platelet count of 31+109/L. He was diagnosed with M5 acute myeloid leukemia with favorable prognosis cytogenetics. Transthoracic echocardiogram revealed severe left ventricular systolic dysfunction (with normal ventricular walls thickness and no wall motion abnormalities) reason why he did not receive standard leukemia therapy. In cardiac MRI there was no oedema, no abnormal myocardial enhancement on late gadolinium images suggestive of fibrosis or myocardial infiltration. No heart failure therapy was given. Initial cytoreductive therapy that did not include anthracyclines produced a good cardiac result, and decision was made to proceed therapy induction with a regimen consisted on anthracyclines. The patient had a complete and persistent cardiac recovery which lead us to consider this cardiac dysfunction as an extramedullary manifestation of the leukemia.

Rapid Fire 6

Monday 25 May 2015 16:30–18:00

Location: Agora

1341

Systemic hypertension and heart failure: insight from different left ventricular ejection fractionA Iorio¹; C Di Nora²; E Zamboni²; S Poli²; C Mazzone¹; D Radini¹; L Tarantini³; G Sinagra²; G Cioffi⁴; A Andrea Di Lenarda¹¹A.S.S. n 1, Cardiovascular Center, Trieste, Italy; ²"Ospedali Riuniti" and University of Trieste, Cardiovascular Department, Trieste, Italy; ³San Martino Hospital, Belluno, Italy; ⁴Villa Bianca Hospital, Trento, Italy**Background:** Although systemic hypertension (SH) as isolated etiology of heart failure (HF) is a relatively frequent observation, the prevalence, clinical characteristics and outcome of hypertensive patients across different HF phenotypes have not been widely studied.**Purpose:** To determine prevalence, characteristics and outcome of HF population with SH as isolated etiology taking into account different left ventricular ejection fraction (LVEF) phenotypes (LVEF \leq 40% - HF_rEF, LVEF 41-49% - HF_bEF, LVEF \geq 50% - HF_pEF).**Methods:** We analyzed all consecutive out-patients with SH and HF from November 2009 to October 2013 whose LVEF had been assessed. HF patients with SH as an isolated etiology factor (HF-SH) were defined as patients with history of hypertension in absence of other triggers of cardiac disease. Patients with ischemic, valvular and congenital heart disease were excluded. Clinical variables of study population were derived from the E-data chart for Outpatient Clinic collected in a regional Data Warehouse.**Results:** We found that 2610 out of 14110 (28%) hypertensive patients had SH and HF. Among them, 1974 (76%) patients were excluded (29% ischemic heart disease, 22% valvular heart disease, 17% ischemic and valvular disease, 3% other acquired/congenital heart diseases). Finally, 636 patients (24% of overall HF population) (55% males, mean age 77 \pm 9 years) showed only SH as etiologic factor associated with HF. Of these, 121 (19%) were identified as HF_rEF, 88 (14%) as HF_bEF and 427 (67%) as HF_pEF. The most significant clinical differences were observed between HF_rEF and HF_pEF group. Patients with HF_rEF were younger, more frequently male, more symptomatic and with less frequent atrial fibrillation. Moreover, ACE-I/sartans and aldosterone treatments were more frequent in HF_rEF, while beta-blockers were similarly prescribed (around 50%) across HF phenotypes. The adjusted mortality for significant predictors at 1-year and mid follow-up term of 28 months (10 to 32) were not significantly different in HF_pEF and HF_bEF group. Conversely, patients with HF_rEF showed a different and significantly higher mortality rates than those with other HF phenotypes.**Conclusions:** Our results showed that in HF patients with SH as isolated etiology, HF_pEF was the most frequent HF phenotype, while one-third of cases presented LV systolic dysfunction. Among different LVEF strata, HF_rEF showed the worst outcome.

1342

The prevalence of iron deficiency in patients with heart failure with preserved ejection fraction and its association with elevated pulmonary pressure, reduced exercise capacity and quality of lifeT Tarek Bekfani¹; P Pellicori²; N Ebner³; DA Morris¹; A Sandek¹; W Doehner¹; JG Cleland²; M Lainscak⁴; SD Anker³; S Von Haehling³¹Charite - Campus Virchow-Klinikum, Department of Cardiology, Division of Applied Cachexia Research, Berlin, Germany; ²University of Hull, Department of Cardiology, Hull, United Kingdom; ³University Medical Center Göttingen, Department of Cardiology, Göttingen, Germany; ⁴General Hospital Celje, Department of Cardiology, Celje, Slovenia**Purpose:** To describe the prevalence of iron deficiency (ID) in outpatients with heart failure with preserved ejection fraction (HFpEF) and its relation to exercise capacity and quality of life (QoL).**Methods:** In total, 233 symptomatic outpatients with HFpEF (LVEF \geq 50%, mean 58 \pm 7%; age 71 \pm 9 years; NYHA 2.2 \pm 0.7; NT-proBNP 777 \pm 641 ng/L; BMI 31.2 \pm 6 kg/m²) were enrolled as part of the Studies Investigating Co-morbidities Aggravating Heart Failure (SICA-HF) in Germany, England and Slovenia. ID was defined as ferritin <100 μ g/L or 100-299 μ g/L with transferrin saturation (TSAT) <20%. Anaemia was defined as Hb <13 g/dL in men, <12 g/dL in women. Absolute ID was defined as ferritin <100 μ g/L. Patients were divided into 3 groups according to E/e' at echocardiography E/e' \leq 8; E/e' 9-14; E/e' \geq 15. All patients underwent cardiopulmonary exercise (CPX), 6-minute walk test (6MWT), and muscle strength testing as well as QoL assessment and Dual Energy X-ray Absorptiometry (DEXA).**Results:** Overall, 131 had ID (56%), 61 patients had anaemia (26%), and 109 had absolute ID (46.8%). ID was more common in patients with more severe diastolic dysfunction: (E/e' \leq 8: 45.8% vs. E/e': 9-14: 52.4% vs. E/e' \geq 15: 84.2%, Pchi=0.0005). In total, Patients with ID performed worse in 6MWT (416 \pm 125 vs. 367 \pm 138 meters, p=0.05), had worse exercise time in CPX (663 \pm 179 vs. 565 \pm 184 sec, p=0.03) and had less muscle strength/muscle mass in both legs (left leg: 4.4 \pm 1.1 vs. 3.5 \pm 1, p=0.001, right leg: 4.1 \pm 1.3 vs. 3.6 \pm 1.1, p=0.09). Lower values of ferritin were associated with worse exercise time (r=0.31, p=0.01), Peak VO₂ in CPX (r=0.28, p=0.03) and less walked distance in 6MWT (r=0.24, p=0.01). TSAT was inversely correlated with E/e' (r=-0.23, p=0.0005) and estimated pulmonary arterial systolic pressure at echocardiography (r=-0.24, p=0.009). Patients with absolute ID had higher pulmonary artery pressure at echocardiography (patients without ID or anaemia: 33 \pm 10 vs. absolute ID without anaemia: 36 \pm 11 vs. absolute ID with Anaemia 40 \pm 14 mmHg, PANOVA=0.04). Patients with absolute ID and anaemia had worse quality of life in the EQ5D-Questionnaire than those without ID or anaemia (16373 \pm 5304 vs. 19062 \pm 4704, P < 0.05).**Conclusion:** ID is a frequent comorbidity in HFpEF, and is associated with reduced exercise capacity, muscle strength, and QoL. Its prevalence increases with increased severities of diastolic dysfunction.

1343

Relationship between pulse pressure and mortality in heart failure with preserved ejection fraction in the I-Preserve TrialA Pozzi¹; PS Jhund²; PE Carson³; MR Komajda⁴; MR Mckelvie⁵; MR Zile⁶; JJV McMurray²¹Di Circolo Hospital, Cardiology 2, Varese, Italy; ²Cardiovascular Research Centre of Glasgow, Glasgow, United Kingdom; ³Veterans Affairs Medical Center, Washington, United States of America; ⁴Hospital Pitie-Salpetriere, Paris, France; ⁵Population Health Research Institute, Hamilton, Canada; ⁶Medical University of South Carolina, Charleston, United States of America**Purpose:** Low pulse pressure (PP, systolic minus diastolic blood pressure), is associated with poorer prognosis in patients with heart failure and reduced ejection fraction (HF-REF). We examined the association between PP and mortality in patients with heart failure and preserved ejection fraction (HF-PEF) in the Irbesartan in Patients with Heart Failure and Preserved Ejection Fraction trial (I-Preserve).**Methods:** 4128 patients aged \geq 60 years with LVEF \geq 45% and symptomatic (NYHA II-IV) heart failure were enrolled in I-Preserve. PP could be calculated in all patients. Patients were divided by quartile of PP; quartile 2 (Q2) was used as the reference quartile. In a Cox model the association between PP and death was examined with and without adjustment for other variables associated with death.**Results:** Compared to patients in Q2, those in Q1 were more likely to be female (34% vs 14%), have a history of AF and MI, have a lower systolic blood pressure (SBP) and a higher NT-pBNP value. On the other hand patients in the higher quartiles were more likely to have history of DM and hypertension and a higher SBR, compared with Q2. In univariable and multivariable models there was a U shaped relationship between PP and death. There was an interaction between PP, SBP and diastolic BP (p < 0.001) both in the univariable and multivariate analysis.

Table 61272.

	N	N° of deaths	Rate per 100 patient years	Univariable HR (95% CI)	Multivariable HR (95% CI)	Univariable (multivariable) P value
Q1 (10-50 mmHg)	1451	316	5.4	1.38 (1.11-1.73)	1.38 (1.10-1.74)	0.005 (0.006)
Q2 (51-58 mmHg)	618	100	3.9	ref	ref	
Q3 (59-65 mmHg)	1144	245	5.2	1.33 (1.05-1.67)	1.33 (1.05-1.69)	0.02 (0.02)
Q4 (66-124 mmHg)	915	220	5.9	1.52 (1.19-1.92)	1.31 (1.03-1.68)	0.001 (0.03)

*History of HF, history of DM, (log)NT-pBNP, (log) neutrophils, EF, history of COPD, history of ischaemic heart disease, history of myocardia infarction, hear rate, age, eGFR

Table 1345.

Stiffnes-coefficient β	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	p
Age	46 (41-55)	50 (43-60)	53 (45-62)	59 (52-66)	64 (57-69)	<0.001
Female gender	40%	49%	52%	54%	50%	<0.001
Diabetes	2%	4%	5%	9%	13%	<0.001
BMI	25 (23-28)	26 (23-28)	26 (23-29)	27 (24-30)	28 (25-31)	<0.001
Dyslipidemia	26%	27%	26%	30%	36%	<0.001
Hypertension	31%	38%	48%	59%	74%	<0.001
eGFR	95 (86-103)	93 (85-102)	92 (82-100)	89 (78-97)	86 (77-93)	<0.001
Smoking	20%	21%	22%	19%	15%	0.004

Conclusion: In patients with HFpEF, both extremes of the PP range were associated with higher mortality. It is likely that the reasons are different at different ends of the PP spectrum, with those at the lower end resembling patients with HFReF. At the upper end, arterial stiffness and abnormal ventriculo-vascular coupling may be more important prognostically.

1344

Diastolic pressure gradient predicts outcome in patients with heart failure and preserved ejection fraction

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Purpose: Pulmonary hypertension due to heart failure with preserved ejection fraction (PH-HFpEF) is associated with poor outcome. According to the diastolic pressure gradient (DPG) with a cut-off of 7 mmHg, affected patients can be further sub-classified into isolated postcapillary PH (lpc-PH) and combined pre- and pc-PH (Cpc-PH). However, the clinical significance and prognostic value of DPG remains to be elucidated.

Methods: Patients with HFpEF diagnosed according to current ESC guidelines were enrolled in our prospective registry. Borderline PH was defined as a mean pulmonary arterial pressure (mPAP) between 21 - 24mmHg, and manifest PH was diagnosed, if mPAP \geq 25mmHg. DPG was calculated as difference between diastolic PAP and mean pulmonary arterial wedge pressure. Hospitalization for HF and/or death for cardiac reason were defined as the primary study endpoint.

Results: Between Dec. 2010 and Dec. 2014, 193 HFpEF patients were registered. 19 patients refused right heart catheter and were excluded. Of the remaining 174 patients, 11 (6.3%) had no PH, 15 (8.6%) had borderline PH and 148 (85.1%) a manifest PH. PH patients (66% females, mean age 70 \pm 7 years) were further sub-classified into lpc-PH (n=126) and Cpc-PH (n=22).

Patients with a Cpc-PH had a shorter six-minute walk distance (253.5 \pm 128.7 vs. 318.4 \pm 117.1 m; P=0.021), a higher NT-proBNP (3816.9 \pm 5977.8 vs. 1651.6 \pm 1883.5 pg/ml; P=0.001), larger right ventricles (42.1 \pm 8.9 vs. 37.4 \pm 7.1 mm, P=0.010) and a lower PaO₂ (63.4 \pm 9.8 vs. 73.3 \pm 11.6 mmHg; P=0.001) compared to patients with lpc-PH. During a median follow-up time of 25.2 months, 55 patients (33.7%) reached the combined endpoint. DPG was found to be an independent predictor of outcome (HR 1.167, 95% CI 1.047 - 1.299; P=0.005). The worst outcome was recognized in the group of patients with Cpc-PH, as compared to lpc-PH patients (log rank test, P=0.015).

Conclusion: The presence of PH in HFpEF is associated with adverse outcome. The subgroup with Cpc-PH had a worse clinical status and event-free survival as compared to the remainder of the group. Although it remains unclear which subset of patients is prone to develop superimposed pulmonary vasculature remodeling, our data indicate a potential contribution of hypoxemia.

1345

Risk factors for heart failure with preserved ejection fraction are associated with a steeper LV end-diastolic pressure-volume relationship in healthy subjects: data from the Gutenberg health study

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Background: Heart failure with preserved ejection fraction (HF-PeF) is linked to different pathologies, e.g. increased myocardial stiffness, leading to lower left ventricular (LV) end-diastolic capacitance and a steeper LV end-diastolic pressure-volume relationship (EDPVR). We associated these haemodynamic alterations to the presence of typical risk factors for HF-PeF in a large, healthy cohort.

Methods: The Gutenberg Health Study (GHS) is a large-scale prospective, population-based study investigating healthy individuals. Based on echocardiographic data from 4562 participants without history of heart failure, we calculated LV end-diastolic capacitance (i. e., LV end-diastolic volume at an end-diastolic pressure of 30mmHg, LV VPed30), as well as the EDPVR's stiffness-coefficient β using a single beat estimation from echocardiographic data. We associated these parameters with typical risk factors for HF-PeF.

Results: A higher stiffness-coefficient β was associated with all investigated risk factors including increasing age, female gender, diabetes, obesity, dyslipidemia and hypertension (see table). Increasing age, female gender and lower eGFR were associated with lower LV VPed30, while the presence of diabetes, obesity, dyslipidaemia and hypertension were associated with higher LV VPed30. Smoking had no association with LV VPed30, but was associated with lower β -values.

Conclusion: In healthy individuals, the presence of risk factors for HF-PeF was associated with a steeper EDPVR. Estimating the EDPVR using non-invasive, echocardiographic data may be a promising tool to identify patients at high risk for developing HFPEF. Further studies will evaluate the EDPVR as a predictor for outcome.

1346

Riociguat treatment for patients with pulmonary hypertension due to heart failure with preserved ejection fraction

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Purpose: Riociguat, a stimulator of soluble guanylate cyclase, is a novel pulmonary and systemic vasodilator that has been approved for pre-capillary forms of pulmonary hypertension (PH). In a proof of concept study, single-dose administration of riociguat has shown favourable effects in patients suffering from PH due to heart failure with preserved ejection fraction (HFpEF). The aim of the present study was to evaluate safety and efficacy of riociguat administration in consecutive patients diagnosed with PH-HFpEF.

Methods: This was a prospective, open-label, non-randomized single-centre study. Eligible patients (n=12) received riociguat in addition to standard heart failure treatment. Riociguat was started at a dose of 0.5mg per day and was up-titrated within 8 weeks to a maximum of 2.5mg per day. Baseline work-up of patients and re-evaluation after 6 months of therapy included the assessment of blood pressure, NYHA functional class, exercise capacity as measured by the 6-minute walk test (6MWT) as well as serum NT-proBNP.

Results: Mean treatment duration was 127 ± 58 days. No adverse events occurred during the observation period. No systemic blood pressure drops were encountered (144/77mmHg at baseline and 142/71mmHg at follow-up; p=0.351). NYHA functional class significantly improved from NYHA: 2.8±0.39 at baseline to 2.33±0.5 (p=0.014). NT-proBNP levels decreased from 1530 pg/ml±2718 to 620 pg/ml±527 (p=0.476). The baseline 6MWT improved from 316±96 m to 368 m±63; (p=0.243).

Conclusion: Although preliminary, our data indicate that long-term treatment with riociguat is safe in patients with HFpEF. The trend towards beneficial clinical effects of long-term treatment remains to be confirmed.

1347

Factors associated with all-cause and heart failure rehospitalization in chronic heart failure patients with reduced and preserved ejection fraction

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Background: Rehospitalization in heart failure is frequent and is associated with worse outcome and increased health-care costs. Many of the studies that have analyzed factors associated with readmission have studied patients from randomized controlled trials or patients with heart failure with reduced ejection fraction (HFrEF). Therefore, the aim of this study was to identify factors associated with readmission in a real-world heart failure cohort and analyze whether differences exist between HFrEF and heart failure with preserved ejection fraction (HFpEF).

Methods: Post-hoc analysis of a single-center prospective cohort of 1072 patients with reduced (n=559) and preserved (n=513) chronic heart failure. HFpEF was defined as an ejection fraction ≥45%. The association of all-cause rehospitalization (ACR) and heart failure rehospitalization (HFR) with baseline characteristics was assessed using a χ^2 and t-test, both in HFpEF and HFrEF. Multivariable Cox proportional hazard regression models to evaluate the effect of ejection fraction (HFpEF vs. HFrEF) on all-cause (ACR) and heart failure rehospitalization (HFR) were developed.

Results: During a median follow-up of 10 [5.5-15.8] months, ACR and HFR rate were 47% and 29%, respectively. Four factors were independently associated with HFR in Cox analysis both in HFrEF and HFpEF: previous hospitalization due to heart failure the last year (HR 2.2; 95%CI(1.2-3.9) in HFrEF and HR 2.8; 95%CI(1.5-5.5) in HFpEF), chronic obstructive pulmonary disease (COPD) (HR 1.8, 95%CI(1.2-2.5) and HR 1.4, 95%CI(1.0-2.0), respectively), NYHA functional class III-IV (HR 1.5, 95%CI(1.1-2.1) and HR 1.6, 95%CI(1.1-2.2), respectively) and heart rate >70 beats per minute (HR 1.5, 95%CI(1.1-2.1) and HR 1.4, 95%CI(1.0-1.9), respectively), all p<0.05. Anemia (HR 1.4, 95%CI(1.1-1.9), p=0.044) and log-NTproBNP (HR 1.4, 95%CI(1.1-1.9), p=0.048) were associated with HFR in HFrEF but not in HFpEF. The presence of COPD, anemia, history of heart failure the previous year, heart rate >70 beats per minute and log-NTproBNP were independently associated with ACR in both HFrEF and HFpEF. In HFpEF, NYHA class III-IV was also associated with ACR.

Conclusions: Heart failure hospitalization the previous year, COPD and heart rate >70 beats per minute are independently associated with ACR and HFR both in HFrEF and HFpEF. Other factors frequently associated with ACR and HFR are NYHA functional class III-IV, log-NTproBNP and anemia. These factors allow the identification of patients at high-risk of readmission.

1348

Fluid overload predicts adverse outcome in patients with heart failure and preserved ejection fraction

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Purpose: Fluid overload plays an important role in the pathogenesis of Heart failure with preserved ejection fraction (HFpEF) and is a well-known predictor of rehospitalization in patients with acute heart failure. Whether fluid status in HFpEF is associated with outcome is currently unknown.

Materials and Methods: Between December 2010 and July 2013, 97 consecutive patients with HFpEF and pulmonary hypertension (PH) as confirmed by right

heart catheter, were enrolled in our prospective registry. Patients with clinically overt decompensation were excluded from the protocol (n=6). To assess the fluid status we performed a bioimpedance spectroscopy in every patient. An overhydration value ≥ 90th percentile for the healthy population was defined as fluid overload. The primary outcome measure was a combined endpoint consisting of hospitalization for HF and/or death for cardiac reason.

Results: 58 (63%) patients were hypo- or normovolemic (overhydration relative to extracellular water [OH-ECW] mean -0.7±5.7 %) and 33 (36%) patients presented with fluid overload (OH-ECW mean +11.5±2.7 %). During a median follow-up of 11.3 months (IR: 4.3-24.2), 27 (29.6%) patients reached the combined endpoint, 1 (1.1%) patient died due to a non-cardiac reason. No patients were lost to follow-up. Multivariate Cox hazard analysis identified fluid overload (HR: 3.17; 95% CI: 1.25-8.02; p=0.015) as independent predictors of adverse outcome. Moreover, higher pulmonary arterial systolic pressure measured by echocardiography (HR: 1.04; 95% CI: 1.00-1.07; p 0.02) and NT-pro BNP (HR: 1.00; 95% CI: 1.00-1.01; p 0.013) were associated with hypervolemia in multivariate regression analysis.

Conclusion: Fluid overload was identified as a predictor of an adverse prognosis in patients with HFpEF. Biospectroscopy devices could therefore help to guide diuretic therapy in the clinical setting, as they are easy to use and provide an accurate assessment of affected patients.

Table 1. Baseline characteristics

Variable	Normohydrate (n = 58)	Fluid overloaded (n = 33)	P-value
Sex female, n (%)	44(75.8)	17(51.5)	0.018
Age, years	69.2±8	73.2±8	0.026
Six minute walking test, m	359.4±101.3	304.7±132.5	0.029
NT-pro BNP, pg/ml	786.4±596.6	786.4±596.6	0.001
Transpulmonary pressure gradient, mmHg	12.3±6.4	15.3±5.6	0.038

NYHA: New York Heart Association

1349

Polymorphisms of AGTR1, AGTR2 genes and left ventricular hypertrophy in patients with arterial hypertension and hypertensive heart disease

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The activation and remodeling of renin-angiotensin system is an important link in the pathogenesis of arterial hypertension (AH) and progression of hypertensive heart disease (HHD). It may be determined by functional interaction of receptors for angiotensin II and polymorphisms of genes which control them.

The purpose of the research: analysis of the distribution of polymorphisms AGTR1 and AGTR2 genes and assessment of the degree of left ventricular hypertrophy (LVH) depending on the distribution of the isolated and combined polymorphisms of these genes in patients with AH and HHD in Ukrainian population.

Materials and Methods: 128 patients with AH and HHD were examined (ISH 2011). In the surveyed group polymorphism A1166C of AGTR1 gene and polymorphism G1675A of AGTR2 gene were determined by PCR. Subsequently, the patients were divided into 4 subgroups: subgroup (1) with isolated polymorphism of AGTR1 gene, subgroup (2) with isolated polymorphism of AGTR2 gene, subgroup (3) with combination of two polymorphisms and subgroup (4) with "normal genotypes" of these genes. In each subgroup we additionally studied the IMMLV.

In the surveyed group of patients with AH and HHD subgroup (1) consisted of (15,63%/20) patients, subgroup (2) - (11,72%/15), subgroup (3) - (64,06%/82), subgroup (4) - (8,59%/11). There is a high frequency of occurrence of these polymorphisms in the studied population. In subgroup (1) IMMLV was (145.2±6.4 g/m², p1-2=0,54, p1-3=0,02, p1-4=0,43), subgroup (2) - (142,5±5.6 g/m², p1-2=0,54, p2-3=0,03, p2-4=0,51), subgroup (3) - (132,4±4,2 g/m², p1-3=0,02, p2-3=0,03, p3-4=0,03), subgroup (4) - (141,8±4.7 g/m², p1-4=0,43, p2-4=0,51, p3-4=0,03). Noteworthy that the lowest IMMLV was in patients with combination of "pathological genotypes" of both genes, that may indicate their partial functional antagonism. Polymorphisms A1166C of AGTR1 and G1675A of AGTR2 genes and their combination in the studied population are associated with AH and HHD and also may determine features of formation and progression of LVH in these patients. AGTR2 gene polymorphism is significantly more frequent on the background of existing of AGTR1 gene polymorphism. The presence of the AGTR2 gene polymorphism on the background of the AGTR1 gene polymorphism may have partially adaptive effect on the severity of LVH.

1350

The relationships of blood levels of apelin with types of the remodeling of heart in hypertension patients with type 2 diabetesK Lushko¹; S Koval¹; T Starchenko¹; E Vysotskaya¹; A Strashnenko¹¹L.T.Malaya Institute of Therapy, NAMS of Ukraine, Kharkiv, Ukraine

Purpose: The endogenous peptide apelin has expressed inotropic, antihypertensive and antidiabetic properties. At the same time did not understand the role of apelin in the processes of the remodeling of heart in hypertensive patients with type 2 diabetes (T2D). The aim of this study was to investigate the apelin blood levels depending from the type of the remodeling of heart, in particular left ventricle hypertrophy (LVH), and its relationships with structural parameters of the left ventricle (LV) in hypertensive patients with T2D.

Methods: We examined 63 hypertension patients grades 2-3 with concomitant T2D (33 men and 30 women), aged 43 to 70 years. The investigation complex included physical examination, echocardiography with measurement of LV internal dimension at end diastole, septal wall thickness at end-diastole (SWTd), posterior wall thickness at end-diastole (PWTd) and calculation of relative wall thickness (RWT), LV mass (LVM) and LVM index. Types of cardiac remodeling we determined according to ESH/ESC 2013 and the patients were divided into the following groups: concentric remodeling of LV - 10 patients (16%), concentric LVH - 29 patients (49%), eccentric LVH - 24 patients (38%). Control group consisted of 14 volunteers. The apelin blood levels were determined by ELISA.

Results: The levels of apelin in hypertensive patients with T2D were significantly lower than in volunteers (0,882(0,788;0,924) ng/ml versus 1,097(0,944;1,171) ng/ml, $p < 0,001$). Correlation analysis revealed significant negative relationships of apelin with SWTd ($R = -0,50$, $p < 0,001$), PWTd ($R = -0,46$, $p < 0,001$), RWT ($R = -0,29$, $p < 0,05$), LVM ($R = -0,39$, $p < 0,01$) and LVM index ($R = -0,42$, $p < 0,001$). In all groups of patients the levels of apelin were lower than in control group: in patients with concentric remodeling of LV - 0,918(0,892;0,984), ng/ml ($p < 0,05$ - versus control), in patients with concentric LVH - 0,855(0,722;0,899) ng/ml ($p < 0,001$ - versus control), in patients with eccentric LVH - 0,884(0,856;0,929) ng/ml, ($p < 0,001$ - versus control). Patients with concentric LVH had significantly lower levels of apelin than in patients with concentric remodeling of LV, $p < 0,05$.

Conclusions: It was established that in hypertensive patients with T2D lowering blood levels of apelin is associated with the development of remodeling of heart, especially with concentric LVH. At the same time, in hypertensive patients with T2D observed negative correlation of apelin with cardiac structural parameters, which characterize LV wall thickness and LVM, that indicating a role of deficiency of apelin in the development of LVH.

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Association of cystatin C with heart failure with preserved ejection fraction. Potential role of myocardial fibrosisMinistry of Economy and Competitiveness (Spain) and FP7 of the European Commission A Gonzalez Miquel¹; A Huerta²; B Lopez¹; O Belouqui²; R Querejeta³; G San Jose¹; S Ravassa¹; E Zubillaga⁴; G Rabago⁵; J Diez¹¹CIMA, University of Navarra, Program of Cardiovascular Diseases, Pamplona, Spain; ²University of Navarra Clinic, Department of Internal Medicine, Pamplona, Spain; ³Donostia University Hospital, Department of Cardiology, San Sebastian, Spain; ⁴Donostia University Hospital, Department of Internal Medicine, San Sebastian, Spain; ⁵University of Navarra Clinic, Department of Cardiology and Cardiovascular Surgery, Pamplona, Spain

Purpose: Cystatin C has been shown to be associated with heart failure with preserved ejection fraction (HFPEF). Some experimental data suggest that an excess of cystatin C in the myocardium may contribute to alterations in the extracellular matrix. On the other hand, myocardial fibrosis has been shown to be involved in the development of diastolic dysfunction in HFPEF. Therefore, we hypothesized that increased cystatin C levels may be associated with myocardial fibrosis, contributing to diastolic dysfunction in HFPEF patients.

Methods: The population consisted of 156 patients with HFPEF of hypertensive origin. Cardiac morphology and function was assessed by echocardiography. Circulating levels of cystatin C, the pro-fibrotic matricellular protein osteopontin, and biomarkers of collagen type I synthesis (carboxy-terminal propeptide of procollagen type I, PICP) and degradation (matrix metalloproteinase-1, MMP-1, and its inhibitor TIMP-1) were analyzed by ELISA. 25 normotensives with no cardiac or renal disease were used as a control group. In vitro studies were performed in cardiac human fibroblasts.

Results: Compared to controls, cystatin C was increased ($P < 0.01$) in HFPEF patients, even in those with normal estimated glomerular filtration rate (eGFR). Cystatin C was directly correlated with TIMP-1 and osteopontin ($P < 0.001$) and inversely correlated with MMP-1:TIMP-1 ($P < 0.01$). Furthermore, E:E' was directly correlated with cystatin C ($P < 0.01$), osteopontin and TIMP-1 ($P < 0.001$), and inversely correlated with MMP-1:TIMP-1 ($P < 0.05$). All these associations were independent of the eGFR. Additionally, cystatin C levels were higher ($P < 0.05$) in those HFPEF patients with an abnormally high estimated pulmonary capillary wedge pressure (< 15 mmHg) compared to the patients with normal filling pressures. Interestingly,

in human cardiac fibroblasts an excess of cystatin C induced osteopontin ($P < 0.01$) and TIMP-1 ($P < 0.001$) accumulation in the cell culture media without changes in mRNA or intracellular protein content, pointing to an inhibition of their degradation, which in turn could favor myocardial fibrosis.

Conclusion: In HFPEF patients of hypertensive origin, cystatin C is increased and associated with diastolic dysfunction and biomarkers of myocardial fibrosis independently of eGFR. An excess of cystatin C may contribute to elevated filling pressures by facilitating myocardial fibrosis via accumulation of osteopontin and TIMP-1.

1352

Clinical pattern and evaluation of NT-proBNP and galectin-3 in decompensated HF-PEFY Yulia Dubolazova¹; O Drapkina¹¹I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation

Purpose: To identify clinical differences between HF-PEF and HF-REF and evaluate the potential of galectin-3 and NT-proBNP as biomarkers of decompensated heart failure both with preserved and reduced EF.

Methods: 30 patients with HF-PEF (17 women, 13 men, age 65 ± 8) and 30 patients with HF-REF (11 women, 9 men, age 63 ± 11) were included in the study. All patients were undertaken physical examination, clinical state rate scale, 6-minute walk test, echocardiography, tissue doppler imaging, evaluation of plasma NT-proBNP and galectin-3 levels.

Results: Dyspnea at rest, edema, orthopnea were significantly more rarely in HF-PEF patients (6%, 46% and 6% vs. 43%, 83% and 47% in HF-REF) ($p < 0.05$). Decompensation in HF-PEF patients was significantly less often accompanied by weight gain (30% vs. 60% in HF-REF) ($p < 0.05$). Small bubbling rales (53% vs. 70%), tachycardia (30% vs. 50%), third heart sound (7% vs. 27%), jugular venous distention (40% vs. 77%), hepatomegaly 20% vs. 60%), cardiomegaly (0% vs. 57%) also were significantly more rarely in HF-PEF compared to HF-REF ($p < 0.05$). HF-PEF patients was found to have significantly higher exercise tolerance (mean 334 m. by 6-minutes walk test) compared to HF-REF patients (mean 238 m.) ($p < 0.05$). There was no significant difference in mean NT-proBNP levels in HF-PEF patients ($153,23 \pm 114,44$ fmol/mL) compared to HF-REF patients ($142,45 \pm 90,82$ fmol/mL) ($t = 0,4$, $p = 0,68$). The higher mean NT-proBNP level in both groups was associated with more expressed signs and symptoms of HF ($r = 0,46$, $p < 0,05$, 95% CI). The higher mean NT-proBNP level is associated with lower exercise tolerance in HF-PEF patients ($r = -0,41$, $p = 0,02$, 95% CI) and worse clinical state ($r = 0,48$, $p = 0,006$, 95% CI). Mean galectin-3 plasma level was significantly higher in HF-PEF patients ($0,98 \pm 1,93$ ng/mL) compared to HF-REF patients ($0,13 \pm 0,07$ ng/mL) ($t = 2,41$, $p = 0,01$). Direct correlation between mean plasma level of galectin-3 and LV EF in HF-PEF patients was found ($r = 0,45$, $p = 0,012$, 95% CI). There was no correlation between galectin-3 mean plasma level and signs and symptoms of HF, exercise tolerance and clinical state in both HF-PEF patients and HF-REF patients.

Conclusions: Clinical signs and symptoms are significantly less expressed in HF-PEF. Use of NT-proBNP allows finding out decompensated both HF-PEF patients and HF-REF patients. Galectin-3 cannot be used as biomarker of decompensation of HF, but can help to identify HF-PEF patients. Combined use of NT-proBNP and galectin-3 allows identifying patients with decompensated HF-PEF.

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Less effective NT-proBNP-guided heart failure therapy in elderly HF patients: is there an age-dependent effect of attaining a target on mortality or is the attainability of targets age-dependent?Netherlands Heart Foundation Susan Stienen¹; K Salah¹; LMW Eurlings²; P Bettencourt³; M Metra⁴; A Bayes-Genis⁵; V Verdiani⁶; L Bettari⁷; YM Pinto¹; WE Kok¹¹Academic Medical Center, University of Amsterdam, Department of Cardiology, Amsterdam, Netherlands; ²Maastricht University Medical Centre (MUMC), Maastricht, Netherlands; ³Sao Joao Hospital, Porto, Portugal; ⁴Civil Hospital of Brescia, Brescia, Italy; ⁵Germans Trias i Pujol Hospital, Badalona (Barcelona), Spain; ⁶Careggi University Hospital (AOUC), Florence, Italy; ⁷Hospital of Cremona, Cremona, Italy

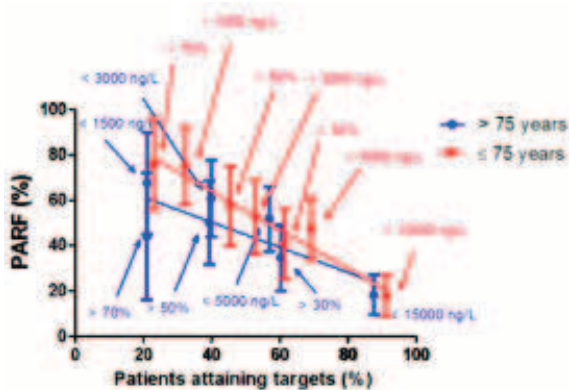
Purpose: (NT-pro)BNP-guided therapy was demonstrated to be less effective in elderly heart failure (HF) patients. Little is known about a possible age-dependent NT-proBNP-guided treatment during admission for HF (ADHF). Our aim was to investigate whether the proportion of mortality that theoretically could be prevented by attaining NT-proBNP targets is different between young and elderly ADHF patients.

Methods: Our study population was assembled from 7 ADHF cohorts. NT-proBNP was measured at admission and discharge. We defined NT-proBNP discharge targets: < 1500 , < 3000 , < 5000 and < 15000 ng/L, and relative reductions from admission to discharge of > 30 , > 50 and $> 70\%$. Population attributable risk fraction (PARF) is the proportion of all-cause mortality within 6 months after discharge that

could be reduced if a risk factor (NT-proBNP level above target) was not present. PARF was determined for each target in pts aged <75 vs ≥75 and presented as % (±95%CI). Regression lines of PARFs vs % of pts attaining NT-proBNP target levels were compared using ANCOVA, to differentiate the effects of slope and intercept

Results: Of 1266 pts (60% male, median age 74), 47% was aged ≥75. The relationship between PARF and % of pts aged <75 vs ≥75 attaining different NT-proBNP targets is depicted in the Figure. Regression slopes of the age groups for the relationship PARF vs attainability were not significantly different ($F(1;10)=2$, $p=0.2$). A significant elevation of the regression line was present in patients aged <75 ($F(1;11)=5$, $p=0.04$)

Conclusion: In ADHF, the proportion of mortality that could be prevented by attaining NT-proBNP targets is similar for young and elderly patients. However, attainability of the targets is lower in elderly patients. There is no need for age-dependent NT-proBNP targets to guide treatment



PARF vs attainability in ADHF patients

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Differences in renin-angiotensin-aldosterone system (RAAS) partially explain differences in prognosis between preserved and depressed ejection fraction

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Introduction: Baseline characteristics of heart failure with preserved (HFpEF) and reduced (HFrEF) ejection fraction are different, and prognosis of HFpEF seems to be better than that of HFrEF. Differences in neurohormonal activation between HFrEF and HFpEF have been described. The aim of this study was to analyze whether renin-angiotensin-aldosterone system (RAAS) activation is different between HFpEF and HFrEF and its relationship with prognosis.

Methods: Post-hoc analysis of a cohort of 1018 chronic ambulatory heart failure patients from a single-center study evaluating RAAS activation by measuring baseline plasma levels of aldosterone (ALD, pg/mL, n=978), plasma renin activity (PRA, ng/mL/h, n=982), plasma angiotensin-converting enzyme activity (PACe, pg/mL, n=993) and NTproBNP (NTproBNP, pg/mL, n=1018). Data are given in median [interquartile range]. HFpEF was defined as left ventricular ejection fraction (LVEF) ≥45%. Multivariate analysis using a General Linear Model (GLM) adjusted for covariates was constructed to analyze the relationship between RAAS markers and HFpEF. Cox regression was constructed to analyze the relationship of HFpEF and cardiovascular (CV) mortality.

Results: Mean LVEF was 60% in HFpEF and 31% in HFrEF. Patients with HFpEF (n=496) were older, more frequently female and hypertensive, with less coronary artery disease as a cause of HF, and higher prevalence of chronic kidney disease, anemia and atrial fibrillation. Functional class was similar (NYHA III-IV in 43% of the cohort). HFpEF patients received less frequently treatment with beta blockers, ACEI/ARBII and mineralocorticoids antagonists. Use of diuretics was similar. There was a negative correlation of NT-proBNP, ALD, PRA and LVEF ($p < 0.006$). NTproBNP was significantly lower in HFpEF [1277 [647-2873] vs 1998 [749-4687], $p < 0.001$] as were ALD and PRA [92 [44-156] vs 104 [58-186], $p = 0.004$ and 2.7 [0.9-8.3] vs 3.5 [1.1-10], $p = 0.043$, respectively]. No differences in PACe was seen between HFpEF and HFrEF. In GLM adjusted for covariates, PRA ($p = 0.021$) and NT-proBNP ($p < 0.001$) were lower in HFpEF compared to HFrEF.

During a median follow-up of 12 (6-18) months, CV mortality was higher in HFrEF (11% vs 7%, $p = 0.021$). In multivariate Cox analysis adjusting for demographic and comorbid conditions, cardiovascular death was higher in HFrEF (HR 1.62; 95%CI 1.03-2.53, $p = 0.036$). However, this difference was lost when markers of RAAS activation were taken into account (HR 1.47; 95%CI 0.91-2.35, $p = 0.11$).

Conclusions: RAAS activation is lower in HFpEF, partially explaining the differences in prognosis compared to HFrEF.

1355

Vitamin D deficiency and the prognosis of patients suffering from diastolic dysfunction or heart failure with preserved ejection fraction

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Purpose: Vitamin D deficiency is prevalent in heart failure (HF) and is known to be associated with a poor outcome in patients with HF and reduced ejection fraction (HFrEF). The association of 25-hydroxyvitamin D [25(OH)D] serum levels with prognosis in patients with asymptomatic diastolic dysfunction (DD) or HF with preserved ejection fraction (HFpEF) has not been investigated so far.

Methods: We measured 25(OH)D serum levels in n=787 outpatients with risk factors for DD or with previous diagnosis of HF. The mean value of E/e' medial was 13 and 15% of the patients had HFpEF according to the Paulus scheme. Serum 25(OH)D measurement were performed at baseline by a competitive binding protein assay with an interassay coefficient of variation of 10-15%. Physical examination, echocardiography, six-minute walking test and blood sampling were obtained. Patients were followed for 5 years.

Results: Patients with lower 25(OH)D levels (≤10.9 ng/ml; n=263) were older ($p = 0.002$) and more symptomatic (oedema, fatigue; both $p < 0.001$) than those with higher 25(OH)D levels and had more often HF signs and symptoms ($p < 0.001$). Lower 25(OH)D levels were also associated with lower GFR ($p = 0.012$), lower HDL ($p = 0.044$), and higher uric acid ($p < 0.001$). Patients with lower 25(OH)D also demonstrated reduced exercise capacity (six-minute walk distance, SF-36-physical functioning score; both $p < 0.001$) and had higher values of LAVI ($p = 0.005$). A lower level of 25(OH)D (per 10 ng/ml) was significantly associated with increased NTproBNP ($p = 0.001$), uric acid ($p < 0.001$) and LAVI ($p = 0.001$) and decreased SF-36 physical functioning score ($p < 0.001$). Furthermore a lower level of 25(OH)D (per 10 ng/ml) was associated with HF ($p < 0.001$), DD ($p = 0.002$), atrial fibrillation ($p = 0.004$), oedema ($p < 0.001$) and the application of diuretics and anticoagulants (both $p = 0.001$). The associations remained significant after adjusting for age. A lower level of 25(OH)D (per 10ng/ml) tended to be associated with higher 5-year-mortality ($p = 0.05$, HR 1.55). Further, a lower level of 25(OH)D was related to an increased rate of cardiovascular hospitalizations ($p = 0.023$, HR=1.74). This finding remained statistically significant after adjusting for age ($p = 0.046$, HR=1.63) and NTproBNP at baseline ($p = 0.047$, HR=3.5).

Conclusion: Lower 25(OH)D levels are associated with reduced functional capacity in patients suffering from DD or HFpEF. A lower level of 25(OH)D was, also after adjusting for age and NTproBNP, significantly predictive for an increased rate of cardiovascular hospitalizations.

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Prognostic significance of atrial arrhythmias in heart failure with preserved ejection function: insights from KaRen

ederation francaise et société française de cardiologie, medtronic europeE Erwan Donal¹; C Bosseau¹; LH Lund²; E Oger¹; C Hage²; C Linde²; JC Daubert¹

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The prognosis of atrial arrhythmias in heart failure with preserved ejection function (HFPEF) remains controversial. The objective of this KaRen sub-study was to assess prognostic significance of atrial arrhythmias in patients with HFPEF.

Methods: KaRen is a prospective, multicenter, international registry aiming at characterizing HFPEF which enabled inclusion of 538 patients having a LVEF > 45%. We compared patients who remained in sinus rhythm versus patients with atrial tachyarrhythmias at the 4-8 week visit for the primary study endpoint: death from all causes or first hospitalization for heart failure (HF).

Results: A total of 413 patients (244 patients in sinus rhythm, 134 with atrial tachyarrhythmias) were analyzed with a mean follow-up of 28-months. This study

included elderly patients (mean age 76.2 years-old. Patients with atrial arrhythmias had a similar survival-free from the primary study endpoint than those in sinus rhythm ($p=0.89$). At the 4-8 week-visit, heart rate, treatments were not associated with prognosis. Nevertheless, echocardiographic characteristics (table I), the natriuretic peptides were in favor of a more severe heart condition in atrial arrhythmia patients.

Conclusion: In this elderly population with high prevalence of non-cardiovascular comorbidities, the survival-free from the primary endpoint was similar between the patients in sinus rhythm and those presenting atrial arrhythmias. The prognosis of atrial arrhythmias in HFPEF seems to be independent on patient's echocardiographic characteristics.

Table I

Characteristics	Sinus rhythm	AF or Flutter	p
N=204	N=118		
LVES diameter	31.41 ± 6.62	33.05 ± 6.10	0.0325
Stroke volume	32.50 ± 9.02	29.03 ± 7.28	0.0020
LAVI¶	42.07 [35.24-51.75]	53.07 [43.30-63.47]	<.0001
E/e'	12.00 [9.41-16.55]	10.27 [7.57-14.92]	0.0024
TAPSE	18.96 ± 4.51	14.47 ± 3.57	<.0001
LV GLS	-15.58 ± 3.76	-12.67 ± 3.41	<.0001
RV GLS	-20.70 ± 5.08	-16.07 ± 4.46	<.0001

Poster Session 3

Monday 25 May 2015 08:30–18:00

Location: Poster Area

ACUTE HEART FAILURE

P1366

Reverse Takotsubo cardiomyopathy after percutaneous epidural neuroplasty

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Reversible stress-induced cardiac dysfunction is frequently seen as a complication of acute stress states. Takotsubo cardiomyopathy [TCM] may mimic myocardial infarction. Echocardiography typically show transient left ventricular apical wall motion abnormalities. We report a case of TCM with reverse echocardiography finding occurrence in a 47-years-old female after percutaneous epidural neuroplasty (PEN). She had not discomfort after PEN, but after 1 day presented with complained of sudden dyspnea and chest discomfort during epidural saline injection. He has had no prior medical history and cardiac disease. Preoperative ECG was normal finding. She complained severe pain during epidural injection. Oxygen saturation was depressed and ECG showed ST depression at chest leads(Fig1). Severe pulmonary edema was developed (Fig2) and cardiac enzyme was elevated. Transthoracic echocardiogram during end-diastole (a) and end-systole (b) showed basal and midventricular segmental hypokinesis of the left ventricle (Fig3). Coronary angiographic finding was normal (Fig4). She was recovered after conservative treatment 1 week later. Inverted takotsubo pattern is a stress-induced cardiomyopathy that could be encountered in patients with percutaneous neuroplasty and is generally of good prognosis.

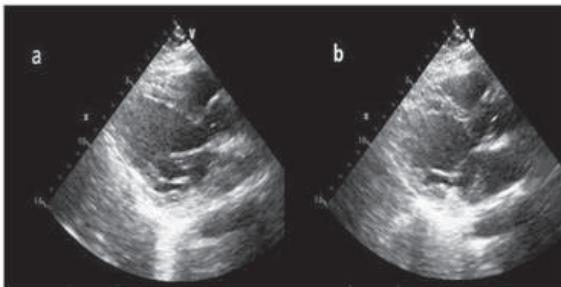


Fig3

P1367

Clinical significance of severe tricuspid regurgitation on admission in patients with acute heart failure

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Tricuspid regurgitation (TR) is frequently present in patients admitted with acute heart failure (AHF). The aim of our study was to demonstrate if patients with AHF and severe TR on admission represent a subset of patients with higher risk.

Methods: We processed the data of 50 patients with AHF. On the basis of echocardiographic findings on admission, the patients were divided into two groups: (1) with severe TR (TR+, 14 men, 4 women, mean age 68,2 years), and (2) with mild/moderate TR (TR-, 23 men, 9 women, mean age 67,3 years). Using chi-square statistics we compared the clinical, prognostical and paraclinical (ECG, echocardiography, laboratory) data of the two groups (significant $p < 0,05$).

Results: In the TR+ group we found a significantly increased prevalence of the following parameters: important mitral regurgitation ($p = 0,0206$), systolic blood pressure < 120 mmHg ($p = 0,0279$), major RBBB ($p = 0,0352$), dilated right ventricle ($p = 0,0353$), signs of right ventricular overload ($p = 0,0158$), increased left atrial size ($p = 0,0101$), presence of atrial fibrillation ($p = 0,0154$), left ventricular ejection fraction $< 40\%$ ($p = 0,0223$), oral anticoagulat treatment ($p = 0,0006$), hospital stay > 10 days ($p = 0,0018$). We did not find significant differences regarding gender ($p = 0,6478$), age ($p = 0,4794$), right ventricular hypertrophy on ECG ($p = 0,2386$), high doses of loop diuretics ($p = 0,639$) and CORE (Yale University) mortality index $> 15\%$ ($p = 0,2265$).

Conclusions: In AHF the presence of severe TR correlates well with the severity of cardiac functional and structural alterations, especially with those of right ventricle. However, probably due to its highly dynamic feature, its prognostic value requires further clarifications.

P1368

Introduction of natriuretic peptide testing to acute NHS hospitals needs education to maximise impact

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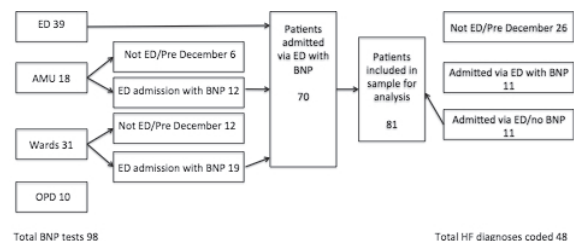
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Purpose: BNP reduces uncertainty in acute heart failure (HF) diagnosis but has not been routinely available to Emergency Departments (ED) in the UK. New guidance encourages their use but cost remains a concern. We report the very early experience of their availability in our general hospital.

Methods: All BNP tests in December 2013 were recorded and the ED record reviewed if the patient was seen there. Symptoms, signs and ED diagnosis were recorded. All patients coded with a discharge HF diagnosis were also reviewed and the ED record reviewed if they were assessed there. In all cases the discharge summary diagnosis was recorded.

Results: 70 patients presented to the ED and had a BNP during their admission. A further 11 patients with a HF diagnosis had been seen in the ED: all with signs and symptoms of HF recorded and 5 diagnosed as such. 3 were discharged from ED with early investigation planned. Of the 39 having BNP in the ED 4 were discharged, 2 prompted by the result. 16 had an ED diagnosis of HF (median BNP 297g/ml, range 1-1254) and 8 retained this to discharge. 3 of the 16 had a BNP < 100 and all final non-HF diagnoses. Review suggests 11 of the 66 (17%) admitted from ED could have been discharged with early specialist follow up. Cases of significantly elevated BNP were seen and not incorporated into ED or final discharge diagnosis.

Conclusions: Out initial experience shows BNP is initially often used to confirm a diagnosis of HF rather than its powerful negative predictive value being exploited. Its introduction into practice needs education stressing the value of a negative result, along with mechanisms to facilitate early discharge with specialist assessment when safe to do so. The limited results also suggest more heart failure cases are likely to be identified.



81 ED notes were analysed as shown

P1369

Incremental value of mean platelet volume as a marker of decompensation in patients with congestive heart failure

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Purpose: Congestive heart failure (HF) is a major public health problem that is related to substantial morbidity, impaired quality of life and diminished survival. When HF patients decompensate, increased intra and extracellular fluid accumulation leads to various symptoms. We hypothesized that intracellular fluid accumulation during decompensation may lead to an increase in parameters related to cellular dimensions such as mean platelet volume (MPV). The aim of the study is to investigate whether there is a difference in terms of MPV in HF patients between decompensated and stable states.

Methods: Patients who were hospitalized due to decompensated HF were enrolled to the study. Transthoracic echocardiographic examination and routine blood tests including hemogram were performed upon admission to hospital. All patients received diuretic (furosemide) treatment during hospitalization. Functional capacities, urine output and weight loss of the patients were recorded during hospitalization. Control hemogram was tested before discharge from the hospital in a stable state.

Results: Ninety-six patients with decompensated HF were enrolled. The most common symptom was orthopnea and mean left ventricular ejection fraction was 0.24 ± 0.12 . Six patients died due to cardiac arrest and 3 patients had acute cerebrovascular embolisation during hospital stay. The mean hospitalization time was 7 ± 4 days and mean daily diuretic dose per patient was 96 ± 72 mg. The mean daily urine output per patient was 2.8 ± 2.1 L and mean weight loss per patient was 14.8 ± 12.1 kg. Mean MPV during decompensation was significantly higher than that of compensation before discharge (14.7 ± 6.9 vs. 10.8 ± 4.1 ; $p = 0.021$). Also there was a positive correlation between the quantity of weight loss and the difference between MPV values during hospitalization ($r^2: 0.93$; $p < 0.001$).

Conclusion: MPV is increased in decompensated HF patients and decreases in response to diuretic treatment during hospitalization. So, MPV may be used as a marker of decompensation during the follow up of HF patients and gives the clinician an opinion about the success of the diuretic treatment.

P1370

Hyponatremia in children hospitalized with acute decompensated heart failure: prevalence, severity and association with clinical outcome

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Objective: To determine the prevalence, severity and outcomes of hyponatremia in children hospitalized with acute decompensated heart failure (HF).

Methods: Consecutive patients (pts) at a single institution who required hospitalization for treatment of acute decompensated heart failure were studied. Inclusion criteria: pts age 3 months to 21 years hospitalized for HF attributable to ventricular dysfunction. Exclusion criteria: acute graft rejection, disease of the central nervous system, HF attributable to left-to-right intracardiac shunts, cyanotic heart disease, treatment with vasopressin during hospitalization. Admission serum sodium (Na) concentration and lowest Na before the primary end-point or discharge were examined. The primary end-point was death, transplant or use of mechanical circulatory support.

Results: One hundred forty-one patients met study criteria. Etiologies of HF included: dilated cardiomyopathy (n=89, 63%), acute myocarditis (n=27, 19%), ischemic cardiomyopathy (n=17, 12%), restrictive cardiomyopathy (n=5, 4%), hypertrophic cardiomyopathy (n=5, 4%). The cohort included 48 (34%) pts with pre-existing HF. Mean serum Na at admission was 137 ± 4 mmol/L. Hyponatremia (serum Na <135 mmol/L) was present in 45 (32%) pts at admission. Hyponatremia subsequently developed in 72 (51%) pts during their hospitalization and dropped below 130 mmol/L in 50 (35%) pts. The primary end-point occurred in 58 (41%) pts. Those pts who were hyponatremic at admission were more likely to reach the primary end-point than pts who had normal or high Na concentrations at admission (26/45 pts [58%] vs 32/96 [33%], $p = 0.006$). The mean lowest serum Na concentration before the primary end-point was $128 (\pm 4)$ mmol/L. Hyponatremia at admission was independently associated with death, transplant or the use of mechanical circulatory support during hospitalization (OR 3.1, $p = 0.003$).

Conclusions: Hyponatremia occurs commonly in children hospitalized with acute decompensated heart failure and is associated with increased risk of in-hospital mortality, transplant and need for mechanical circulatory support.

P1371

Influence of activity of rheumatism on the progression of heart failure in patients with rheumatic heart disease

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Purpose of the study: influence of activity of rheumatism on linear and volumetric indicators of the left ventricle (LV) and its contractive function in patients with rheumatic heart disease.

Materials and Methods: 115 patients with rheumatic heart disease were studied. Depending on the degree of activity of the rheumatic disease, the patients were divided into 2 groups. In the 1st group there were 48 patients with no activity of rheumatism (ESR -7.5 ± 1.5 mm/h), in the 2nd group there were 7 patients with clinical signs of rheumatism activity and with high indicators of ESR (18.0 ± 1.8 mm/h) and positive value of CRP (1.43 ± 0.1). All the patients went through clinical-instrumental and laboratory methods of examination.

Results: According to the echocardiography, LV parameters of Group 1 patients were within normal limits: end-systolic size (ESS)- 3.5 ± 0.1 cm, end-systolic volume (ESV)- 52.3 ± 6.9 ml, end-diastolic size (EDS)- 5.2 ± 0.1 cm, end-diastolic volume (EDV)- 130.9 ± 7.7 ml. In Group 2 patients, ESS increased by 7.9%, ESV by 20.9%, EDS by 8.8%, EDV by 17.7% ($p < 0.05$). Also, an increase was observed in the sphericity index of systole ($-C\Phi c - 0.67 \pm 0.02$ cm) by 16.5%, indexed myocardial mass (IMM)- 173.9 ± 11.6 g/m² by 26.8%, myocardial stress in diastole (MSd)- 82.5 ± 3.9 g/cm² by 19.2% ($p < 0.05$), and reduction of the integral systolic remodeling index (ISRI)- 67.3 ± 1.9 by 10.2% ($p < 0.05$) compared with patients of Group 1. EF was normal in all groups. For patients of Group 1, normal LV geometry was characteristic, for Group 2 it was eccentric LV hypertrophy ($p < 0.05$) Consequently, the activity of rheumatism enhances the expansion of LV cavity, directly affecting the processes of myocardial remodeling. Moreover, the low values of ISRI in our patients indirectly indicate the progression of myocardial insufficiency and reduced contractility of the left ventricle.

Outcome: activity of rheumatic process is probably one of the factors contributing to the progression of chronic heart failure in patients with rheumatic heart disease.

P1372

The efficacy of the handheld echocardiography for the severity stratification of the acute dyspnea during the urgent cardiological consultation

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Purpose: to evaluate the feasibility and accuracy of the handheld echocardiography (HHE) for the severity stratification of the patients with acute dyspnea referred for urgent cardiological consultations (UCC) compared with standard transthoracic echocardiography (STE) and its impact on the further management of these patients.

Methods: we performed a prospective study on 55 patients (32 females, mean age 67 ± 15 years) referred for UCC for acute dyspnea from different departments of a multidisciplinary hospital in whom the bedside ECG performed during the UCC was considered as non-diagnostic.

Results: the most frequent findings were left ventricle systolic dysfunction (kappa coefficient of agreement between HHE and STE = 0.82) and left atrium dilatation ($k = 0.91$) while the less frequently seen was pericardial effusion. Mitral valvular abnormalities were detected by HHE in 46% of the cases vs. 65% of STE ($p = 0.04$) and aortic valve abnormalities in 32% of the cases vs. 52 % ($p = 0.04$). The waiting time for the examination by HHE was 18 ± 6 minutes compared with 61 ± 17 minutes ($p < 0.01$) for STE. The duration of the examination was 13 ± 4 minutes by HHE vs. 31 ± 11 minutes by STE ($p < 0.001$). In the 19 (34.5%) patients that were immediately hospitalized the HHE had excellent correlation with STE.

Conclusions: HHE performed during the UCC for acute dyspnea is feasible and its accuracy compared to STE was able to correctly stratify the severity of the patients. This facilitated the urgent management of the patients by significantly reducing the time until the required medical action (hospitalization or intervention) was done.

P1373

Combined cardiac and lung ultrasound protocol for differential diagnosis of acute dyspnea in the emergency department

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Objectives

To combine Echo and LUS into a "thoracic FAST exam", a rapid ultrasound protocol to be used for examining acutely dyspneic patients immediately after arrival in the emergency department (ED). To use the protocol for diagnosing AHF with pulmonary congestion, and to examine its yield in differential diagnosis among these patients.

Methods: We included 99 cognitively intact adult patients presenting with dyspnea at rest in our ED. Patients with mitral stenosis or pulmonary fibrosis were excluded. LUS of 2-3 pulmonary fields and pleuras bilaterally, medial E/e' and visual estimation of the right side of the heart were performed. Other alarming findings were reported if seen. The patients were classified as having AHF if E/e' was >15, and either bilateral B-lines (BBL) or rightsided/bilateral pleural fluid (PF) was present on LUS.

Results: According to the protocol, 53 (53,5 %) of the 99 patients had AHF, and 46 (46,5 %) an alternative diagnosis. The mean E/e' was 21,14 (SD 4,30) for AHF patients, and 9,75 (SD 2,96) for the control group (p < 0,001). In the AHF group 51 patients (96,2 %) had BBL, and 37 (69,8 %) PF, compared with 7 (15,2%) and 2 (4,3%) in the non-AHF group (p < 0,001 for both).

In the non-AHF group, the thoracic FAST protocol was indicative of an alternative diagnosis in 21 (56,7 %), and normal in 18 (39,1 %) of the patients (see table below). The ED- clinicians used standard measures to establish their clinical diagnosis as usual, and they would also have access to the Echo and LUS exams if they wished to.

Conclusion: A focused ultrasound protocol combining LUS and Echo might be a fast and helpful tool in diagnosing AHF, also providing aid with differential diagnosis of other potentially life threatening conditions among dyspneic patients in the ED.

		Thoracic FAST findings	
FAST positive	AHF	E/e' >15 in all	B/Lines
	53/99 (53.5%)	51/53 (96.2%)	37/53 (69.8%)
		Bilateral or right-sided pleural fluid	
FAST negative (other diagnosis)	Pneumonia	11/21 (52.4%)	10/21 (47.6%)
	Obstructive pulmonary disease	2/18 (11.1%)	3/18 (16.7%)
	Decompen. NAD	7/17 (41.2%)	7/17 (41.2%)
	Secondary pulmonary hypertension	4/15 (26.7%)	4/15 (26.7%)

FAST findings according to diagnosis

P1374

Blood transfusions as heart failure cause after cardiac surgery

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Bleeding during and after cardiac operations and the hemodilution effects of cardiopulmonary bypass commonly result in blood transfusions. Despite institutional efforts to avoid the frequency of blood transfusions in cardiac operation, the frequency remains high.

If transfusions were completely safe, differing thresholds would not matter. However, the adverse reactions associated with transfusions are: febrile reactions, post-transfusional syndrome, pulmonary oedema acute, haemolytic and infectious complications may occur. Most recently, blood transfusions have been linked to postoperative wound infections, pneumonia, renal dysfunction, severe sepsis, hospital mortality and increased 5-year mortality.

Aims: Bleeding occur frequently in patients undergoing cardiac surgery. Although unexpected bleeding after this surgery is common, reducing this bleeding is a desirable clinical goal, because such bleeding is associated with adverse outcomes. Our study was performed to identify those patients receiving blood transfusions and heart failure as a complication.

Methods and Results: A prospective preliminary study was realized involving 200 patients (A-100, B-100) at our Intensive Care and Heart Transplantation Unit. All patients signed consent for blood transfusions if necessary. All patients were studied before surgical procedure and underwent a total of 100 routine follow up echo cardiography study for fraction ejection control. All patients received homologous blood transfusion during and after open heart surgery. Minimum was transfused among 5 and 10 blood units.

Complications (Table I) were considerable important, because the recovery time was too long comparing with those patients not getting blood. The fraction ejection control was successful increased faster in not transfusions patients.

Conclusions: Evidently, several blood transfusions in open heart surgery represent a big group of complications in relation with a long recovery time leading to graft rejection and death.

When is possible to realize a surgical procedure no in emergency status, is necessary the hemodynamical patient stability, controlling the lack of blood before procedure, the basal mean hematocrit value, avoiding myocardial ischaemia and the subsequent use of recombinant erythropoietin to treat postoperative anaemia. Heart failure

is not an uncommon complication and we must be carefully and take the necessary diuretic control after first concentrate.

P1375

Very low-dose dopamine combined with furosemide compared with continuous infusion of furosemide in acutely decompensated heart failure

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Introduction: Several studies suggested that low dose dopamine administration has no additional benefit on diuresis, renal function and clinical outcome in patients with acute decompensated heart failure (ADH). However, 'renal dose' may not be the same for all patients. Drug discontinuation due to tachycardia is reported even at doses of 2 mcg/kg/min. The aim of this study was to evaluate the effect of very low-dose dopamine (1 mcg/kg/min) in ADH patients.

Methods: We retrospectively evaluated 100 consecutive patients (63 males, 37 females, mean age 67 ± 12 years) admitted with ADH and divided the group as very low-dose dopamin + furosemide (VLD+F) and continuous infusion furosemide (CF) groups. The effects on diuresis, renal function on 24th and 72nd hours, mortality and rehospitalization due to AHF in 60th and 180th days were recorded.

Results: Systolic blood pressure (125 ± 12 mmHg), creatinine (1.27 ± 0.6 mg/dl) and NT-proBNP (9624 ± 10256 ng/dl) on admission and total furosemide dose (120 mg/day) during treatment were similar between the two groups. Rate of diuresis was higher (24th hour: 3272 ml vs. 2696 ml, P=0.05; 72nd hour: 8468 ml vs. 7597 ml, P=0.06) and length of hospital stay was slightly but not statistically shorter (VLD+F: 8 ± 3 days vs. CF 9 ± 4 days, p=0.08) in VLD+F group. Creatinine at 24th (VLD+F 1.35 ± 0.8 mg/dl vs. CF 1.33 ± 0.8 mg/dl, P=0.07) and 72nd hours (VLD+F 1.44 ± 0.6 mg/dl vs. CF 1.41 ± 0.8 mg/dl, P=0.84) and electrolytes were not different. Mortality (180th day: VLD+F 3 patients vs. CF 2 patients) and rehospitalization rates (180th day: VLD+F 3 patients vs. CF 2 patients) at 30 and 180 days were also not different. The effects of VLD+F on diuresis and hospital stay was more marked in patients with a systolic blood pressure <120 mmHg. However, other endpoints were not affected.

Conclusions: Very low dose dopamin combined with furosemide have similar effect and safety as continuous furosemide infusion in ADH.

P1376

Pre-hospital management and vital status of patients transferred to emergency department by emergency medical services compared to non-EMS patients

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The role of early management of acute heart failure (AHF) has been underscored in the recent literature. The real-life data on prehospital AHF management and possible differences in vital signs before and after transportation to hospital are scarce.

Purpose: To analyze EMS treatment relevant for AHF and whether vital signs differ 1) between initial prehospital values and those on admission to emergency department (ED) in EMS patients and 2) between EMS and ambulatory non-EMS patients on admission to ED.

Methods: We included patients with AHF from three academic emergency departments and divided them to those transferred by emergency medical services (EMS group) and non-EMS group from July 2012 to 2013. Data was collected from electronic EMS and hospital databases.

Results: Of total 873 AHF admissions, 100 were EMS patients (11.5%). Minority was medicated in EMS: 21% received morphine, 21% oral nitrate aerosol, 7% nitrate infusion, and 7% bronchodilator. None of the patients received iv diuretics. Vital signs are shown in Table.

Conclusion: Few AHF patients arrive to hospital by EMS and few receive medication before admission. No major differences exist in vitals in EMS patients between home and ED or EMS and non-EMS patients in ED.

Vital signs of EMS and non-EMS patient			
Patient groups	1. EMS: pre-hospital values	2. EMS: ED values	3. Non-EMS: ED values
SBP (mmHg)	139.0 (32.1)	140.6 (27.0)	139.6 (29.7)
Heart rate (/min)	89.2 (22.5)	84.5 (19.0)†	84.3 (31.1)
Respiratory rate (/min), n=718	22.9 (6.6)	22.3 (6.7)	22.5 (7.6)
SpO2 (%)	90.3 (8.6)	91.8 (8.5)	92.9 (6.6)

Values are mean (SD). SBP, systolic blood pressure. †P-value for comparison between 1 and 2 =0.024

P1377

Characterization of in-hospital adverse events by day of hospitalization in patients admitted with pulmonary edema - data from RO-AHFS study

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Purpose: Pulmonary edema (PE) is a common manifestation of acute heart failure syndromes (AHFS) and is associated with a dramatic clinical presentation and poor in-hospital outcomes. Present study was a post-hoc analysis of adverse in-hospital events in PE patients in relation to time since hospital admission.

Methods: The Romanian AHFS (RO-AHFS) registry prospectively enrolled 3224 consecutive patients between January 2008 and May 2009 admitted with a primary diagnosis of AHFS at 13 medical centers. On admission all patients were divided into 5 clinical profiles, 924 patients being classified as PE. In-hospital adverse events were defined as: in-hospital all cause mortality (ACM), need for ICU admission, need for iv inotropes, and need for invasive mechanical ventilation (IMV).

Results: Patients admitted with PE had a mean age of 71 ± 10.4 , 49.7% were male, ischemic etiology was noted in 70.8% and mean ejection fraction was $39.2 \pm 13.2\%$. A proportion of 7.4% patients died during hospitalization, 17.2% required ICU admission, 18.4% received iv inotropes, and 7% required IMV. All in hospital adverse events were significantly more frequent in the first 24 hours and steadily declined afterwards (Table 1).

Conclusions: Since the rate of adverse events is the highest in the first 24 hours, appropriate triage decisions and the quality of the initial life saving measures may be crucial for in-hospital outcome.

Table 1

	Day 1	Day 2-5	Day 5-10	Day >10	p value*
ACM (%)	57%	18%	11%	14%	$p < 0.001$
ICU (%)	71%	23%	6%	0%	$p < 0.001$
Iv inotropes (%)	48%	25%	24%	3%	$p < 0.001$
Invasive mechanical ventilation (%)	68%	19%	8%	5%	$p < 0.001$

* p values adjusted for multiple comparisons between Day 1 and the rest

P1378

The profile of patients with acute heart failure managed in prehospital setting

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Purpose: To describe the profile and management of patients with acute heart failure (AHF) in pre-hospital area.

Methods: Registry data of the Emergency medical system (EMS) of South Moravian region of Czech Republic were used. Patients were enrolled consecutively during the period of January 2010 - December 2011. Excluded were patients who died or were resuscitated before the arrival of the EMS. We compared patients transported to the hospital with those treated in outpatient manner. Mortality within the first 30 days after the initial EMS contact was assessed as the main endpoint.

Results: From the 86584 of patients who called EMS, 1310 were transported to the hospital and 35 were treated in outpatient manner as having AHF. Median age of the study population was 78 years, the most common comorbid condition was hypertension (67.0%), nearly one half of the study population had signs of pulmonary oedema (46.4%). Patients not transported to the hospital were more frequently of male gender (71.4% vs. 49.1%, $p < 0.05$), with lower incidence of comorbid conditions (ischaemic heart disease 17.1% vs. 45.0%, diabetes mellitus 8.6% vs. 36.0%, hypertension 20.0% vs. 68.2%, $p < 0.001$), did not have a signs of respiratory distress (median oxygen saturation 96% vs. 87% in those transported to the hospital, $p < 0.05$) and nobody had signs of pulmonary oedema in this population. The most common drug applied in pre-hospital care is furosemide (74.0% patients), intravenous nitrates were used in 30.6%. The all-cause 30-day mortality rate of the whole study population reached 20.7% and was 21.1% in group transferred to the hospital in comparison with 2.9% of patients treated in outpatient manner ($p < 0.001$).

Conclusion: AHF represents less than 2% of all emergency calls for acute symptoms. The vast majority of patients are transported to the hospital with the assumption of hospitalization. Early mortality rates of these patients are high.

P1379

The magnitude and management of acute heart failure in the Netherlands

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Purpose: To understand the magnitude and management of patients hospitalized for acute heart failure (AHF) in the Netherlands (NL) in order to identify possible opportunities for improving medical care.

Methods: A survey of heart failure specialists in NL utilising a structured iPad-based questionnaire with the following items: number of patients hospitalized with AHF per week; percentage of patients hospitalized for AHF presenting as 'de novo'; baseline blood pressure at admission; the diagnostic regimen used to diagnose AHF; first line treatment for AHF; criteria used to determine improvement in the patient's condition; length of hospital stay and guideline adherence for CHF therapy at discharge.

Results: A total of 45 cardiologists and 3 cardiology residents from 8 university hospitals (UH) and 40 general hospitals (GH), together representing 52% of hospitals in NL, took part in this survey conducted Nov 2013 to Dec 2014. On average 6.1 (range 1 - 20) patients were hospitalised for AHF per week in each hospital; of which 28% presented as de novo. The diagnostic regimen in all UH consisted of a physical exam, blood pressure measurement, chest x-ray, echocardiography and/or ECG. Whereas 77% of GH reported a standard diagnostic approach consisting of a blood pressure measurement, echocardiography and/or ECG and an NTpro-BNP measurement. A chest x-ray and physical exam, as part of the diagnostic work-up, was reported in approximately 50% of GH. First line treatment for AHF consisted of: diuretics (100%), nitrates (75%), oxygen (67%) and opiates (25%). All participants reported using signs and symptoms to determine improvement in a patient's condition, whereas other parameters were used less frequently: biomarkers (22%), heart rate (33%) and oxygen saturation (50%). Participants reported that guideline recommended therapy for (CHF) was initiated in more than 80% of patients prior to hospital discharge. Diuretics were given in 73% of patients and a MRA in over 50%, whereas nitrate use was limited to 14%.

Conclusions: This survey revealed that AHF is a significant medical issue in NL, with a similar magnitude of approximately 29,000 AHF hospitalisations per year. Establishing a standard approach in diagnosing AHF could lead to an improvement in heart failure care in NL. Interestingly, signs and symptoms still remain the criteria used to determine improvement in the patient's condition despite advances in biomarkers research. Guideline-recommended medication for AHF at admission and CHF at discharge was being followed in the majority of patients.

P1380

Comparison of the efficacy of urapidil and nitroglycerin in older women with non valvular heart failure

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Abstract: Objective: To evaluate whether the α -1 blocker, urapidil, provides additional therapeutic benefits compared to nitroglycerin in treatment of non valvular heart failure complicated by hypertension and diabetes mellitus in elderly patients.

Method: Forty-six elderly patients were randomized into two groups which received treatment with either urapidil or nitroglycerin, respectively. All patients were monitored for blood pressure (BP), heart rate (HR), and received tests for metabolic activity and cardiovascular function prior and after treatment.

Results: Patients receiving urapidil had significantly lower systolic blood pressure (SBP) than their counterparts in nitroglycerin group ($F=4.53$, $P < 0.05$). Moreover, patients in urapidil group showed lower NT-proBNP levels compared to patients in nitroglycerin group ($F=8.93$, $P < 0.01$). While both urapidil and nitroglycerin decreased fasting plasma glucose (FPG) levels, there was no significant difference of FPG levels between these two groups ($P > 0.05$).

Conclusions: Urapidil demonstrated better efficacy than nitroglycerin on lowering and stabilizing SBP, attenuating cardiac afterload, and improving cardiac function. Urapidil is a therapeutic option for the MHF patients complicated with hypertension and DM.

P1381

Differences between index and following acute heart failure episodes

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Background: Nobody takes in doubt that Acute Heart Failure (AHF) is the cardiovascular pandemic of the 21st Century, the progressive aging of the population and

the improve in survival allows its prevalence to continuously increase. It has a high repercussion on the sanitary budget. Guidelines told us to manage in different ways the index episode and the following ones.

Objectives: Analyzing the characteristics and management between of the index episode and the successive ones in a hospital with a health population of 210.000 persons. Establishing the differences between the medical specialties implicated from quality and efficiency indicators. Then we compare it with the desirable.

Methods: We analyze 600 discharges which main diagnosis was CIE 428 (AHF). We calculate the costs per patient by analytic accountability. We study the hospitalization time, the use of diagnostic tests, the costs and the characteristics of the patients. Results (Table 1) shows the different results comparing index and followings episodes.

Conclusions: 1. Our percentage of index cases is higher than the found in literature, representing one third of the discharged patients. They are shared in similar percentage between the three specialties. Following cases rarely go to Cardiology 2. There is a low use of Ultrasonography (NICE guides recommend doing it to all index cases). This is particularly low in Geriatrics and Internal Medicine.

3. There are no significant differences in costs between index episode and the followings. This could be because high use of diagnosis tests in the index episode is compensated by the prolongation of the hospitalization days in the following cases.

4. There is a tendency in index episode to be in younger persons and to take fewer hospitalization days

5. There are more index episode in patients with heart function preserved

Table 1

	Index	Following	p
Discharges(%)	196(34)	386(66)	
US(%)	54%	26%	<0.01
Coronariography(%)	14%	4%	<0.01
Costs(€)	2848	3128	0.362
Age	79	81	0.089
Hospitalisation(days)	7.70	8.65	0.005

P1382

Maximizing the cGMP system with the combination of PDEV inhibition and BNP IN preclinical systolic and diastolic dysfunction (stage B heart failure)

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Introduction: Preclinical systolic dysfunction (PSD) is defined by LVEF < 45% without symptoms of heart failure (HF), while preclinical diastolic dysfunction (PDD) is defined as normal systolic function, moderate or severe diastolic dysfunction determined by Doppler criteria but with no symptoms of HF. There is an impaired cardiorenal response to acute volume loading (AVL) in these preclinical entities. Type V phosphodiesterase (PDEV) metabolizes cGMP, second messenger of the B-type natriuretic peptide (BNP). Preclinical studies have demonstrated that PDEV inhibition (PDEVi) enhances cardiorenal actions of BNP.

HYPOTHESIS: The combination of PDEVi and BNP will result in a greater enhancement of the cardiorenal response to AVL as compared to PDEVi alone in PSD and PDD.

Methods: Randomized double-blind single placebo-controlled cross-over study in 21 PSD and 20 PDD subjects. We determined the cardiorenal effects of PDEVi with Tadalafil (T) 5 mg alone and in combination with sc BNP (Nesiritide 10 µg/Kg), in response to AVL (normal saline at 0.25 ml/kg/min for 1 hour). Each subject had 2 study visits, separated by at least 1 week, performing echocardiogram and renal clearance with iohalate and PAH to measure GFR and renal plasma flow (RPF), before and after AVE. Patients were randomized to receive either T plus placebo or sc BNP at the first visit and the other on the second one.

Results: In both PSD and PDD, T+BNP resulted in smaller LA volume index (p< 0.05) and lower right ventricular systolic pressure (p< 0.05) in response to AVL as compared to T alone. Furthermore, T+ BNP also resulted in a significant reduction of plasma ANP and LV end-systolic volume in response to AVL while T alone did not. However, in PSD T+BNP, there was a greater reduction in systolic blood pressure (-21 ± 16 vs 10 ± 6 mmHg p< 0.05), GFR (-9 ± 22 vs 9.2 ± 24 ml/min/1.73m², p< 0.05), RPF (-48 ± 121 vs 58 ± 106 ml/min/1.73m², p< 0.05) as compared to T alone. Whereas in PDD, T+ BNP did not result in any differences between RPF, GFR and urine flow, as compared to T alone.

Conclusions: Maximizing the cGMP system with the combination of PDEVi and BNP reduced cardiac filling pressure in response to AVL in stage B HF subjects, as compared to PDEVi alone. However, this combination did not enhance renal response to AVL. In PSD, the combination of PDEVi and BNP resulted in lower GFR in response to AVL, due to the greater decrease in blood pressure. This suggests a

differential cardiac versus renal response to the maximization of cGMP system with PDEVi and BNP.

P1383

Congestion reduction evaluated by BIVA and clinical signs at discharge are predictive for 90 days cardiovascular events in patients admitted for acute heart failure

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Purpose: Acute Heart Failure (AHF) is a frequent reason for patients to be admitted with consequent related high costs. Exacerbation of chronic heart failure is linked with a progressive worsening of the disease with increased incidence of death. Fluid overload is the main mechanism underlying acute decompensation in chronic heart failure patients. Bioelectrical Impedance Vector Analysis (BIVA) is a validated technique able to identify and quantify the presence of fluid overload differentiating dyspnea from cardiac origin, and its assessment at discharge is useful in identifying patients at risk for future cardiovascular events. Aim of this study was to investigate the prognostic role of quantitative reduction of congestion during hospitalization assessed by physical examination and BIVA serial evaluations in patients admitted for acute heart failure.

Methods: this is a prospective, multicenter, observational study in AHF and no AHF patients (control group) in 3 Emergency Departments centres in Italy. Clinical data and BIVA evaluations were performed at admission, and at discharge. A follow-up phone call was carried out at 90-days.

Results: 336 patients were enrolled (221 AHF and 115 no AHF patients). At admission, congestion detected by BIVA was present only in AHF group, and it significantly decreased at the moment of discharge. In AHF patients an increase of Resistance >11 Ohm/m was associated with increased survival. Clinical signs of congestion at discharge showed the most powerful prognostic significance.

Conclusions: In patients hospitalized for AHF, BIVA showed a quantitative reduction of congestion during hospitalization obtained as a consequence of medical therapy. The absence of clinical signs of congestion at discharge and an increase of dR/H >11 Ohm/m during hospitalization were associated with increased 90 day survival.

P1384

Clinical efficacy and safety of urapidil and nitroglycerin injection for treatment of hypertension in older patients with acute systolic heart failure: a multi-center, randomized, parallel controlled

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Introduction: Urapidil improves cardiac function in heart failure (HF) by reducing cardiac afterload. However, data from large-scale, multi-center clinical trials are lacking. We compared the effects of urapidil and nitroglycerin for acute-phase treatment of older patients with hypertension and systolic HF.

Objective: To evaluate whether the a-1 blocker, urapidil, provides additional therapeutic benefits compared to nitroglycerin in treatment of acute-phase treatment of older patients with hypertension and systolic HF

Methods: 120 patients aged 65-86 (mean 77.74) years with hypertension and acute systolic HF (ejection fraction <50%) were randomized to treatment with a total of 10 mg of nitroglycerin or 100 mg urapidil administered over 140 hours. Systolic (SBP) and diastolic blood pressure (DBP) and N-terminal pro-brain natriuretic peptide (NT-proBNP) were measured at days 0, 1, 2, 3, and 7. Lipids, liver and kidney function, glucose metabolism and echocardiographic indices were also evaluated. Continuous data were analyzed using repeated-measures analysis of variance (ANOVA).

Results: Between these two groups, SBP (F = 27.42), DBP (F = 29.32), and heart rate (F = 31.24) were all significantly lower after treatment. Inter-group ANOVA showed no significant difference between urapidil and nitroglycerin (P > 0.05). However, After 48 hours of treatment urapidil (F = 57.24) had a more favorable effect than nitroglycerin on NT-proBNP (P < 0.05). (Table1-2).After 7 days of treatment, the urapidil group had higher left ventricular ejection fraction (t = 4.312, P < 0.05) than the nitroglycerin group. Fasting plasma glucose was lower in the urapidil group than the nitroglycerin group after 7 days.

Conclusions: Urapidil controls blood pressure without adversely affecting HR in older patients with systolic HF. It also improves left ventricular diastolic and systolic

functions and may also have beneficial effects on lipid and glucose metabolism. For hypertensive crisis, acute HF, and surgical procedures, urapidil is comparable or superior to other first-line antihypertensive drugs.

P1385

The management of acute heart failure in Greece. A sub-analysis of the heart failure pilot survey (ESC-HF pilot)

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Aim: The objective of this survey was to produce evidence on the management of acute heart failure (HF) in Greece.

Methods: A prospective, multi-centre, observational survey conducted in 136 cardiology centres from 12 European countries, including eight Greek centres. In this analysis, all Greek patients admitted for acute HF have been followed-up for one year with follow-up visits at 3, 6 and 12 months. The clinical and epidemiological data of these patients have been collected in a central database. Appropriate statistical tests have been performed for the analysis of the data.

Results: A total of 177 patients have been admitted for acute heart failure, 79.7% were classified as NYHA III and IV and 20.3% as NYHA I and II. The mean age of the patients was 70.1 ± 11.6 years (range 30 - 98 years old) and most of them were male (73.9%). More than half were current or former smokers (66.7%) with a history of hypertension (53.1%) and atrial fibrillation (51.4%). About one third were diabetics (37.2%) with a history of chronic kidney disease (32.8%). The most of the patients have been admitted with decompensated HF (61.7%) and 28% with pulmonary oedema. About 20% received inotropic support, mainly levosimendan (12.4%). The rate of use of pharmacological treatments before hospitalisation and at discharge were: for ACEi/ARBs 62.7% before and 79.7% after, b-blockers 65.5%/80.2%, aldosterone antagonists 44.6%/63.3% and for diuretics 84.2%/94.9%. The mean length of hospitalisation was 8.36 ± 6.81 days. About one fifth (21.4%) of the patients have also admitted in the intensive care unit with a mean stay of 4.49 ± 3.16 days among them.

Conclusion: This study has produced valuable data about the management of acute HF in Greece and demonstrated that Greek patients with acute heart failure are multi-morbid patients that require a complicated multi-drug therapeutic scheme and long hospitalisation.

P1386

Lipids and inflammatory markers in acute heart failure patients with metabolic syndrome

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Purpose: Heart failure (HF) is an abnormality of cardiac structure or function lesion leading to failure of the heart to deliver oxygen at a rate commensurate with the requirements of the metabolizing tissues, despite normal filling pressures. Metabolic syndrome (MS) is present at 35% of patients (pts) with acute HF (AHF). MS is major concomitance in HF thus its pathogenesis pathways are among emphasized areas to investigate. The aim of this study was to investigate concomitance of MS and AHF with emphasized relationship between lipids and biomarkers.

Methods: Study was performed as observational, prospective study on AHF pts recruited from the Emergency Department (ED) from January 2014 to January 2015. Participants were divided in two groups depending on presence of MS and compared according to levels of lipids and biomarkers. Pts were treated by standard protocol for AHF by ESC Guidelines. Study was approved by local Ethics committee. Written informed consent was obtained from each pt according to Good Clinical Practice and Helsinki Declaration principles. Pts' history, clinical presentation, diagnostic procedures and laboratory tests were recorded.

Results: Analysis included data for 100 pts presenting with AHF admitted in the ED and hospitalized. Interestingly there were 53% female pts and 47% male, average age 73 years. Most common clinical presentation of AHF was acute worsening of chronic HF. Unexpectedly, 90% of pts had high (III or IV) New York Heart Association (NYHA) Functional Classification. Increased BMI was observed for 70% of pts, 40% were classified as obese with BMI >30 kg/m², 23 of them were male. It was observed that 89% pts had hypertension, 54% diabetes mellitus, 42% hypercholesterolaemia, 40% hyperlipidaemia and 30% anemia. Family history of cardiovascular disease had 48% of pts and 26% were smokers. Remarkably, 59% of investigated pts had MS, equally by gender. Average cholesterol level was 4.11 (mmol/L), 4.12 for pts with MS, 4.08 for pts without MS. Average HDL level for pts with MS was 0.943, 1.05 for patients without MS, average triglyceride level was 1.22 (mmol/L), 1.33 for pts with MS, 1.05 for pts without MS. 30-day mortality was 15%. Clinical improvement was most common recorded outcome.

Conclusions: MS is important concomitant factor in development of AHF. It was detected in 59% of hospitalized pts. Excitingly, pts in our study had

highly elevated BMI, NYHA score and overlapping MS. The results of this research offer MS as treatment focus for improving outcome of AHF pts. It is obligatory to provide further research in order to produce impact on clinical practice.

P1387

Occurrence and predictor of new onset-acute heart failure in patients admitted with acute coronary syndrome

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Introduction: Acute Heart Failure (HF)-complicating acute coronary syndrome (ACS) has been reported to have an increased risk of 30-days mortality. However, little is known about timing and associated clinical factors. This study is aimed to describe the occurrence and timing of new onset-heart failure in patients admitted with ACS in our national cardiovascular center.

Methods: Data of 495 consecutive ACS patients admitted to emergency department during October-December 2014 were analyzed. HF at presentation was defined as the presence of mild to moderate lung congestion. New-in hospital cases of HF included new onset of pulmonary edema and cardiogenic shock during hospitalization.

Results: Among 495 ACS patients, 195 (39.4%) had HF at presentation. Within 300 patients with no HF at presentation, 64 (21.3%) developed acute HF in hospital and another 18 (6%) patient had cardiogenic shock. Patients presenting with HF or developing HF during hospitalization were more often with ST elevation ACS (142 pts, 54.8%), smoker (166 pts, 64.1%), non-diabetes (140 pts, 54.1%), had higher TIMI score for ST elevation ACS and higher GRACE score for NSTEMI-ACS, and all had elevated troponins. Higher heart rate on admission (HR>100 bpm, p < 0.001) and no revascularization (157 of 259 pts with HF, vs. 11 of 236 pts with no HF, p < 0.001) were associated with development of HF in hospital. We also observed high in hospital mortality for patients with new onset cardiogenic shock following ACS (10 of 18, 55%).

Conclusion: We have described the occurrence and clinical characteristic for development of HF in ACS. Further follow up and analysis are needed to predict clinical outcomes in those patients.

P1388

Predictors of early readmission in acute heart failure

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Background: Early readmission after acute heart failure (AHF) is a very common problem (15.93 % in our region), resulting in a high burden for both the patients and health care system.

Purpose: We aimed to determine predictors of 30-day readmission after hospitalization for AHF to identify potential targets for intervention.

Methods: Using hospital administrative and clinical data, we analyzed 599 patients with AHF (mean age of 80 years; 40.64% males) admitted in our Hospital from January to December 2013 and determined their readmission status within 30 days after an index hospitalization. Clinical, economical, administrative, echocardiographic and social variables were obtained at baseline to determine predictors of early readmission.

Results: Out of 599 patients with AHF, 58 (9.68%) were readmitted within 30 days. Readmission rates were significantly higher in patients older than 75 year-old and in those patients without an echocardiogram during index hospitalization. There were no differences in costs or length of stay.

Conclusions: Early readmission rate in our institution was acceptable and it was lower than regional rate. Older patients and those without echocardiogram during index AHF hospitalization had the highest readmission rates. This might be a call to change clinical practices to prevent early readmission rates in AHF, making a better study during index hospitalization with echocardiogram in all the patients, and increasing the follow-up and medical attention after the discharge in older patients.

RR of 30-day readmission for AHF

	RR	95% CI	p-value
Age >75 year-old	2.20	1.02-4.75	0.035
No echocardiogram during index AHF hospitalization	1.69	1-2.98	0.043
Ventricular dysfunction	0.11	0.66-1.87	NS

RR, relative risk; CI, confidence interval; NS, non-significant.

P1389

Acute heart failure pathway in a tertiary cardiac centre. To be or not to be?

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Background and Aim: Heart failure is one of the most common reasons for admission to hospital and carries a prognosis worse than most types of cancer with a one year mortality of over 30%. An independent review of our local trust in 2013 has shown marked variations in outcomes for patients, both in terms of mortality and length of stay, depending on where they are seen. The aim of this study was to test the hypothesis that a new acute heart failure pathway will facilitate assessments of all patients with suspected heart failure within 24 hrs of admission to improve clinical outcomes.

Method: All patients admitted with suspected heart failure between February and April 2014 had NT proBNP level measured on admission. A raised NT proBNP level $\geq 400\text{ng/l}$ triggered a clinical review by a heart failure nurse and echocardiography. All patients with confirmed left ventricular systolic dysfunction were reviewed by a consultant cardiologist with special interest in heart failure. Referral to review and admission to review times, length of stay (LoS), 30-day readmission and in patient mortality rates were compared between the old clinical practice and the new pathway.

Results: 178 cases were triaged with 118 (66%) had raised NT pro BNP level and required echocardiography. 93 cases (53%) had confirmed LV systolic dysfunction and required consultant reviews. The table below shows the results for the various end points.

Conclusion: A dedicated acute heart failure team's review soon after patient's admission with suspected acute heart failure has a significant positive impact on reducing readmission rates. The new model showed a trend towards reducing IP mortality and LoS but was not statistically significant. It will be useful to reassess this new pathway in a bigger and sufficiently powered cohort of patients over a longer period of time in multiple sites.

Results

	Old Pathway	New Pathway	p value
Time admission to referral (days)	4 (+/-3)	1.7 (+/- 0.7)	0.04
Time referral to review (days)	1 (0-1)	1 (0-1)	0.28
Time admission to review (days)	5 (+/-3)	1.7 (+/- 0.7)	0.03
LoS (days)	15 (8-24)	13 (9-26.7)	0.49
30-day Readmission	54 (22.25%)	29 (13.7%)	0.02
IP mortality	6.2%	5.1%	0.71

P1390

NSTE-ACS with ST elevation in aVR: higher incidence of pulmonary edema and mortality rates

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INTRODUCTION: Lead aVR contains important short-term prognostic information in patients with acute pulmonary oedema (PE) in NSTE- acute coronary syndromes (ACS). ST elevation (STE) greater than 1 mm in aVR may be useful in the early identification of left main or 3-vessel disease (LM/3-VD) in ACS patients (pts) with ST depression. Early detection of the clinical entity by the presenting electrocardiogram (ECG) should result in immediate aggressive clinical management.

PURPOSE, Materials and Methods: We performed multivariable analysis to determine (1) the independent prognostic significance of STE in aVR for life-threatening events like acute pulmonary oedema (PE) and death and (2) its association with significant ($\geq 50\%$ stenosis) LM/3-VD.

Results: Among 250 pts with NSTE- ACS, 149 (59.6%) had no STE in aVR, 54 (21.6%) had minor (0.5-1 mm) STE in aVR, and 47 (18.8%) had major (>1 mm) STE in aVR; Among the enrolled pts, 226 were discharged and 24 died; their in-hospital mortality rates were 3.36%, 14.81%, 23.4% respectively ($p = 0.001$). Of the 250 pts without prior coronary bypass surgery was 218 pts who underwent cardiac catheterization, the prevalence of LM/3-VD was (43) 28.86 %, (18)33.33%, and (29) 61.7% for the groups with no, minor, and major STE in aVR, respectively. The prevalence of PE was 18.12%, 20.37% and 44.68%. Pulmonary oedema and mortality rates were significantly higher in patients with STE in aVR lead (both $p = 0.001$).

Conclusion: There is a correlation of STE in aVR lead with poor outcome in NSTE-ACS.

P1391

Predicting early death in patients with acute aortic dissection

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Acute aortic syndromes mortality remains high, justifying predictive tools to identify patients(pts) at higher risk of death.

Aim: Identify prognostic factors of early death(<30days) and establish a "Score" for risk stratification of pts with thoracic aorta dissection (TAD).

Methods: Of 56pts admitted to our center with acute aortic pathology we selected those with TAD. We identified the variables associated with higher mortality and attributed 1 or 2 points(p) according to the OR obtained ($p < 0.05$) in univariate analysis: previous history of arterial hypertension(1p) and vasculitis(1p); neurological deficits(2p), posterior thoracic pain(1p) and acute myocardial infarction(MI)(1p) on admission; presence of pericardial effusion (1p). We established a Score cut-off (ROC curve) of 2.5p. Then we analyzed if the score was predictor of early death (survival analysis Kaplan-Meier).

Results: We studied 24pts with TAD (20Stanford type A), 54.2% males, age 62 ± 14 years old. On admission: 12pts had predominantly non-anginal chest pain and 4pts had neurological deficits. Blood pressure profile: normal 46%, hypertensive 29%, hypotensive 25%. There were complications in 17pts (71%): 7cardiac tamponade, 5acute aortic regurgitation, 3MI, 4cerebral ischemia, 7acute kidney injury and 2hemothorax. Three pts died in the acute event. Eighteen pts underwent urgent surgical intervention and 2 died soon postoperatively. Early death rate was 22.7%. A Score>2.5 proved to be an independent predictor of early death (OR 3.5;CI 1.08 to 11.3), $p = 0.001$ (Fig1).

Conclusion: Pts with acute aortic dissection are a heterogeneous group with varied clinical presentation and high incidence of complications and death. The proposed Score, using easy available variables, proved to be an independent predictor of early death in this pts.

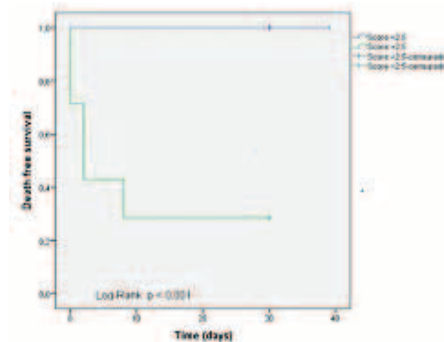


Figure 1

P1392

Neuro-humoral activation is the main prognostic determinant in acute heart failure

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Background: Neuro-humoral activation has proved prognostic value in heart failure (HF). The role of under nutrition and inflammation has been suggested; however, its independence of natriuretic peptide system activation is still to be proved. We aimed to assess prognostic determinants in acute HF in a sample of age-, sex- and admission B-type natriuretic peptide (BNP)-matched patients.

METHODS: We conducted a case control-study to assess prognostic predictors of mortality at 6 months in acute HF.

From a prospectively recruited population of hospital-admitted acute HF patients we retrospectively selected a convenience sample of age-, sex- and admission BNP-matched patients. The ratio of BNP in cases and controls was between 0.80 and 1.20. Patients surviving and not-surviving the 6-month period were compared: McNemar test, paired samples t test and Wilcoxon test. Prognostic predictors of death were analysed using a Cox-regression analysis. A multivariate model was built. Variables entering the model were: atrial fibrillation, hypertension history, admission heart rate and systolic blood pressure, haemoglobin, urea, albumin, prognostic modifying therapy, systolic dysfunction, admission New York Heart Association class and ischemic aetiology.

Results: A total of 224 patients were analysed, 112 surviving and 112 not surviving a 6-month period. Ninety two percent of the patients had>85% admission BNP concordance. Median age was 80 years, 42.9% of the patients were male and 63.9% of the patients had systolic dysfunction. Patients surviving the first 6 months after hospitalization had higher admission heart rate, higher admission systolic blood pressure, higher haemoglobin, lower plasma urea and more often had >30%

decrease in BNP during hospitalization; they were also more often discharged on HF prognostic modifying therapy. In a Cox-regression analysis no inflammatory, nutritional or even hemodynamic parameters predicted death. The only independent predictor of 6-month death was BNP decrease: patients in whom BNP did not decrease over 30% during hospitalization had an HR of death of 1.75 (95% CI: 1.12-2.73).

Conclusions: In admission BNP matched acute HF patients no comorbidities and no clinical parameters or laboratory parameters except for BNP decrease were associated with death risk. Natriuretic peptide system activation appears to be the most important prognostic predictor and other predictors suggested in the literature may not be independent of neuro-humoral activation.

P1393

Affective disorders in patients with acute heart failure and acute myocardial infarction

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Purpose: to investigate affective disorders in patients with acute heart failure (AHF) on a base of primary acute myocardial infarction (AMI).

Methods: 92 patients with AHF with AMI were examined. Patients were divided into 3 groups according to the AHF classification by Killip. The 1st group-22 patients with AHF class I (13 men and 9 women, 58.4 ± 6.8 years of age), the 2nd group-46 patients with AHF class II (27 men and 19 women, 59.4 ± 7.3 yrs), 3d group included 24 patients with AHF class III (13 men and 11 women, 63.6 ± 8.7 yrs). To estimate the degree of anxiety and depression scale Beck Depression Inventory was used. The evaluation was done on the 2nd day of the beginning of AHF and on 12-14th day on a background of standard therapy of the main disease, the correction of affective disorders was carried by fluoxetine use. Also on 2nd and 12-14 days from the onset of the disease in all patients were evaluated according to the Minnesota life with heart failure questionnaire (MLHFQ).

Results: During the initial testing in 1st group there were patients with predominant subdepression-15 (13 ± 2 points on a Beck's scale) and 7 patients had mild depression (17 ± 2 points), in patients of the 2nd group were identified symptoms of mild depression (18 ± 1 points) in 14 patients and moderate severity depression (23 ± 3 points)-in 32 patients, in the 3rd group 10 patients had significant depression (26 ± 2 points), 14 patients-severe depression (36 ± 3 points). According to MLHFQ patients of the 1st group showed 56.3 ± 3.1 points, in the 2nd group-67.8 ± 2.7 points, in the 3rd group-83.8 ± 4.9 points. Subdepressive disorders in patients did not require additional correction and regressed by usage of standard therapy of the main disease. Patients with mild, moderate and severe depression were prescribed fluoxetine at a dosage of 20 mg, 40 mg and 60 mg per day, respectively. When repeated testing positive dynamics was observed in all groups as a reduction of the affective disorders by 4 points in 1st gr., by 5 points in the 2nd and in the 3d gr.-7 points. Quality of life improved in all patients mainly by psycho-emotional component: in 1st group-by 64 %, in 2nd gr.-by 47% and in the 3rd-by 38%.

Conclusion: 1) Worsening of the depression symptoms with an increase of the AHF severity in patients with AMI was observed. 2) A direct relationship between the severity of affective disorders and decreasing of life quality in patients with AHF was found. 3) Fluoxetine can be recommended for treatment of the patients with AHF on a base of AMI due to absence of negative cardiac influence and positive effect in correction of somatogenic depressions.

P1394

A descriptive analysis of patients with chronic heart failure hospitalized for acute venous thromboembolic disease

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Background: Acute venous thromboembolic disease (VTED) is a very common condition with high incidence in heart failure (HF) patients.

Objectives: To establish the clinical profile of patients with chronic HF and VTED, and also to compare their clinical outcome respect to those without such complication.

Methods: A descriptive observational study assessing a cohort of 70 patients consecutively admitted to a Spanish Community Hospital with the diagnosis of VTED (pulmonary embolism and / or deep vein thrombosis) and a previous diagnosis of symptomatic HF during a 5-year span.

Results and discussion: Pulmonary embolism was detected in 60% of patients and / or deep venous thrombosis in the remaining 40%. HF with reduced EF (54.3%) was slightly prevalent over HF with preserved EF (45.7%). The patients in our cohort were more frequently women (58.6%) with a mean age of 78 ± 11 years old. Cardiovascular risk factors were frequent: arterial hypertension (77.1%), dyslipidemia (45.7%), diabetes mellitus (25.7%), morbid obesity (BMI > 35) (12.9%) and smoking (7.1%). Regarding other comorbidities, 30% of patients presented

a history of ischemic heart disease, 27.1% malignant neoplasia, 27.1% chronic kidney disease, 22.9% chronic obstructive pulmonary disease, 14.5% stroke and 8.6% obstructive sleep apnea-hypopnea syndrome. Antecedent of previous VTED was found in 18.6% of cases, and atrial fibrillation in 38.6%. Remarkably, 25.6% of patients were in chronic anticoagulant therapy (17.1% with acenocumarol), yet suboptimal INR level was often recorded (mean INR=1.32 ± 0.566). Most patients (90.1%) received low molecular weight heparin as the preferred therapeutic option. The in-hospital clinical outcomes were as follows: acute HF exacerbation 48.6%, infection 51.4%, shock of any etiology 7.1%, intracranial hemorrhage 1.4%, other non-fatal bleeding 17.1%, and death 20%. Comparison of these figures with those of other HF patients rendered significant differences in all studied variables.

Conclusions: Patients with stage C HF admitted for VTED should be considered a high-risk population, with frequent serious comorbidities and high in-hospital complications and overall mortality.

P1395

Rate and predictors of bioimpedance vector analysis compensation in patients with acute decompensated heart failure

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Objective: Systemic congestion is the known main cause of hospital readmissions of patients with acute decompensated heart failure (ADHF). The aim of the study was to evaluate changes of hydration status assessed by clinical criteria and bioimpedance vector analysis (BIVA).

Methods: In 48 patients admitted with ADHF (56% male, 67.1 ± 11.6 years (M±SD), arterial hypertension 94%, ischemic heart disease 85%, myocardial infarction 45%, atrial fibrillation 66%, diabetes mellitus 54%, known chronic kidney disease 29%, left ventricular ejection fraction (EF) 46 ± 9%) hydration status was assessed and graded according ESC 2010 Scientific statement and by BIVA using resistance (R) and reactance (Xc), standardized by height (h). Mann-Whitney and Wilcoxon tests were performed. P < 0.05 was considered statistically significant.

Results: 45 (94%) patients discharged with clinical improvement (patients lost weight, reduced edema, had improvement in dyspnea and NYHA functional class (p < 0.05)). Only 28 (58%) patients attained compensation assessed by BIVA. In spite of failure of attainment BIVA compensation in 42% of patients R/h and Xc/h significantly increased in both groups (meaning decrease of overhydration severity): from 235 ± 46 to 298 ± 55 Om/m and from 18 ± 8 to 24 ± 8 Om/m in patients with BIVA compensation (p < 0.001), from 225 ± 54 to 284 ± 56 Om/m and from 17 ± 7 to 23 ± 5 Om/m in patients without BIVA compensation (p < 0.001). Patients with versus without compensation by BIVA had lower baseline distance attained during a 6-minute walk (6MWD) (133 ± 65 vs 170 ± 42 meters, p < 0.05), EF (42 ± 9 vs 49 ± 8%, p < 0.05), more pronounced edema (2.3 ± 0.7 vs 2.0 ± 0.5 points, p < 0.05). Patients did not differ by baseline BIVA parameters or outpatient therapy. Patients with versus without compensation by BIVA had higher rate of in-hospital therapy with beta-blockers (100 vs 75%, p = 0.006), higher dose of i/v loop diuretics (p = 0.02), lower rate of thiazide diuretics (18 vs 50%, p = 0.03) and longer duration of hospitalization (17.4 ± 2.9 vs 13.4 ± 2.6 days, p < 0.001).

Conclusion: 42% of patients admitted with ADHF discharged with subclinical congestion according BIVA assessment. Higher severity of clinical hyperhydration, worse baseline functional status as well as non-optimal regime of medical therapy may be associated with failure to attain BIVA compensation.

P1396

Characteristics and outcome of acute heart failure patients according to their clinical profile

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Purpose: The aim of this regional registry was to evaluate the epidemiology, clinical presentation, in-hospital management and evolution of patients hospitalized with acute heart failure.

Methods: In this study we evaluated all consecutive patients (P), enrolled over a 5-month period during 2012 at our clinical county hospital with a primary diagnosis of acute heart failure. Patients were divided into 5 clinical profiles of heart failure according to the 2008 ESC guidelines: acute decompensated heart failure (ADHF), cardiogenic shock (CS), pulmonary edema (PE), right heart failure (RHF) and hypertensive heart failure (HTHF). For statistical analysis we used independent t test for comparison of continuous values, Pearson χ^2 test for comparison of categorical values, and multivariate logistic regression for predictors of in-hospital mortality.

Results: A total of 364 consecutive patients with acute heart failure (215 males and 149 females) were enrolled. Mean age was 68 ± 10 years and mean ejection fraction was 35 ± 10%. The percentage of patients with ADHF was 50.5%, PE 18.7%,

CS 4,7%, HTHF 14% and RHF 12,1%. Ischemic etiology was predominant among ADHF, CS and RHF profiles. Atrial fibrillation was present in 50,7% of P whereas diabetes and chronic kidney disease were present in 39,6% and 30,5% of P. Atrial fibrillation was significantly associated with the ADHF profile ($p=0.014$, $OR=1.4$). In-hospital mortality was 7,4%. CS was associated with the highest in-hospital mortality rates ($p < 0.0001$, $OR=37$). Blood urea nitrogen was found to be an independent risk factor for in-hospital mortality. Combined evidence based heart failure therapy (ACE inhibitors/angiotensin receptor blocker+beta-blocker+diuretic) increased from admission to discharge from 22% to 44,2%.

Conclusions: Cardiogenic shock profile carries the worst in-hospital survival rates and is associated with ischemic etiology. These P have frequently atrial fibrillation, diabetes and chronic kidney disease. Atrial fibrillation was more frequent among ADHF profile. Blood urea nitrogen is an independent risk factor for in-hospital mortality. Despite improvement in heart failure therapy, at discharge combined heart failure therapy remains under 50%.

P1397

Correlation of pacemaker lead impedance with clinical signs and chest radiography at the time of heart failure hospitalization

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Purpose: Patients with Heart failure (HF) are frequently hospitalized for fluid overload. A reliable method for chronic monitoring of fluid status is, therefore, desirable. Intrathoracic impedance, measured with special equipment, falls as the amount of conductive intrathoracic fluid increases with pulmonary congestion. We hypothesized that monitoring of conventional pacemaker lead impedance (PLI), may also provide an early warning means of congestion. The purpose of this study was to evaluate PLI and to determine its correlation between clinical and chest radiography signs at the time of HF hospitalization.

Methods: Thirty six patients with NYHA class III/IV HF and previously implanted PM, were admitted to our department with acute decompensation of chronic HF. The right JVP was assessed at admission and before discharge. The PLI was measured in VVI mode with unipolar pacing at 5V using the PM analyzer. Correlation of this measurement with the "reference" PLI was used to quantify the magnitude and duration of any PLI changes leading up to hospitalization. A "reference" impedance value was established as the average of the last 3 consecutive measurements from the PM clinic. A chest x-ray was also evaluated in all patients.

Results: PLI was low on admission (mean value 350 ± 40 Ohms) and increased after intensive diuresis in 33 patients (mean value 390 ± 50 Ohms). In two patients, the PLI recorded soon after diuresis, was not significantly increased (340vs355 Ohms). In these two patients, the decrease in PLI was attributed to fluid accumulation due to causes other than pulmonary congestion (pneumonia and PM pocket infection). JVP was high (mean value $22\text{cmH}_2\text{O}$), and decreased after treatment (mean value $13\text{cmH}_2\text{O}$) in all but one patient. This patient had marked pulmonary hypertension and right heart failure. Radiographic signs of pulmonary congestion were present in 33 out of the 35 patients (sensitivity 94%). They were absent in the two patients in whom PLI did not increase after treatment. There was an inverse correlation between the PLI and JVP ($p < 0.001$) as well as between PLI and degree of congestion ($p < 0.001$), during hospitalization.

Conclusions: This prospective observational study describes first clinical experience with PLI used as guiding tool for pulmonary congestion. PLI value is correlated closely with HF severity as reflected by the JVP and chest x-ray findings of congestion. The findings from this study suggest that monitoring of PLI at regular intervals during HF therapy may provide quantitative information on the severity of volume overload and a warning sign of impending HF decompensation.

P1398

Electrocardiographic patterns differentiating "apical ballooning" from anterior myocardial infarction

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Purpose: Left ventricular apical ballooning (AB) mimics anterior myocardial infarction (AMI). This study assessed if the ECG can differentiate between these two syndromes with a similar clinical presentation.

Methods: Among 2086 patients (pts) with an ACS, 33 (1.6%) with AB were identified (29 f, 4 m, median age 77 years) and compared to 28 consecutive age and sex matched AMI pts undergoing PCI of the LAD with similar findings on LV angiography.

Results: AB pts arrived at the hospital later after symptom onset (median 21 vs 5 hours; $p < 0.001$). On the admission ECG, the number of leads with ST-segment elevation (4 [3-6] vs 5 [5-7], $p = 0.005$) and the magnitude of ST-segment elevation (0.7 [0.5-0.9] vs 0.9 [0.7-1.5] mV, $p = 0.002$) were greater in AMI. Reciprocal ST-segment depression was similar (27% vs 54%, $p=ns$). A positive T wave in aVR was more frequent in AB (49% vs 7%, $p < 0.001$).

During follow-up, AB pts had more leads with T-wave inversion (8 [8-9] vs 6 [5-8], $p < 0.001$) and a larger magnitude of T-wave inversion (2.9 [2.2-4.6] vs 1.4 [0.9-2.3] mV, $p < 0.001$). T-wave inversion was similar in I, aVL and V2-V5. AB pts, however, showed negative T-waves also in lead II (74% vs 22%, $p < 0.001$), III (34% vs 4%, $p = 0.004$), aVF (51% vs 11%, $p = 0.001$) and a positive T wave in aVR (100% vs 70%, $p = 0.005$). The QTc interval was longer in AB (515 [482-543] vs 458 [435-484] ms, $p < 0.001$). An abnormal Q wave on admission was more frequent in AMI (21% vs 79%, $p < 0.001$) and persisted but was absent in AB at discharge (0% vs 61%, $p < 0.001$). Ventricular tachycardia was similar (2% vs 14%, $p=ns$) but atrial fibrillation occurred only in AB (21% vs 0%, $p = 0.013$). The ECG normalized in all AB but in only 1 AMI pt ($p < 0.001$).

Overall, despite a similar ejection fraction (54 ± 15 vs 55 ± 13 %) and lower troponin I values (7.5 ± 6.9 vs 238 ± 221 ng/ml, $p < 0.001$), AB pts developed significantly more adverse events compared to AMI pts (52% vs 18%, $p < 0.008$).

Conclusion: ECG patterns in AB are significantly different from those in AMI. On admission, the extent of ST-segment elevation and the number of Q waves are greater in AMI. During follow-up, no Q wave, a longer QTc interval, a greater extent of T-wave inversion and a positive T wave in aVR are typical findings in AB. Adverse events are more frequent in AB than in AMI.

P1399

Usefulness of serial liver enzymes in prognostication of patients with cardiogenic shock

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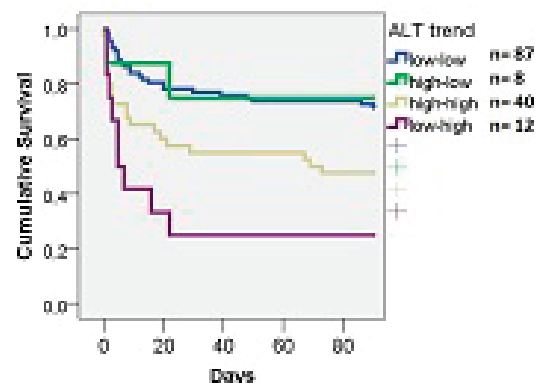
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Liver dysfunction predicts dismal prognosis in heart failure (HF) patients. We have analyzed if serial liver enzyme alanine transferase (ALT) has effect on in-hospital or 90-day mortality in cardiogenic shock patients.

Material and methods. This is a substudy of Cardshock study (220 patients). Blood samples were drawn from patients at 0 h, 12h, 24h, 36h, 48h, 72h, 96 and 120h, and analyzed in a central laboratory in Finland. The effect of ALT mortality was analyzed statistically. ALT was considered to be high if it was $> \text{ULN}$ (upper normal limit, 70 U/l).

Results: 178 patients were included (male 132, mean age 66.2 yrs, SD 12.3). In-hospital mortality was 38% and 90-d mortality was 42%. In Cox univariate regression analysis high ALT predicted both in-hospital and 90-d mortality at all time points up to 48 h being strongest at 12h (in-hospital mortality HR 2.8, 95CI 1.6-4.8, 90-d mortality HR 2.6, CI 1.6-4.3). It remained significant also in multivariate analysis adjusted with gender, age, coronary and HF history, NT-proBNP, hs-CRP, other liver enzymes (aspartate transferase, alkaline phosphatase, glutamyl transferase and bilirubin), and albumin, baseline hs-TnT and creatinine, and etiology of cardiogenic shock (in-hospital mortality HR 2.6, 95CI 1.4-5.0, 90-d mortality HR 2.6, CI 1.4-4.9.). In figure is presented 90-d mortality Kaplan-Meier curves for different ALT trends during the first 12h. Prognosis was worst if ALT raised rapidly from low to high.

Discussion and Conclusions: High ALT predicted both in-hospital and 90-d mortality during the first two days, strongest at 12h. If ALT raised rapidly from low to high the 90d prognosis was very dismal. The total number of such patients was only 12. Our results support using ALT in prognostication of cardiogenic shock patients.



P1400

Association between heart rhythm at discharge in patients hospitalized for acute heart failure and probability of readmission

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The aim of this study was to evaluate if heart rhythm at discharge, stratified by ejection fraction (EF), in patients hospitalized for acute heart failure (AHF) is associated with an increased readmission rate for heart failure.

A cohort study of patients admitted to our centre for AHF was conducted. The patients were divided in three groups: 1) sinus rhythm (SR), 2) pacemaker (PM), 3) atrial fibrillation (AF). We evaluated time to readmission, stratifying by EF (reduced ejection fraction <45%, HF rEF; preserved ejection fraction ≥ 45% HF pEF). We excluded those patients under cardiac resynchronization.

We included 555 patients (303 with HF rEF; 252 with HF pEF; mean age of 72 ± 12 years; 41,9% women). Figure 1 shows time to readmission in the three groups stratified by EF. The cumulative probability of readmission at 2 years was 34% (group 3), 21% (group 2) and 17% (group 1). After stratifying by EF, group 2 had a higher risk of readmission in patients with HF rEF (Vs group 1 p=0.024 and Vs group 3 p=0.03) and group 3 in those with HF pEF (Vs group 1 p=0,028 and Vs group 2 p=0,9).

In patients with HF rEF pacemaker stimulation increases the rates of readmission due to heart failure. In those with HF pEF being in atrial fibrillation is associated with higher rates of rehospitalization.

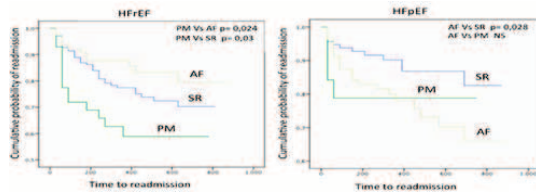


Figure 1

CHRONIC HEART FAILURE

P1401

Risk of pulmonary embolism in patients with chronic heart failure

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Purpose: to investigate risk of pulmonary embolism (PE) in patients with different cardiovascular diseases complicated by chronic heart failure (CHF).

Methods and Results: 113 patients with cardiovascular pathology complicated by chronic heart failure were examined (64 female and 49 male). To estimate the risk of pulmonary embolism the pulmonary embolism clinical score system was used: Geneva scale and Wells scale. Patients were divided into 3 groups according to the classification of PE risk. The 1st group - low risk - 48 patients (23 men and 25 women, 56,8 ± 3,4 yrs), among them 42% of pts with atherosclerotic cardioclerosis, 25% with stable angina, 33% with non QMI, unstable angina 5%, the 2nd group- intermediate risk - 42 patients (17 men and 25 women, 62,5 ± 4,6 yrs): 43 % stable angina, 7% unstable angina, 10% non QMI, 20 % QMI, atherosclerotic cardioclerosis 17 %; 3d group - high risk - 14 patients (7 men and 7 women, 64,6 ± 6,7 yrs) 10% stable angina, 18% unstable angina, 22% QMI, 62 % atherosclerotic cardioclerosis. It was found that complications such as atrial fibrillation, extrasystolic arrhythmia, COPD, Chronic bronchitis, autoimmune thyroiditis, worsen the prognosis and increase the risk of PE in patients with cardiovascular diseases. High and intermediate risk was mostly seen in patients with nonQ and QMI, with decompensated CHF, comparing to compensated CHF, but it was found that the highest amount of patients with intermediate risk were among patients with stable angina and atherosclerotic cardioclerosis, also patients with atherosclerotic cardioclerosis showed a 62 % of high risk of PE. This might confirm a propiate anticoagulant therapy in patients with unstable angina, non Q and QMI, but insufficient anticoagulation in patients with stable angina and atherosclerotic cardioclerosis.

Conclusion: All patients with chronic heart failure have a risk of developing pulmonary embolism no matter if they had any history of PE in anamnesis or no. Complications such as (atrial fibrillation, extrasystolic arrhythmia, COPD, chronic bronchitis, autoimmune thyroiditis worsen the prognosis and increase the risk of PE in patients with chronic heart failure. More intensive anticoagulant/antiaggregant therapy should be included into protocols of treatment of the patients with stable angina and atherosclerotic cardioclerosis due to high risk of development PE in such patients.

P1402

Safety of spironolactone in patients with chronic heart failure in Malaysia

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Background: Use of mineralocorticoid receptor antagonist in heart failure has been well established. However, concerns over its safety remain an important issue. This study examines the safety of spironolactone in patients with heart failure in a heart failure (HF) clinic setting in Malaysia.

Method: The cohort included all heart failure patients in our HF clinic whom spironolactone was added on top of standard therapy (53% n=57). Baseline and clinical characteristics, including renal profile was observed for at least 3 months.

Results: Median age was 56 years, 61% were males. 54% diabetics and 83% had HF rEF. 90% patients were on beta blocker, and 84% on ACE/ARB. Spironolactone dosing was 12.5mg (44%, n=25), 25mg (53%, n=30) and one patient each at 37.5mg and 50mg. Paired testing using Wilcoxon Signed Ranks revealed no significant difference between the baseline (Kb) and followup (Kf) potassium levels in the entire cohort (median Kb=4.2; Kf=4.1; p=0.646), however, 3 patients (5.3%) developed hyperkalaemia (K>5.5 mmol/L) during follow-up. All were diabetics. We also noted a small, albeit significant reduction in GFR between baseline and followup (median GFRb = 60.5mls/min; GFRf = 58.5 mls/min; p=0.032). This reduction was amplified in diabetic patients (median GFRb = 60mls/min; GFRf = 51 mls/min; p=0.002) and was independent of gender, EF, dose of spironolactone and concomitant therapy.

Conclusions: Although the sample size was small, we have demonstrated that spironolactone therapy on top of ACE/ARB and Beta blocker is well tolerated among Asian patients with heart failure. However in diabetics, GFR has to be regularly monitored.

P1403

Use of bedside thoracic ultrasound as a diagnostic tool in the outpatients with heart failure

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Purpose: Description of the results of thoracic ultrasound performed in outpatient setting to patients with a history of heart failure and assesses its potential usefulness as a diagnostic and/or prognostic tool.

Methods: We collected information from patients with programmed visits to the outpatient clinic specialised in heart failure, which belongs to the department of internal medicine of a Spanish hospital (referenced for 200,000 inhabitants), between May 2014 and July 2014. All of them were patients with a history of at least one previous hospitalization due to congestive heart failure. Thoracic ultrasound was performed to all patients by a no-radiologist physician, unrelated to clinical follow up of the patient. Chest ultrasound areas described in the Blue Protocol, were examined and classified according to the number of B lines and the presence or absence of pleural effusion. Ultrasound interstitial syndrome (UIS) was defined as the presence of more than 3 lines B in anterior chest wall, or more than 5 in lateral or posterolateral chest wall or unilateral or bilateral pleural effusion.

Results: 30 patients were included in the study, with a mean age of 79 years, 17 women and 13 men. All but one suffered from hypertension, 86.7%(26) had dyslipidemia and 40%(12) diabetes mellitus. 37%(11) were current or former smokers. 76.7%(23) had a normal LVEF.

UIS was observed in 14 of the 30 patients. 30% of patients had pleural effusion. Lines B predominated in posterolateral chest areas (58% had more than 3 lines B and 21% more than 5), lateral areas (43%>3, 10%>5), finding the lowest percentage of B lines in anterior areas (25%>3 lines and only 6.7%>5).

The mean red cell distribution width was 14.6% in patients without UIS and 16.1% in those with UIS, with a statistically significant difference (p=0.001).

Pro-brain natriuretic peptide levels were higher in patients with UIS (mean 3840pg/ml) compared to patients without UIS (mean 2160) although no statistically significant differences were found between groups. Drug therapy was modified in 13 of the 30 patients after assessment in outpatient, based on clinical-analytical features. 5 of the 6 patients whose diuretic drug was increased had UIS. Only 1 of the 7 patients whose diuretic was reduced had UIS.

Conclusions: Chest ultrasound may be useful for monitoring patients with chronic heart failure. In our sample, there has been an increase in the level of NTproBNP in patients with UIS. Patients with this syndrome were more likely to increase diuretic therapy. Further studies are needed to elucidate the usefulness of thoracic ultrasound in non-emergency patients.

P1404

Right ventricular systolic function in heart failure: a moroccan experience

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Background: The right ventricle (RV) has received less attention than the left in heart failure patients probably because morbidity and mortality associated with left ventricular disease is clinically more apparent.

In our study, we tried to prove the importance to characterize the prevalence and clinical significance of right ventricular (RV) systolic dysfunction (RVD) in patients with heart failure.

Methods and Results: We studied 1613 patients with chronic heart failure at the HF Registry of the university hospital Ibn Rochd Casablanca, during a follow up of 6 years. RVF (RV function) was determined by echocardiography, RV dysfunction defined by ($S'VD < 10 \text{ cm/s}$ and $TAPSE < 16 \text{ mm}$). The primary endpoint was the occurrence of acute heart failure decompensation (AHFD).

Results: RVD was present in 117 patient (7.17%), this group had an average age of 64 years, they were more likely to be men (sex ratio: 2,1), to have atrial fibrillation, and chronic diuretic therapy. At echo, patients with RVD had slightly lower LVEF (75% lower LVEF and 25% preserved LVEF), worse diastolic dysfunction, lower blood pressure and cardiac output, higher pulmonary artery systolic pressure (PASP) 23%, and more severe RV enlargement and tricuspid valve regurgitation. Patients with RV dysfunction had 11.54% of AHFD occurrence. The association of both RVD and pulmonary hypertension increased the risk of AHFD (14.28%), while patients with normal RVF had only 1.48% to develop AHFD. Adjusting for age, sex, PASP and comorbidities, RVD defined by TAPSE and echo Doppler tissue imaging, was associated with higher risk of HF decompensation.

Conclusions: In our community, RVD is common in HF patients, associated with clinical and echocardiographic evidence of more advanced HF and predictive of poorer outcomes so it had independent prognostic utility.

We should give more attention to the RVF in our systematic assessment of HF patients.

P1405

Early outcome of a dedicated heart failure clinic in Malaysia

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Heart failure is common cause of admission and has a high rate of mortality in Malaysia. Our hospital has initiated a dedicated heart failure clinic since 2013. Recently we undertook an audit to look at the readmission rate and the survival rate of the patients recruited in our clinic.

Method- We have enrolled 95 consecutive patients from our heart failure clinic. Symptom were reviewed and medication were up titredwith adherence to the treatment per international guidelines. In the audit we look at the patients survival rate at 3, 6, 9, 12 and 18 months respectively. We also monitor the readmission rates.

Demography- Median age is 57. Sixty-six percent (n=63) patients are male. Fifty-nine percent (n=53) were Malays, 24% (n=23) were Indian, 17% (n=16) were Chinese and 3% (n=3) were of other races. Seventy-nine percent (n=75) has underlying hypertension, 79% (n=75) has ischaemic heart disease and 52% (n=49) has DM. 84% (n=80) has HF rEF. 79% (n=75) are on Ace/Arb, 84% (n=80) are on a beta blocker, 61% (n=58) on spironolactone and 10% (n=8) are on ivabradine.

Result - survival rates at 3,6,9,12,18 months were 100%, 98.9%,98.9%, 96 % and 86%. 14% (n=13) were readmit during this 18 months duration, in which (10/13) 77% were admission due to worsening heart failure symptoms. Improvement of >1 NYHA status at 3,6,12,18 months were 21%, 34 %, 31% and 44%.

Conclusions- With strict adherence to the international guidelines for heart failure we found that in an Asian cohort early survival rate at 18 months was high and readmissions rate for worsening symptoms was kept low. There was also a gradual improvement of NYHA status with time.

P1406

RAAS genetic polymorphism analysis in chronic heart failure patients

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51 patients with heart failure (27 women, 24 men, mean age - 73.1 ± 11.3 years old), who had 3-4 functional classes (NYHA).

Having analyzed genomic DNA with PCR - analysis (PCR-express) followed by electrophoresis detection we estimated type I angiotensin II (AGTR1) A1166C receptor polymorphism, polymorphism of T174M and M235T AGT gen of ACE.

Results are presented as genotype (homozygote in allele 1, allele 2 or heterozygote) detection for AGTR1 genes and AGT and in detection allele D-deletion or allele I - insertion Alu - consequences in intron ACE gen. Data were statistically processed with standard methods.

Results: homozygote 1166A was found in 45.1%, homozygote 1166C - in 9.2%, heterozygote - 45.1% of patients with CHF. Allel 174MM was found in 27.5%, 174TT - in 43.1% and heterozygote variant T174M - in 27.4% of patients. Genotype TT

M235T was found in 19.6%, MM - in 19.6%, heterozygote variant - in 60.8%. Allel D ACE was found in 51%.

Conclusion: In our research we found relatively low RAS polymorphism frequency, which is responsible for IHD and AH association. ACE Allel D, associated with high ACE inhibitors efficacy, and was found in about 50% of cases. Assuming vague results of genetic polymorphism investigation in different racial groups and investigations that were performed on rather small population give controversial results, further functional significance of RAS genes polymorphism researches in CHF patients are required.

P1407

The influence of heart failure on heart rate variability in patients with newly diagnosed arterial hypertension

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Purpose: To compare the rates of frequency analysis of heart rate variability (HRV) in patients with newly diagnosed arterial hypertension (AH), depending on the degree of heart failure (HF) in order to determine the risk of cardiovascular events (CVE).

Methods: A total of 79 patients with newly diagnosed AH were examined (mean systolic and diastolic blood pressure: $154,4 \pm 6,8 \text{ mm Hg}$ and $95,6 \pm 4,7 \text{ mm Hg}$, respectively), mean age - $42,4 \pm 2,1$ years, 32 women; HF stage I (36 patients - group 1) and HF stage II-A (43 patients - group 2). All patients underwent an electrocardiogram (ECG) in the morning on an empty stomach 08.00-09.00 with a 5-minute interval recording. The following data of the spectral analysis of HRV were analyzed: high-frequency component (HF), low frequency component (LF), their ratio (L / H) and the total power spectrum (TP). The control group consisted of 14 healthy individuals.

Results: The average heart rate (HR) per day didn't differ in all groups. The average heart rate of patients of group 2 at rest was significantly higher than the one in the control group ($70,4 \pm 1,2$ and $64,4 \pm 1,5$ per 1 min, respectively ($p < 0,05$)). The analysis of HRV showed reduction of spectral analysis indexes, which was more pronounced in patients of group 2. Patients of groups 1 and 2 demonstrated a decrease of TP ($1359,4 \pm 72,7 \text{ ms}^2$ ($p > 0,05$); $943,8 \pm 49,6 \text{ ms}^2$ ($p < 0,05$), respectively; control group $1682,8 \pm 83,2 \text{ ms}^2$); significant reduction of HF ($325,7 \pm 44,9 \text{ ms}^2$ ($p < 0,05$); $271,5 \pm 34,7 \text{ ms}^2$ ($p < 0,05$), respectively; control group $486,2 \pm 41,4 \text{ ms}^2$) and decrease of LF ($204,3 \pm 21,5 \text{ ms}^2$ ($p < 0,05$); $175,3 \pm 19,4 \text{ ms}^2$ ($p < 0,05$), respectively; control group $295,5 \pm 18,2 \text{ ms}^2$).

Conclusions: Patients with newly diagnosed hypertension demonstrate a decrease of HRV spectral characteristics at an early stage of HF formation, thus reflecting the adverse prognostic significance in relation to the development of the CVE and stipulating the necessity for active treatment.

P1408

Effect of ivabradine on functional exercise capacity in patients with systolic heart failure

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Selective sinus-node inhibitor ivabradine has been proved effective in patients with systolic heart failure improving survival and hospitalization rate. Functional exercise capacity provides strong independent insight into the prognosis of patients with heart failure. Evaluation of functional capacity in patients with heart failure by 6-minute walk test is simple, safe and inexpensive alternative to cardiopulmonary exercise testing. We aim to evaluate prospectively the additional effect of ivabradine to optimal medical therapy on functional capacity of patients with heart failure by 6-minute walk test.

We enrolled 25 stable outpatients who were receiving optimal medical treatment for systolic heart failure (mean age 65 ± 11). They had sinus rhythm and their resting heart rate was more than 70 bpm despite optimal beta-blocker therapy. They had left ventricular systolic dysfunction (ejection fraction < 40%) with NYHA functional classes II heart failure. Before the initiation of ivabradine (5-7.5 mg b.i.d) and six months later, the patients underwent clinical evaluation, 6-minute walk test to evaluate functional exercise capacity and echocardiographic evaluation. After six months of additional ivabradine treatment, the maximum distance walked by 6-minute walk test was significantly increased by 25% (from $310 \pm 21 \text{ m}$ at baseline to $387 \pm 20 \text{ m}$; $p < 0.001$). Their mean resting heart rate was decreased by 30% (from $79 \pm 5 \text{ bpm}$ to $61 \pm 5 \text{ bpm}$; $p < 0.001$). All patients remained at NYHA functional classes II and there was no death or new hospitalization of patients during six months. There was no significant difference between echocardiographic parameters.

High resting heart rate is an independent prognostic value in patients with heart failure. Many patients maintain a resting heart rate > 70 bpm despite optimal beta-blocker therapy. In clinical practise only 30-35% of patients achieve the therapeutic target dose of beta-blocker therapy as established in randomized clinical trials. Target resting heart rate can be achieved by additional ivabradine treatment.

The addition of ivabradine to optimal medical therapy in patients with heart failure is associated with significant improvement in functional capacity and quality of life.

P1409

Poor knowledge of heart failure among primary healthcare workers in Malawi

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Purpose: Heart failure continues to grow in Sub-Saharan Africa. The current focus in healthcare delivery in Sub-Saharan countries is on primary healthcare. This study sought to determine the knowledge of heart failure among primary healthcare workers in Northern Malawi.

Method: Semi-structured interviews were conducted with 23 community health workers in the Mzuzu area of Northern Malawi. This addressed healthcare worker demographics, knowledge of heart failure, awareness in community, diagnosis and management

Results: 23 community health workers were interviewed. Average age was 38.1 years. Six were male. There were four nurses, 1 clinical officer and 18 health surveillance assistants. None were aware of guidelines for the management of heart failure. 65% had no method to measure blood pressure. 100% had heard of heart failure and 78% knew someone with heart failure. 78% knew the symptoms of heart failure which were described as "shortness of breath" and "feeling hot". 26% would do nothing if they thought someone had heart failure as there were no facilities available for management and the remainder would send to hospital if they thought someone had heart failure. 78% did not know of any medications for heart failure. Of those who did report a medication digoxin, diuretics and phenobarbitone were reported as being medications relevant to heart failure.

Conclusion: Despite heart failure being a common condition in Sub-Saharan Africa knowledge of heart failure management among community health workers remains poor. This is likely due to a focus on acute and infectious diseases and will require a change in focus to chronic conditions also.

P1410

Therapeutic education for patients with heart failure: effect on medication adherence and clinical outcomes

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Background: Successful treatment of Chronic Heart Failure (CHF) require not only evidence-based drug therapy, but a set of non drug interventions aimed on improving of self-care skills and formation of appropriate health-related behavior. The key role in this process belongs to structured therapeutic education, which can be not only improve patients medication adherence, but increase their quality of life and decrease rehospitalisations.

Aim: To test an efficiency of structured therapeutic education program for CHF patients and assess clinical outcomes in patients, that took part in this program in comparison to those on standard treatment.

Methods: Study included 120 hospitalized CHF patients mean age - 71 years. Participants were randomized in education group which included 60 patients and control group - 60 patients. During hospital admission all patients received standard evidence based treatment with the patients of education group participated in 1-hour one-on-one teaching session before hospital discharge. After discharge subjects were contacted by telephone every 3 months with second visit after 1 year. The primary end-points of study were death or total number of rehospitalisations during follow-up period. The secondary end-points were MLHFQ and Morisky-Green scale score, results of 6-minute walk test and serum concentration of TNF-alpha.

Results: Among 120 patients, 11 (5 in education group and 6 in control group) discontinued the study. After 1-year follow up number of deaths from all causes was 3 in education group and 8 in control group (OR = 0,33 CI: 0,08-1,33; p < 0,05). Total average number of rehospitalisations was 2,6 in education group and 1,7 in control group (p > 0,05). Patients in education group showed higher average Morisky-Green (3.25 in education group and 2.1 in control group, p < 0.01) and lower MLHFQ score (24 in education group and 51 in control group, p < 0.05). Serum concentration of TNF-alpha was 18.6 pg/ml in education group and 32.1 pg/ml in control group (p > 0,05).

Conclusion: Therapeutic education can be important tool in enhancing medication adherence clinical outcomes in CHF patients.

P1411

BNP absolute value but not 6 month BNP variation is a powerful prognostic marker in a prospective systolic heart failure follow up

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BNP is recognized as a powerful prognostic marker in chronic heart failure (CHF). However, BNP plasma levels could increase or decrease due to therapeutic improvement or heart failure progression. In acute heart failure, a decrease of BNP is associated with a better short time prognostic but in a chronic setting, the respective prognostic performance of absolute value or 6 month BNP variation are not yet determined.

We have analyzed BNP variation in a prospective cohort of 1310 consecutive patients followed in our heart failure out patient hospital with systolic heart failure. Mean follow up was 52 months (6- 84 months). 3287 medical examinations pairs were finally analyzed.

Our patients were mostly male (70%) and young (mean age 63 years old (15-96), 70% were in sinus rhythm, 10% demonstrate clinical congestion (lower limb oedema). Mean LVEF was 36 % (+- 10). Mean BNP was 424 (+-200) pg/ml. HF aetiology was dilated in 50% and ischaemic in 40% of patients. During follow up 387 events (death or HF hospitalizations) followed out patient hospitalizations.

BNP demonstrate a linear association with the risk of death or rehospitalisation for HF. BNP < 50 pg/ml regardless of LVEF was associated with a risk of events lower than 5% in the next 6 months. The 6 month increase respectively to 7, 11, 20 and 27 % for BNP plasma level of 100, 200, 500 or 1000 pg/ml. Interestingly BNP mean variation in our cohort was only - 5% in our study. According to tertiles we have analysed the impact of a BNP significant decrease (more than 30%), BNP no change or BNP significant increase (increase more than 30%). BNP variation is associated to a prognostic change only if initial BNP is higher than 500 pg/ml and not if the BNP is lower than this cut off.

Conclusion: In systolic heart failure patients follow up, BNP absolute value is a powerful prognostic marker but BNP variation between two sampling is not, unless BNP is higher than 500 pg/ml.

P1412

Identifying patients at risk for heart failure hospitalization: out-of-range intrathoracic impedance versus fluid index threshold crossings

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Background: Monitoring intrathoracic impedance can be a useful tool to detect worsening heart failure (HF). Medtronic CRT and/or ICD devices traditionally convert impedance data into a fluid index (OptiVol), which triggers an alert when a predefined programmable threshold (nominal set at 60 ohm-days) is exceeded.

Aim: To determine if intrathoracic impedance (Z) based diagnostic can be used to stratify patients at the risk of HF hospitalization (HFH), and compare the performance of the novel approach to OptiVol.

Methods: Existing device data from 109 patients (age 70 ± 11 years, 76% male) followed for 21 ± 10 months with adjudicated HFHs were used for analysis. Data from the first 6 months were excluded because Z is known to rise slowly during this period. Thereafter, a 30-day segment with no HFH was used to compute the mean and establish baseline Z. Daily Z was tracked using a 7-day moving average, and percentage change (ΔZ) from the baseline Z was calculated. An out of range Z was triggered if ΔZ crossed a pre-specified band of $\pm 6\%$, $\pm 7\%$ and $\pm 8\%$ of baseline Z for 1, 2, 3 or 4 days. A trigger was considered positive if HFH occurred within 30 days. Generalized Estimating Equation (GEE) adjusted sensitivity and positive predictive value (PPV) were calculated for various combinations to account for multiple observations per patient.

Results: For a $\pm 6\%$ band, the sensitivity of HFH detection was 79.1% and PPV was 5.0%. PPV increased and sensitivity decreased gradually when 2, 3, or 4 Z measurements outside Z band were required for the trigger. Also, selecting a larger Z band increased PPV and decreased sensitivity (Table shows performance at two bounds for each band). OptiVol had a sensitivity of 73.7% and PPV of 5.4%.

Conclusion: Out-of-range Z values can be used to predict HFH with PPV and sensitivity that is comparable to OptiVol.

Performance of out-of-range Z approach

	$\pm 6\%$ Z Band	$\pm 7\%$ Z band	$\pm 8\%$ Z Band		
Days out-of-range	1	4	1	4	1 4
Sensitivity	79.1%	69.2%	72.1%	63.7%	68.4% 58.8%
PPV	5.0%	5.6%	5.9%	6.9%	7.4% 8.5%

P1413**Effect of atrial fibrillation on renal function and neutrophil gelatinase associated lipocalin values in chronic heart failure patient with reduced ejection fraction**

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Aim- Both atrial fibrillation (AF) and renal dysfunction are common comorbidities in patients with chronic heart failure with reduced ejection fraction (HFrEF). In aim of this study was to evaluate the effect of AF on renal function in HFrEF and to investigate the relationship of neutrophil gelatinase-associated lipocalin (NGAL) levels with presence of AF and renal dysfunction.

Methods - A total of 130 patients with chronic HFrEF (EF ≤ 0.45) and functional class of NYHA 2-4 were included into the study. Sinus rhythm was present in 68 of the patients (37 men, 31 women, mean age 61 ± 13 years) and 62 of them had permanent AF (37 men, 25 women, mean age 68 ± 14 years). A healthy control group (22 men, 28 women, mean age 57 ± 11 years) was selected for comparison of renal function and NGAL levels. Estimated GFR was calculated according to MDRD, CKD-EPI, Cockcroft-Gault formulas. NGAL was measured with ELISA method. The relationship between eGFR, rhythm and NGAL values were examined with univariate and multivariate analysis.

Results - Mean eGFR levels of HF patients were significantly lower than the control group but the difference between patients with sinus rhythm and AF was not statistically significant. Renal failure (GFR by CKD-EPI < 60 ml/min/1.73 m²) was detected in 25 patients (37%) with sinus rhythm and in 32 patients (52%) with AF ($p=0.09$). Other GFR estimation formulas were also slightly lower in patients with AF, but the difference again did not reach statistical significance value.

NGAL values were higher in HF patients compared to controls (119 ± 69 ng/ml in HF with sinus rhythm, 130 ± 63 ng/ml in HF with AF and 82 ± 26 ng/ml in the control group; $p < 0.001$). Again, there was no significant difference between AF and sinus rhythm groups.

In linear regression analysis adjusted for clinical, biochemical and echocardiographic variables with significant correlations in univariate analysis, independent associates of renal dysfunction beside of age and weight were ferritin, NGAL, mitral annular early diastolic velocity and pulmonary artery systolic pressure. In ROC analysis, NGAL had the highest AUC after age and weight for a GFR < 60 ml/min/1.73 m² and a cut-off value of 110 ng/ml had a 67% sensitivity and a 71% specificity.

Conclusion - Presence of AF does not make a significant additional contribution to progression of renal dysfunction in patients with HFrEF. Independent association of NGAL with renal dysfunction suggest, that functional deterioration of the kidneys in these patients is associated with increased inflammatory response and ongoing kidney injury inherent in the disease rather than the rhythm.

P1414**Effect of ivabradine on quality of life of Greek patients with chronic heart failure and left ventricular systolic dysfunction. The OPTIMIZE QOL study**

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Introduction: Chronic heart failure (CHF) is a complex clinical syndrome with increased morbidity, which reduces quality of life (QOL).

Purpose: To record the effect of ivabradine on QOL, NYHA classification and symptoms in patients with CHF (NYHA II-IV) and left ventricular systolic dysfunction (LVSD) (left ventricular ejection fraction $\leq 35\%$). In addition, to record the global assessment of the effect of ivabradine treatment by the patient and by the treating physician.

Methods: In this observational study 1245 patients with CHF and LVSD were prospectively studied in 102 cardiology hospital clinics and private offices. Data were recorded at baseline and at 1 and 4 months after inclusion. Patients' QOL was assessed at all visits by using the Left Ventricular Dysfunction (LVD 36) questionnaire, while the effect of treatment was assessed by the patient and by the treating physician at the 2nd and 3rd visit, using the Patient Global Assessment (PaGA) and the Physician Global Assessment (PhGA).

Results: Of 1245 CHF patients who participated in the study, 52 (4.2%) prematurely discontinued treatment. From the 1st to the 3rd visit, ivabradine administration (mean dosage 10.1 ± 1.5 mg and 12.0 ± 2.6 mg respectively) changed the NYHA classification from 0%/47.3% (for NYHA I & II respectively) to 18.2%/62.9% and from 52.7% (NYHA III & IV) to 18.9%. In addition, symptoms decreased significantly, since fewer patients reported dyspnea (47.0% less), orthopnea (31.8% less), angina (25.7% less), reduced exercise capacity (24.2% less) and fatigue (28.5% less). As a consequence, QOL assessed by means of the LVD 36 was significantly improved by 29 points (from 58.4 ± 26.6 to 29.4 ± 24.8) ($P < 0.001$), while the PaGA and PhGA showed the favorable effect of 4 months' ivabradine treatment, since 90% of patients and 90.4% of treating physicians reported an improvement. Mean heart

rate values decreased from 83.5 ± 10.6 bpm (baseline), to 66.9 ± 7.3 bpm (study completion) ($P < 0.001$).

Conclusions: Treatment with ivabradine significantly improves QOL in patients with CHF and LVSD in conjunction with improvement in symptoms and NYHA classification. The above mentioned results are confirmed by the LVD 36 questionnaire data, as well as by the assessments by the patients and by the treating physicians.

P1415**Survival rates after implantation of a left ventricular assist device: results of a new LVAD program**

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Background: Left ventricular assist devices are a growing therapeutic option for patients with end-stage or acute decompensated left ventricular heart failure. Since the beginning of this decade, the rate of implantation of continuous, non-pulsatile devices significantly increased. However, less is known how mortality and survival rates changed in the first years of this implantation program. Therefore, we analysed the outcome of a new started LVAD program with continuous, non-pulsatile blood flow support over the last four years.

Methods: Since 2010 all patients receiving a LVAD system were included into the study. The mean age of patients was 60 ± 10.3 y and most of the patients were male (86,7%). Most common reason for terminal heart failure and LVAD implantation was dilated cardiomyopathy (53,6%), followed by ischemic heart failure (39,3%) and myocarditis (7,1%). Patients were mainly in Internmacs - stage I-IV. Mean BNP before implantation had been 1352 ± 1276 pg/ml and the ejection as a marker of dysfunction was 15,6% ± 6 . All patients were followed for a time period of 360 days and data were presented by Kaplan-meier diagram.

Results: With the beginning of the program more than 100 LVAD had been implanted. Overall the survival rate of these patients with end-stage heart failure was 44,3% after 360 days of follow-up. Comparing the one year results of LVAD patients the mortality rates significantly declined over time. While 75% of all patients in the first year (2010) did not survive the 360 days of follow-up, this rate significantly improved by less than 25% in the last year (2013).

Summary: LVAD system improves survival of patients with end-stage heart failure and it is undoubted that the survival rates of LVAD patients significantly increased in the first time of an improved heart failure program. However, it remains unknown if this success is due to an improved selection of patients, a better implantation technique or standardized follow-up care.

P1416**Effect of the angiotensin receptor neprilysin inhibitor LCZ696 compared with enalapril according to baseline risk in PARADIGM-HF**

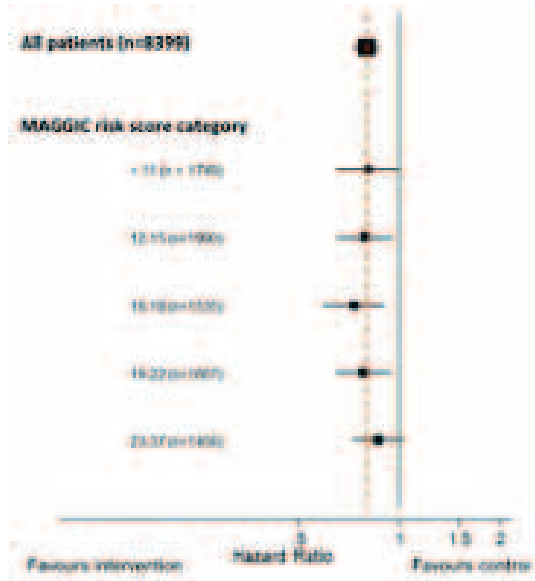
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Background: The angiotensin receptor neprilysin inhibitor LCZ696 reduced cardiovascular morbidity and mortality in patients with heart failure in the PARADIGM trial. We utilized a comprehensive measure of heart failure severity, the MAGGIC risk score, to determine the benefit of LCZ696 across the spectrum of heart failure severity.

Methods: In PARADIGM-HF, 8399 patients with NYHA functional class II-IV heart failure (HF), a LVEF $\leq 40\%$ and a mildly elevated BNP/NT pro BNP concentration were randomized to the angiotensin receptor neprilysin inhibitor (ARNI) LCZ696 (sacubitril-valsartan) 200mg bid or enalapril 10mg bid. The primary endpoint was a combination of cardiovascular (CV) death or HF hospitalization. The MAGGIC risk score is a validated risk score in heart failure and assigns points based LVEF, sex, age, systolic BP, BMI, creatinine, NYHA class, smoking status, diabetes, COPD, beta-blocker use and duration of HF. We determined whether risk, based on the MAGGIC score, modified the treatment effect of LCZ696. Patients were divided into 5 categories of risk (Figure).

Results: In PARADIGM-HF, 70% of patients were in NYHA functional class II and 24% in class III. The median MAGGIC score was 16 (IQR 12, 21). Each point of increased score was associated with a 4% increased risk of the primary endpoint ($p < 0.001$) and a 5% increased risk of cardiovascular death. The benefit of LCZ696 over enalapril for the primary endpoint was similar across the spectrum of risk (p for interaction = 0.23, Figure).

Conclusion: Although most patients PARADIGM-HF had mild symptoms, there was a broad spectrum of risk of CV death or HF hospitalization. The benefit of LCZ696 over enalapril was similar regardless of baseline risk estimated using a validated score.



P1417

Endothelial dysfunction and inflammation in patients with coronary heart disease with preserved systolic function in combination with nonalcoholic hepatic steatosis depend from body mass index

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Objective: To compare the relationship of endothelial dysfunction, inflammation, serum levels of aminotransferases depend from body mass index (BMI) in patients with coronary heart disease with preserved systolic function in combination with nonalcoholic hepatic steatosis.

Methods: We studied 20 patients with coronary heart disease with preserved systolic function in combination with nonalcoholic hepatic steatosis. Allocated 2 groups according to BMI: one group consisted of 10 (50%) people with first degree of obesity (BMI 30,0 to 34,9 kg/m²) mean age 53,7 ± 5,4, group 2 - 10 (50%) people who are overweight (BMI 25 to 29,9 kg/m²) mean age 57,2 ± 7,04. Patients with diabetes were excluded. All patients not taking statins. All patients have had left ventricular ejection fraction >45%. The reactive hyperemia test for assessment of endothelial dysfunction was consecutively performed in all patients. Brachial artery enlargement by less than 10% was considered as a sign of endothelial dysfunction. Studied biochemical parameters: the levels of C-reactive protein (CRP), alanine transaminase (ALT), aspartate transaminase (AST), gamma-glutamyl transpeptidase (GGT).

Results: According to the reactive hyperemia test date, endothelial dysfunction was found in 9 patients (90%) in a group A and in 6 patients (60%) in a group B, vasospastic response observed in 1 patient (10%) in a group A. The mean level reactive hyperemia index (RHI) changes did not significantly differ between the two groups (5,4 ± 4,3 % and 5,3 ± 1,4 %, p > 0,05). The mean level CRP in a group 1 was higher (4,6 ± 0,6 mmol/l) than in group B (2,2 ± 0,34 mmol/l) (p < 0,05). The mean value of ALT in a group A was higher (36,1 ± 10,9 mmol/l) than in a group B (26,2 ± 12,2 mmol/l) (p < 0,05); of AST: 27,3 ± 2,2 mmol/l and 20,1 ± 2,4 mmol/l (p < 0,05); of GGT 61,2 ± 8,02 mmol/l and 48,2 ± 3,7 mmol/l (p < 0,05). There was correlation between the endothelial dysfunction and level of AST (r = 0,89; p < 0,05) in a group 1 however in a group 2 such connection was not observed. The level of CRP in a group 1 associated with level gamma-glutamyl transpeptidase (GGT) (r = 0,88; p < 0,05) than in group 2.

Conclusion: In patients with coronary heart disease with preserved systolic function in combination with hepatic steatosis and first degree of obesity (BMI 30,0 to 34,5 kg/m²) inflammation were more expressed in those who had overweight (BMI 25,0 to 29,9). There was an association between endothelial dysfunction and level of AST, level of CRP and level GGT in a group 1 however in a group 2 such connection was not observed.

P1418

Effectiveness of heart failure treatments according to leading guidelines: a meta-analysis

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Purpose
 The primary aim of this systematic review of randomized controlled trials (RCTs) is to evaluate the benefit of treatment with recommended drugs and devices on mortality and heart failure (HF) hospitalization, and thus to provide clinicians with useful effect sizes.

Methods: RCTs listed in two recent and widely used guidelines in the Western world were evaluated for use in the primary meta-analyses. Studies written in English on HF patients with reduced ejection fraction (rEF) examining angiotensin-converting enzyme inhibitors (ACE inhibitors), angiotensin receptor blockers (ARBs), beta-blockers, aldosterone receptor antagonists, digoxin, ivabradine, cardiac resynchronization therapy (CRT) devices or intracardiac defibrillator devices (ICDs) were included.

The primary outcome collected from the studies was total mortality and HF hospitalization. Meta-analyses based on the number of randomized patients and the number of events in the intervention and control group were made with the effect size being risk ratio (RR). The random effects model was used when moderate to high heterogeneity was found, otherwise the fixed effect model was used.

Results: A total of 50 RCTs were included in the primary analysis, with 50 studies included for mortality and 35 for HF hospitalization. The average age of patients was 63.4 years and 22.4 % were women.

Please see Figure 1.

Conclusions: The majority of recommended HF treatments showed to be significantly effective on HF patients. However, many of the included studies were from the 1990's or earlier with a preponderance of middle-aged men. Therefore, whether these results can be reasonably translated to contemporary HF patients is uncertain.

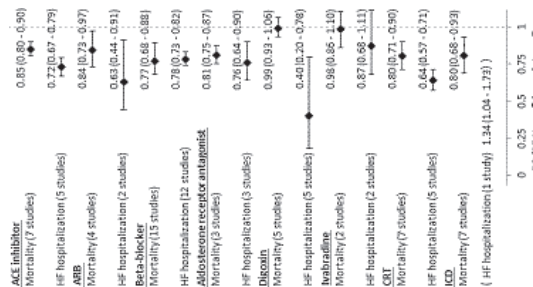


Figure 1

P1419

Clinical outcomes after PCI in ischaemic patients with severe left ventricular dysfunction admitted for heart failure decompensation

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Purpose: PCI in ischaemic patients with severe left ventricular dysfunction admitted for HF decompensation, is a reasonable therapeutic approach, maybe not to improve survival, but to relieve symptoms and clinical outcomes. We present our experience in these patients management.

Methods: We selected patients with ischaemic myocardial infarction and LVEF ≤ 0.35 admitted for HF. After adjusting medical treatment, all of them were made a coronary angiography. According to the heart team decision, some of them were applied a PCI in the suspected culprit arteries. They were followed-up in HF unit considering as outcomes: admission for HF, TRC/ICD implantation and coronary angiography.

Results: 53 patients were followed-up during a mean of 56 months. Basal characteristics are reported in table 1. In medical treatment group there was a significant increase in betablocker, MRA and diuretics use, and in the PCI group in ACE-I/ARB, betablocker, MRA and diuretics ones. PCI was performed in 26 patients.

During the follow-up, an increase in LVEF was reported in the medical treatment group (0.28 vs. 0.38; p = 0.01) and also in the PCI group (0.26 vs. 0.37; p = 0.001). Medical treatment alone does not improve NYHA class (p > 0.05), but there were a significant improvement in PCI group (p = 0.01).

There were no statistical differences neither in the rest of the clinical outcomes nor in survival.

Conclusions: In our sample, in patients with ischaemic myocardial infarction and severe LVEF dysfunction admitted for HF, PCI of the suspected culprit arteries along with

medical treatment optimization, improve functional class and LVEF, whereas only medical treatment do improve LVEF but not symptoms.

Table 1. Basal characteristics

	PCI (N=26)	Medical treatment (N=27)	p value
Age (years)	71 (9)	69 (8)	ns
Sex (male)	21	23	ns
NYHA before to admission: I II III IV	1/11/13/1	3/13/9/2	ns
NYHA after admission: I II III IV	4/15/6/0	2/14/4/3	ns
Drugs before to admission: ACE-I/ARB, BB, MRA, Digoxin, Diuretics	17/14/4/2/18	18/18/9/7/17	ns
Drugs after admission: ACE-I/ARB, BB, MRA, Digoxin, Diuretics	26/25/13/4/23	25/23/15/7/27	ns

P1420

Matrix metalloproteinase-2 (MMP-2) and its tissue inhibitor, TIMP-2, in patients with chronic heart failure

This research has been a part of the statutory activity of the Cardiology Department, Medical University of Wrocław, Poland. M Kobusiak-Prokopowicz¹; J Krzysztofik¹; K Kaaz¹; B Jolda-Mydlowska¹; A Mysiak¹

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Matrix metalloproteinases (MMPs) and their endogenous tissue inhibitors (TIMPs) are responsible for cardiac extracellular matrix remodelling, and the alternations in the balance between MMPs and TIMPs play an important role in pathological cardiac remodelling. The aim of the study was to assess MMP-2 and TIMP-2 serum levels in patients with diverse types of heart failure (HF) and concomitant disorders.

Methods: 101 patients (65.2 ± 11.0 years) with chronic HF were enrolled in the study. Each patient had the levels of MMP-2, TIMP-2, NT-proBNP assessed, and echocardiography performed. Patients were divided into subgroups based on LVEF level, degree of LV diastolic dysfunction, or presence of concomitant diseases i.e. diabetes mellitus, hypertension, ischemic heart disease and chronic kidney disease (CKD).

Results: The LVEF as a factor defining HF type was not associated with MMP-2 and TIMP-2 levels. Among patients with HF, aetiology was not related to MMP-2 levels. The level of TIMP-2 in patients with the most advanced diastolic dysfunction was significantly lower compared to groups with less advanced dysfunction. The patients with HF/CKD(+) exhibited higher MMP-2 and TIMP-2 levels compared to the HF/CKD(-). However, the association between MMP-2 and TIMP-2 was retained in both groups. The patients with a reduced LVEF produced significantly higher levels of NT-proBNP. HF, in the course of coronary artery disease, was also related to higher NT-proBNP levels.

Conclusions: 1. Among patients with HF, neither aetiology nor LVEF values were related to MMP-2 and TIMP-2 serum levels. 2. The degree of diastolic dysfunction was correlated with TIMP-2 levels, suggesting a diminished contribution of MMP-2 inhibitors in the pathophysiology of diastolic dysfunction. 3. Elevated levels of MMP-2 and TIMP-2 were found in patients with chronic kidney disease; in addition, serum levels of MMP-2 were correlated with the degree of kidney failure.

Parameters in HF/CKD(+) versus HF/CKD(-)

Parameter	HF/CKD(+) group n=38	HF/CKD (-) group n=61
MMP-2 [ng/ml]	249.7±278.5 (100.4)	145.3±198.4* (62.5)
TIMP-2 [ng/ml]	163.4±48.1 (166.8)	143.8±40.2* (142.3)
NT-proBNP [ng/ml]	1.28±0.52 (1.25)	1.11±0.47 (1.0)
Creatinine [mg/dl]	1.47±0.35 (1.36)	0.99±0.17** (0.98)
LVEF [%]	49.3±17.9 (56.0)	48.2±17.9 (50.0)

Median values are given in parentheses. *p < 0.05; **p < 0.0001

P1421

Serum erythropoietin levels in patients with chronic heart failure and preserved ejection fraction of left ventricle

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Purpose: To study the levels of erythropoietin and their relationships with symptom's severity, parameters of cardiovascular system, haemoglobin and N-terminal pro-BNP (NT proBNP) levels in patients with different functional classes of CHF.

Methods: We examined 28 patients aged 68-84 years with CHF (I-III classes according to NYHA functional classification system) with preserved ejection fraction of left ventricle (LVEF>50%). Erythropoietin, NT proBNP, haemoglobin levels and echocardiography parameters were assessed in this group of patients.

Results: Patients with the more severe forms of CHF exhibited significantly elevated levels of erythropoietin. Although mean erythropoietin concentrations in healthy patients were 9.2 ± 1.4 mMe/mL, patients with NYHA classes I, II and III had levels of 18.9 ± 3.1, 27.3 ± 4.9, and 37.9 ± 5.6 mMe/mL, respectively (P < .05). A similar trend demonstrating elevated levels of NT-proBNP with rise in the NYHA class was also evident and significant. A significant correlation was found between serum erythropoietin and NT-proBNP (r = 0.43; p < 0.05) and creatinine levels (r = -0.32; p < 0.05). No association was found between LVEF and erythropoietin serum levels. Yet no significant correlation was found between circulating erythropoietin levels and hemoglobin levels in the CHF patients, nor was there an association between age of patients and erythropoietin levels.

Conclusion: Progression of CHF in patients with preserved ejection fraction of left ventricle is accompanied by increasing levels of serum erythropoietin. No association was found between LVEF and erythropoietin serum levels in this group of patients.

P1422

Accuracy of a pacemaker-derived algorithm for the diagnosis of sleep disordered breathing in heart failure

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Purpose: Sleep disordered breathing (SDB) is highly prevalent in patients with heart failure and its presence is associated with a worse prognosis. Treatment with continuous positive pressure is beneficial for those with obstructive sleep apnoea (OSA), however the treatment of central sleep apnoea (CSA) is under investigation. Many centres do not have routine access to sleep polygraphy or polysomnography and SDB is frequently under-diagnosed. A novel pacemaker algorithm uses variation in transthoracic impedance with breathing to quantify apnoeas and hypopnoeas. It is commercially available on ICD and CRT devices. The aim of this study is to assess the accuracy of this algorithm compared to standard multichannel sleep polygraphy.

Methods: Patients with symptomatic heart failure, ejection fraction <40%, not on nocturnal non-invasive ventilation and with compatible pacing or ICD devices underwent home sleep polygraphy at least 6 weeks following device implantation or box change, followed by download of data from the pacemaker. The data for the study night was compared using correlation coefficients and a Bland Altman plot.

Results: 18 patients (mean ±SD: age 68 ± 14 years, 78% male, NYHA 2.1 ± 0.5, BNP 469 ± 417ng/l, EF 26.8 ± 9.5%) underwent home polygraphy and pacemaker download. Mean apnoea-hypopnoea index by polygraphy (PG-AHI), analysed according to the American Academy of Sleep Medicine 2012 criteria, was 16.0 ± 17.8 events/hr. Mean pacemaker-derived AHI (PM-AHI) was 31.1 ± 11.4/hr. The PM-AHI demonstrated good correlation with PG-AHI overall (r = 0.79, p < 0.01). The pacemaker algorithm performed well in those with moderate to severe SDB, defined as AHI > 15/hr, (r = 0.93, p < 0.01) but was less accurate in those with mild or no SDB (r = 0.28, p = 0.37). The accuracy of the algorithm was not significantly different between those with CSA and OSA. The algorithm over-estimated SDB by a mean difference 15.94 ± 11.39 in this cohort. In detecting those with moderate to severe SDB (AHI > 15/hr) the sensitivity was 100% with specificity 8%; positive predictive value 35% and negative predictive value 100%.

Conclusions: This pacemaker algorithm is a sensitive but non-specific means of diagnosing SDB, with a strong negative predictive value. The algorithm over-estimates severity of SDB but is more accurate in those with moderate to severe SDB. The PM-AHI may prove a useful tool for screening for SDB in patients with chronic heart failure.

P1423

The effect of non-pharmacologic treatment on clinical status of patients with heart failure

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Introduction: Heart failure (HF) is closely related to diet and physical activity, and this variables are capable of improving or deteriorating the patients clinical condition. However, there is not specific nutritional or physical therapy for patients with HF.

Purpose: To evaluate the effect of non-pharmacologic treatment over clinical status of patients with HF.

Methods: Randomized clinical trial. We recruited 122 patients with HF (from the HF clinic of INCMNSZ), which were randomly assigned into two groups: intervention group (n=84), who followed a diet and physical therapy plan consisting of aerobic and resistance exercises; and a control group (n=38), which received a diet plan only. The trial had a follow up period of four months, with assessments every two months. The variables evaluated were: blood pressure, hand strength, total body water, oxygen saturation and heart rate.

Results: Baseline population characteristics were similar between the two study groups. After two months of follow up, the intervention group had a decrease in diastolic blood pressure (71 to 64 mmHg, $p=0.004$) and a trend in reducing systolic blood pressure (126 to 119 mmHg, $p=0.10$), whereas in the control group, no statistically significant changes were observed. Non-statistically significant differences were observed in the intervention group.

Conclusions: non-pharmacologic treatment decreased blood pressure.

P1424

Cardiorenal relations in patients with chronic heart failure and chronic obstructive pulmonary disease

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Aim of the study was to examine the peculiarities of cardiorenal relations in patients with chronic heart failure (CHF) with chronic obstructive pulmonary disease (COPD). A total of 134 patients aged from 45 to 78 years, comparable by age and sex, with CHF II of functional class (FC) III of ischemic origin. The main group consisted of patients with CHF II, FC III with concomitant COPD II, stage III (n=74). The control group (group II) represented patients with CHF II, FC III without disrupting of respiratory function (RF) (n=60). The study of morpho-functional state of the myocardium showed that for the same functional class of CHF in patients with concomitant COPD, compared with patients with CHF without COPD we observe a significant increase in the size of the right atrium (RA), right ventricular (RV), the average diameter of the pulmonary artery (ADPA); significantly more often we observe arterial hypertension, left ventricular hypertrophy (LVH), prognostically unfavourable types of LV remodeling (concentric and eccentric), the number of people with "delayed" type of diastolic dysfunction of the left ventricle (DD LV) is decreased due to increasing the proportion of patients with an intermediate "pseudonormal" violation of DD LS.

In patients with CHF and COPD compared with those without COPD more frequently we observed clinically significant: increase in serum creatinine (35.1% vs 10%, respectively, $p < 0.05$), reduced glomerular filtration rate (GFR) ($< 60 \text{ ml/min/1.73m}^2$) (47.3% vs 25.0%, respectively, $p < 0.05$), exhausted functional renal reserve (FRR) (47.3% vs 15%, respectively, $p < 0.05$) microalbuminuria (MAU) (89.2% vs 61.7%, respectively, $p < 0.05$). It is discovered that increasing the MAU is associated with dilation of the right parts of the heart, reduction of tolerance to physical exercise and an increase in the severity of CHF. The increase of Urine Specific Gravity (USG) is due to decrease in RV dilatation.

It is proved that the maximum percentage of patients with MAU and exhausted FRR, clinically significant reductions in GFR, increased KK and decrease of the relative density of urine was observed among patients with stage III COPD, as well as in patients with FC III of CHF. It is determined that eccentric hypertrophy and concentric hypertrophy of the LV are accompanied by a more symptomatic deterioration in glomerular and tubular nephron function. Thus, there is a direct correlation between progressive nephropathy and adverse myocardial remodeling.

P1425

Heart failure after kidney transplantation

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Purpose: To determine the prevalence of heart failure in kidney transplant patients and prevalence of major pathogenic risk factors for heart failure in kidney transplant patients. To determine whether there is a difference in the prevalence of heart failure and major pathogenic risk factors for heart failure among kidney transplant patients and patients treated with hemodialysis.

Methods: We conducted a prospective study that included 90 patients. All patients had their anamnestic data taken, electrocardiogram, complete physical examination and echocardiography. In our patients heart failure was diagnosed if the following criteria were met: persistent symptoms of heart failure, objective findings of cardiac dysfunction and positive response to the treatment of cardiac insufficiency. The difference in frequency of the observed parameters was tested by chi-square test.

Results: Patients were divided into two groups: kidney transplant patients (60 patients) and patients treated with hemodialysis (30 patients). There were 42 men and 18 women in the group of kidney transplant patients. The group of patients treated with hemodialysis consisted of 15 men and 15 women. The mean duration of dialysis before kidney transplantation in the group of kidney transplant patients was $43,00 \pm 9,19$ months. The average kidney graft survival was $9,1 \pm 9,68$ years. The mean duration of dialysis in the group of patients treated with hemodialysis was $87,00 \pm 15,6$ months. Congestive heart failure had 2 kidney transplant patients and 5 patients treated with hemodialysis. Hypertension had 18 kidney transplant patients and 20 patients treated with hemodialysis. Left ventricular hypertrophy had 30 kidney transplant patients and 23 patients treated with hemodialysis. Coronary heart disease had 8 kidney transplant patients and 11 patients treated with hemodialysis. Atrial fibrillation had 6 kidney transplant patients and 8 patients treated with hemodialysis. Diastolic dysfunction of the left ventricle was verified by echocardiography in 27 kidney transplant patients and 11 patients treated with hemodialysis. Tricuspid regurgitation had 20 kidney transplant patients and 12 patients treated with hemodialysis. Mitral regurgitation had 20 kidney transplant patients and 17 patients treated with hemodialysis.

Conclusion: We found statistically significant difference in the frequency of congestive heart failure, hypertension, left ventricular hypertrophy, coronary heart disease, valvular heart disease and atrial fibrillation among kidney transplant patients and patients treated with hemodialysis.

P1426

Liver dysfunction in chronic heart failure: prevalence, characteristics and prognostic significance: moroccan profil

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Background: Abnormal liver function tests are common in ambulatory chronic heart failure but characterization and importance of liver dysfunction are poorly defined. The aim of this study was to evaluate the incidence of liver dysfunction in ambulatory patients diagnosed with chronic heart failure in order to establish a correlation with the risk factors, evolution and prognosis.

Methods: 1613 consecutive ambulatory patients with chronic heart failure were enrolled from 2006 to 2013 and registered in the therapeutic unit of chronic heart failure. Clinical, echocardiographic and biological data were investigated.

In only 358 HF patients, liver function was determined by aspartate and alanine aminotransferase (AST, ALT). We divided our population into three groups: group 1 with elevated ALT > 45 U/l, group 2 with elevated AST > 45 U/l and group 3 with normal liver enzymes.

Results: Liver dysfunction was present in 13.68%. Mean serum levels of ALT and AST were 98.44 U/l and 88.43 U/l respectively. Liver dysfunction was associated with male sex ($p=0.019$), dyslipidemia, smoker and coronary heart disease ($p=0.004$). Compared with a normal liver function, those with dysfunction had a higher heart rate and more cardiac right and left decompensation. Also Transaminases elevated were associated with more tricuspid regurgitation ($p < 0.00001$), pulmonary hypertension ($p < 0.00026$), right ventricular dysfunction ($p=0.02$), kidney dysfunction (DFG $< 60 \text{ ml/min/m}^2$) ($p=0.018$), higher doses of diuretics ($p < 0.02$), whereas beta-blockers were inversely associated ($P < 0.0001$). No correlation between liver function and using statins and spironolactone was found ($p=0.8$ and 0.1 respectively).

Conclusions: Liver dysfunction is frequent in chronic heart failure. Patients with heart failure and abnormal liver function had less optimized treatment with more hospitalizations for cardiac decompensation.

P1427

Resting heart rate and mortality risk in patients with long term conditions: a community based study

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Background: Evidence that raised resting heart rate is adversely associated with poor outcomes in patients with cardiovascular disease (CVD) and diabetes individually exists. However, there is no data in patients with multiple co-morbidities (heart failure and/or chronic pulmonary disease or diabetes). This study addresses this issue.

Methods: The relationship between baseline resting heart rate and all-cause mortality was examined in 764 patients with 2 or more long term conditions under the care of a community heart failure team over a 5 year period.

Results: During the follow-up 187 (24.4%) patients died. In heart failure patients alone, the relative risk of all cause mortality was increased by 7% for every 10 beats/minute increase in heart rate (adjusted HR: 1.07 [1.01-1.32], $p < 0.001$). However, this was not observed for every 10 beats/minute in heart rate (adjusted HR: 1.02 [0.89-1.21]) in patients with 2 or more concurrent long term conditions.

Conclusions: An increased resting heart rate is not associated with adverse outcomes in patients who have chronic co-morbidities and does not appear to be a risk factor. This observation requires further investigation.

P1428

Relationship between functional capacity and diastolic function in chronic heart failure patients

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Background: Dyspnea is the frequent cause of exercise intolerance and physical inactivity among chronic heart failure patients. Diastolic dysfunction has shown significant correlation with exercise capacity.

The aim is to study whether there is interaction between left ventricular diastolic dysfunction and functional capacity in our CHF patients.

Methods: 1613 consecutive ambulatory patients with chronic heart failure were enrolled from 2006 to 2013 and registered in the therapeutic unit of chronic heart failure. Clinical, echocardiographic and biological data were investigated. We divided our patients into 2 groups as follow: group 1 with reducing filling pressure (64 years, 67% were male), group 2 with elevated filling pressure (EFP) (69 years, 61% were male). We analyzed New York heart association (NYHA) status and the 6 minutes' walk test. Assessment of diastolic function as determined by Doppler-derived mitral and pulmonary venous flow velocities recorded by transthoracic pulsed doppler echocardiography.

Results: There was no significant difference in baseline characteristic and ejection fraction. The mean of 6 minutes' walk in groups were 349 and 212m respectively. Group 2 (EFP) was significantly associated with more NYHA grade III/IV ($p < 0.00001$), inversely associated with NYHA grade I/II ($p < 0.0001$). The 6 minutes' walk test was shorter in EFP patients than others ($P < 0.01$).

There was a significant correlation between diastolic dysfunction and cardiac decompensation ($p = 0.00001$), right ventricular dysfunction ($p = 0.00001$), pulmonary hypertension ($p = 0.00001$), dilated vena cava and higher doses of diuretics ($p = 0.00001$). Also, beta-blockers were inversely associated ($P < 0.0001$).

Conclusion: diastolic dysfunction is significantly associated with impaired functional capacity and dyspnea among CHF patients.

P1429

Age-related multiple hormone deficiencies in chronic heart failure

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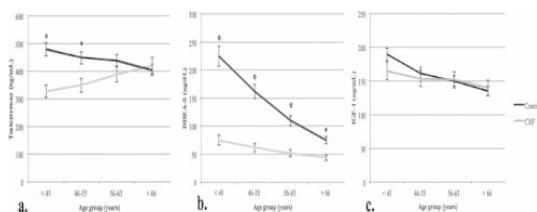
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Background: Anabolic hormones are endowed with powerful actions on both the cardiovascular system and the skeletal muscle. An age-related decline of anabolic hormones including IGF-1, testosterone and DHEA-S is extensively described, and thought to contribute to sarcopenia, visceral adiposity and osteopenia. However, very few studies have described its prevalence in mild-to-moderate CHF, particularly focusing on age-related trends.

Methods: 107 male subjects with CHF, NYHA class I-III, were enrolled. Biochemical hormonal deficiencies were defined as follows: DHEA-S and IGF-1 below the 10th percentile of our sex and age-matched control population; serum total testosterone levels below 300 ng/dL and free triiodotironine levels (T3) below 2.0 pg/mL (in the presence of normal TSH levels). We next divided the CHF and healthy controls in four subgroups according to the following age: < 45 yrs. (n=10), 46-55 yrs. (n=29), 56-65 yrs. (n=32) and > 66 yrs (n=36) (Fig 1 a,b,c,d).

Results: Overall, 18% of CHF patients had no hormonal deficiency, 75% had either 1 or 2 deficiencies, and a small proportion showed 3 or 4 deficits (7%). Interestingly, CHF heavily impacted on the age-related decline of anabolic hormone, which was apparently attenuated with regard to DHEA-S and IGF-1, and paradoxically reversed with regard to testosterone (Fig. 1b,c,d). The latter findings suggest that anabolic decline of CHF males can be age-independent and MHDS be more relevant in younger than older ages, as depicted in figure 1.

Conclusion: the high prevalence of HD in CHF patients particularly in younger patients supports the role for a hormonal screening in these patients.



Levels of hormones in CHF and CTRL

P1430

How to measure the functional status of obese heart failure patients?

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Background: Obesity is a high risk factor and has been described as an independent risk for heart failure (HF). Obese patients suffer dyspnea earlier than others. Our aim to explore the functional status of obese heart failure patients.

Method: This retrospective study including 685 patients (66 years, 436 were male) admitted in the therapeutic unit of heart failure, We divided the patients into 3 groups regarding their body mass index (the weight in kilograms divided by the square of the height in meters): normal weighted <18.5 to 24.9 kg/m²> (67 years, 72% were male); overweight <25.0 to 29.9 kg/m²> (65.3 years, 60% were male); and obese <30.0 kg/m² or more> (65.6 years, 37% were male); We analyzed new York heart association (NYHA) status, the 6 minutes' walk test a simple and reliable way to assess the exercise capacity of CHF patients.

Results: Baseline characteristics and ejection fraction was comparable in the 3 groups.

Female sex, diabetes, hypertension, dyslipidemia were significantly associated in overweight and obese groups ($p = 0.0001$).

NYHA grade III/IV were significantly lower in the normal weighted patients ($p = 0.01$); no difference in NYHA grade I/II was observed. There was significant correlation between groups in distance covered in the 6 minutes' walk test ($p = 0.03$). Patients incapable to walk were significantly obese ($p = 0.003$).

Conclusions: These results show that NYHA score and 6 minutes' walk test are useful to discriminate functional status in obese patients compared to others but unsatisfying because can surestimates severity of obese heart failure patients, the VO2 max is more useful.

P1431

Relationship between neuropsychological performance and left ventricular dysfunction in male patients with ischemic heart disease

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Purpose: Many researches interrelate overt heart failure (HF) and cognitive dysfunction, while there are few evidences on the relationship left ventricular (LV) dysfunction (ejection fraction, EF <40%) and neuropsychological and neurophysiological performance in ischemic heart patients independently of the HF presence. Aim of our pilot study has been to test this relation.

Methods: We enrolled 25 elderly male outpatients with stable CAD (CCS class I) divided in groups A and B (respectively without or with LV dysfunction) with Mini Mental State Examination (MMSE) > 25, without history of depression, TIA or stroke, diabetes, persistent/permanent atrial fibrillation, aortic stenosis, severe hepatic and kidney failure, and COPD. Global functional capacity was measured with 6MWT. None of the patients were in NYHA class III or IV and had a Boston score > 4. We assessed cognitive profile with comprehensive neuropsychological battery and Event-Related Potentials (ERPs), recorded while participants performed a visual word recognition task consisting of a test phase in which they were asked to judge whether visual stimuli had been previously presented in a learning phase ('old'), or not ('new').

Results: Two groups (A 12; B 13 subjects) not significantly differ in mean age (A 75,3 ± 1,9; B 73,1 ± 2,3 years), BMI (A 28,0 ± 1,5; B 26,9 ± 0,9 kg/m²), distance walked at 6MWT (A 508 ± 59; B 501 ± 34 meters) and MMSE (A 28,93 ± 0,5 B 27,9 ± 1,9 $p = 0,18$). The mean EF was 63 ± 3% in group A, 31 ± 2% in group B ($p < 0,001$). We found significant differences on memory performances, in particular delay recall, evaluated by Buschke-Fuld Test ($p = 0,01$), verbal fluency ($p = 0,02$), constructional praxis evaluated by Rey's Complex Figure ($p = 0,02$) and on executive functions evaluated by Trail Making Test (TMT) ($p = 0,02$). The only echocardiograph parameter significantly correlated with this cognitive profile was EF. The distance walked at 6MWT was significant related with alteration in executive functions (TMT B Rho = -0,447; TMT B-A Rho = -0,460). Concerning neurophysiological performance, a late positive ERP component (as a memory process index) peaking around 500 ms was differentially modulated in the two groups: a clear old/new effect (enhanced amplitude for "old" respect to "new" items) was observed in Group A, whereas group B did not show such a old/new effect.

Conclusions: Our preliminary data show a strong relation between reduced EF and cognitive performance evaluated both neuropsychological and neurophysiological assessment, independently from HF presence.

P1432

Relation between serum NT-proBNP level and severity of coronary artery disease in chronic heart failure patients

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Purpose: The aim of the study is to evaluate the relation between serum NT-proBNP level and severity of coronary artery disease in patients with chronic heart failure undergoing cardiac catheterization.

Methods: The study included 58 patients with chronic heart failure - NYHA functional class I - III and symptoms of stable angina pectoris. NT-proBNP concentrations were measured before an angiographic procedure that allowed diagnosis of CAD and measurements of left ventricular end-diastolic pressure. Echocardiographic assessment of LVEF was performed in all patients. Systolic dysfunction was defined at LVEF < 50%.

Results: NT-proBNP concentrations in patients with 1-, 2- and 3-vessel coronary artery disease were $681, 18 \pm 354.08$ pg/ml, 592 ± 559.72 pg/ml and $965, 44 \pm 521, 91$ pg/ml, respectively. Linear regression analysis showed positive correlation between NT-proBNP serum levels and the presence of CAD ($p < 0.001$, $R^2 = 0.194$, confidence interval 95%). According to our data NT-proBNP levels < 100 pg/ml in patients with preserved ejection fraction have negative predictive value for CAD - 80% sensitivity and 65 % specificity (AUC 0,728; $p = 0,003$). Significant positive correlation between NT-proBNP and LVEDP ($p = 0,001$) and negative correlation between NT - proBNP and LVEF ($p = -0,001$) were observed.

Conclusion: NT-proBNP is elevated in patients with chronic heart failure and stable angina pectoris and has a close correlation with the severity of CAD.

P1433

Epidemiology characteristics in a cohort of elderly and pluripathologic patients with chronic heart failure

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Purpose: To describe epidemiology characteristics associated to survival in aged and pluripathologic patients with chronic heart failure (HF) registered in our cohort.

Methods: Retrospective cohort study from a database of patients with chronic HF followed in a specialized unit of a tertiary hospital during at least two years. Continuous variables are reported as means and standard derivation (SD), and qualitative variables are expressed as percentages. The significance for all comparison tests was set at $p < 0.05$.

Results: The study involved 157 patients from 2007 to 2014. Mean (SD) age was 83.50 (10.46) yrs, 59% were females. The prevalence of comorbidities was: 95% for hypertension, 36% for diabetes, 18% for chronic air flow obstruction (COFA), 14% for any level of cognitive impairment, 71% for atrial fibrillation, and 47% for advanced chronic renal failure (glomerular filtration rate, GFR < 60 ml/min). Echocardiographic evaluation described 30% of cases of systolic ventricular dysfunction and 22% of diastolic dysfunction. Patients followed treatment with ACEI/ARA II in 76% of cases, 43% beta-blockers, 28% digoxin. Prevalence of treatments with loop diuretics, potassium-sparing diuretics and thiazides was 84%, 40% and 13% respectively. Mortality rate recorded after first and second year of follow up was 13.4% and 33%, respectively. Regarding baseline characteristics, main factors associated with mortality during the first year of follow up were CAFO (47.8 vs 12.6%, $p = 0.006$), and GFR < 30 ml/min (33.5% vs 8.5%, $p = 0.02$). For baseline echocardiographic, mortality was related to both lower left ventricular ejection fraction (LVEF) (43 (15) vs 54 (16)%, $p < 0.022$) and higher systolic pulmonary arterial pressure (PAPs) (55 (8) vs 48 (8) mmHg, $p < 0.017$). Mortality was associated to lower mean sodium values (137 (5) vs 141 (3) mEq/l, $p < 0.023$), higher mean urea values (87 (47) vs 67 (31) mg/dl, $p < 0.27$) and higher median Nt-ProBNP values (3272 vs 1603 pg/ml, $p < 0.006$). According to baseline treatment, lower mortality rates during the first year were found among those taking potassium-sparing diuretics at baseline (31% vs 69%, $p = 0.013$), lower doses of loop diuretics (furosemide 38.6 (28.3) vs 57 (24.6) mg/day, $p < 0.021$), and lower doses of thiazides (16 vs 50 mg/day, $p < 0.001$).

Conclusions: In elderly aged and pluripathologic patients with chronic HF, comorbidities profile, PAPs and LVEF as well as sodium, urea and Nt-ProBNP levels appear to be associated to mortality after one year of follow up. Treatment strategies including distal sparing diuretics and lower doses of loop diuretics are related to lower mortality rates in our cohort.

P1434

Detection of ventricular arrhythmias in patients with acute Q-MI and left ventricular diastolic dysfunction

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Objective: to estimate the relationship between ventricular arrhythmias (VA) and left ventricular diastolic dysfunction (LVDD) in patients with Q-wave myocardial infarction (MI).

Materials and Methods: The study involved 87 male patients with primary Q wave MI. Echocardiography, Doppler sonography study and long-term ECG recording were carried out. To characterize ventricular premature beats were used gradation and classification B.Lown M.Wolf (1971) and prognostic classification J.Bigger (1982).

Results: Depending on the frequency of ventricular premature beats on the results of Holter monitoring, patients were divided into 2 groups: the first consisted of 50 patients with either a lack of or a rare and up to 10 per hour ventricular premature beats, the second - 37 with the presence of potentially dangerous VA (PDVA). In the analysis of clinical and anamnestic data revealed that the group of patients with the presence of PDVA presented by patients with anterior MI localization, complicated course of the disease as early postinfarction angina. At the same time, significant differences were revealed only in terms of signs of heart failure (40.9% vs. 14%, $\chi^2 = 4.54$; $p < 0.05$) at the time of the survey, as well as the detection of two or more complications in the acute phase of MI (36.3% versus 10% $\chi^2 = 4.38$; $p < 0.05$).

When analyzing the data we have identified the following Doppler options LVDD: type I at 43.7% in type II in 31%, by type III in 25.3% of patients. In the group of patients with PDVA detection frequency LVDD was 43.5%, 29.6% and 26.9%, respectively I, II and III types of LVDD.

Conclusion: The data analysis showed an association between potentially dangerous heart rhythm disorders and severity of left ventricular diastolic dysfunction in patients with Q-myocardial infarction.

P1435

Effects of cultural aspects on quality of life in patients with heart failure after beta-blocker up-titration: CIBIS-ELD trial results

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Purpose: Quality of life (QoL) depends on patient's emotional and social status, traits of treatment setting, medication and clinical factors during treatment. Since the effect of cultural aspects on QoL hasn't been fully explored so far, we decided to analyze the data from CIBIS-ELD in which QoL for Serbian and German patients with heart failure (HF) were available.

Methods: CIBIS-ELD was a trial in elderly patients (>65 y) with moderate to severe HF, who were randomly assigned to up-titration with bisoprolol vs. carvedilol. The physical and psychosocial component scores on the short-form health survey (SF36) were recorded at baseline and after 3 months (final visit). Age and clinical parameters such as NYHA class (NYHA I-II vs. NYHA III-IV) at baseline, objective physical performance in the 6-min walk test, LVEF, initial medication and final dosage of study medication at follow-up (0, 1/2, 1/4, 1/2, > 1/2 of the targeted dose) were also recorded for the analyses. Complete data were available for 136 German (67 female) and 426 Serbian (117 female) patients. We ruled out QoL differences due to unplanned study visits, by controlling their number and its interaction with NYHA class and nation.

Results: Physical and mental QoL differed between men and women, $F > 6.6$, $ps < .01$: Men reported better QoL. When comparing the effect of Nation for QoL, Serbians reported better physical QoL. Concerning treatment effects, both QoL scores improved from baseline to follow up, effect sizes $d > .17$, $ps < .001$. This treatment response was moderated by nation for both mental ($F = 7.22$, $ps < .001$) and physical QoL ($p = .087$): Serbians showed a more pronounced response on physical and mental QoL compared to Germans ($d = 0.3-0.34$ vs. $d = 0.07-0.12$). A closer look revealed that cultural differences in treatment response were strongest for the facets that are less affected by beta-blockers. Treatment effects associated to NYHA class were only observed on physical QoL, $F = 9.38$, $p = .002$. For patients in NYHA classes III-IV the treatment resulted in a larger improvement of physical QoL than for NYHA I-II and their physical QoL did not differ from that of patients with less severe HF at follow-up, $p > .10$.

Conclusions: Careful analysis showed that Serbian patients had a stronger positive response to treatment with beta-blockers. This effect might be because of differences in health care systems or cultural aspects related to the perception of interpersonal factors as nation effects were more pronounced on the psychosocial than on the physical QoL facet.

P1436

Iron deficiency, intravenous iron and re-hospitalizations in patients with chronic heart failure: a multicentre study of 2172 patients

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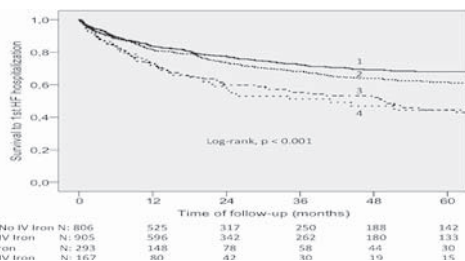
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Purpose: Treatment with intravenous (IV) Iron in patients with chronic heart failure (CHF) and iron deficiency (ID) has been shown to improve functional capacity and reduce re-hospitalizations. We aimed to evaluate the risk of re-hospitalization due to decompensated CHF or any cause according to ID and IV Iron treatment.

Methods: We evaluated ID in patients with CHF at entry to a heart failure unit of 3 university hospitals. ID was defined as a ferritin < 100 ug/L or a Transferrin Saturation < 20% if ferritin between 100 and 299 ug/L. We retrospectively assessed treatment with IV Iron at any point after entry. Time to first hospitalization due to decompensated CHF or any cause was evaluated using Kaplan Meier survival curves.

Results: We included 2172 patients, 65% males, median age of 72 years and median left ventricular ejection fraction of 36%. Median glomerular filtration rate was 53 ml/min, NT-proBNP of 1484 pg/mL, haemoglobin of 12.7 g/dL and 37% in NYHA functional class III-IV. ID was present in 55% and 461 patients (21%) received IV Iron and 6% EPO. Median follow-up was 19 months. Figure 1 shows how patients with ID had more re-hospitalizations due to CHF than those without ID, however IV iron was associated with more re-hospitalizations due to CHF. A similar picture was seen with re-hospitalizations due to any cause.

Conclusions: Patients with CHF and ID had more re-hospitalizations due to decompensated CHF or to any cause. Paradoxically, treatment with IV Iron was associated with more re-hospitalizations. We do not think IV Iron caused more re-hospitalizations. Because IV Iron was assessed at any point in time during follow-up, this finding probably reflects the current pattern of use of IV Iron, where it is more often used if the patient decompensates and not up-front.



Re-hospitalizations in CHF

P1437

How comorbidity, self-care confidence and self-care behaviors interact to predict hospitalization in heart failure patients

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Purpose: As many as 70% of heart failure (HF) patients suffer from at least one other chronic condition. Comorbidity in HF is associated with frequent hospitalizations. Self-care can mitigate poor outcomes. Yet, lack of confidence is known to interfere with self-care when more than one chronic condition exists. The mechanism by which comorbidity, self-care confidence and self-care behaviors interact to predict hospitalization in HF patients is unclear. The aim of this study was test an explanatory model of predictors of hospitalization by: 1) identifying the contribution of comorbidity to HF self-care behaviors and hospitalization, and 2) testing comorbidity as a moderator of the relationship between self-care confidence and HF self-care behaviors.

Methods: We conducted a secondary analysis of data from a cross sectional study of 628 HF patients enrolled across Italy. All participants: 1) had a confirmed diagnosis of HF; 2) were stable in the preceding month; 3) were age > 18 years; and 4) had symptoms in the last month so that we could analyze their symptom management behaviors. Both comorbidity, as measured by the 12 item Charlson Comorbidity Index total score, and hospitalization were evaluated from medical record review. Self-care was measured with the Self-Care of HF Index v.6.2. All three scales (maintenance, management, confidence) yield standardized scores ranging 0-100 with higher scores indicating higher HF self-care. Structural equation modeling and post-hoc simple slope analysis were used to analyze the data.

Results: Participants were primarily male (58%), older (73 years old, SD = 11) and NYHA class II or III (75%). In model testing, higher numbers of hospitalization were associated with lower self-care maintenance (i.e. treatment adherence and symptom monitoring) and higher comorbidity. Higher self-care maintenance was associated with higher self-care confidence. Higher self-care management (i.e. symptom management behaviors) was associated with lower comorbidity and higher self-care confidence. Slope analysis showed that comorbidity moderated the relationship between self-care confidence and self-care maintenance. As the level of comorbidity increased, the effect of self-care confidence on self-care maintenance decreased. The final model fit the data well (fit indices: CFI = 0.99, RMSEA = 0.03).

Conclusion: Self-care confidence plays a key role in the relationship between comorbidity and self-care in influencing hospitalization. When patients have comorbid conditions, interventions designed to improve self-care confidence may help to decrease hospitalizations.

HEART FAILURE DIAGNOSIS

P1438

First HF admission: doppler echocardiographic differences based on left ventricular ejection fraction

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Purpose: The heart failure (HF) syndrome has been divided according to the left ventricle ejection fraction (LVEF) into two different entities: HF with reduced ejection fraction (HF REF, LVEF < 50%) and HF with preserved ejection fraction (HF PEF, LVEF ≥ 50%). Nevertheless, diastole and systole are part of a continuum process which makes this classification somewhat artificial. The aim of this study was to compare the Doppler diastolic echocardiographic parameters among HF patients hospitalized for the first time. **METHODS** We prospectively collected data from 116 patients admitted to the Cardiology or Internal Medicine Units during 3 months. We only included patients whom LVEF was not previously known. Patients with advanced chronic renal disease, high output HF, congenital heart disease, mitral or aortic prosthesis or severe mitral or aortic native valve disease. **RESULTS** Out of the 116 patients, 82 had PEF and 34 REF. Average age (SD) was 79.7 years (8.4) among HF PEF patients and 76 (12.9) in the REF group (p = 0.064). HF PEF was found predominantly in women (87.5% vs 12.5%, p < 0.0001). Patients with HF REF were more frequently admitted to Cardiology (p = 0.007). The median (IQR) of the NT proBNP was higher in the HF REF group, 6474 (14463) ng/l vs 1831 (3969) ng/l, p = 0.003. The main baseline echocardiographic characteristics of both cohorts are summarized in Table 1. HF REF had worse LV diastolic dysfunction: the early diastolic velocity of mitral annulus obtained by DTI (e') was lower and the E/e' ratio of the mitral inflow E wave to the tissue Doppler e' wave was higher among patients with LVEF < 50%. The E wave deceleration time was also lower among HF REF patients. **CONCLUSIONS** Hospitalized HF patients with HF REF had worse diastolic function than patients with HF PEF.

Table 1. Echocardiographic differences

	LVEF < 50% X (SD)	LVEF ≥ 50% X (SD)	p
LVEDVI ml/m ²	65,76 (28,06)	38,47 (15,74)	<0,0001
LVEF Simpson %	29,85 (12,70)	65,73 (7,87)	<0,0001
e' mitral annulus wave cm/s	4,8 (1,6)	6,6 (2,1)	<0,0001
E/e' septal ratio	19,5 (6,9)	15,6 (6,6)	0,005
E/e' lateral ratio	15,0 (6,1)	12,9 (6,1)	0,126
E wave deceleration time ms	177 (87)	214 (86)	0,039
Left ventricular dp/dt mmHg/s	757 (440)	1515 (1136)	<0,0001

LVEDVI: Left ventricle end-diastolic volume index

P1439

Ultrasound diagnosis of pulmonary edema in congestive heart failure; simplified approach

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Pulmonary edema (PE), due to fluid retention and redistribution is the cardinal manifestations 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: 400 patients with II-IV NYHA functional class HF were evaluated (105 patients with diastolic and 295 with systolic HF). The control group consisted of 160 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 MHz convex or sector probe, from 10 points on thoracic wall (cross points of midclavicular line with II, IV and V intercostal spaces and anterior axillary 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

Table P1441. Changes of NT-proBNP & EDV during PLET

Parameters	HF functional class		Chi ²	p			
	1st (n=16)	2nd (n=20)					3rd (n=20)
EDV before PLET (ml)	105.2 (11.5)	111.9 (16.4)		112.6 (10.8)	130.7 (20.7)	8.99	0.003
EDV after PLET (ml)	118.5 (10.9)*	122.2 (16.4)*		142.2 (20.2)*	160.8 (27.7)*	17.9	0.0005
ΔEDV (ml)	13.2 (6)	10.3 (7)		29.6 (19)	30.1 (15)	21.0	0.0001
EF before PLET (%)	72.3 (5.3)	68.3 (4)		54.4 (8.3)	58.3 (10.6)	22.4	0.0001
EF after PLET (%)	65.3 (7.9)*	62.4 (6.2)*		49.7 (11.3)*	55 (8)*	15.2	0.0017
ΔEF (%)	7 (4)	5.9 (5)		4.6 (7)	3.2 (5)	6.18	0.1
IVST (mm)	10.3 (1.1)	9.3 (1.1)		11.9 (1.2)	12 (1.2)	23.7	<0.0001
NT-proBNP before PLET (pg/ml)	8.7 (8)	81.4 (71)		292.9 (173.9)	1399.6 (427.1)	42.8	<0.0001
NT-proBNP after PLET (pg/ml)	14.4 (11)*	101.1 (85)*		366.9 (232.7)*	1656.7 (510.8)*	48	<0.0001
ΔNT-proBNP (pg/ml)	5.7 (4)	19.7 (24)		74.1 (86.8)	257.1 (241)	29.3	<0.0001

Results are shown in M (SD). ΔParameter - difference between Parameter before and after PLET. * - p < 0.05 in comparison with parameter before PLET in each group of HF functional class.

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

P1440

Rationale: preserved and reduced ejection fraction epidemiological regional study in stockholm (PREFERS)

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Purpose: Heart failure (HF) with preserved (HFpEF) and reduced ejection fraction (HFrEF) are conditions associated with poor prognosis and poor quality of life. While HFrEF shows a decreasing incidence and has effective HF treatment, HFpEF is increasing with no established therapy. PREFERS Stockholm is an epidemiological study performed within the 4D HF project which aligns improved clinical care with better prerequisites for good clinical research. We aim to include patients with incident HF (1000/year) in Stockholm (population of 2 million inhabitants). The goal is to find targets for new drug developments in HFpEF (<https://internwebben.ki.se/en/project-4d-bridging-gap-between-healthcare-and-research>).

Methods: Patients will be characterized at baseline and at a one year follow up by clinical characteristics entered into standardized electronic medical records including standardized protocols for echocardiography and ECG transferred online to a database. Blood samples will be stored in a biobank. One subset of patients will undergo an MRI, another subset of patients undergoing elective coronary bypass surgery (n=200) will be characterized into 3 groups: pEF with a) normal versus b) abnormal diastolic function, or c) rEF. Myocardial biopsies from the right atrial appendage and the right and left ventricles as well as central and peripheral blood will be collected during surgery.

Results: The purpose is to characterize and compare new onset HFpEF and HFrEF patients by using high quality clinical and imaging data, by new blood and cardiac biopsy markers through Science for Life Laboratory platforms of genomics, transcriptomics and proteomics as well as established biomarkers of fibrosis, inflammation, hemodynamics, hemostasis and thrombosis. and All these data will be explored by state of the art bioinformatics methods to investigate gene expression patterns, sequence variation, DNA methylation, posttranslational modifications and systems biology approaches including pathway and network analysis.

Conclusions: In this large scale epidemiologic study of both HFpEF and HFrEF, with an initiating phase of biopsy studies, we hope to identify new biomarkers of disease progression and to find pathophysiological mechanisms to support explorations of new treatment regimens for HFpEF.

P1441

Evaluation of functional class of heart failure using passive legs elevation test in patients with ischemic heart disease

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The number of people suffering from ischemic heart disease (IHD) and heart failure (HF) continues to increase in the world. The levels of NT-proBNP are associated with HF functional class. NT-proBNP is secreted by cardiomyocytes in response to the dilatation of the heart chambers.

The purpose of the study is to develop a method of estimating HF functional class (HF fc) in view of changes of NT-proBNP concentration in response to heart chambers enlargement during the passive legs elevation test (PLET).

We examined 68 patients with IHD (angina 1-4 fc, normosystolic AF) complicated by HF 1-4 fc. Mean age of patients - 70 (14) years. In all patients EchoCG and the venous blood sampling (to determine the values of NT-proBNP) were performed. Then the patient's legs raised at an angle of 45° for 15 minutes. Then EchoCG and blood sampling were repeated. HF fc was determined by using the 6MWT.

Statistical significance was defined at the level of methods for p < 0,05. Results are shown in Table 1. Performing linear multivariate regression analysis found relationships between HF functional class and values of ΔNT-proBNP, ΔEDV and IVST: HF fc = -0.192+0.386*ΔNT-proBNP+0.319*IVST+0.139*ΔEDV; R²=0.45, adj R²=0.42, F=17.5, p < 0.0001.

Thus, the results of the study indicate that executing PLET and assessing of ΔNT-proBNP allows to verify the HF functional class.

P1442

Effect of preload change on transmitral antegrade flow and movement of mitral annulus in hypertensive patients

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Purpose: Modification of preload can unmask altered filling pattern and movement of left ventricle (LV). Transmitral antegrade flow velocity and mitral annulus movement traced by tissue Doppler is measurable in practically every case and do not require very good visibility. Our goal was to prove impact of preload change on observed values and its difference between patients with arterial hypertension and control group.

Methods: 27 patients with treated arterial hypertension and 10 healthy individuals had undergone echocardiographic study and measurements to reveal possible diastolic dysfunction. We focused on inflow pattern and movement of mitral annulus. Measurements were repeated in terms of passive leg rise to simulate increased preload and Valsalva maneuver to simulate decreased preload.

Results: Our study group had on average grade 1 diastolic dysfunction. 9 patients did not meet current criteria for diastolic dysfunction. The highest measured was grade 3 diastolic dysfunction. In resting position there was difference in medial E/E' (p = 0.001). During Valsalva maneuver we showed expected decrease in E/A, but also statistically significant smaller decrease in medial and lateral E' (p = 0.003, p = 0.005) in study group. Consequently, E/E' medial (mean -3.70 vs. -0.40, two-tailed probability p = 0.0007) and E/E' lateral (mean -6.54 vs. -1.63, two-tailed probability p = 0.0005) presented with lower values in hypertensive group.

Passive leg rise caused significant rise in E/A ($p < 0.0001$) in control compared to study group and significantly lower lateral mitral annulus motion in hypertensive group; E/E' lateral (mean 1.36 vs. -1.11, two-tailed probability $p = 0.0009$).

Conclusions: This study showed that movement of mitral annulus is significantly decreased in patients with arterial hypertension. Decreased preload caused by Val-salva maneuver has the greatest impact on mitral annulus motion. Nevertheless, increase of preload in passive leg rise causes decreased mitral annulus motion in hypertensive patients compared to increased motion in healthy individuals. These simple maneuvers can be useful in determination of diastolic function in patients with exertional dyspnoea where standard criteria for diastolic dysfunction are not fulfilled.

P1443

Impairment of preload reserve in experimental heart failure with preserved ejection fraction: can spectral analysis contribute to diagnosis?

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Background: Roughly half of elderly patients diagnosed with heart failure fall into the preserved ejection fraction (HFpEF) category. Though the underlying mechanisms are still controversial, a severe pattern of cardiovascular stiffness involving both the left ventricle and arteries at end-diastole and end-systole, respectively. A joint assessment of both is possible by analysing beat-to-beat changes in stroke volume index (SVI) as a transfer function of end-diastolic pressure (EDP) during ventilation. We applied this concept in a naturally occurring genetic rat model of metabolic syndrome and HFpEF.

Methods: Seventeen-week-old healthy Wistar-Kyoto (Ctrl), hypertensive ZSF1 lean (HT), and ZSF1 obese rats (HF) with metabolic syndrome and HFpEF ($n=6$ each) underwent left ventricular (LV) pressure-volume loop evaluation under halogenate anesthesia and spontaneous breathing. Beat-to-beat EDP, ED volume (EDV) and SVI were linearly interpolated and resampled at 8 Hz, detrended and subdivided into overlapping segments for spectral analysis using fast Fourier transform. Transfer function gain and coherence were calculated between EDV and SVI and EDP and SVI. Overall coherence was good (>0.9). Groups were compared with one-way ANOVA. Data: mean \pm SEM. Two-tailed $P < 0.05$.

Results: Respiratory rate was higher in HF compared with both HT and Ctrl (1.3 ± 0.0 vs 0.7 ± 0.0 and 0.7 ± 0.0 Hz, respectively; $P < 0.001$) as well as fluctuations in EDP with ventilation as assessed by power spectral density (PSD) analysis (56 ± 12 vs 23 ± 12 and 34 ± 5 mmHg², respectively; $P = 0.04$). Conversely, transfer function of EDP into SVI was lower in HF compared with both HT and Ctrl (0.024 ± 0.005 vs 0.035 ± 0.01 and 0.050 ± 0.006 mL.cm⁻².mmHg⁻¹, respectively; $P = 0.017$) whereas no difference was observed for the transfer function of EDV into SVI.

Conclusions: We provide experimental support that preload reserve is impaired in HFpEF by PSD analysis. Increased effort of breathing can contribute to elevated EDP and lung congestion in HFpEF. Results suggest that similar analyses carried out on non-invasive estimates of SVI and EDP may aid the diagnosis of HFpEF.

P1444

Initial management of patients with low BNP elevations could be carried out in primary care without specialist assessment

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Purpose

NICE guidance suggests specialist assessment of patients with symptoms suggestive of heart failure and a BNP > 100 pg/ml, or urgently if > 400 . The value of specialist input in those with BNP at the lower end of this range has been questioned.

Methods: All patients referred to our heart failure diagnostic clinic in 2013 were identified from a prospective database. Those with a BNP 100-399 were included and the clinic assessment and echocardiogram reviewed to identify symptoms, risk factors, whether a heart failure syndrome was or had recently been present, and echocardiographic parameters. The age-gender adjusted normal upper BNP level was obtained for each patient.

Results: 232 patients were referred. 42 were excluded with BNP > 400 and a further 46 had no BNP (previous MI or secondary care referral) or didn't attend. 144 patients had a BNP 100-399 as shown. 40% of these had a BNP 100-149: only 3 with significant LV systolic dysfunction requiring targeted therapy (1 previous diagnosed with DCM abroad and on therapy and 1 with a delay of seven months between BNP and referral). 25 (43%) in this range had a BNP below the 95th centile of the normal age-gender adjusted population. 88% in this group were discharged without diuretic or follow up, usually with advice on blood pressure and/or AF control. AF was common, and in 10% (particularly with BNP < 200) respiratory assessment, usually for OSA symptoms was advised.

Conclusions: In patients with BNP levels just above the current threshold initial strategy of BP control, screening for AF and OSA without specialist assessment would be appropriate with referral for those remaining symptomatic. Raising the referral threshold to 150 would permit rapid primary care management and enable all above to be seen more expediently in specialist services.

BNP level (pg/ml)	N (%)	Heart failure syndrome (%)	Significant LVSD (%)	AF (%)	BP/AF advice & no follow up (%)
100-149	58 (40)	9 (16)	3 (5)	11 (19)	51 (88)
150-199	33 (23)	10 (30)	2 (6)	15 (45)	27 (82)
200-249	16 (11)	8 (50)	1 (6)	10 (63)	10 (63)
250-299	18 (13)	8 (44)	5 (28)	11 (61)	9 (50)
300-349	14 (10)	7 (50)	3 (21)	6 (43)	6 (43)
350-399	5 (3)	5 (100)	3 (60)	3 (60)	1 (20)
TOTAL	144	47 (33)	17 (12)	56 (39)	104 (72)

ATRIAL FIBRILLATION

P1445

Left atrial mechanical dysfunction analysis using strain rate parameters

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Purpose: Global and segmental deformation analysis for the left atrial (LA) function may be obtained by speckle tracking analysis. We aimed to evaluate the role of strain rate (SR) in the recognition of LA mechanical dysfunction in a population after electrical cardioversion (CV) for atrial fibrillation (AF).

Methods: We evaluated 39 patients with AF after CV in the last year. Eleven (28.2%) patients were at sinus rhythm (SR) and 28 (71.8%) had an AF recurrence. A group of 22 patients with no cardiovascular disease were used as control group. The strain rate analysis was made according to the three groups: group 1 - AF after CV ($n=28$, 45.9%); group 2 - SR after CV ($n=11$, 18.0%); group 3 - control patients at SR ($n=22$, 36.1%). LA transthoracic SR from lateral and septal walls were measured with offline analysis.

Results: There was no difference between groups regarding gender prevalence, while group 3 patients were significantly younger (47 years vs. 64-66 years). The mean longitudinal SR for the S wave was significantly lower in group 1 patients than in group 2 and 3 (1.24 ± 0.39 vs. 1.47 ± 0.53 vs. 2.45 ± 0.68 , $p < 0.001$). The mean longitudinal SR for the E wave was also lower in the same groups (-1.03 ± 0.43 vs. -1.57 ± 0.82 vs. -2.01 ± 0.56 , $p < 0.001$).

Conclusions: The reduced atrial mechanical function was more evident in AF patients, while in SR patients that underwent electrical CV for a previous AF episode, the deformation properties are still not comparable to SR control patients.

P1446

Incidence and prognostic significance of atrial fibrillation in chronic heart failure

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Objectives

We aimed to assess the incidence and prognosis of atrial fibrillation (AF) in patients with chronic heart failure (CHF).

Methods: All the consecutive patients with CHF were prospectively analyzed by Holter monitor 24 hours during normal activity. The population was divided into two groups: no-AF and symptomatic AF.

Results: Among the 1613 patients with CHF, 188 (12%) developed symptomatic AF. Compared with the no-AF group, patients with AF were markedly older (76 vs. 62 y, $p < 0.001$), more frequently women (43% vs. 30%, $p = 0.006$) and less likely to be smokers (20% vs. 36%, $p < 0.001$). They had impaired left ventricular ejection fraction (LVEF) and left atrial (LA) enlargement. By multivariate analysis, age, history of AF, indexed LA area and LVEF were identified as independent predictors of symptomatic AF. Hospitalisation and mortality rates were markedly higher in AF group when compared with no-AF patients (41.8% vs 21.0% and 10.4% vs. 1.3%, respectively).

Conclusion: Our study showed that AF is frequent in moroccan population with CHF, its appearance associated with an unfavorable prognosis which requires adequate care with a long-term monitoring.

P1447

Left atrial speckle tracking analysis for assessment of thromboembolic risk in patients with paroxysmal and persistent atrial fibrillation

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Purpose: To evaluate the relationship between left atrial (LA) speckle tracking measurements and thromboembolic (TE) risk in patients (pts) with paroxysmal and persistent AF.

Methods: Sixty pts [mean age 65 (60; 72) yrs, 45% men] with paroxysmal (n=26) and persistent (n=34) AF were included in study comparing echocardiographic measurements in the sinus rhythm period. AF duration was 28 (20; 59) months. Seven (12%) pts had previous stroke, 16 (27%) pts had history of prior MI, 14 (23%) pts had diabetes mellitus. Apical four- and two-chamber views images of 6 myocardial segments in the filling phase were obtained to assess global peak left atrial longitudinal strain (PALS) and strain rate (PALSr) in the reservoir (r) and contractile (c) phase.

Results: Pts with paroxysmal AF had significantly higher PALSr to compare with pts with persistent AF [15,1 (12,2; 16,4) vs 11,2% (8,0; 12,9), $p=0.0002$] and PALSr [-15,0 (-16,2; -12,7) vs -12,0% (-13,0; -9,4), $p=0.0002$]. PALSr significantly differed in paroxysmal and persistent AF groups [2,16 (1,95; 2,34) vs 1,65 s-1(1,35; 1,90), $p=0.0003$] as well as PALSr [-2,02 (-2,25; -1,95) vs -1,56 s-1(-1,85; -1,38), $p=0.0008$]. Higher CHA2DS2-VASc scores were significantly ($p < 0.05$) related with LVMI ($r=0,31$), PALSr ($r=-0,39$), PALSrR ($r=-0,44$) and PALSrC ($r=0,47$).

Conclusions: TE risk was positively correlated to LVMI and PALSrC, and negatively correlated to PALSr and PALSrR in pts with paroxysmal and persistent AF.

P1448

INR variability in the elderly with nonvalvular atrial fibrillation and decompensated heart failure

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Aim: To analyse the influence of decompensated heart failure (DHF) on INR variability (INRV) in the elderly with non valvular atrial fibrillation (NVAF) treated with warfarin. Method. We included 134 patients (pts) 78 +/- 10 years old, 75 (55.97%) women, with chronic heart failure and chronic warfarin treatment for nonvalvular atrial fibrillation, admitted for acute decompensation. We excluded pts with SGOT and/or SGPT elevation more than 2 times the normal values and creatinine clearance less than 35 mL/min/1.75m² at discharge. We noted NYHA class, left ventricular ejection fraction (LVEF), NTproBNP (normal <850 pg/mL in man and < 650 pg/mL in woman) at discharge and we determined INR twice a week for 2 weeks thereafter. Any variations more than 0.5 were considered as INRV. Data were analyzed by Statistica 8.

Results: 87 pts (64.92%) were in NYHA II and 47 (35.07%) in NYHA III, ($p < 0.01$) without differences between women (W) and men (M). Mean LVEF was 43 +/- 8% without significant differences between pts in NYHA II and III ($p = 0.1$). 31 (41.3%) W and 25 (42.37%) M ($p=NS$) had high NTproBNP at discharge, without correlation with NYHA class ($r = 0.3$, $p = 0.1$). 51 pts (38.05%) had INRV, 20 (39.2%) pts having normal NTproBNP and 30 (58.8%) high NTproBNP ($p < 0.01$). 29 (56.8%) pts with INRV were in NYHA III and 22 (43.1%) pts in NYHA II ($p < 0.01$). There was no correlation between INRV and LVEF. Multivariate analysis showed a significant correlation of INRV only with high NTproBNP.

Conclusions: There is a significant correlation between ambulatory INRV and high NTproBNP level at the moment of discharge after DHF in elderly pts treated with warfarin for NVAF.

P1449

Very elderly patients with atrial fibrillation: multimorbidity and high mortality

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Purpose: Atrial fibrillation is the most common arrhythmia encountered in clinical practice. It is associated with increased morbidity and mortality, due to the risk of thromboembolic events and associated risk factors. The purpose of the study was to analyze the clinical characteristics of very elderly patients (> 80 yo) with permanent atrial fibrillation admitted in the Internal Medicine Clinic of a University Emergency Hospital over a period of one year.

Methods: The total number of admissions in 2013 was 3470. From these, 273 patients were over 80 years old (7.86%); 195 had permanent atrial fibrillation and represented our study group. We analyzed data from the hospital record database.

Results: The distribution by sex in the study group: 81 men (41.53%) and 114 women (58.46%). The mean age was 84.5 yo. 42.56% of the patients were institutionalized in nursing homes. The main comorbidities were: arterial hypertension 78.46%, coronary artery disease 61.02%, heart failure 47.17%, chronic obstructive pulmonary disease 44.61%, peripheral artery disease 42.05%, cerebrovascular disease 40.51%, valvular heart disease 39.48%, diabetes 31.79%, dementia 14.35%, chronic kidney disease (eGFR <60 mL/min/1.73 m²) (MDRD) 9.74%. As compared to non-institutionalized patients, those residing in nursing homes

were older and had higher comorbidity score. 173 patients (88.71%) received anticoagulants: 129 patients (74.56%) received cumarinic oral anticoagulants and 44 patients (25.43%) new anticoagulants (dabigatran). The mean CHA2DS2-VASc score was 5.2. In-hospital mortality rate in very elderly patients with atrial fibrillation was 10.76%. Rates of mortality, heart failure, coronary artery disease and stroke increased with older age and higher CHA2DS2-VASc scores.

Conclusions: Atrial fibrillation is a frequent arrhythmia in very elderly patients. Very elderly patients with atrial fibrillation have many comorbidities, arterial hypertension, coronary artery disease, heart failure and chronic obstructive pulmonary disease being the most frequent. In-hospital mortality rate of very elderly patients with atrial fibrillation is high. Adequate control of arterial hypertension and management of heart failure in patients with atrial fibrillation, alongside with stroke prevention are key priorities for the management of very elderly patients with atrial fibrillation and improving quality of their life.

P1450

Atrial fibrillation in patients with chronic systolic heart failure due to chagas disease: clinical characteristics, prognostic determinants, and survival

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Atrial fibrillation (AF) is frequently found in patients with chronic Chagas disease (CD). The clinical characteristics of AF as well as its impact on patients with chronic systolic heart failure (CHF) due to CD is not known. The present study was undertaken in an attempt to fill this gap.

A total of 246 patients with a positive serologic test for CD with left ventricular systolic dysfunction on echocardiography followed at our ambulatory from January, 2000 to January, 2010 were included. Sixty-nine (28%) patients had AF on the 12-lead ECG. Mean age was 61 ± 12 years in patients with AF and 52 ± 14 years in those without AF ($p < 0.005$). Permanent pacemaker was worn by 43 (62%) patients with AF and by 81 (46%) patients without AF ($p=0.02$). Digoxin was prescribed to 56 (81%) patients with AF and to 120 (68%) patients without AF ($p=0.04$); spironolactone was used by 53 (77%) patients with AF and by 112 (63%) patients with no AF ($p=0.04$). Right ventricular dimension was 27 ± 8.1 mm in patients with AF and 24.3 ± 7 mm in those without AF. The other clinical characteristics were similar in patients with AF and in those with no AF. On multivariate analysis, age (hazard ratio=1.03, 95% CI 1.01 to 1.05, $p < 0.005$), right ventricular dimension on echocardiography (hazard ratio=1.04, 95% CI 1.01 to 1.08, $p=0.002$), and spironolactone use (hazard ratio=2.26; 95% CI 1.24 to 4.12, $p=0.008$) were independent predictors of atrial fibrillation. Survival probability for patients with AF was lower than that of patients with no AF as seen on Kaplan-Meier curve (Figure 1).

In patients with CHF secondary to CD, those with AF have a distinctive clinical profile in comparison to patients with no AF. AF portends a poor prognosis in patients with CHD due to CD.

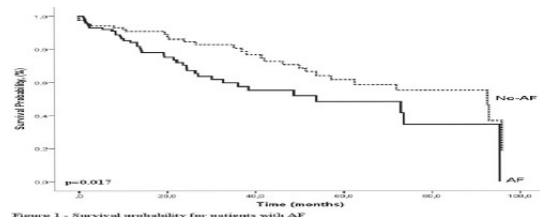


Figure 1

P1451

Heart failure in patients with acute myocardial infarction and new onset atrial fibrillation

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Purpose: New-onset atrial fibrillation (AF) is common complication of acute myocardial infarction (AMI), with an incidence between 6-21% and usually the new-onset AF during the hospital course is associated with an increase in mortality and adverse events in post-myocardial patients. The aim of the study was to evaluate the incidence of heart failure in patients with AMI and new onset AF during the 4-year follow-up.

Methods: We included 600 patients with AMI in the study. At entry, all patients were in sinus rhythm and patients with congenital cardiac disease, organic mitral regurgitation, healed endocarditis and any other disease limiting survival were excluded.

The AF group included patients with AMI and new onset AF and control group included patients with AMI without AF during the hospital course. The patients were followed up for four years with visits every 6 months and with assessment of clinical signs of heart failure.

Results: We observed 600 patients, 290 STEMI and 310 NSTEMI. Mean age of patients was 63.6 ± 10.6 years, between them 425 were men and 275 women, mean BMI was 26.8 ± 2.6 kg/m². During hospital course of AMI 48 patients had new onset AF-AF group and in control group were 552 patients. The patients in AF group were older (69.9 ± 9.4 years in AF group versus 63.1 ± 11.4 in control group) and with higher BMI (28.0 ± 2.6 kg/m² in AF group versus 26.7 ± 2.6 kg/m² in control group), p < 0.01. Physical examination found that in AF group 72.9% of patients had Killip I class, 18.8% of them Killip II class, 6.3% of patients had Killip III class and 2.1% had Killip IV versus 88.0%, 10.0%, 1.3% and 0.7% in control group during the hospital course, p < 0.01. LVEF was lower in AF group 0.417 ± 0.046 versus 0.439 ± 0.049 in control group, and a left atrial diameter was bigger (43.6 ± 3.9 vs 40.4 ± 3.63 mm), p < 0.01. The incidence of heart failure was 42% for four years of follow up, 45.8% in AF group and 41.7% in control group, p > 0.05.

Conclusions: The incidence of heart failure during hospital course was significantly higher in AMI patients with new onset AF, but there was no significant difference in the incidence of heart failure during follow up for four years between the AF group and control group.

P1452

ABC-, VEN- and frequency analysis of treatment of atrial fibrillation in out-patients in a city Russian Federation

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Purpose: carrying out ABC-,VEN- and frequency analysis of treatment of atrial fibrillation (AF) in out-patients of a city of Russia

Materials and Methods: the analysis information about 97 out-patients with the diagnosis of AF addressing at least 1 time to the physician from 1.01.2013 for 31.12.2013 was carried out. Average age of patients is 74,7 ± 8,8 years. There are 66 (68%) women and 31 (32%) men. The part of patients with permanent AF made 55,6%, with changeable forms - 44,4%.

Results: In total for treatment of patients with various forms of AF 114 names of drugs were used. The general expenses for 2013 for the medicines made 1 102 030,6 rubles in 2013 (among 34 438,45 \$). The group A (80% of costs of medicines) included 24,56% of preparations (28 names). The group B (15% of expenses) included 18,42% (21 names). The group C (5% of expenses) included 57,02% of drugs (65 names). After carrying out of VEN-analysis there are 48 names of medicines, expenses made 78,17% of the general expenses. The group E included 23 names and expenses in group B made 16,81%. Costs of drugs in group N - 4,87% (43 names).

Conclusions: After carrying out ABC/VEN-analysis it is revealed that the greatest number of money is spent for a small amount of names of expensive preparations, and the smallest quantity of finance is spent for more often used preparations. More than 70% of money is spent for vital drugs (V), group's N (Non-essential) share of the expenses is about 10% of general expenses, it corresponds to the recommended indicators.

P1453

Influence of heart failure in atrial fibrillation progression

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Background: Heart failure (HF) and previous stroke or TIA (2 points), chronic obstructive pulmonary disease (COPD), age >75, and hypertension (1 points) are well known predictors for AF progression in patients (pts) with paroxysmal atrial fibrillation (AF) within 1 year (HATCH score).

Purpose: The purpose of this study was to evaluate the accuracy of the HATCH score to predict progression and to assess influence of HF functional class (FC) in paroxysmal AF.

Methods: We retrospectively studied 137 pts (mean age 55 ± 13 years; 68% men) with paroxysmal AF (>2 onset per 3 months) after cardioversion. Previous stroke identified in 4% pts, HF (I-III classes by NYHA) in 31%, hypertension in 69%, COPD in 21%. Amiodarone or propafenone prescribed in 82% pts in addition to upstream therapy. Progression of AF was defined, if paroxysmal AF at baseline becoming permanent AF. The primary end point was rhythm status at 1 year follow-up (mean 24 ± 15 months). We used correlation analysis, logistic regression and receiver operating characteristic (ROC) curve and calculated the area under the curve to estimate the HATCH score's accuracy of predicting AF progression. All statistics were calculated by SPSS version 22.

Results: During the 1 year only 12 (8,8%) pts had progression to permanent AF (progression group). The total mean HATCH score was 1.67 ± 1.5. In AF progression group the mean HATCH score at baseline was significantly higher than without

AF progression (3.75 ± 1.6 vs 1.47 ± 1.4, P < 0.0001). According to HATCH score only 8 (6%) pts had >5 points. Of these, 50% of pts progressed versus 6%, who were in low or moderate risk (p < 0.0001). Correlation analysis revealed that previous stroke (0.276, p < 0.0001), HF (0.387, p < 0.0001) and Age > 60 (0.182, p < 0.01) were highly associated with AF progression. The HATCH score's ROC area under the curve was 0.820 (95% CI, 0.701-0.939, p < 0.0001). According to logistic regression analysis, only 2 predictors was associated with a risk of AF progression: HF (OR: 8.33 95% CI: 1.4-49.3, P = 0.02) and history of stroke (OR: 3.2, 95% CI: 1.1-9.7, P = 0.033). Among pts with HF 33% pts with II, III FC had progression versus 7.6% pts with 0-I FC, p > 0.15.

Conclusions: Patients with baseline HATCH score >5 points had 8.3 times higher incidence of AF progression than those who had <5 points. Only HF and history of stroke or TIA were independent risk factors associated with AF progression according to logistic regression analysis. Among pts with HF, no significant difference was found between FC by NYHA and the percentage of pts who experienced AF progression.

P1454

Novel oral anticoagulants: patient satisfaction, common and severe side-effects in a district general hospital

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AIM

Dabigatran and Rivaroxaban, two novel oral anticoagulants (NOACs), have recently been approved for use in a small district general hospital. We constructed a quality improvement study to ascertain patient satisfaction and to identify common or life-threatening side-effects experienced in our elderly population.

Methods: Patients on NOACs for non-valvular atrial fibrillation were obtained using the pharmacy dispensary list. A satisfaction questionnaire was designed and posted to each patient with a pre-paid return envelope. The patient list was cross-referenced with blood-bank records to identify any patients who had required blood products since NOAC approval. Hospital coding services were also consulted to identify any patient's admitted with acute bleeds.

Results: 135 patients identified
Questionnaire response rate of 75% (n=101)

Mean age = 71.87

63% female.

Mean eGFR = 69.38

Mean CHADS2 Score = 2.81

26% reported general side-effects including GI upset and skin rash. 22% had minor bleeding or bruising. Of these, 59% did not seek medical attention. 85% were satisfied or very satisfied. 9% stopped taking the medication due to side-effects.

4 patients were admitted with acute bleeding. 3 presented with rectal bleeding/melaena whilst 1 presented with gum bleeding. 2 had an abnormal clotting profile. Only 1 required blood products which were for an upper GI bleed in an intensive care setting.

Conclusions: In an elderly population in west Wales, patient satisfaction and tolerance to NOACs was high. Only 1% had severe bleeding requiring blood products. These finding supports the use of NOACs in our elderly population with good tolerability for the majority.

Parameters	RELY Trial (Dabigatran)	Rocket AF (Rivaroxaban)	Our Study
Percentage of Discontinuation At one year	110 mg- 14.5% 150mg- 15.5 %	23.7% over study period	9 %
Mean CHADS2 score	2.1	3.5	2.81
Mean Age	71	Median-73	71.87
Major Bleed	110mg-2.71% 150mg-3.11 %	3.6%	3/101

P1455

Association with acute ischemia and predictors of new-onset atrial fibrillation in st-segment elevation myocardial infarction

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Introduction/goal

New-onset atrial fibrillation (NOAF) is a relatively common complication of acute myocardial infarction, associated with more adverse events and higher mortality. Proposed mechanisms are complex and still misunderstood and include atrial and ventricular ischemia with consequent neuro-humoral abnormalities and hemodynamic changes. The aims of this study were to evaluate the relationship between

acute ischemia and NOAF and to identify predictors of NOAF in ST-segment elevation myocardial infarction (STEMI) patients (pts).

Methods: We retrospectively analysed the registries of pts with STEMI included in the Portuguese National Registry of Acute Coronary Syndromes, between October of 2010 and October 2014. NOAF was defined as paroxysmal or persistent atrial fibrillation unknown prior to admission. Demographic data, cardiovascular risk factors and previous history, admission data, coronary angiography results, treatment and complications during hospitalization were analysed and multivariate analysis was performed in order to identify predictors of NOAF.

Results: A total of 4566 STEMI pts were considered, 306 (6.7%) with NOAF. These pts were significantly older, more frequently hypertensive and diabetic and had a higher prevalence of previous heart failure (HF), valvular heart disease, stroke, peripheral artery disease, renal failure, chronic obstructive lung disease and dementia. They presented more frequently with HF at admission (27.8% of NOAF pts had a Killip class >1 vs 13.8% of pts without NOAF; $p < 0.001$). There were no differences between the two groups regarding total ischemic time (TIT), culprit lesion, number of diseased vessels and percentage of reperfused pts. Stroke (2.0% vs 0.8%; $p = 0.043$), need for blood transfusion (5.2% vs 1.9%; $p < 0.001$) and in-hospital mortality (15.7% vs 5.3%; $p < 0.001$) were higher among NOAF pts. In multivariate analysis older age (OR 1.03, CI95% 1.02-1.05; $p < 0.001$), dementia (OR 2.54, CI95% 1.16-5.56; $p = 0.020$) and Killip class>1 at admission (OR 1.82, CI95% 1.23-2.69, $p = 0.003$) were independently related to the risk of developing NOAF.

Discussion/Conclusions: In this analysis of STEMI pts no clear association between NOAF and acute ischemia was found as the two groups were similar regarding TIT, culprit lesion, number of diseased vessels and percentage of acute reperfusion. NOAF was associated with in-hospital stroke and mortality. Older age, dementia and HF at admission were independent predictors of NOAF.

CARDIOMYOPATHY

P1456

Impact of female gender in the development of heart failure in patients with hypertrophic cardiomyopathy - a portuguese multicenter study

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Introduction: Hypertrophic cardiomyopathy (HCM) may lead to the development of heart failure. Little is known about gender differences in HCM.

Aim: To identify gender differences in patients with HCM and to determine if female gender has impact on the development of heart failure in patients with HCM.

Methods: Portuguese multicenter study involving 9 hospital centers and including all patients diagnosed with HCM. We evaluated demographic, clinical, genetic, electrocardiographic, echocardiographic and cardiac magnetic resonance data. We evaluated the gender differences in patients with HCM and then conducted a multivariate analysis to determine if female gender is an independent predictor of heart failure in patients with HCM.

Results: We included 356 patients with HCM, 42.1% females. Heart failure was present in 45% of patients.

In patients with HCM, females were older (67 ± 12 vs 59 ± 15 years, $p < 0.001$), presented more heart failure (59.9% vs 35.1%, $p < 0.001$), angina (22.4% vs 13.9%, $p = 0.037$), history of stroke (7.5% vs 2.5%, $p = 0.027$), diabetes mellitus (19.7% vs 11.9%, $p = 0.044$) and hypertension (55.1% vs 43.6%, $p = 0.033$). No gender differences were found regarding other demographic, clinical, genetic, electrocardiographic, echocardiographic and cardiac magnetic resonance data.

In the multivariate analysis, female gender was an independent predictor of heart failure in HCM ($p = 0.015$).

Conclusion: In this Portuguese population of HCM, female patients were older and more symptomatic and had more history of stroke, diabetes mellitus and hypertension. Female gender was an independent predictor of heart failure in patients with HCM.

P1457

Abnormal q waves and sudden cardiac death in hypertrophic cardiomyopathy: experience of a tunisian center

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Background: Electrocardiographic (ECG) abnormalities are common in hypertrophic cardiomyopathy (HCM) and have been associated with the distribution of

left ventricular hypertrophy and myocardial fibrosis. Such abnormalities may predispose patients to electrophysiologic instability, ventricular arrhythmias, and sudden cardiac death (SCD).

Objective: The aim of the present study was the evaluation of the presence of Q waves as a new potential risk factor for SCD in HCM.

Methods: We hereby report a retrospective study about 48 patients with HCM followed between 1997 and 2013. Primary endpoint was life-threatening ventricular arrhythmias including SCD, resuscitated SCD and appropriate implantable cardioverter defibrillator therapy. The mean follow-up period was 5 years.

Results: The 48 patients were predominately young at diagnosis with a mean age of 37 ± 16 years and most of them were male (65%). At the 12 lead ECG evaluation, 50% of patients had abnormal Q waves that were located predominantly in the inferior and lateral leads. During the follow-up period, 12 patients (25%) had life-threatening ventricular arrhythmias. The annual rate of life-threatening ventricular arrhythmias was 5%. In our study, the overall probability of SCD was significantly greater among patients with abnormal Q waves than among those without ($p = 0.046$). However, a multivariate analysis based on the Cox regression didn't identify the presence of abnormal Q waves as a predictive factor of life-threatening ventricular arrhythmias in our cohort study ($p = 0.152$).

Conclusions: In our cohort study, the presence of abnormal Q waves was associated with a potential risk of life-threatening ventricular arrhythmias and may be useful in risk stratification for SCD.

P1458

Comparison of current guidelines for primary prevention of sudden cardiac death in hypertrophic cardiomyopathy - is clinical practice consistent?

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Purpose: Sudden cardiac death (SCD) is a common mode of death in hypertrophic cardiomyopathy (HCM), but identification of patients who are at a high risk of SCD is challenging as shown by the variety of proposed risk stratification guidelines. The aim of this study was to compare eligibility for implantable cardioverter defibrillator (ICD) implantation in the primary prevention of SCD based on presently used guidelines.

Methods: The study included 187 pts, mean age 59.2 ± 14.5 yo, 45% males, diagnosed with HCM. Indications for ICD implantation in primary SCD prevention were identified based on present guidelines: 2014 ESC guideline on management of HCM (ESC2014), 2011 ACC/AHA guidelines on management of HCM (ACC2011), 2006 ESC guidelines for prevention of sudden death (ESC2006).

Results: Ninety-five pts (50.8%) had obstructive HCM with high rest LVOT gradient, 36 (19.2%) had latent obstruction, while 28 (14.9%) presented with apical forms. Average HCM Risk-SCD Score (based on ESC2014) of the group was $2.65 \pm 2.40\%$ (limits 0.67-18.44%). Twelve pts (6.4%) had a high calculated 5-year risk of SCD >6%. We found significant differences between the 3 guidelines in use, with the largest number of ICD indications from American guidelines ($p < 0.001$ for differences between all groups). This difference was mainly driven by an ACC2011 indication of class Ia in patients with ESC2014 HCM Risk-SCD Score <4% due to unexplained syncope (8 pts), SCD family history (5 pts) and LV wall thickness >30mm (3 pts).

Conclusions: There are significant inconsistencies among guidelines in use for the ICD implantation indication for primary SCD prevention in HCM. ACC/AHA guidelines appear to have the highest yield of implantations, hence economic burden. Formal prospective validation with comparison of current indications is necessary both for establishing optimal treatment and minimizing costs.

	ESC2014 Ind Ia	ESC2014 Ind Ib	ESC2014 Ind III
ACC2011 Ind Ia	11	8	8
ACC2011 Ind Ib	1	4	6
ACC2011 Ind III	0	3	146
ESC2006 Ind Ia	7	0	0
ESC2006 Ind Ib	5	12	14
ESC2006 Ind III	0	3	146

P1459

Detection of myocardial fibrosis in patients with hypertrophic cardiomyopathy evaluated by biological markers

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Introduction and Aim: Hypertrophic cardiomyopathy (HCM) is autosomal dominant disease characterized by variable penetrance. This condition is based on cell disorganization with a matrix remodeling leading to fibrosis more to less extensive. This fibrosis is associated with an increased risk of rhythm disorder and left ventricular dysfunction as shown by magnetic resonance studies.

Predictors of sudden death or prognostic factors are being reassessed and still looking for new ones.

Aim: The purpose of our study was to investigate biological markers which are the amino terminal pro peptide of type III collagen (PIIINP), a synthetic indicator which may reflect the rate of myocardial fibrosis, a metalloproteinase (MMP3) involved in the regulation of degradation and accumulation of collagen and its specific tissue inhibitor TIMP2. We aim to determine serum concentration of the PIIINP, MMP3 and TIMP2 in patients with Hypertrophic cardiomyopathy.

Methods: we recruited 107 patients and 175 controls who received a clinical study, ultrasound and rhythm assessment. the concentrations of the PIIINP, MMP3 and TIMP2 was assayed at a peripheral vein in patients with Hypertrophic cardiomyopathy and in the control group.

We studied the association of serum levels of these markers to clinical, echocardiographic, electric and biological parameters.

Results In the study population, the mean age was 49 years, 60 were male, 75% were symptomatic (palpitations in 38% of cases, chest pain in 28% of cases, syncope or faintness dans 25% of cases) the rate of PIIINP was significantly higher in patients compared with controls (261,92s vs 242,80ng / ml; $p=0.036$). It was the same for MMP3 and TIMP2 (12.16 vs 10.4 and 63.4 vs 57, respectively, $p=0.03$).

We note that the MMP3 / TIMP2 report is correlated to left ventricular (LV) mass and the surface of the left atrium, the PIIINP is correlates to the maximum thickness of VG, VG Strain and LV mass.

Patients with a history of syncope and episodes of non-sustained ventricular tachycardia, had a younger age, a significantly higher rate of PIIINP and more impaired LV function (EF and global LV Strain).

Conclusion: Hypertrophic cardiomyopathy is characterized by ventricular and atrial remodeling, collagen accumulation may be reflected in the determination of serum MMP3 / TIMP2 report and PIIINP concentration. These parameters correlated with LV function may represent potential risk factors for the ventricular dysrhythmia and LV dysfunction.

P1460

New guidelines for hypertrophic cardiomyopathy: the impact on prophylactic cardioverter-defibrillator implantation

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Introduction: Sudden cardiac death (SCD) continues to be the most devastating complication of hypertrophic cardiomyopathy (HCM). The new guidelines of the European Society of Cardiology (ESC) define the current standard for estimation of SCD risk as an integral part of clinical management. The aim of this study was to compare the 2014 and 2011 implantable cardioverter-defibrillator (ICD) recommendations in HCM patients (pts).

Methods: We studied 80 HCM ambulatory pts, in our hospital. The recommendation for ICD was assessed using previous (ACCF/AHA Guideline for the Diagnosis and Treatment of Hypertrophic Cardiomyopathy -2011) and current guidelines (ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy -2014). All statistics analyses were performed using SPSS 20.0 version.

Results: The mean age of our population was 50 ± 18 years and 65% were male. The majority of pts were in NYHA class I (71%) or II (27%) and had septal HCM (65%). Mean left atrial size was 43 ± 7 mm and maximum left ventricular wall thickness 19 ± 6 mm; 22% had family history of SCD and 22% non-sustained ventricular tachycardia. By 2011 guidelines, 51% of pts had a classe IIa recommendation for ICD and 49% had no ICD indication (class III). In comparison, by 2014 guidelines, we found much more pts without ICD indication (82%; $p < 0.001$), fewer pts with a class IIa recommendation for ICD (8%; $p < 0.001$) and 10% of pts had a class IIb indication.

Conclusion: In our population, we found several differences in regarding recommendation for prophylactic ICD between previous and current guidelines. Overall there were fewer pts with ICD indication than before.

P1461

Prognostic value of left ventricular two-dimensional strain analysis in patients with hypertrophic cardiomyopathy: a 2- years follow-up study

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Introduction and Aims: Hypertrophic cardiomyopathy (HCM) is the first cause of sudden cardiac death in young people and it's frequency is probably more than 1/500. Stratifying this risk is a major issue in the management of HCM. Existing

risk factors have low positive predictive value and new parameters are needed. Determination of myocardial deformation (strain) by 2D Speckle tracking is a new methodology for determining LV regional function and could correlate with myocyte disarray and fibrosis. The aim of this study was to assess the relationship between strain analysis and the occurrence of a major adverse cardiac event (MACE) in HCM subjects.

Methods: 105 patients with HCM were studied and compared to 30 age-matched controls. All underwent standard echocardiographic and two-dimensional strain examination with the evaluation of left ventricle (LV) longitudinal strain (GLS), radial strain (RS) and circumferential strain (CS) Echocardiographic parameters were correlated with MACE defined as congestive heart failure, atrial fibrillation, syncope, non sustained ventricular tachycardia, during a mean follow-up period of 22 ± 6 months.

Results: The mean age was 49. Despite apparently normal left ventricular function, all components of strain were significantly reduced in HCM. Average longitudinal, circumferential, and radial strain in patients with HCM and controls were ($-13.81 \pm 6.19\%$ Vs $-21.85 \pm 1.46\%$ for GLS), ($-12.83 \pm 7.55\%$ Vs $-19.6 \pm 5.2\%$ for CS) and ($22.33 \pm 9.63\%$ Vs $36.8 \pm 17.2\%$ for RS). During the follow up, 26 patients (24.7%) had cardiac events. All myocardial deformation values were significantly lower in HCM subjects with MACE than in those without MACE ($-11.97 \pm 7.92\%$ Vs $-14.5 \pm 5.41\%$ for GLS) ($18.51 \pm 9.03\%$ Vs $24.64 \pm 9.48\%$ for RS) and ($-10.63 \pm 6.73\%$ Vs $-14.10 \pm 7.82\%$ for CS). By Kaplan-Meier analysis, MACE were more frequent in HCM subjects with GLS values $\geq -15\%$ ($P=0.06$). MACE were also more frequent in HCM subjects with RS values $< 20\%$ ($p=0,01$) and with CS $\geq -19\%$ ($p=0,01$) during the observation period.

Conclusion: Two-dimensional strain is a new simple, rapid, and reproducible method to measure different components of systolic strain in HCM patients with normal chamber function. It might provide useful information on myocardial fibrosis and cardiac events and consequently can indicate a poor prognostic.

P1462

Functional capacity in familial dilated cardiomyopathy by cardiopulmonary exercise testing and its relationships with echocardiographic parameters

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Purpose: Ejection fraction (EF) and New York Heart Association functional class (NYHA) are largely used parameters in the prognostication of heart failure. However, they frequently misrepresent the actual functional status of patients with dilated cardiomyopathy. The aim of this study was to explore the association of diastolic and systolic functional echocardiographic parameters with functional capacity as assessed by both cardiopulmonary exercise testing and NYHA class, in patients with mild or moderately reduced EF (35-50%).

Methods: Patients with familial dilated cardiomyopathy (EF 35-50%) were prospectively enrolled ($n=11$; age 47 ± 17 years; female 55%). They all underwent transthoracic echocardiography and cardiopulmonary exercise testing the same day of the outpatient clinic evaluation. The echocardiographic study included diastolic (E/A ratio, indexed left atrial volume, systolic to diastolic pulmonary waves ratio, atrial pulmonary wave duration and E/e' ratio) and systolic (EF) functional parameters; functional capacity was assessed by cardiopulmonary exercise testing (peak oxygen uptake per kilogram [VO₂], oxygen uptake efficiency slope [OUES], and peak oxygen uptake to heart rate ratio [VO₂/HR]) and clinical interview (NYHA class). Non-parametric tests were used for statistical analysis.

Results: Ten patients were asymptomatic or mildly symptomatic (NYHA class I=7 and II=3, respectively) at the time of evaluation. Only one patient was significantly symptomatic (NYHA class III; age 70). Among diastolic parameters, E/e' showed correlation with VO₂, and OUES ($\rho = -0.86$, $p = 0.003$, and $\rho = -0.63$, $p = 0.05$, respectively), and indexed atrial volume was correlated with VO₂ ($\rho = -0.83$, $p = 0.003$). Regarding systolic function, EF showed correlation with VO₂, OUES, and VO₂/HR ($\rho = -0.72$, $p = 0.02$; $\rho = -0.71$, $p = 0.02$; and $\rho = -0.78$, $p = 0.02$, respectively). On the other hand, the only echocardiographic parameter close to a significant association with NYHA class was EF ($p = 0.05$). None of the cardiopulmonary exercise testing-derived parameters was associated with NYHA class.

Conclusions: In relatively young patients with familial dilated cardiomyopathy and mild or moderately reduced EF, echocardiographic parameters such as E/e' ratio, indexed left atrial volume and EF may together reflex their actual functional capacity as assessed by VO₂. Our findings support a comprehensive echocardiographic evaluation, versus NYHA class gradation, in the prognostication of heart failure.

P1463

Left ventricular reverse remodelling and fibrosis in nonischaemic dilated cardiomyopathy

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Purpose: In nonischemic dilated cardiomyopathy (NICM), myocardial fibrosis at cardiovascular magnetic resonance (CMR) is associated with worse prognosis. We investigated whether myocardial fibrosis progresses during follow-up and whether its absence is associated with left ventricular reverse remodelling (LV-RR).

Methods: One-hundred-and-twenty-five NICM patients (age 51 ± 16 years, 82 male) were enrolled and underwent baseline CMR; patients with ischemic, valvular, congenital heart disease, other cardiomyopathies or contraindications to CMR were excluded from study entry. After a 24-month follow-up on optimal medical therapy, all patients underwent a second CMR; patients who died, underwent device implantation or declined a second CMR, were also excluded from the study. Late gadolinium enhancement (LGE), an index of myocardial fibrosis, was quantified on post-contrast CMR images. Left ventricular (LV) reverse remodelling (RR) was defined as an increase in LV ejection fraction ≥10 U or decrease in LV end-diastolic volume ≥10% at follow-up.

Results: Mean LV ejection fraction was 41 ± 11% at baseline, 47 ± 12% at follow-up. LGE was present in 48 (38%) patients at baseline (mean extent 5 ± 6% of LV mass), in 76 (61%) patients at follow-up (mean extent 7 ± 7%, $p < 0.01$ vs. baseline). LV-RR was observed in 59 patients (47%), with no age or gender difference ($p = NS$). Patients experiencing LV-RR during follow-up presented a baseline worse LV ejection fraction (36 ± 12%) than no-LV-RR patients (45 ± 9%, $p < 0.01$), greater LV volumes (123 ± 38 vs. 110 ± 22 ml/m², $p = 0.02$) and worse right ventricular ejection fraction (54 ± 12% vs. 59 ± 10%, $p = 0.02$). Nevertheless, only 17 (29%) LV-RR patients presented LGE compared to 31 (47%, $p = 0.04$) no-LV-RR patients. Moreover, among LGE-positive patients ($n = 48$), only 17 (35%) developed LV-RR, while among LGE-negative patients ($n = 77$), 42 (55%) developed LV-RR ($p = 0.04$). Multivariate regression analysis showed that the absence of LGE at baseline CMR was a strong predictor of LV-RR ($p = 0.02$), even after correction for age, New York Heart Association class, LV volumes and systolic function.

Conclusions: In patients with idiopathic dilated cardiomyopathy, LGE tended to increase during follow-up; the absence of LGE at baseline was a strong independent predictor of LV-RR at 2-year follow-up, irrespective of the initial clinical status and the severity of ventricular dilatation and dysfunction.

P1464

The use of next generation sequencing to determine genotype-phenotype correlations in dilated cardiomyopathy

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Background: Dilated cardiomyopathy (DCM) is the leading cause of non-ischaemic heart failure and causes 10,000 deaths/year in Europe. Studies suggest that 50% of patients with DCM have a genetic predisposition and that mutations within genes coding for structural and functional cardiac proteins accounts for up to 40% of familial disease. The relevance of genotype to clinical phenotype, treatment and prognosis is poorly understood. This study aimed to characterise probands with familial DCM using next-generation sequencing (NGS) to determine genotype-phenotype correlations in DCM.

Methods: 72 probands with DCM were recruited. All received genetic counselling and provided written consent. Patients were clinically characterised using a standard phenotyping protocol. Genomic data was collected and screened for all major genes involved in cardiomyopathies and selected candidate genes using NGS. Eighty-six genes with 1528 exons representing 500kb of coding sequence, were studied using target enrichment methods (Agilent SureSelect System) followed by sequencing on the Illumina HiSeq 2000 platform. Clinical parameters were correlated with genotype findings.

Results: Variant calling from 72 probands (male 54%, mean age 41 years (range 14 to 68 years) generated 1415 exonic and splice-site calls. After filtering, 420 distinct candidate variants were reported, 253 of which are published pathogenic mutations, 112 of which are frameshift insertion/deletion or splice-site variants predicted to cause loss of function (thus likely to be pathogenic). A further 55 novel variants were considered potentially pathogenic on the basis of preliminary in silico analysis. Each proband, on average, carried 3 published pathogenic variants which included known mutations associated with DCM and other forms of cardiomyopathy. Up to two further variants predicted to be pathogenic were identified per DCM proband illustrating genetic heterogeneity. However, there was no simple correlation between a specific mutation or number of mutations and phenotype. Furthermore, there was no evidence of a 'poly-hit' theory of multiple mutations contributing to a worsened phenotype nor of specific variant demonstrating causality of phenotype.

Conclusions: This study demonstrates the utilisation of next generation sequencing in clinical practice. It highlights the genetic heterogeneity and high frequency of novel variants with uncertain effects on gene function in DCM which presents considerable challenges for clinical interpretation. Large-scale phenotyping is therefore required to fully understand genotype-phenotype relations in DCM.

P1465

Long-term characterization and prognosis of dilated cardiomyopathy in children compared to adult population: the trieste heart muscle disease registry experience

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Purpose: Dilated cardiomyopathy (DCM) in childhood has a high incidence of major cardiovascular events. In this study we compared outcome of pediatric and adult DCM populations.

Methods: Between 1988 and 2014, 927 DCM patients were consecutively enrolled in the Heart Muscle Disease Registry. We performed baseline evaluation and regular evaluations for a median follow-up of 110 months (IQR: 54 - 185). We excluded secondary forms of DCM.

Results: Pediatric population (≤18 years old at enrollment) counted 47 patients (5%). Family history of cardiomyopathy was significantly higher among pediatric population (34.8% vs 17.5%; $p = 0.03$). At presentation pediatric patients had a significantly lower systolic arterial blood pressure (116 ± 20 vs 125 ± 17 mmHg; $p = 0.01$) and a lower presence of left bundle branch block (4.4% vs 31.9%; $p < 0.0001$). Left ventricular ejection fraction (LVEF) was significantly higher compared to older patients (36 ± 13 vs 32 ± 11; $p = 0.03$). There were not significant differences about the use of evidence-based pharmacological and non-pharmacological treatments. Because of the huge size difference between the two groups and the presence of the above cited baseline differences, we compared the survival of pediatric patients with a sample of older patients, randomly matched on the basis of several baseline variables (presence of LBBB, family history of DCM, heart failure duration, blood pressure and LVEF) in a 3:1 ratio. Survival free from death/heart transplantation at Cox regression for matched data was significantly lower among pediatric patients ($p < 0.001$). Similar results were obtained for sudden death/major ventricular arrhythmias and pump failure death/heart transplantation ($p = 0.001$). Long-term longitudinal trends of main echocardiographic parameters (indexed end diastolic diameter, indexed end diastolic volume, LVEF, restrictive filling pattern) was similar in the two subgroups. Finally at multivariable Cox analysis in the pediatric population, baseline lower LVEF and NYHA III-IV emerged as independent negative prognostic features, while beta blockers were protective.

Conclusions: Pediatric DCM population has worse prognosis compared to older patients also after adjustment for other significant covariates and despite higher baseline LVEF and a similar clinical-echocardiographic long-term evolution.

P1466

Long term follow up of patients with idiopathic dilated cardiomyopathy treated with intracoronary infusion of autologous bone marrow cells

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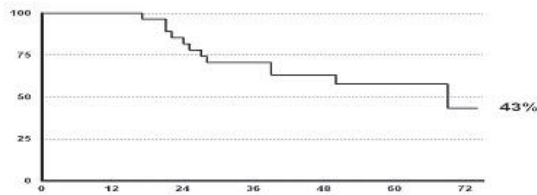
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Different studies have shown left ventricular ejection fraction improvement in idiopathic nonischemic dilated cardiomyopathy treated with intracoronary infusion of autologous bone marrow mononuclear cells. This trial investigates the long-term results in patients with idiopathic dilated cardiomyopathy treated with intracoronary cell therapy and factors influencing good result at 5-year follow-up.

Methods: 27 patients received intracoronary infusion of autologous bone-marrow mononuclear cells. Flow cytometry and functional analyses of the cells were also performed. NYHA functional class, brain natriuretic peptide, left ventricle ejection fraction by echocardiography and major events were recorded after 53 ± 14 months follow-up. Death, need for heart transplant, need for resynchronization therapy and hospitalization for heart failure were considered major events.

Results: 15 patients had no major events at follow-up (group I); 12 patients had major events (group II): death ($n = 3$), hospitalization for heart failure ($n = 3$), need for resynchronization therapy ($n = 6$). Last mean determination of brain natriuretic peptide was 156 ± 450 pg/mL (69 ± 58 pg/mL in group I vs 280 ± 750 pg/mL in group II; $p < 0.03$). Last transthoracic echocardiography left ventricle ejection fraction was 35 ± 13% (42 ± 11% in group I vs 26 ± 5% in group II; $p < 0.005$). The mean left ventricle ejection fraction gain (last follow-up - Baseline) was 7.4 ± 11% (11.6 ± 12.1% in group I vs 2.5 ± 7.4% in group II; $p < 0.01$).

Conclusions: More than half of patients had favourable evolution 5 years after cell therapy. They remain in functional class I-II and event-free. Younger and baseline better clinical condition patients with smaller diameter and greater gain greater benefit from intracoronary cell-therapy at long-term follow-up.



Free probability of events in months

P1467

Association of plasma taurine levels with left ventricular function in patients with idiopathic dilated cardiomyopathy

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Backgrounds

Taurine was reported to prevent cardiac fibrosis and structural remodeling in an experimental animal heart failure model. To explore in vivo evidence for potential role of taurine in human failing heart, we measured plasma taurine levels in patients with biopsy-proven idiopathic dilated cardiomyopathy (DCM) and evaluate association between its levels and the clinical parameters concerned with cardiac function.

Methods: Consecutive 59 patients with DCM (M/F: 43/16, mean age: 62 years) and 35 patients with normal cardiac dysfunction (Control group) were enrolled. Plasma taurine levels, B-type natriuretic peptide (BNP) and A-type natriuretic peptide (ANP) were measured in peripheral blood samples. Left ventricular ejection fraction (LVEF) and fractional shortening (FS) as determined by echocardiography were used as LV function parameters.

Results: Mean plasma taurine levels in DCM were comparable to those in control subjects with normal LV function. However taurine levels in severely reduced LV function (LVEF <30%) (n=27) were significantly lower than those of remainings (54.1 ± 21.2 vs 68.2 ± 17.8, p=0.014). Also plasma levels of taurine showed a significant positive association with LVEF (r=0.362, p=0.009) and FS (R=0.334, P=0.019). There were no significant differences between the mean plasma taurine levels and BNP and ANP.

Conclusion: The plasma taurine could be a novel biomarkers of ventricular dysfunction and the extent of heart failure in patients with DCM.

P1468

Red flags in dilated cardiomyopathy: a not so uncommon finding

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Introduction: In 2012, Rapezzi et al proposed a diagnostic work-up in cardiomyopathies with the premise that a systematic search for diagnostic clues or "red flags" can help identify particular disorders and guide rational selection of diagnostic tests.

Methods: We performed a retrospective analysis, in patients (pts) with dilated cardiomyopathy (DCM), to search for ECG, laboratory tests and cardiac magnetic resonance (cMRI) abnormalities suggestive of specific diagnosis. For each pt, we analyzed, when available, the ECGs and 24h HOLTER monitor in search for conduction abnormalities and the cMRI in search for specific patterns of late gadolinium enhancement (LGE) and fatty replacement within LV wall. We also performed a systematic search of blood chemistry abnormalities (creatinine kinase (CK), serum iron, ferritin).

Results: We identified 76 patients (pts) with DCM. Eight pts (10,5%) had atrial or atrial-ventricular (AV) conduction abnormalities (two had atrial paralysis with normal AV conduction and 6 pts had either congenital or acquired AV block). None of the ECGs available showed low P wave or QRS amplitude. CK was measured in 51 pts and 11 (21,5%) pts had elevated levels (>172u/L). One of these pts had a permanent pacemaker due to atrial paralysis (this pt has a suspected diagnosis of limb-girdle muscular dystrophy). Serum iron, ferritin and transferrin saturation measurements were available for 37 pts (48,7%) and none met the criteria suggestive of hemochromatosis. Fifty-four patients underwent cMRI of who 24 (44,4%) had LGE. LGE was present in the septum of 21 (87,5%) pts and had a midwall distribution in 19 (79%) cases. No pt had postero-lateral akinesia/dyskinesia. One pt had fatty replacement within the LV wall (this particular case was a women whose son was submitted to heart transplantation at a very young age due to dilated cardiomyopathy). A total of 11 pts (20% of those submitted to MRI) met the criteria for LV non-compaction in at least one segment.

Discussion: In our sample of patients with DCM, the presence of the so-called "red flags" that may help identify specific diagnosis was not uncommon. The prevalence of these abnormalities varied from 10,5% (for conduction abnormalities) to 25% for

the presence of midwall LGE. This latter proportion may be even higher if we consider that not all pts underwent cardiac MRI. In this population, a total of 35 pts (46%) presented with at least one abnormality considered as a diagnostic clue for a DCM with a genetic cause (elevated CK, midwall LGE, conduction abnormalities and/or LV non-compaction).

P1469

Neural cell adhesion molecule (NCAM) expression in dilated cardiomyopathy is associated with cardiomyocyte diameter and intramyocardial inflammation

Deutsche Forschungsgemeinschaft through the SFB TR19 "Inflammatory Cardiomyopathy" (TP B2 to MN, and TP Z1 to HPSM Noutsias¹; HP Schultheiss²; KO Ostermann²

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Background: The etiopathogenesis of dilated cardiomyopathy (DCM) has been linked to intramyocardial inflammation. Inflammation can induce hypertrophy, and re-expression of embryologically confined genes. NCAM (neural cell adhesion molecule) is an adhesion molecule which is expressed during cardiac organogenesis, but is absent in adult cardiomyocytes under healthy conditions. We investigated NCAM expression and its expression pattern in DCM hearts, as well as its possible association with inflammatory markers (infiltrates: CD18+, LFA-1+, Mac-1+, CD3+, TNFα+; cell adhesion molecules linked to inflammation: CD29 and ICAM-1) and hypertrophy in endomyocardial biopsies (EMB) from DCM patients.

Methods: EMB from DCM patients (n=85; LVEF<45%) and autptic hearts from non-cardiac deaths (n=17; controls) were immunostained. Quantification of immunostainings and of the mean diameter of cardiomyocytes was carried out by digital image analysis (DIA).

Results: Whereas the controls did not present any NCAM immunoreactivity, n=46 (54%) of the DCM EMBs demonstrated NCAM expression on the intercalated discs and the sarcolemma. These EMBs had significantly higher infiltration densities, expression of ICAM-1 and CD29, and the mean cardiomyocyte diameter as a measure of hypertrophy. DIA-quantified NCAM expression correlated with immunocompetent infiltrates (CD18, LFA-1/CD11a, Mac-1/CD11b, CD3, TNFα expressing infiltrates), with the expression of CD29 and ICAM-1, and the mean cardiomyocyte-diameter.

Conclusions: De novo expression of NCAM, confined to the embryological phase of myocardial organogenesis under healthy conditions, is present in ca. 50% of DCM hearts, and is associated with intramyocardial inflammation and the mean cardiomyocyte diameter / hypertrophy. These data indicate that intramyocardial inflammation might be involved in the induction of the embryologically confined NCAM, and of cardiomyocyte hypertrophy in DCM. Thus, NCAM might be a useful marker in EMBs indicating both inflammatory and hypertrophy pathways.

P1470

Left ventricular noncompaction and heart rate variability: is there any prognostic impact?

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Purposes: Low Heart Rate Variability (HRV) has been shown to have a prognostic impact in ischemic cardiopathy. However, the effect of HRV on cardiomyopathies is still uncertain. No link has been found associating low HRV and hypertrophic cardiomyopathy with a worse prognosis. Is HRV of any value in Left Ventricular Non-Compaction (LVNC)?

The objective of the study is to determine the prognostic impact of HRV in patients (P) diagnosed with LVNC at one year follow-up.

Methods: The study followed 20 patients diagnosed with LVNC based on the echocardiographic Jenni criteria. In 24 hour Holter (H24h) testing performed after diagnosing LVNC, the statistical measure of HRV was calculated as the standard deviation of every NN interval (SDNN24h). The P were distributed into groups determined by the SDNN24h tertiles: Group (G) 1 < 116 ms; G2 116-164ms; G3 >164 ms. P were followed for one year after initial H24h monitoring, during which the following events were recorded: death by any cause; hospital admission due to supraventricular or ventricular tachycardia; acute heart failure (AHF); cardiac transplant. Tests were considered statistically significant when p<0,05.

Results: The average age at diagnosis was 43.6 ± 20 years, 50% being males. There was no statistically significant difference found when comparing initial clinical symptoms of LVNC. H24h testing was performed on average 8.19 months following LVNC diagnosis. The P were distributed accordingly: G1- 20%; G2- 45%; G3 35%. No statistical difference was found between tertiles when analyzing the use of beta blockers (40% of the study population) and amiodarone (30% of the P). No difference was observed when comparing the prevalence of AHF symptoms. Also, no statistical difference was found between study groups when reviewing electrocardiograms and echocardiograms. During the follow-up period, no statistical difference was

observed when comparing endpoint amongst study populations (G1- 25%; G2- 12.5%; G3- 50%; $p=0.298$).

Conclusion: Though the prognostic impact of HRV in other cardiomyopathies is well documented, its impact in LVNC is still undetermined. Further larger studies are needed to determine HRV significance.

P1471

Predictors of complete in-hospital recovery of left ventricular systolic function in Takotsubo cardiomyopathy - a portuguese multicenter study

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Introduction: Takotsubo cardiomyopathy (TC) is characterized by a transient left ventricular (LV) dysfunction. The speed of LV function recovery is variable. There are no studies determining the predictors of in-hospital recovery of LV systolic function in TC.

Aim: To identify predictors of in-hospital recovery of LV systolic function in TC.

Methods: A Portuguese multicenter study involving 11 hospital centers and including all patients diagnosed with TC in the last 10 years. We evaluated demographic, clinical, electrocardiographic and echocardiographic data. We determined the factors that were associated with in-hospital recovery of the LV systolic function and then conducted a multivariate analysis to establish the independent predictors of in-hospital recovery of LV systolic function in patients with TC.

Results: We included 142 patients with TC, predominantly women (89.4%). The mean age was 67 ± 12 years.

Complete recovery of LV systolic function occurred in 45.1% of patients with TC during hospitalization (mean length of stay 7.2 ± 6.9 days).

In patients with TC, the following factors were associated with complete recovery of LV systolic function during hospitalization: the absence of a history of angina (98.4% vs 79.5%, $p=0.001$) and the absence of Q waves in the initial ECG (92.2% vs 71.8%, $p=0.002$).

In the multivariate analysis, the absence of a history of angina ($p=0.011$) and the absence of Q waves in the initial ECG ($p=0.006$) were identified as independent predictors of complete recovery of LV systolic function during hospitalization of patients with TC.

Conclusion: In patients with TC, complete recovery of LV systolic function occurs during hospitalization in about half of the cases. This study identified the absence of a history of angina and the absence of Q waves on the admission ECG as independent predictors of complete recovery of LV systolic function during hospitalization of patients with TC.

P1472

Idiopathic dilated cardiomyopathy vs. left ventricular non compactation with systolic dysfunction, differences in clinical evolution and its relationship with basal ecocardiographic features

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Aim: The purpose of this study is to compare the echocardiographic features in patients (p) with left ventricular non compactation cardiomyopathy (LVNC) and left ventricular dysfunction, against those p with idiopathic dilated cardiomyopathy (IDCM) with similar systolic dysfunction of the left ventricle (LV). As well as to compare the differences in clinical evolution and establish the relationship between clinical events and basal ecocardiographic features.

Methods and Results: A comparison between 2 groups of p, A: p with IDCM and left ventricular dysfunction and B: p with LVNC and similar left ventricular ejection fraction (LVEF) was done. The whole group had LVEF below 50%. An echocardiogram was performed at the beginning of the study, a clinical follow up through personal interviews and telephone calls, during a 2 years period was developed. Primary end points as a combination of Cardiovascular Death, Cardiac Transplantation and need for a cardiodefibrillator (ICD) as secondary prevention were defined.

A total of 45 p fulfilled the inclusion criteria, 21 p with IDCM and 24 p with LVNC. 55% were men, mean age 62 ± 10 y/o, 45% had hypertension, 24% diabetes and 39% dyslipidemia. There were no significant differences in most of the basal features between groups, except in terms of age. Yet we didn't find a correlation between age and echo differences nor with the development of the primary end point. There were no differences when comparing features regarding systolic function, mean LVEF

was $24,6\% \pm 6,4$ in p with IDCM and $28,6\% \pm 7,8$ in p with LVNC ($P=0.07$). We found statistically significant differences in variables related to diastolic function, left atrial area was larger in p with IDCM ($31 \text{ cm}^2 \pm 8$ vs $24 \text{ cm}^2 \pm 5$, $P=0.0001$) and when diastolic dysfunction was evaluated as 0 = normal, 1 = impaired relaxation, 2 = pseudonormal, 3 = restrictive, it was worse in p with IDCM than in p with LVNC, (2 ± 0.77 vs 1.3 ± 0.88 $P=0.01$). There was no difference in terms of mitral regurgitation. At the end of the follow up period the combined primary end point was more prevalent in p with IDCM than in p with LVNC (45% vs 14%, $P=0.03$). At multivariate analysis, both the etiology of the cardiomyopathy and the diastolic dysfunction were independent predictors of the primary end point.

Conclusion: IDCM and LVNC present important echocardiographic differences especially in terms of diastolic function. This is directly related with a better clinical evolution, after 2 year follow up, in p with LVNC compared to IDCM.

P1473

Hereditary transthyretin related amyloidosis - cardiac phenotype in patients with glu89gln mutation

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Background: Hereditary transthyretin - related amyloidosis (ATTR) is an autosomal dominant multisystem disease, caused by a mutation in the transthyretin gene. Cardiac involvement is very common with significant phenotypic heterogeneity depending on the type of mutation. More than 100 mutations are known up to now.

Purpose: The purpose of this study was to evaluate cardiac involvement in a group of ATTR patients with Glu89Gln mutation.

Material and methods

Thirty five consecutive patients with ATTR, with genetically confirmed Glu89Gln mutation were prospectively evaluated, 17 male and 18 female patients at mean age of 57.2 ± 6.3 years, in the range of 42 to 71 years. A clinical examination, 12-channel ECG, standard 2D, Doppler and tissue Doppler echocardiography were performed.

Results: Median age of symptom onset was 52.3 ± 6.4 years, in the range of 35 to 68 years. A family history was present in 24 (68.6%) patients. Peripheral polyneuropathy was present in all the evaluate patients at diagnosis. Symptoms from the autonomous nervous system were found in 23 patients. Cardiac involvement was evident on echocardiography at diagnosis in all patients. In the majority of patients (27) the presenting symptoms were from the peripheral nervous system, in 6 - from the heart and 2 patients had gastrointestinal complaints. 13 patients suffered from carpal tunnel syndrome. Echocardiography revealed an infiltrative cardiomyopathy with significant increase in left and right ventricular wall thickness. Varying degrees of diastolic dysfunction were found - mild in 11 (31.4%), moderate in 10 (28.6%) and severe in 14 (40%) patients. Reduced LV ejection fraction $<50\%$ was found in 6 (17,1%) of the patients. A common finding were significantly reduced mitral annular myocardial velocities (s'av- $5,7 \pm 2,1$ cm/s, e'av- $5,3 \pm 1,6$ cm/s). Pericardial effusion was found in 9 patients.

Pathological ECG was present in 30 (85,7%) of the evaluated patients - atrial fibrillation in 3 patients, A-V block first degree in 8 and left anterior fascicular block in another 8 patients, low voltage in 13, pathological Q wave in 10, left bundle branch block in 3, right bundle branch block in 2 and nonspecific increase in QRS duration in 5 of the patients.

Conclusion: We found a various degree of cardiac involvement in all the evaluated ATTR patients with Glu89Gln mutation at the time of diagnosis, but peripheral neuropathy was more common presenting condition. Our results add some knowledge to the phenotypic expression of this relatively more rare mutation and show the need for a multidisciplinary approach to these patients.

P1474

Predictors of heart failure on takotsubo cardiomyopathy, a portuguese multicenter study

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Introduction: Takotsubo cardiomyopathy (TC) is characterized by a transient left ventricular (LV) dysfunction that may lead to the development of heart failure. Little is known about the predictors of heart failure in TC.

Aim: To identify predictors of heart failure in patients with TC.

Methods: A Portuguese multicenter study involving 11 hospital centers and including all patients diagnosed with TC in the last 10 years. We evaluated demographic, clinical, electrocardiographic and echocardiographic data. We determined the factors that were associated with the development of in-hospital heart failure and then conducted a multivariate analysis to establish the independent predictors.

Results: We included 142 patients with TC. During the hospital stay (7.2 ± 6.9 days), heart failure occurred in 25.4% of patients. Other complications: cardiogenic shock (9.9%), atrial fibrillation (8.5%), complete auriculo-ventricular block (2.8%), acute pulmonary edema (3.5%), stroke/transient ischemic attack (2.1%), ventricular tachycardia (2.1%), LV thrombus (1.4%) and death (1.4%).

In patients with TC, the factors associated with the development of heart failure were the history of heart failure (5.6% vs 0%, $p = 0.015$), chronic renal failure (19.4% vs 1.9%, $p < 0.001$), the clinical presentation with dyspnea (44.4% vs 10.4%, $p < 0.001$) and worse LV ejection fraction ($35.9 \pm 10\%$ vs $46.4 \pm 11\%$, $p < 0.001$).

In the multivariate analysis, chronic renal failure ($p = 0.005$) and worse LV ejection fraction ($p = 0.005$) were identified as independent predictors of the heart failure during hospitalization of patients with TC.

Conclusion: TC has a high rate of in-hospital heart failure. The development of heart failure in patients with TC is associated with a history of heart failure and chronic renal failure, clinical presentation with dyspnea and worse LV ejection fraction. Chronic renal failure and worse LV ejection fraction were identified as independent predictors of heart failure in patients with TC.

P1475

The impact of 6- months therapy of carvedilol on systolic and diastolic left ventricular function in patients with peripartum cardiomyopathy

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The Aim: To assess the impact of carvedilol on systolic and diastolic cardiac function in patients with peripartum cardiomyopathy (PDCM).

Methods: The study included 23 patients with PDCM with investigation of an electrocardiogram, EhoKG (left ventricle systolic (LVSF) and diastolic function (LVDF)) the definition of cardiothoracic index (CTI) by chest X-ray. Intracardiac hemodynamic parameters were evaluated at baseline and after 6 months of continuous therapy. By the time of entry into the study, patients were stabilized on basic therapy (BT) of heart failure, which allowed applying Carvedilol with a starting dose of 3.12 mg 2 times a day with a standard titration step.

Results: III NYHA class was observed in 17 (73.9%), IV NYHA class- in 6 (26.1%) patients. The treatment with carvedilol led to dose titration to achieve an average dose 16.5 ± 2.8 mg/day: in III NYHA class on 19.6 ± 2.8 mg, in IV NYHA class on 14.8 ± 2.6 mg / day. Cardiomegaly of II degree recorded in 8 (34.8%), III degree - in 15 patients (65.2%). We observed restrictive type ($E / A > 2$) at 12 (52.2%) patients, pseudonormal type of diastolic dysfunction at 11 (47.8%) patients. The six months therapy with BT characterized by improvement of left ventricular ejection fraction on 24.7% (from 41.6 ± 2.1 to $51.9 \pm 1.9\%$; $p < 0.01$), accompanied by improved diastolic function (DF) LV: Ve index decreased on 6.1% (from 0.83 ± 0.04 to 0.78 ± 0.03 ; non respectively) with an increase of Va on 24.4% (from 0.45 ± 0.03 to 0.56 ± 0.04 ; $p = 0.03$), as a consequence of significantly reduced rate Ve / Va on 22.6% (from 1.99 ± 0.1 to 1.54 ± 0.1 ; $p < 0.01$).

Conclusions: Thus, the 6- months therapy to CHF against BT in individually dosed at patients with PDCM and severe heart failure can improve the clinical status, systolic and diastolic function.

P1476

The role of treg markers detection in patients with inflammatory cardiomyopathy endomyocardial and blood samples

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Aim: To evaluate the expression of functional Treg markers in endomyocardial biopsies and blood samples in patients with inflammatory cardiomyopathy (ICMP).

Methods: 35 patients mean age 41 ± 11.4 (21 male, 14 female), I-III Class NYHA, mean LVEF $33.3 \pm 5.7\%$, with symptomatic heart failure for median $2.0 [1.0; 3.0]$ years and suspected inflammatory cardiomyopathy underwent endomyocardial biopsy (EMB). EMB specimens were investigated with histological and molecular-genetic methods with PCR detection of cardiotropic viruses. Diagnosis was based on World Health Organization criteria. Leucocytes and macrophages criteria amount was ≥ 14 . Endomyocardial and blood samples were analysed for expression and sera testing of markers, characterizing Treg(FoxP3, TGF β , IL-10).

Results: The total number of EMB patients was 35 (100%). ICMP was diagnosed in 18 cases (54, 5%) [9 cases (25, 7%) were virus-positive and 9 cases (25, 7%) were virus-negative]. DCMP without signs of active inflammation have been revealed in

$n=17$ [(45, 4%), 11 cases (31, 4%) were virus positive and 6 cases (17,1%) were virus negative]. Mean NYHA FC was $2, 06 \pm 0, 77$ in ICMP pts group and $2, 17 \pm 0, 7$ in DCMP pts group ($p = 0,6$). According to EMB results, the median of lymphocytes, that expressed CD4+ and CD8+ in the myocardium of patients with ICMP [relatively $2,0(2,0;4,0)$ and $10,0(6,0;11,7)$] was significantly higher compared with DCMP pts without active inflammation [relatively $0(0,0;2,0)$, $p < 0,0001$ for CD4+ and $3,1(1,5;4,2)$, $p < 0,0001$ for CD8+].

According to the frequency of FoxP3 myocardial expression, 4 pts (22,2%) in ICMP group were positive and 14 pts (77,8%) were negative, compared with relatively 8 pts (46,2%) and 9 pts (53,8%) in DCMP group without signs of active inflammation ($p = 0,1$). In the same time, the frequency of FOXP3 expression was significantly higher in DCMP pts blood samples: 13 (76,4%) pts were positive and 4 pts (23,6%) were negative compared with relatively 7 (38,8%) and 11(61,2%) pts in ICMP group ($p = 0,028$).

Sera level of TGF β (pg/ml) was significantly higher in pts with ICMP: $10614 [3622;49392]$ pg/ml vs $7030[0,0;9956]$ pg/ml in pts without signs of active inflammation ($p = 0,01$). Positive value of IL-10 (2,0 pg/ml) was detected only in one patient with DCMP.

Conclusion: Treg cells play an important role in the development of cardiomyopathy. Higher level of TGF β in ICMP patients may reflect the compensatory reaction of the inflammatory process.

P1477

Usefulness of 99mTc-HMDP scintigraphy for the etiologic diagnosis and prognosis of cardiac amyloidosis

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Background: Amyloidosis is characterized by extracellular deposits of insoluble proteins that cause tissue damage. The three main types are monoclonal light chain (AL), wild-type transthyretin (wt-TTR), and mutated transthyretin (m-TTR) amyloidosis. Cardiac amyloidosis (CA) raises diagnostic challenges.

Objective: To assess the diagnostic accuracy of 99mTc-HMDP-scintigraphy for typing CA, differentiating CA from non-amyloid left ventricle hypertrophy (LVH), and predicting outcomes.

Methods: 121 patients with suspected CA underwent 99mTc-HMDP-scintigraphy in addition to standard investigations.

Results: CA was diagnosed in all AL (n=14) and wt-TTR (n=21). Among m-TTR (n=34), 26 had CA, 4 neuropathy without CA and 4 were asymptomatic carriers. Of the 52 patients with non-amyloid heart disease, 37 had LVH and served as controls. 99mTc-HMDP cardiac uptake occurred in all wt-TTR, in m-TTR with CA except two, and in one AL. A visual score ≥ 2 was 100% sensitive and specific for diagnosing TTR-CA. Among TTR-CA, heart-to-skull retention (HR/SR) correlated with CA severity (LVEF and NT-proBNP). Median follow-up was 111 days (50;343). In a multivariate Cox model including clinical, echocardiographic, and scintigraphic variables, NYHA III-IV and HR/SR > 1.94 predicted acute heart failure and/or death.

Conclusions: 99mTc-HMDP-scintigraphy allows differentiating transthyretin from AL-CA and CA from other LVHs and also provides prognostic information.

P1478

Predictors of heart failure in left ventricular non-compaction cardiomyopathy - a portuguese multicenter study

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Introduction:

Left ventricular non-compaction cardiomyopathy (LVNC) may lead to the development of heart failure. Little is known about the predictors of heart failure in LVNC.

Aim: To identify predictors of heart failure in patients with LVNC.

Methods: A Portuguese multicenter study involving 11 hospital centers and including all patients diagnosed with LVNC. We evaluated demographic, clinical, electrocardiographic, echocardiographic and cardiac magnetic resonance data. We determined the factors that were associated with the development of heart failure and then conducted a multivariate analysis to establish the independent predictors of heart failure in patients with LVNC.

Results: We included 72 patients with LVNC. Heart failure was present in 37.5% of patients. In patients with LVNC, the factors associated with the development of

heart failure were presence of symptoms on diagnosis (88.9% vs 53.3%, $p=0.002$), higher LV end-diastolic diameter ($61 \pm 8\%$ vs $53 \pm 7\%$, $p < 0.001$), lower LV ejection fraction ($39 \pm 13\%$ vs $55 \pm 14\%$, $p < 0.001$), diastolic dysfunction (69.2% vs 21.1%, $p=0.006$), atrial fibrillation on ECG (22.2% vs 2.2%, $p=0.006$) and left bundle branch block (22.2% vs 4.4%, $p=0.020$). Patients with LVNC and heart failure had a tendency to higher frequency of death in the 48 months of follow up (7.4% vs 0%, $p=0.064$). In the multivariate analysis we could not identify any independent predictors of heart failure in LVNC patients.

Conclusion: Heart failure is a common complication of LVNC. The presence of heart failure in patients with LVNC was associated with the presence of symptoms on diagnosis, higher LV end-diastolic diameter, lower LV ejection fraction, diastolic dysfunction, atrial fibrillation on ECG and left bundle branch block. Patients with LVNC and heart failure had a higher frequency of death in the follow-up.

P1479

Does heart failure development during hospitalization predict the prognosis of takotsubo cardiomyopathy? A portuguese multicenter study

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Introduction: Takotsubo cardiomyopathy (TC) is characterized by a transient left ventricular (LV) dysfunction. The severity of LV dysfunction may lead to the development of heart failure; little is known about the impact of heart failure during hospitalization on the prognosis of TC.

Aim: To determine if the development of heart failure during hospitalization influences the prognosis of TC.

Methods: A Portuguese multicenter study involving 11 hospital centers and including all patients diagnosed with TC in the last 10 years. It was determined whether patients with heart failure during hospitalization had worse prognosis.

Results: We included 142 patients with TC. During the hospital stay (7.2 ± 6.9 days), heart failure occurred in 25.4% of patients. A mean follow up of 40 ± 31 months was performed. Heart failure development was associated with a higher incidence of atrial fibrillation (17% vs 5.7%, $p=0.040$) and complete atrioventricular block (8.3% vs 0.9%, $p=0.021$) during hospitalization. Heart failure development was also associated with a higher incidence of death (5.6% vs 0.0%, $p=0.015$) and recurrence of TC (11% vs 2.2%, $p=0.047$) in the follow-up.

Conclusion: In this Portuguese multicenter study, patients with TC that developed heart failure during hospitalization had worse short and medium term prognosis.

P1480

Predictors of reversibility in tachycardia induced cardiomyopathy

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Introduction: Tachycardia induced cardiomyopathy (TIC) is a rare but potentially reversible cause of heart failure. The recovery of ventricular function after termination of or control of the tachyarrhythmia is extremely variable. Recovery may be complete or partial. The aim of this study was to identify predictors of recovery level of left systolic ventricular function in patients with TIC.

Methods: This was a retrospective study of 39 patients admitted in a single centre with TIC, between January 2008 e October 2013, accordingly to the following criteria: symptoms and/or signs of heart failure, reduced left ventricle ejection fraction (LVEF < 50%); tachyarrhythmia; significant recovery (improvement of LVEF > 15%) or normalization of LV function after control of tachycardia; no other cause of reversible cardiomyopathy found. The patients were divided into two subgroups according to the level of LVEF recovery (complete vs partial) and compared regarding their demographic, clinical and echocardiographic characteristics and type of treatment received (rhythm control versus rate control). Comparisons between groups were performed with an unpaired Student t test. Categorical variables were compared with a chi-square test and Fisher's test. A value of $p < 0.05$ was considered statistically significant.

Results: Mean age of the population was 67.6 ± 9.7 years, with a female predominance (59%). Atrial fibrillation was the underlying arrhythmia in 69.2% and atrial flutter in 30.8%. In 27 patients (69.2%) it was observed total recovery with normalization of LVEF, the other patients had a significant improvement of their LVEF but maintained LVEF < 50%. There were no significant differences between groups for sex, mean age, underlying arrhythmia, therapeutic strategy, and presence of arterial hypertension or diabetes. In our population, the pts who had partial recovery had more severe left ventricular dysfunction (LVEF of 24% vs 34% ; $p=0.001$), high

mean heart rate (HR 160,7 vs 145,6 bpm; $p=0.019$), higher percentage of patients with right ventricular (RV) dysfunction associated (50% vs 18,8%; $p,020$) and greater end-diastolic left ventricular diameter (LVIDd) (58,4mm vs 53,7 mm, $p=0,011$) at admission.

Conclusions: Restoration of LV function and reversal of LV remodeling can be achieved with successful elimination of tachycardia in the majority of pts. The severity of LV dysfunction, the presence of associated RV dysfunction, LVIDd dimensions and heart rate at admission were predictors for the level of improvement of left ventricular function in our population with TIC.

P1481

Left ventricular non-compaction: an entity in search of an identity

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Introduction: Left ventricular non-compaction (LVNC) can occur in association with several neuromuscular diseases and several causative mutations have been identified in genes encoding tafazzin (X-linked), actin, and lamin A/C among others. It is not clear whether LVNC is a distinct cardiomyopathy or a trait shared by different cardiac diseases. Little is known about distinctive markers of LVNC.

Methods: In a population of patients (pts) with dilated cardiomyopathy (DCM) who were submitted to cardiac magnetic resonance imaging (cMRI), we identified those who met the criteria for LVNC in at least one left ventricular segment (ratio of non-compacted myocardium to compacted myocardium >2,3). We performed a retrospective analysis to search for eletrocardiographic, biochemical and cMRI abnormalities that may be specific of LVNC.

Results: Of 55 pts with DCM who were submitted to cMRI, 11 (20%) met the criteria for LVNC, and in 9 (82%) non-compaction was present in the apical-lateral segment. Indexed left ventricular end-diastolic and end-systolic volumes, indexed myocardial mass and ejection fraction were not different between groups ($p=0,74$, $p=0,9$, $p=0,56$ and $p=0,9$ respectively). Compared to pts without LVNC, pts with LVNC did not present any specific pattern of late gadolinium enhancement (LGE) ($p=0,125$ for midwall LGE; $p=0,33$ for subepicardial LGE; $p=0,8$ for subendocardial LGE) and LGE was equally prevalent in both groups ($p=0,5$). Mean QRS duration was 121 ± 30 ms in pts without LVNC and 123 ± 27 ms in pts with LVNC ($p=0,8$). Presence of left bundle branch block (LBBB) was also not different between groups ($p=0,578$). Creatinine kinase serum levels were available for thirty-five patients, and were significantly different between groups (108 ± 64 u/L in pts without LVNC and 223 ± 170 u/L in pts with LVNC, $p=0,046$). Brain natriuretic peptide serum levels were available in 51 pts and were not significantly different between groups, although there appears to be a trend towards lower values in patients with LVNC (424 ± 833 ng/L VS 118 ± 274 ng/mL; $p=0,062$). **DISCUSSION:** In our sample of patients with DCM who were submitted to cMRI, 20% met the criteria for LVNC. Left ventricular volumes and ejection fraction were not different between groups, nor was the presence or pattern of LGE. QRS duration and prevalence of LBBB were also similar between groups. We observed a statistically significant difference between CK serum levels that were higher in patients with LVNC. This finding may be related to the known association between LVNC and neuromuscular diseases. Further studies are needed in order to better characterize this entity.

P1482

Which clinical factors at presentation predict deterioration to fulminant course in acute myocarditis patients?

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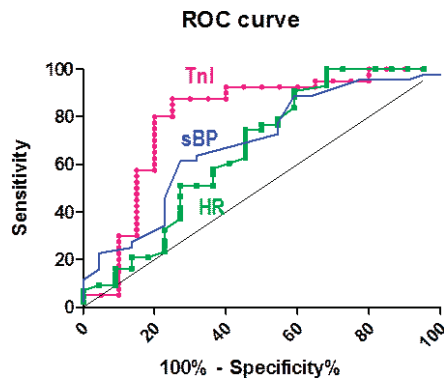
Purpose: Clinical factors at presentation which might be associated with deterioration to fulminant course in acute viral myocarditis are not fully described. Herein, we evaluated the initial clinical characteristics related to acute deterioration.

Methods: From January 2004 to August 2014, 66 patients from single center who were finally diagnosed with acute (viral) myocarditis were included in this study. We predefined the clinical deterioration to fulminant myocarditis within 48 hours from the arrival of the hospital; 1) high dose of inotropics ($\geq 20 \mu\text{g/kg}$) or 2 more inotropic agents requirement, 2) IABP or ECMO requirement.

Results: Mean age was 45 years old, and 62% were male. Predefined fulminant progression was noticed in 22 patients (fulminant group; 33.3%). Among them, 14 patients (63.6%) were received MCS device. Predictors of clinical deterioration were assumed to be initial systolic blood pressure (OR 0.925, CI 0.856-1.000, $p=0.05$), and initial troponin I level (OR 1.119, CI 0.997-1.255, $p=0.056$) with marginal significance by multivariable logistic regression model. Overall in hospital mortality rate was 12.1% (8 patients) and all of them were noticed in fulminant group (36.4%) especially during hospitalization. Long term mortality rate was 12.1% during average 888 days of follow-up period.

Conclusion: From our single center experience, the short-term and long-term prognosis of acute myocarditis were good especially in patients who did not get

into fulminant course within 48 hours from presentation. Clinical predictors of progression to fulminant course were only initial systolic blood pressure and troponin I. Close monitoring in early hospital days with vital signs and stratification will be helpful to manage acute myocarditis patients.



ROC curve for fulminant course

P1483

Plasma HMGB1 is increased in inflammatory cardiomyopathy but not in ischemic cardiomyopathy

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Purpose: HMGB1 (High mobility group box 1) is a nuclear protein and plays a central role in multiple inflammatory and autoimmune diseases boosting and sustaining inflammation. It can either be secreted by activated inflammatory cells in infection or passively released by necrotic cells as happening in ischemia and reperfusion. Myocarditis is an inflammatory heart disease which can result in dilated cardiomyopathy and heart failure. Clinical differentiation between inflammatory or ischemic causes in patients with unclear cardiomyopathy can be difficult and often requires invasive diagnostics. The aim of this study was to evaluate the plasma levels of HMGB1 in patients with acute and chronic myocarditis and post-inflammatory dilated cardiomyopathy as compared to patients with acute myocardial infarction or chronic ischemic cardiomyopathy.

Methods: We investigated HMGB1 levels in blood samples from patients with endomyocardial biopsy proven acute or chronic myocarditis (n=15), patients with post-inflammatory dilated cardiomyopathy (n=15), patients with acute myocardial infarction (n=15) and chronic ischemic cardiomyopathy (n=15). Age-matched healthy volunteers served as controls (n=15). Plasma samples were analyzed for HMGB1 by quantitative Western blots and densitometric analyses. Endomyocardial biopsies were investigated by histopathological analysis, immunohistochemistry and molecular biological detection of viral genomes by PCR and in situ hybridization.

Results: Patients with myocarditis and inflammatory dilated cardiomyopathy showed similarly increased plasma levels of HMGB1 as compared to healthy controls and as compared to patients with ischemic pathology (5 to 6-fold increase). Contrary to this, there was no significant difference in HMGB1 plasma levels between healthy controls, acute myocardial infarction and chronic ischemic cardiomyopathy patients.

Conclusions: Myocarditis is associated with increased plasma levels of pro-inflammatory HMGB1, which persist in patients with dilated cardiomyopathy indicating ongoing inflammation. These observations might help develop new diagnostic strategies for differentiation of ischemic and inflammatory cardiomyopathy and could lead to the development of new therapeutic strategies for the prevention of dilated cardiomyopathy.

P1484

Clinical presentation of acute myocarditis predicts left ventricular function as assessed by cardiac MRI

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Purpose: The purpose of our study was to evaluate any possible correlation between the clinical presentation of acute myocarditis and the findings of the cardiac MRI at admission.

Methods: We retrospectively analysed the data of consecutive patients with acute myocarditis presented at our emergency department within an 80-month-period spanning from January 2007 to August 2013. Our definition of acute Myocarditis included all the patients with a recent onset of symptoms of dyspnea, chest discomfort, palpitations/arrhythmia symptoms or fatigue, with or without history of recent respiratory or gastrointestinal infection and angiographically confirmed absence of significant coronary artery disease (absence of stenosis $\geq 50\%$), who fulfilled at least two of the following criteria: 1. Troponin I increase at presentation or during the hospitalisation period, 2. Edema/LGE of classical myocarditic pattern at the admission cardiac MRI, 3. positive myocardial biopsy, as defined by positive Dallas histopathologic criteria and/or immunohistochemistry and/or PCR-amplification of viral genome. The clinical variables under investigation were categorised in four groups: 1. chest discomfort, 2. dyspnea, 3. palpitations/arrhythmia symptoms and 4. other. The following MRI-variables were studied: LVEF (normal, mildly-, moderately- and highly-reduced), presence of myocardial edema and extend of LGE (expressed as the sum of involved segments based on a standardised myocardial segmentation according to the 17-segment model).

Results: A total of 52 patients were studied. The majority of the patients were male (71,1%, n=37), aged $34,2 \pm 11,6$ years. Patients presenting with dyspnea demonstrated, as compared to those without dyspnea, a highly reduced LVEF at admission-MRI (66,7% vs. 7,9%, $p < 0,001$). Inversely, only 8,3% patients with dyspnea vs. 65,7% of those without dyspnea at presentation had a normal LVEF ($p < 0,001$). Interestingly, presentation with chest discomfort displayed, in comparison to presentation due to other symptoms, a significant correlation with a normal LVEF at admission (69,2% vs. 28,8%, $p < 0,006$). No significant correlation was pointed out between the type of clinical presentation and myocardial edema or the extend of LGE at the admission-MRI.

Conclusion: In the setting of acute myocarditis dyspnea at admission correlates with a highly reduced left ventricular systolic function, whereas chest discomfort at admission is associated with a normal LVEF. No other association could be detected between other MRI variables and other types of clinical presentation.

P1485

Peak laboratory values correlate well with cardiac MRI findings in patients with acute myocarditis

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Purpose: To evaluate the correlation between laboratory variables in the context of acute myocarditis and indices of left ventricular involvement as determined by cardiac MRI findings at admission.

Methods: We retrospectively analysed the data of consecutive patients with acute myocarditis presented at our emergency department over an 80-month-period spanning from January 2007 to August 2013. Our definition of acute Myocarditis included all the patients with a recent onset of symptoms of dyspnea, chest discomfort, palpitations/arrhythmia symptoms or fatigue, with or without history of recent respiratory or gastrointestinal infection and angiographically confirmed absence of significant coronary artery disease (absence of stenosis $\geq 50\%$), who fulfilled at least two of the following criteria: 1. Troponin I increase at presentation or during the hospitalisation period, 2. Edema/LGE of classical myocarditic pattern in cardiac MRI, 3. positive myocardial biopsy, as defined by positive Dallas histopathologic criteria and/or immunohistochemistry and/or PCR-amplification of viral genome. The laboratory variables under investigation were peak Troponin I, peak CRP and peak BNP during hospitalisation. The following MRI variables were studied: LVEF (normal or mildly, moderately and highly reduced), presence of myocardial edema and extend of LGE (expressed as the sum of involved segments based on a standardised myocardial segmentation according to the 17-segment model).

Results: A total of 52 patients were studied. The majority were male (71,1%, n=37), whereas the mean age of the study group was $34,2 \pm 11,6$ years. Patients with a normal LVEF exhibited, compared to patients with reduced LVEF, significantly lower peak BNP levels ($50,6 \pm 35,7$ vs. $472,1 \pm 546,8$ pg/ml, $p = 0,007$). Accordingly a highly reduced LVEF was associated with higher peak BNP levels ($659,2 \pm 550,5$ vs. $131,2 \pm 301,0$ pg/ml, $p < 0,001$). No significant association was demonstrated between the LGE extend and any of the aforementioned variables. Interestingly, the presence of myocardial edema was related to higher peak Troponin levels ($5,94 \pm 6,09$ vs. $1,15 \pm 1,54$ ng/ml, $p = 0,003$).

Conclusion: As expected, any reduction of left ventricular systolic performance was associated with significantly higher peak BNP levels. Importantly the presence of edema, a substantial feature of the acute inflammatory reaction in the myocardium, was associated with a more pronounced increase of peak troponin levels.

P1486

Gadolinium late enhancement and septal thinning predict adverse events in cardiac sarcoidosis

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Purpose: The diagnostic value of cardiac magnetic resonance imaging (CMR) in cardiac sarcoidosis (CS) is well known. The purpose of this study was to investigate the prognostic value of CMR in CS.

Methods: We retrospectively reviewed the CMR studies and follow-up data of the 60 CS patients who underwent CMR in our institution from February 2004 to July 2014. Criteria used for CS diagnosis included imaging finding consistent with CS combined with histological verification of CS (myocardial biopsy, n=31; mediastinal lymph node, n=19; other extra-cardiac tissue, n=9; autopsy, n=1). The late gadolinium enhancement (LGE) mass was calculated by the full width half-maximum threshold method and the amount of LGE was expressed as a percentage of the total left ventricular (LV) mass. Thickness of the basal septum (defined as the thinnest point of American Heart Association segments 2 and 3) was measured.

Results: There were 21 males and 39 females with a mean age of 46 years (range 18-66). The mean left ventricular ejection fraction (LVEF) by CMR was 43% (range 12-69). Major adverse cardiovascular events (MACE) included death (n=4), cardiac transplantation (n=2), ventricular fibrillation (n=8) or ventricular tachycardia requiring ICD therapy (shocks or ATP) or external defibrillation (n=17), whichever occurred first. The median follow-up from the CMR study to end of follow-up or first MACE was 14 months. All patients exhibited LGE with a median of 17% (range 2 - 52) of LV mass. The extent of LGE was a strong predictor of MACE (HR 1.054; 95%CI 1.018-1.091; p=0.003 by Cox regression). The thickness of basal septum was <4 mm in 6/55 patients. These patients had significantly worse MACE-free survival (5/6 MACE, median MACE-free survival 2 months vs. 18/49 MACE; median MACE-free survival 60 months; logrank p=0.008). LVEF did not predict MACE in these patients.

Conclusion: CMR with quantitative LGE analysis helps to assess prognosis in CS. Both overall LGE extent and abnormal LV septal thinning predict an increased risk of MACE.

P1487

Short and long-term outcome of acute myocarditis: what can we expect?

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Introduction: Myocarditis is a relatively common inflammatory disease that affects the myocardium. Current data suggest a good overall prognosis for patients with myocarditis. We thought to evaluate the in-hospital and long-term outcome of patients diagnosed with acute myocarditis in our tertiary referral center.

Methods: Retrospective analysis of 91 consecutive patients hospitalized with acute myocarditis between June 2006 and June 2014. Clinical features, complications, baseline and follow-up echocardiograms and cardiac magnetic resonance imaging were reviewed.

Results: The mean of age was 33 ± 10 years and 75 (82%) patients were men. Hypertension and dyslipidemia were present only in a few pts (17% and 15%, respectively). A viral prodrome was found in 76% of patients and chest pain was the commonest symptom (93%). All patients presented elevated levels of troponin I (mean peak level of 27 ± 36ng/ml). Mean BNP, C-reactive protein values at admission were 204 ± 371 pg/ml and 86 ± 94 mg/dl, respectively. ST segment elevation (58%) was the most frequent ECG changes. Coronary angiography performed in 38 (42%) patients was normal in all of them. Left ventricular (LV) systolic dysfunction (ejection fraction <55%) was present at admission in 23 patients (25%). Myocardial oedema was present in 62% and late gadolinium enhancement in 96%, predominantly subepicardial (63%), with an inferior-lateral location in most cases (39%) and involving 4 or more myocardial segments (58%). In-hospital complications occurred in 5 patients (5%) and included cardiogenic shock (n=2); atrial fibrillation (n=2) and sustained ventricular tachycardia (n=1). There were no in-hospital deaths. After a mean follow-up of 36 months, residual LV dysfunction was reported in 3% without cases of heart failure. Recurrences occurred in 9% of cases. No other cardiac re-hospitalizations or deaths were recorded. In a multivariate analysis, the presence of oedema in T2 weight imaging on admission was the only determinant of normalization of LV systolic function (p=0.042).

Conclusions: In this cohort, most of patients with acute myocarditis were male, at 3rd decade of life, without cardiovascular risk factors. Despite the favorable outcome, some patients do not fully recover LV function and others had recurrence of myocarditis. Myocardial oedema as defined by CMR was the only predictor of LV systolic function recovery.

P1488

Cardiac magnetic resonance findings in follow-up

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Background: Myocarditis is characterized by acute or chronic inflammation of myocardial tissue. Cardiac magnetic resonance (CMR) has become an established

non-invasive diagnosis tool for acute myocarditis. However, it is less established as a prognostic tool. Our aim was to assess the CMR findings after the first episode of acute myocarditis.

Methods: We studied 33 patients with acute myocarditis whose CMR was performed during clinically acute myocarditis and 9 ± 3 months later. A CMR protocol was applied and the prognostic value was assessed using a combination of death, heart transplant, hospitalization for cardiac cause and recurrent myocarditis as main outcome.

Results: The mean of age was 32 ± 9 years and 24 (72%) patients were men. Troponin I elevation was found in all patients (mean peak level of 22 ± 23 ng/ml). Mean BNP, C-reactive protein values at admission were 241 ± 443 pg/ml and 96 ± 93 mg/dl, respectively. An abnormal ECG was present in 21 (64%) patients. CMR was displayed at 4 ± 2 days after admission and mean left ventricular (LV) ejection fraction was 55 ± 10% (12 (36%) patients presented ejection fraction <55%). Late gadolinium enhancement (LGE) was presented in all patients, mostly subepicardial and involving 4 or more myocardial segments (mean 5 ± 3). Myocardial oedema was found in 25 (76%). After 9 ± 3 months all cases had persistence of LGE, although but less expressive, involving less myocardial segments (mean 3 ± 2). No one had myocardial edema. All patients, except one, presented LV ejection fraction recovery but systolic dysfunction persisted in 8% cases. The LV end-systolic and end-diastolic volumes and LV mass decreased. At 38-month clinical follow-up, only two suffered a second episode of acute myocarditis. No deaths, heart transplant or re-hospitalizations for other cardiac cause occurred.

Conclusion: In our population we found a high persistence of LGE in CMR follow-up studies after an acute myocarditis episode. Although the low rate of cardiovascular events, persistence of LGE had no impact on prognosis. Many doubts still exist and clinical implications of imaging findings must be clarified, to help us better identify patients with a poor prognosis due to a complicated course myocarditis.

CO-MORBIDITIES

P1489

Impact of body mass index on prognosis in systolic heart failure patients: moroccan profile

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Background: Higher body mass index (BMI) is associated with incident chronic heart failure but it is paradoxically associated with better prognosis.

The objective of the study was to analyze the relationship between body mass index and HF in a moroccan profil.

Methods: We enrolled 685 patients admitted to the therapeutic unit of chronic heart failure from 2006 to 2013 as follow: underweight (BMI < 18.5 kg/m², n=35), normal (18.5 ≤ BMI < 25, n=349), overweight (25 ≤ BMI < 30, n=200) and obese (BMI ≥ 30, n=101) and compared the results from their clinical data, laboratory tests and echocardiography.

Results: The prevalence of obesity and overweight in chronic heart were 15 and 29% respectively. Obese group had a higher prevalence of obesity-related comorbidity (hypertension: p=0.0001, diabetes mellitus :p=0.0001 and dyslipidemia: p=0.001).

Age, Ischemic heart disease, stroke attack, stage NYHA, heart rate, hospitalization rate for cardiac decompensation, left right ventricular systolic function did not differ among the groups. However male sex, anemia and diastolic dysfunction were higher in the underweight group than in the other groups (p < 0.0001 and p = 0.03 respectively).

Conclusion: High body mass index (overweight and obesity) was frequent in chronic heart failure and it was not predictor of cardiac decompensations and hospitalizations. Furthermore, lower BMI was associated with diastolic dysfunction.

P1490

Efficacy, safety and prognostic benefit of intravenous iron therapy in patients with heart failure due to left ventricular dysfunction

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Introduction: Deficit of iron deposits is associated with congestive heart failure (CHF), sometimes conditioning the functional status and prognosis of these patients. Several studies have shown the benefit of correcting this deficit with a very high safety profile. The aim of our study was to evaluate the clinical and laboratory efficacy of intravenous ferric carboxymaltose infusion in patients with CHF and deficit of iron deposits.

Methods: 52 patients that were being followed up in our CHF unit, with CHF, depressed ejection fraction, and absolute or relative deficit of iron deposits were

studied between June 2012 and April 2014. Intravenous iron therapy was administered to all patients in one or two doses. Deficit of iron deposits was defined as absolute if ferritin levels were less than 100 mcg/L, or relative, if ferritin levels were between 100 and 300 mcg/L, being the transferrin saturation (TSAT) less than 20%. Intravenous iron infusion was performed with ferric carboxymaltose, from 800 to 2000 mg, according to the calculated deficit of each patient. Iron deficit was calculated for each patient individually by the Ganzoni formula. Baseline characteristics of patients and analytical values of CBC and NT-proBNP were analyzed before and after the infusion, as well as clinical response measured by hospitalizations or emergency room visits due to acute decompensated CHF.

Results: The mean age of patients was 68.73 years, most frequently men (63.5%), with a mean follow-up of 11 months (11.05 +/- 3.95). Statistical significance ($p < 0.05$) was obtained for the statistical analysis of the mean values of hemoglobin (13.04 mg/dL vs 13.78 mg/dL), hematocrit (39.61 % vs 42.38%), iron (67.85 mg/dL vs 109.11 mg/dL), ferritin (79,65mg/dL vs 424.62 mg/dL) and TSAT (17.23% vs 33.64%), before and after the treatment. Mean value of NT-proBNP was 2229.47 +/- 3209.79 mg/dL before the treatment and 1648.66 +/- 2594.49 mg/dL after the treatment ($p = 0.037$). Reduced hospitalizations and emergency room visits due to acute decompensated CHF after receiving iron therapy was observed (50% vs 13.5%, $p < 0.005$). There were no complications associated with the infusion and all patients had good treatment tolerance.

Conclusions: 1. Intravenous iron therapy allowed the correction of iron deposits deficit in a safe and efficient way. 2. In the mean-term follow up, reduction in emergency room visits and hospitalizations due to acute decompensated CHF was observed.

P1491

Prevalence of iron, vitamin B12 and folate deficiencies in Heart Failure: does ejection fraction matter?

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Anemia is a frequent comorbidity in Heart Failure patients. Classically it was known to be related with inflammation and chronic disease. Current guidelines recommend evaluation and treatment of iron deficiency (ID), but there are no recommendations regarding vitamin B12 and folates. Little is known about these hematologic parameters regarding HF, specially those with preserved ejection fraction, with few studies showing that these values are low in only a minority of HF patients. Nevertheless HF patients are old, with multiple comorbidities and many dietary defaults, making them a risk population for deficiency anemia.

Objectives: To evaluate the prevalence of anemia caused by nutritional deficits in an HF Unit.

Methods: Prospective study of patients admitted consecutively admitted in a HF Unit over a period of one year. Anemia was diagnosed according to World Health's Organization criteria. ID was considered when ferritin <100 ng/ml (absolute ID) or 100-299 ng/ml and transferrin saturation <20% (functional ID) and vitamin B12 and folate deficit when its levels were below 200 pmol/L and 6.25 nmol/L, respectively.

Results: 202 patients were included; mean age was 74,95 ± 11,84 years, 30,2% (61) were male, with an ejection fraction of 57,9%. Anemia was found in 69,7%: 40,2 % absolute ID, 19,1% functional ID, 14,5% vitamin B12 deficiency and 2,7% folate deficiency. 13% had both ID and Vitamin B12 deficiency, 1,2% ID and folate deficiency.

Patients with Heart failure with Reduced Ejection Fraction (HF-REF) Vs HF with Preserved Ejection Fraction (HF-PEF) and ID Anemia: 18% Vs 31,4% ($p = 0,509$). Patients with HF-REF Vs HF-PEF and Vitamin B12 Deficiency: 4% Vs 10,7% ($p = 0,192$). Patients with HF-REF Vs HF-PEF and Folic acid Deficiency: 1,7% Vs 1,2% ($p = 0,302$).

Conclusion: In HF, the systolic ejection does not seem to affect the type of anemia. Anemia should be fully studied and treated accordingly in all HF patients.

P1492

Heart disease in patients with end-stage liver disease

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Background and Purpose: Involvement of the cardiovascular system in patients with end-stage liver disease (ESLD) is well recognized and may be seen in several scenarios in adult liver transplantation (LT) candidates. Patients with hepatopulmonary syndrome (HPS) have higher cardiorespiratory mortality than those without. Pre-operative assessment of the cardiac status of LT candidates is thus critically important for risk stratification and management. Cardiac imaging plays an integral

role in the assessment of LT candidates. The purpose of our study is to evaluate the presence of cardiac involvement and the prevalence of HPS in patients with ESLD previous to hepatic transplant.

Methods: A total of 115 chronic liver disease patients aged 48(SD 11) years fulfilled the criteria for this study and were subjected to clinical examination, laboratory investigations, and agitate saline contrast transthoracic echocardiography.

Results: Alcohol abuse was the main cause of liver disease (50%), followed by hepatitis C virus infection (26%). The prevalence of HPS was 17%, mild hypoxemia was observed in 74% of these patients and moderate in 24%. Left ventricle (LV) was dilated in 10% (ETDV 100 ml, SD 33) and LV hypertrophy (LVH) was found in 44%. LVEF was 69% (SD 6) and LV systolic dysfunction was observed in only 6%, however diastolic dysfunction was present in 76% of patients (type I 57% and type II in 19%) with elevated LV filling pressures in 8% of cases. Aortic calcification was present in 34% of patients and mitral calcification in 36%. Aortic stenosis was present in 6% (severe in 1 case and mild in the rest), aortic regurgitation in 11% (moderate in 1 case) and mitral regurgitation in 46% (all mild except for 3% moderates). Left atrium was enlarged in 57% of patients. RV was dilated in 21% of cases but RV systolic dysfunction was observed in only 2%. Systolic arterial pulmonary pressure was 32 mm HG (SD 7) with PHT in 24% of cases (mild in all patients). Pericardial effusion was present in 6% of patients and pleural effusion and free abdominal fluid in 5% of cases. Coronariography was performed in 32% of patients and significant coronary disease was found in a 35% of them.

Conclusions: The presence of cardiac involvement especially LVH, diastolic dysfunction and valvular calcification are common in patients with ESLD. Coronary disease is not uncommon in a selected group of these patients. Cardiac examination should be routine in order to evaluate the possible causes and repercussions of hepatic diseases besides the evaluation of HPS.

P1493

Impact of airflow limitation on COPD in chronic heart failure

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Purpose: To investigate prevalence, treatment and quality of life (QOL) of COPD in patients (pts) diagnosed with heart failure (HF).

Methods: 205 HF pts stable for >1 month, irrespective of LV ejection fraction, smoking status and age >50 years were included from our outpatient cardiology clinic. Patients performed a comprehensive lung function test, a six-minute walking test (6-MWT) and completed the Kansas City Cardiomyopathy Questionnaire (KCCQ). The BODE and ADO index, risk scores in COPD pts, were used.

Results: 33% fulfilled the criteria of significant COPD and 6% (n=13) had restrictive lung disease, the latter being excluded from further analysis. Based on the new COPD classification ABCD, 4% had severe COPD. Importantly, 43pts were undiagnosed with COPD and 8% used inhalation therapy without diagnosis of COPD. Pts with COPD had more complaints of dyspnea despite little difference in HF severity and similar comorbidities (table). KCCQ was significantly worse in the COPD group. The ADO - and BODE index was significantly different in both groups. Survival for COPD versus non-COPD pts did not differ ($P = 0.54$).

Conclusion: COPD is very common in unselected patients with HF, but often not diagnosed and many received treatment without being diagnosed with COPD. Presence of COPD seems to worsen dyspnea and negatively affects cardiac specific quality of life.

P1494

Prediction of poor left ventricle systolic function in obese patients with coronary heart disease

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Purpose: Obesity is an important risk factor for cardiometabolic diseases, including: coronary heart disease (CHD), diabetes, hypertension, and dyslipidemia. Therefore, poor left ventricle systolic function and heart failure due to ischemic heart disease is common among these patients. The aim of this study was to find parameters significant for prediction of poor systolic function in these patients.

Methods: A cohort study enrolled 77 obese patients, with body mass index (BMI) ≥ 25 kg/m², and coronary artery disease (44 males and 33 females) determined by previous coronary angiography. All patients underwent anamnesis, clinical examination, laboratory analyses, and transthoracic echocardiography. Poor systolic function was determined by ejection fraction $\leq 45\%$, estimated by transthoracic echocardiography. BMI ≥ 30 kg/m², and high waist circumference (hWC), > 88 cm for women, and > 102 cm for men, were parameters of significant obesity. Analyzed laboratory parameters were CRP and glycosylated hemoglobin (HgbA1c). Univariate and stepwise multivariate logistic regression were conducted

Table 61354. Baseline characteristics

	All (n=186)	NO-COPD (n=118)	COPD (n=68)	P-value
Age	76 [68-82]	76 [67-82]	76 [70-73]	0.55
Male sex	129 (70%)	78 (66%)	51 (75%)	0.25
LVEF, % Preserved EF	44 [32-54] 57 (31%)	46 [32-57] 40 (38%)	43 [30-50] 17 (27%)	0.11 0.18
Cause of HF CAD Dilated CM Hypertensive HD	91 (49%) 35 (19%) 33 (18%)	51 (43%) 25 (21%) 23 (20%)	40 (59%) 10 (15%) 10 (15%)	0.33
Co-morbidity Hypertension Diabetes mellitus Hypercholesterolemia	114 (61%) 49 (26%) 133 (72%)	77 (65%) 32 (27%) 86 (73%)	37 (54%) 17 (25%) 47 (69%)	0.16 0.86 0.62
Smoking status Non smoker Current smoker Former smoker	49 (26%) 22 (12%) 106 (57%)	42 (37%) 10 (9%) 61 (54%)	7 (11%) 12 (19%) 45 (70%)	0.001*
Symptoms NYHA I NYHA II NYHA III NYHA IV	47 (25%) 99 (53.2%) 38 (20%) 2 (1%)	38 (32%) 61 (52%) 18 (15%) 1 (1%)	9 (13%) 38 (56%) 20 (29%) 1 (2%)	0.014*
Clinical findings 6-MWT, m (n=141) Saturation (n=134) Systolic blood pressure	397 [318-460] 97 [96-98] 125 (±21)	402 [308-462] 98 [97-98] 129 (±21)	393 [318-442] 97 [96-98] 118 (±19)	0.68 0.005* <0.001*
QOL KCCQ score	78 (±20)	82 (±19)	73 (±21)	0.005*
Risk of mortality ADO score BODE score	4 [3-5] 1 [0-4]	4 [3-4] 0 [0-3]	4 [3-6] 2 [0-5]	0.001* 0.004*

CAD (coronary artery disease), CM (Cardiomyopathy) Frequency(%), Mean(±SD)and Median [IQR]

with Hosmer-Lemeshow goodness-of-fit statistics for model calibration and receiver operating characteristic (ROC) curve for model discrimination.

Results: There were 28.6% of patients with BMI ≥ 30 kg/m², and 61% with hWC. High level of HgbA1c was found in 52% pts; CRP level higher than 3 mg/L was found in 51% pts. Triple vessel coronary artery disease was found in 54.5% of pts and 64.5% of pts have had the diagnosis of previous myocardial infarction. Low ejection fraction was determined in 22 patients (29%). Among the analyzed parameters, triple vessel disease (odds ratio 0.245, 95% CI 0.079 to 0.758, $p=0,015$), previous myocardial infarction (odds ratio 0.204, 95% CI 0.054 to 0.770, $p=0,009$), and high level of HgbA1c (odds ratio 0.29, 95% CI 0.009 to 0.854, $p=0,019$) were significant predictors of low EF, using univariate logistic regression. Analyzing these parameters, after adjusting for confounding variables, using multivariate logistic regression model, significant predictors were: triple vessel disease (odds ratio 0.27, 95% CI 0.084 to 0.86, $p=0,027$), and previous myocardial infarction (odds ratio 0.32, 95% CI 0.058 to 0.877, $p=0,032$). The model discriminated well with a ROC of 0.722 (95% CI 0.606 to 0.838). Conclusion. It appears that previous myocardial infarction and triple vessel coronary artery disease are reliable independent predictors of poor left ventricle systolic function in obese patients with coronary heart disease.

P1495

Impact of heart diseases on the clinical outcome of patients suffering from COPD in comparison with a similar group without cardiopathy. 4 year-follow-up

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Aim: The prevalence of heart diseases (HD) was assessed in patients consecutively hospitalized due to an acute exacerbation of COPD from June 2009 to June 2010. Clinical outcome of both groups (with "G1" or without HD "G2") was analyzed at 4 years follow-up.

Material and Methods: prior cardiological history, electrocardiogram, echocardiogram and NTproBNP values were used for the initial identification of HD in COPD patients (recruiting phase). The following diagnoses were established in the Group 1 (G1): 30.0% Ischemic heart disease, 12.5% Hypertensive heart disease, 12, 5% Cor pulmonale, 10, 0% Non- valvular atrial fibrillation, 7.5% Tachyarrhythmias, 5, 0% Dilated cardiomyopathy, 5, 0% Hypertrophic cardiomyopathy. 17.5% Left ventricular systolic dysfunction of unknown etiology. A 4-year retrospective evaluation of both groups is presented.

Clinical outcome is defined by: 1. readmission due to COPD exacerbation. 2. readmission due to any cardiovascular cause. 3. global readmission. 4. global mortality. 5. ratio of hospitalizations in the year prior to death.

Results: 86 patients (mean age 71.83 \pm 9.3, (95 % men) were recruited and all of them were in GOLD stage III-IV. Group 1 (G1) enrolled 30 subjects (mean age 74,05) and group 2 (G2) 56, (mean age 71,02). At 4 year follow-up this comparative analysis about hospitalizations and mortality was obtained (Table 1)

Taking into account only mortality, and increased ratio of admissions was documented in the prior year in both groups; 4.40 in G1 and 2.66 in G2 group, but significantly higher in G1 ($p=0,017$).

Conclusions: Hospitalizations and mortality due to COPD exacerbation are high in patients in GOLD III-IV. In comparison, both are higher in patients with a coexistent heart disease.

Mortality is usually preceded by an increased number of hospitalizations in the previous year.

Comparative analysis

	G2 (N:56)	G1(N:30)	P
Readmission (COPD exacerbation) n° / %	34/60.7	23/76.6	ns
Readmission (cardiovascular cause) n° / %	7/12.5	7/23.3	ns
Global readmission n° / %	38/67.8	26/86.6	0.033
Exitus n° / %	15/26.8	16/53.3	0.003

P1496

Role of overnight pulse oximetry in heart failure patients

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Objective: To evaluate the efficacy of overnight pulse oximetry (PO) for detecting sleep pattern abnormalities in patients admitted because of decompensated Heart Failure (HF).

Methods: We included consecutive patients (pts) admitted in our Cardiology Ward from May 2013 to January 2014 because of decompensated HF. Inclusion criteria were: 1. not older than 85 years old, 2. Advanced HF without reversible causes, 3. not previously diagnosed of Sleep-Breathing Disorders (SBD). PO was performed to all pts regardless of their history of SBD. All pts in whom an Oxygen desaturation index (ODI)₁₂ was detected by PO were further evaluated with a polysomnography (PSG). Results were manually analyzed following the SEPAR Consensus guidelines.

Results: From 103 patients evaluated during this time, 35 fulfilled our study inclusion criteria, mean age 68 \pm 10.6. PO values were suggestive of SBD in 17 pts (48.5%). 4 patients (23.5%) were diagnosed of Cheyne-Stokes by PSG, 9 (53%) presented Sleep Apnea/Hypopnea Syndrome (SAHS) (8 severe and 1 moderate) and 4 pts (23.5%) had both Chronic Obstructive Pulmonary Disease and SAHS. There were no statistically significant difference regarding either

age (69.41 ± 10.5 vs 69.57 ± 10.7 ; $p = 0.553$) or Epworth sleepiness Scale (8.3 ± 4.7 vs 5.20 ± 5.02 ; $p = 0.31$) among pts with and without SAHS. However we found statistically significant difference in their overnight mean heart rate (70.5 ± 11.81 VS 60.19 ± 13.76 P 0,05)

Conclusions: In patients admitted because of decompensated Heart Failure we found abnormal PO values in 48,5% of them. These patients could be later specifically diagnosed by PSG of SDB and appropriately treated. PO is a very useful tool for Sleep-Breathing Disorders screening in patients with decompensated Heart Failure.

P1497

Polypathology and heart failure in a cardiology's hospitalization unit: influence of comorbidity on the prognosis

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Purpose: The presence of comorbidities is very common in patients hospitalized for heart failure (HF), making more difficult the clinical management and being associated with poor prognosis. We conducted this study in a Cardiology's Hospitalization Unit in order to know the prevalence and type of comorbidities, as well as their influence on these patients prognosis.

Methods: We studied consecutively all the patients admitted in the Cardiology Department of our Hospital during 2012, recording their comorbidities, admission reason, hospital stay, in-hospital mortality and prognostic index of Charlson. Furthermore, we recorded readmissions and mortality during follow-up on polypathological patients (two or more chronic conditions).

Results: Of the 1033 patients (67 years, 35% women), 303 were admitted because of decompensated HF (29.3%). These patients had a significantly higher mean age (71 vs 65 , $p < 0.001$), higher percentage of women (47.2% vs 30.1% , $p < 0.001$) and higher prevalence of depressed LVEF (48.8% vs 31% , $p < 0.001$). As for comorbidities, they had higher prevalence of previous cardiopathy (71% vs 36% , $p < 0.001$), higher prevalence of chronic kidney disease (CKD) (30.4% vs 11.8% , $p < 0.001$), higher prevalence of COPD (21.1% vs 11.4% , $p < 0.001$) and higher prevalence of anemia (8.6% vs 1.8% , $p < 0.001$), being higher the number of polypathological patients (51.5% vs 18.9% , $p < 0.001$) and having a higher Charlson index (5.3 vs 3.7 , $p < 0.001$). In addition, this group had higher in-hospital mortality (4% vs 0.8% , $p = 0.001$) and longer hospital stay (9.4 vs 5.7 days, $p < 0.001$). Polypathological patients had higher readmission rate (60.8% vs 41% , $p = 0.002$) and lower event-free survival (death and/or readmission) (36% vs 53% , $p = 0.005$) at 12 months follow-up. The CKD was identified as an independently associated factor of one-year mortality (HR 2.53, 95%CI: 1.19-5.39, $p = 0.016$), and CKD, anemia and chronic hepatopathy were independent predictors of one-year readmissions (HR 1.93, 95% CI: 1.161-3.218, $p = 0.011$; HR 2.6, 95%CI: 1.403-4.846, $p = 0.002$; HR 6.25, 95%CI: 1.686-23.185, $p = 0.006$; respectively).

Conclusions: 1. Patients admitted because of HF have high prevalence of comorbidities and a high percentage of them are polypathological patients. 2. Patients admitted because HF had longer hospital stay and higher in-hospital mortality. 3. Polypathological patients had higher readmissions rate and lower event-free survival at 12 months follow-up. 4. The CKD was identified as an independently associated factor of one-year mortality, and CKD, anemia and chronic hepatopathy were independent predictors of one-year readmissions.

P1498

Chronic alcoholism as a cause and co-morbidity in heart failure

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Introduction: Chronic alcohol intake can lead to cardiac muscle damage resulting in alcohol-induced cardiac muscle diseases, even heart failure (HF). Excessive ethanol intake is reported in 3% to 40% of patients with dilated (alcoholic) cardiomyopathy. Oxidative stress, myocyte apoptosis, sympathetic system activation are some of the adverse effects of ethanol. Systematic reviews and meta-analyses have not uniformly addressed associations between alcohol use and morbidity and mortality from cardiovascular diseases.

Purpose: The goal of our study was to determine the presence of alcoholism as comorbidity in patients admitted to ICU due to acute decompensation of chronic heart failure and its impact on prognosis.

Results: During 3 months we included in our study 201 consecutive patients; average age was 71.55 ± 10.35 years and 60.7% were male. The average duration of HF was 1.69 ± 1.13 years. In 29.9% of patients the cause of HF was coronary artery disease, in 27.9% dilated cardiomyopathy, in 23.9% arterial hypertension and in 18.4% it was valvular disease. 11 patients (5.5%) had history of chronic alcohol abuse (a daily consumption of ethanol > 80 g in the previous 5 years with

the average duration of 10.7 years) and all were male. They stopped alcohol intake after inclusion in the study. Three (27.3%) of them were in NYHA class II, 6 (54.5%) were in NYHA class III and 2 (18.2%) were in NYHA class IV. The average left ventricle ejection fraction (LVEF) in patients with chronic alcoholism was 29.3% while in other patients it was significantly higher 37.8% ($F = 4.131$, $p = 0.043$). During 1 year of follow up 42.8% of patients died and 5% of them had history of chronic alcoholism. In binary logistic regression analysis, alcoholism had no significant influence on mortality during the first 6 months after inclusion in the study. However, mortality from 6th to 12 months of follow was influenced by low LVEF, female gender, number of co-morbidities, presence of chronic obstructive pulmonary disease, chronic renal failure and alcoholism [OR = 0.03, CI 95% (0.002-0.405), $p = 0.008$].

Conclusion: Chronic alcoholism was presumably a cause of heart failure in 5.5% of our patients. They had lower LVEF than other patients and had higher mortality risk during one year of follow up. Excessive and prolonged alcohol intake leads to alcoholic cardiomyopathy in a minority of alcohol abusers. However, alcoholism is a widespread medical problem, and therefore alcohol abuse may well represent the major cause of dilated cardiomyopathy in Western countries. More attention should be given to its prevention.

P1499

Sleep apnea treatment during cardiac rehabilitation can improve heart failure prognosis? SATELIT-HF

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Background: Sleep-disordered breathing (SDB) is commonly in chronic heart failure (CHF) patients. Exercise training (ET) improves exercise tolerance and reduces cardiac decompensations in CHF population. Otherwise, ventilation therapy (VT) improves prognosis and exercise capacity in CHF patients with SDB. However, the effect of the combination therapy: ET and VT is still unexplored.

The aim of our study is to evaluate the effects on hemodynamic status (cardiac decompensations) of ET and VT in stable CHF patients referred to cardiac rehabilitation (CR).

Methods: We included 118 stable CHF patients with an apnea-hypopnea index (AHI) $> 15/h$ diagnosed by polygraphy. They were randomized into exercise training (ET group n=58) or combined exercise and ventilation (ET+VT group n=60). The follow up period was the 8 weeks during which 20 exercise training sessions were scheduled. Severe episodes of cardiac decompensations were recorded.

Results: The mean age was 62.6 ± 10.3 years, 89 % were males, 50 % NYHA class II and 50 % in class III, mean LVEF was 30 %. 40 % and 60% of patients had respectively obstructive and central and/or mixed apneas, with a mean AHI $34.4 \pm 14.3/h$. Patients of ET+VT group had significantly fewer acute cardiovascular events than those of ET group (2/60 vs. 7/58 ; 3.3 % vs. 15.5%, $p < 0.05$).

Conclusion: Ventilation therapy combined with ET in severe CHF patients seems to reinforce benefits of ET alone. Screening of SDB in CR could be proposed in order to optimize the global management of the heart disease.

P1500

Correlation between diastolic left ventricular heart fonction and sleep apnea syndrome in reduced ejection fraction heart failure population

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Introduction: Several previous studies demonstrated a strong prevalence of the syndrome of sleep apnea in reduced ejection fraction heart failure population. The prevalence of this association was estimated between 47% and 76 %. Many factors were incriminated as favorisants this association. Some studies were interested in the ventricular dysfunction in a general way especially to the central SAS.

The aim of our study: Determine if the diastolic dysfunction is a risk factor for development of the SAS in reduced EF

Materiels et methods: We have realized a cross sectionnal study of our patients followed in the heart failure warm by regular consultations and echocardiography. All patient underwent a polysomnography and they separated into two groups .group 1 heart failure with sleep apnee syndrome, group 2 heart failure without sleep apnea syndrome. After PSG examination, LV functions were assessed by using the conventional and tissue Doppler echocardiographic methods

Resultats: The mean age was similar between the groups. 63 ± 5.3 years old. The ratio of male patients was higher in group 1 % with a sex ratio of 2.20.

The diabetes and the HTA are respectively found at 57 % (n=20) and 48 % (n=17) and higher in group 1

The ischemic etiology of the cardiac insufficiency is found in 52 % (n=18) of the cases against 48 % (n=17) of non ischemic. On the functional class, 50% of patients are in class III of the NYHA, 26 % class IV and 23 % class II.

The cardiac ultrasound was realized at all the patients, the average of EF is $33 \pm 4.2\%$

The SAS is found at 73 % (n=25 =group 1) of the cases. Central sleep (CSAS) was noted in 63 % (n=16) against 37 % (n=9) for Obstructive sleep apnea (OSAS).

The severity of the cardiac heart failure estimated by the average of ejection fraction was not significantly associated with the SAS.

the average EF is 32 % in the group 1 with SAS and 34 % in the group 2 (p=0.06). However, the diastolic dysfunction is associated in a significant way with the group 1 (with SAS) with 78 % Vs 16 % in the group without SAS (p 0.001).

Ratio of early to late transmitral diastolic velocities was lower in group 1 (p=0.01), indicating that impairment of diastolic function was more frequent in OSAS.

Conclusion: According to the results of this study, it has proved that the diastolic dysfunction associated would favor the presence of the SAS in reduced ejection fraction heart failure population. Of more the diastolic dysfunction of type I would favor the obstructive SAS and the type III of dysastolic dysfunction would favor the central SAS.

P1501

Phenotypes of acute kidney injury in patients with non-ST-elevation acute coronary syndrome and non-invasive strategy

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Objective: worsening of renal function occurs frequently in patients with acute coronary syndromes (ACS) and is associated with adverse short- and long-term outcomes. The aim of the study was to evaluate the incidence, phenotypes and prognostic value of cardiorenal interrelations in patients with non-ST-elevation acute coronary syndrome (NSTE-ACS) with conservative strategy.

Methods: 288 patients (36% male, 72 ± 12 years (M \pm SD), body mass index $28.0-4.8$ kg/m², arterial hypertension 92%, previous myocardial infarction (MI) 42%, diabetes mellitus (DM) 23%, heart failure 36%, atrial fibrillation 23%, baseline serum creatinine (SCr) $108-55$ -mol/l, GFRCKD-EPI $61-23$ ml/min/1.73 m²) with NSTE-ACS were examined. Based on ESC Guidelines NSTE-ACS was qualified as NSTEMI or unstable angina (UA) in 186(64.5%)/102(35.5%) patients. Chronic kidney disease (CKD) and acute kidney injury (AKI) were diagnosed according to KDIGO 2012 Guidelines. Mann-Whitney test was performed. P <0.05 was considered statistically significant.

Results: cardiorenal interrelations were found in 130 (45%) patients. CKD was diagnosed in 46 (16%) patients: CKD with/ without AKI - in 21(46%)/26(54%). AKI occurred in 103 (36%) patients, stage 1/2/3 - in 73/14/13% of cases respectively. 82% of AKI developed in first 48 hours. The following incidence of different phenotypes of AKI was revealed: transient/ persistent 54/46%, AKI de novo/AKI on CKD 80/20%, community-acquired/ hospital-acquired AKI 46/54 %. Patients with NSTEMI versus UA had higher incidence of AKI: 46 vs 17% (p < 0.01). Patients with NSTE-ACS with versus without AKI had worse prognosis: higher risk of recurrent MI 11 vs 2% (p=0.0001), in-hospital mortality 17 vs 5% (p=0.003).

Conclusions: Cardiorenal syndromes in patients with NSTE-ACS and non-invasive strategy were found in 45%. AKI was revealed in 36% patients, CKD - in 46 (16%) pts. AKI predominantly developed in first 48 hours and was stage 1 of severity. AKI had negative impact on outcomes and was associated with increased rate of recurrent MI and in-hospital mortality.

P1502

Risk factors and prognostic value of contrast-induced acute kidney injury in patients with delayed percutaneous coronary intervention

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Objective: Contrast-induced acute kidney injury (CI-AKI) is a well-known serious complication of percutaneous coronary intervention (PCI) associated with increased morbidity and mortality. The aim of the study was to evaluate the incidence, predictors and outcomes of CI-AKI in patients with unstable angina pectoris/non-ST-segment elevation myocardial infarction (UAP/NSTEMI) and delayed PCI.

Methods: 236 patients with UAP/NSTEMI and delayed PCI (158 male, 69 ± 14 years (M \pm SD), arterial hypertension 94%, previous MI 36%, diabetes mellitus (DM) 22%, known chronic kidney disease 15%, anemia 15%, heart failure 58%, left ventricular ejection fraction $44 \pm 6\%$) were examined. CI-AKI was defined using 2012 KDIGO Guidelines. Mann-Whitney test and multivariate logistic regression analysis were performed. P <0.05 was considered statistically significant.

Results: 15% of patients developed CI-AKI. Stages 1 and 2 of CI-AKI were found in 71 and 29% of cases accordingly. CI-AKI developed in 61% of cases in first 48 hours after PCI. Patients with versus without CI-AKI had higher baseline serum creatinine (104 ± 32 vs 98 ± 24 μ mol/l, p < 0.05), plasma glucose (8.4 ± 3.9 vs 6.7 ± 2.7 mmol/l, p < 0.05), higher rate of DM (39 vs 19.5%, p < 0.05), anemia (28 vs 12.5%, p < 0.05), stroke (44 vs 20%, p < 0.05), higher rate of therapy with nephrotoxic antibiotics (11 vs 3.5%, p < 0.05), lower rate of postprocedural TIMI3 (83 vs 96 %,

p < 0.05), higher rate of main left coronary artery disease (59 vs 30%, p < 0.001). Main independent predictors of CI-AKI were main left coronary artery disease (odds ratio (OR) 4.45; 95% confidence interval (CI) 1.89-10.50; p < 0.001), therapy with nephrotoxic antibiotics (OR 4.04; 95% CI 1.08-15.12; p < 0.05), stroke (OR 3.20; 95% CI 1.52-6.73; p < 0.05), anemia (OR 2.69; 95% CI 1.16-6.24; p < 0.05), DM (OR 2.63; 95% CI 1.23-5.59; p < 0.05). Patients with CI-AKI had higher risk of hospital mortality (11 vs 1.5%, p < 0.001), 30-days mortality (12 vs 4%, p < 0.05) and similar rate of 6 months rehospitalizations (74 vs 58%, p > 0.05).

Conclusions: CI-AKI in patients with UAP/NSTEMI and delayed PCI developed in 15% of cases, predominantly in first 48 hours after PCI. CI-AKI was associated with higher rate of comorbidities (DM, anemia, stroke), therapy with nephrotoxic drugs, higher baseline serum creatinine and plasma glucose, main left coronary artery disease, lower rate of postprocedural TIMI3. CI-AKI had negative impact on hospital mortality, 30-days mortality.

P1503

Incidence, predictors and outcomes of contrast-induced acute kidney injury in patients undergoing primary percutaneous coronary intervention

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Objective: Patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI) are at high risk of contrast-induced acute kidney injury (CI-AKI), a complication that negatively affects outcomes. The aim of the study was to evaluate the incidence, predictors and outcomes of CI-AKI in patients with STEMI and primary PCI.

Methods: 216 patients with STEMI and primary PCI (143 male, 64 ± 13 years (M \pm SD), arterial hypertension 90%, previous myocardial infarction 27%, diabetes mellitus 21%, known chronic kidney disease (CKD) 7%, anemia 14%, heart failure 62%, left ventricular ejection fraction (LV EF) $44 \pm 15\%$) were examined. CI-AKI was defined using 2012 KDIGO Guidelines. Mann-Whitney test and multivariate logistic regression analysis were performed. P <0.05 was considered statistically significant.

Results: 20% of patients developed CI-AKI. Stages 1 and 2 of CI-AKI were found in 77 and 33% of cases accordingly. CI-AKI developed in 66% of cases in first 48 hours after PCI. Patients with versus without CI-AKI were older (69 ± 13 vs 63 ± 12 years, p < 0.05), had higher baseline serum creatinine (104 ± 31 vs 87 ± 22 mmol/l, p < 0.001), lower LV EF (37 ± 10 vs $41 \pm 14\%$, p < 0.05), higher rate of CKD (21 vs 3.5%, p < 0.001) and higher rate of therapy with nephrotoxic antibiotics (19 vs 3.5%, p < 0.01), loop diuretics (72 vs 39%, p < 0.01), mineralocorticoid receptor antagonists (56 vs 37%, p < 0.05), higher contrast volume (CV) (282 ± 94 vs 236 ± 85 ml, p < 0.05), contrast media volume/estimated glomerular filtration rate ratio (CV/eGFR) (4.02 ± 2.15 vs 2.32 ± 1.08 , p < 0.05), higher rate of multivessel coronary damage (84 vs 59%, p < 0.05). Main predictors of CI-AKI were CKD (odds ratio (OR) 7.37; 95% confidence interval (CI) 2.46-22.06; p < 0.001), therapy with nephrotoxic antibiotics (OR 6.36; 95% CI 2.08-19.49; p < 0.05), loop diuretics (OR 3.98; 95% CI 1.92-8.30; p < 0.01), multivessel coronary damage (OR 3.58; 95% CI 1.51-8.49; p < 0.05), therapy with mineralocorticoid receptor antagonists (OR 2.15; 95% CI 1.09-4.23; p < 0.05). Patients with CI-AKI had higher risk of 30-days mortality (10 vs 3%, p < 0.05) and similar rate of 6 months rehospitalizations (66 vs 46%, p > 0.05).

Conclusions: CI-AKI in patients with STEMI and primary PCI developed in 20% of cases, predominantly in first 48 hours after PCI. CI-AKI was associated with CKD, therapy with nephrotoxic drugs, multivessel coronary damage. CI-AKI had negative impact on 30-days mortality.

P1504

Filtration renal function depending on arterial stiffness in patients with chronic heart failure and preserved left ventricle ejection fraction

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Aim: to evaluate filtration renal function in patients with ischemic chronic heart failure (CHF) and preserved left ventricle ejection fraction (LV EF) depending on CAV1, which is the marker of genuine arterial stiffness and which is detected via sphygmopletismography on VaSera VS-1000 Methods and materials: 60 CHF patients with preserved LV EF and stable angina were examined. Patients were divided into two groups based on CAV1. The 1st group consisted of 40 patients with normal CAV1 < 9. The 2nd group was of 20 patients with CAV1 > 9. Average age was $62,16 \pm 4,39$ yrs. Average FC of stable angina was $2,22 \pm 0,43$, average CHF FC was $2,33 \pm 0,49$. To evaluate renal filtration function serum creatinine and eGFR (MDRD) were used. Also, albumin and creatinine and their ratio in urine were estimated.

Results: patients in groups did not differ in risk factors, comorbidities, CAD and CHF therapy. In 2nd group FC of CHF was reliably higher $2,57 \pm 0,53$ vs $2,20 \pm 0,42$ m/c (p=0,048). Also, FC of stable angina was higher in 2nd group: $2,50 \pm 0,50$ vs $2,15 \pm 0,24$ (p=0,014). Patients in groups differed in creatinine and eGFR (MDRD)

reliably: $75,29 \pm 15,8$ vs $88,67 \pm 14,99$ $\mu\text{mole/L}$ ($p=0,024$) and $75,37 \pm 18,69$ vs $61,72 \pm 10,88$ mL/min/1.73m^2 ($p=0,048$), respectively. There was no significant difference between the groups in albumin and creatinine in urine, but in urinal albumin/creatinine ratio there was reliable difference ($p=0,015$). There were direct reliable correlations between CAV1 and serum creatinine ($r=0,50$; $p=0,027$) and between CAV1 and urine albumin/creatinine ratio ($r=0,61$; $p=0,045$). Indirect reliable correlation between CAV1 and eGFR ($r=-0,46$; $p=0,047$) was also estimated.

Conclusions: in patients with ischemic CHF and preserved LV EF filtration renal function depends on not only severity of CHF and stable angina, but also on genuine arterial stiffness according to CAV1.

P1505

Peculiarities of arterial wall remodeling depending on cystatin C in patients with chronic heart failure and permanent atrial fibrillation

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Aim: to estimate peculiarities of arterial wall remodeling depending on Cystatin C in patients with ischemic chronic heart failure (CHF) and permanent atrial fibrillation (AF).

Methods and materials: 60 ischemic CHF and permanent AF patients were examined. Average age was $57,02 \pm 5,07$ yrs. Average FC of stable angina was $2,51 \pm 0,38$, average CHF FC was $2,61 \pm 0,26$. Sphygmoplethysmography using VaSera VS-1000 (Fucuda, Japan) was performed to evaluate shock-absorbing and conductive functions of arterial wall. To evaluate collagen matrix status TIMP-1 was analysed. All patients were divided into 2 groups based on cystatin C level. The 1st group included 25 patients with normal cystatin C level (average mean $783,2 \pm 86,5$ ng/mL). The 2nd group consisted of 35 patients with elevated cystatin C (average mean $2068,7 \pm 223,4$ ng/mL), ($p<0,001$).

Results: Carotid-femoral pulse wave velocity (PWVcf) appeared to be significantly higher in the patients of the 1st group that is $11,07 \pm 7,06$ m/s compared to the patients of the first group that is $-5,84 \pm 2,51$ m/s ($p=0,036$). Between the groups significant differences in terms of CAV1 ($p=0,028$) were detected. The patients of the first and of the second groups differed significantly in terms of aorta and carotid PWV: $6,72 \pm 3,02$ vs $9,31 \pm 2,07$ m/s ($p=0,013$) and $0,51 \pm 0,18$ vs $0,72 \pm 0,49$ m/s ($p=0,023$) respectively. Augmentation indices C-AI and R-AI in patients of the 2nd group made up $1,52 \pm 0,78$ and $1,35 \pm 0,27$ respectively which is significantly higher than in patients of the 1st group - $1,06 \pm 0,51$ and $1,16 \pm 0,17$ ($p=0,020$ and $p<0,001$ respectively). Also, reliable direct correlations between cystatin C and TIMP-1 ($r=0,67$, $p=0,046$), cystatin C and CAV1 ($r=0,76$, $p=0,032$), cystatin C and C-AI ($r=0,63$, $p=0,021$), cystatin C and C-PWV ($r=0,54$, $p=0,017$) were revealed.

Conclusions: in ischemic CHF patients with permanent atrial fibrillation there unfavorable changes in collagen matrix elevates as well as increase in arterial wall stiffness and decrease of its elasticity along with decrease of renal filtration function.

P1506

N-terminal pro B-type natriuretic peptide and emergency bedside ultrasonography in patients with chronic kidney disease, hospitalized for acute decompensated heart failure

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Introduction: A large number of patients hospitalized for acute decompensated heart failure have some degree of kidney dysfunction.

Purpose: To evaluate in-hospital characteristics of chronic kidney disease (CKD) in patients with acute decompensated heart failure in Internal Medicine Department.

Methods: A retrospective study was conducted on 112 patients admitted in Internal Medicine Department of an emergency clinical hospital for acute decompensated heart failure, from July to December 2014. NT pro-BNP, BUN, serum creatinine and eGFR using MDRD equation were evaluated. Emergency bedside transthoracic echocardiography and abdominal ultrasonography were performed. Serum sodium and potassium levels were monitored.

Results: 64% of patients were male (72) and 36 % were female (40). Mean age was 77.86. CKD was presented in 46.42% of patients (52): stage II in 5.7%, stage III in 69.23%, stage IV in 19.23% and stage V in 7.6% of patients. Lower left ventricular ejection fraction (LVEF<45%) was measured by Simpson method on transthoracic echocardiography in 82.69% of cases. Small kidneys were seen at abdominal ultrasonography in 78.84% of patients. Worsening renal function in-hospital occurred in 28.84% of patients. Treatment with ACE-inhibitors, Angiotensin II receptor blockers, β -blockers, aldosterone antagonists, loop diuretics, IV inotropes were administered in the first day of admission according to LVEF and ultrasonographic aspect of the kidney in emergency bedside ultrasound. In-hospital length of stay was shorter (mean 6.7 day) with clinical improvement at discharge.

Conclusions: Kidney dysfunction was often observed in patients hospitalized for

acute decompensated heart failure. Emergency bedside ultrasound improved treatment schedule, in-hospital length of stay and correlated with NT pro-BNP and eGFR-MDRD.

P1507

Worsening renal function in patients with acute decompensated heart failure

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Purpose: The aim of the study was to evaluate prevalence, predictors and prognostic significance of worsening renal function (WRF) in patients with acute decompensated heart failure (ADHF).

Methods: In our retrospective analysis we enrolled 100 consecutive patients (mean age: 65 ± 13.2 years; 37% women) hospitalized for ADHF. WRF was defined as an increase of serum creatinine level $\geq 0,3$ mg/dl above the admission value. Medical history, treatment administered during hospitalization, clinical and laboratory parameters were compared between patients with and without WRF. Prognostic measures including all-cause mortality, rehospitalization for cardiovascular causes and combined endpoint consisted of death and rehospitalization were collected 1- and 3-years after the date of discharge.

Results: Worsening renal function was observed in 23% of the study population (mean age: 69 ± 11.1 years; 43.5% women). Individuals with WRF in comparison to those without WRF were more likely to have preexisting chronic kidney disease (39.1% vs. 15.6%, $p=0,02$), prior percutaneous coronary intervention (65.2% vs. 35.1%, $p=0,01$), diabetes mellitus (52.2% vs. 29.9%, $p=0,049$), admission systolic blood pressure ≥ 160 mmHg (34.8% vs. 13.0%, $p=0,02$) and received higher mean daily intravenous dose of furosemide during first three days of hospitalization (85.9 ± 57.4 mg/day vs. 65.8 ± 63.3 mg/day, $p=0,048$). Patients who experienced WRF had significantly higher serum creatinine level and lower value of eGFR on the first three days and discharge day of hospitalization. Also the peak and discharge value of BUN were significantly higher in group with WRF. Predictors of WRF were prior percutaneous coronary intervention (OR 5.20; 95%CI 1.66-16.31; $p=0,004$), admission systolic blood pressure ≥ 160 mmHg (OR 4.92, 95%CI 1.37-17.64; $p=0,01$), preexisting chronic kidney disease (OR 4.25; 95%CI 1.29-14.05; $p=0,02$). WRF was not associated with greater risk of mortality and rehospitalization at 1- and 3- years after discharge. Furthermore in Kaplan-Meier analysis event-free survival (rehospitalization, death and combined endpoint) at 1 and 3 years after discharge was similar in patients with and without WRF.

Conclusion: WRF is frequent finding in patients with ADHF. Preexisting chronic kidney disease, prior percutaneous coronary intervention, admission SBP ≥ 160 mmHg and intravenous dosage of furosemide are the risk factors for development of WRF. Occurrence of WRF during hospitalization for ADHF was not associated with adverse prognosis including rehospitalization for cardiovascular causes and all- cause mortality.

P1508

Hemodialysis and outcome in patients with heart failure and chronic kidney disease

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Purpose: Concurrent cardiac and renal disease is associated with increased mortality and morbidity in heart failure patients. Most of the studies concerning cardio-renal syndromes have omitted hemodialysis patients from their research. We wanted to investigate the impact of early hemodialysis treatment of patients with cardio-renal syndrome on mortality and hospital readmission.

Methods: We retrospectively evaluated all patients with cardio-renal syndrome 2 or 4 whom we treated with life-long hemodialysis because of deteriorating kidney function, between July 1st 2004 and Jan 1st 2015 (91% of patients started hemodialysis after Sept 2007). Heart failure was diagnosed according to ESC guidelines and chronic kidney disease was diagnosed according to K/DOQI guidelines. The primary outcomes were all-cause mortality and hospital readmission 1 year after hemodialysis.

Results: We evaluated 67 patients (36 (54%) men, mean age 72.9 ± 11.1 years) who started hemodialysis because of worsening cardio-renal syndrome (baseline NT-proBNP 1954 ± 1582 pg/ml, creatinine 411 ± 197 $\mu\text{mol/l}$, LVEF 49.4 ± 18.6 %). All were NYHA IV functional class when starting dialysis, with main heart failure etiologies being arterial hypertension (50.7 %), coronary artery disease (14.9 %), concomitant arterial hypertension and coronary artery disease (20.9%) and valvular disease (4.5 %). Only 10 patients (14.9 %) were readmitted in the first year after dialysis because of worsening heart failure. Hospital readmission rate due to heart failure decreased after the start of hemodialysis (1 year before dialysis vs. 1 year after dialysis: 0.79 ± 1.32 vs. 0.22 ± 0.65 hospitalizations per year, $p=0,001$) together with the duration of annual hospital stay (1 year before dialysis vs. 1 year after dialysis:

11.4 ± 21.4 vs. 3.7 ± 10.4 days, $p = 0.011$). One-, two-, three-, four- and five-year survival for our patients was 81 %, 61 %, 52 %, 47 % and 39 %, respectively. These survival rates are higher than those of NYHA IV functional class documented in the literature.

Conclusions: Cardio-renal patients treated with hemodialysis have good survival rates compared to general NYHA IV functional class patients. Hospital readmission rate and the number of days hospitalized due to heart failure are lower in the first year after dialysis than prior to it.

CYTOKINES AND INFLAMMATION

P1509

Distribution of leukocyte populations is affected by cardiac resynchronisation therapy

The study was supported by funds from the Leading National Research Centre - Medical University of Białystok K Kaminski¹; K Ptaszynska Kopczynska¹; M Marcinkiewicz Siemion¹; P Singh²; U Radzikowska²; M Rusak³; A Lisowska¹; M Witkowski¹; WJ Musial¹; M Moniuszko²

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Chronic heart failure with reduced ejection fraction (CHF-REF) is characterized by enhanced inflammatory and abnormal immune response. Deeper understanding of the immune processes in CHF-REF is crucial for development of innovative treatment strategies. Cardiac resynchronisation therapy (CRT) created a promise of reversal of CHF symptoms. Investigations of changes of immune response before and after CRT implantation may improve understanding of the processes responsible for development and progression of heart failure. The aim of the study was to analyze the changes of crucial immunomodulatory subpopulations of peripheral blood mononuclear leukocytes: monocytes, Th17 and Treg lymphocytes.

The study enrolled 50 stable CHF-REF patients, NYHA class II-III, EF <35%, and 45 patients without CHF but with similar comorbidities profile, matched for age and sex. All were on optimal medical therapy for at least 3 months and had indications for CRT listed in current ESC CHF guidelines. Patients underwent CRT device implantation and were controlled after 6 months later. All subjects underwent transthoracic echocardiography and venous blood tests. The frequencies of particular subpopulations of monocytes, Th17 and Treg lymphocytes were established using flow cytometry with antibodies against CD14, CD16, CD161, CD 25, CD210 and CD127 respectively.

We were able to show that initially CHF patients had more classical (CD14+CD16-) monocytes in 1 -1 as compared to controls (399 ± 125 vs 288 ± 76 $p = 0.028$). Moreover, they presented lower frequency of Th17 lymphocytes (14.6% 7.1-43.7% IQR vs 41 % 11.6-49.4% IQR $p = 0.02$). In contrast to previous reports of other authors we did not find differences in the number of Treg lymphocytes. Six months after the CRT device implantation the numbers of monocytes from intermediate (CD14+CD16+) and non-classical (CD14++CD16++) subpopulations (by 26% and 23 % respectively $p < 0.05$ in both cases) increased resembling now the distribution of monocyte subpopulations in healthy controls. This phenomenon was observed only in patients with positive clinical response, whereas there was no change in monocytic subpopulations of patients whose clinical status did not improve. No significant change was observed in the frequencies of Th17 and Treg lymphocytes 6 months after CRT.

Our data indicate that CHF is associated with changed distribution of immunomodulatory subpopulations of lymphocytes and monocytes. Moreover, positive clinical response to CRT normalizes composition of monocytic subpopulations in CHF patients, while having no effect on Th17 and Treg lymphocytes.

P1510

IL-10 concentration changes in chronic heart failure patients treated with cardiac resynchronization therapy

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Cardiac resynchronization therapy (CRT) is an additional treatment to pharmacotherapy and is aimed at abolition of heart asynchrony. Progression and therapeutic success of chronic heart failure (CHF) patients is strongly associated with inflammatory response. The aim of the study was to evaluate the influence of CRT treatment on IL-10 concentration in patients with heart failure treated with CRT.

We prospectively studied 26 CHF patients on optimal medical therapy for at

least 3 months, treated with CRT (91.7%-male) and 18 comorbidities matched (CM) controls - without history of HF (66.7%-male). Analysis included parameters commonly used in CHF patients monitoring: NYHA class, left ventricular ejection fraction (LVEF), 6 minute walk test distance (6MWT), cardiopulmonary exercise testing parameters: peak oxygen uptake (VO2peak), ventilation-to-carbon dioxide output slope (VE/VO2 slope) and concentrations of brain natriuretic peptide (BNP), C-reactive protein (CRP). Evaluation was performed before and after 6 months (6M) of CRT. Serum concentrations of IL-10 were measured by ELISA method.

CHF and CM groups were comparable in respect of mean age (63.7 ± 10.9 vs 57.7 ± 13.5 years) and body mass index (28.7 ± 3.9 vs 27.7 ± 3.1 kg/m²). CHF population before device implantation and CM control differ with respect to BNP concentration (349.3 ± 509.4 vs 31.9 ± 27 pg/ml, $p = 0.011$), LVEF (22.5 ± 5.4 vs 63.5 ± 3.4%, $p < 0.001$), 6MWT (381.6 ± 101.5 vs 518.6 ± 93.6m, $p < 0.001$), VE/VO2 slope (31.5 ± 7.7 vs 25.7 ± 3.2, $p = 0.005$), VO2 peak (16.6 ± 7 vs 26 ± 5.8 ml/kg/min, $p < 0.001$). After 6M of CRT three parameters significantly increased: IL-10 concentration (1.2 ± 0.4 vs 2.1 ± 0.7 ng/ml, $p < 0.001$), LVEF (22.5 ± 5.4 vs 31.3 ± 8.1%, $p < 0.001$) and 6MWT (381.6 ± 101.5 vs 412.5 ± 104.7m, $p = 0.011$), but they remained still significantly lower in comparison with CM control (3.5 ± 1.2 ng/ml, $p < 0.001$, 63.5 ± 3.4%, $p < 0.001$, 518.6 ± 93.6m, $p = 0.001$). There was no significant difference in mean CRP concentration in CHF before and after 6M of CRT and in CM control (2.8 ± 3.2, 1.9 ± 1.4, 2.5 ± 1.9 mg/l, respectively). Improvement in NYHA class after 6M was observed in 19 patients (73%). Median NYHA class before CRT was III and significantly improved in 6M observation (median II, $p < 0.001$). NYHA class after 6M negatively correlated with IL-10 concentration ($r = -0.62$, $p = 0.011$).

Conclusions: CRT improves exercise tolerance manifested by prolonged 6MWT, increases LVEF and reduces BNP concentration after 6 months. CRT has an impact on antiinflammatory response reflected in the increase in IL-10 concentration, which relates to NYHA functional class. The underlying mechanisms are still to be elucidated.

P1511

Assessment of high sensitivity c-reactive protein in patients with microvascular dysfunction

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Introduction: About 30% of coronary angiographies done for chest discomfort and positive stress cardiac testing are normal. Patients with chest pain with normal coronary arteries have coronary microvascular endothelial dysfunction and myocardial ischemia. Elevated hs-CRP levels have been related to atherogenesis and endothelial dysfunction. Little is known whether low grade chronic inflammation is a pathogenic mechanism.

Aims and Objectives: To assess high sensitive CRP in patients of typical chest pain with normal coronary arteries (cardiac Syndrome X).

Methods: Cardiac Syndrome - X patients were compared to controls to see any difference of markers of inflammation in the form of HS-CRP. 120 patients with 50 number of well matched controls were studied. All the patients underwent baseline investigations, ECG, ETT, Echocardiography and coronary angiographies. The serum levels of hs-CRP were estimated.

Results: Among the study group (Group-1), the mean age was 48.12 (± 7.87) yrs and 47.48 (± 7.48) yrs among control group (Group-2). In Group-1, 96 (80%) were male and 24 (20%) were female. In Group-2, 40 (80%) were male and 10 (20%) were female. In Group-1, 60% had sedentary lifestyle, 60% were hypertensives, and 50% were diabetics or IGT, 70% were smokers, 40% were dyslipidemics, 30% had family history of CAD and 50% were obese. and serum levels of hs-CRP were found to be significantly higher in Group-1 than in Group-2 patients, (4.10 ± 2.74 mg/L vs 1.18 ± 0.96 mg/L, $p < 0.001$).

Conclusion: hs-CRP levels are higher in patients of cardiac Syndrome-X, suggesting a chronic low grade inflammatory process.

P1512

Limited impact of atorvastatin treatment on endothelial function and inflammatory status in ischemic heart failure patients with renal impairment

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Purpose: Endothelial function has an independent predictive value in patients with cardiovascular disease. Impaired renal function is a major determinant of adverse prognosis in heart failure (HF). We examined the impact of atorvastatin treatment and renal function on endothelial function and biomarkers of inflammation in HF patients.

Methods: We studied the effect of 4 weeks administration of atorvastatin in 23 patients with ischemic HF. The study was carried out on two separate arms, one with atorvastatin 40mg/d and one with atorvastatin 10mg/d (randomized, double-blind,

cross-over design). Endothelial function was evaluated by flow-mediated dilation (FMD) of the brachial artery. Tumor necrosis factor alpha (TNF α), brain natriuretic peptide (BNP) and matrix metalloproteinase-9 (MMP9) levels were measured by ELISA as biomarkers of inflammatory status, left ventricle loading and cardiac remodeling respectively. Total cholesterol (TC) levels were also measured.

Results: Compared to baseline, treatment with 40 mg/d of atorvastatin improved FMD ($3.16 \pm 2.98\%$ vs. $6.05 \pm 2.45\%$, $p = 0.001$), TNF α ($p = 0.01$) and MMP9 levels ($p = 0.04$) while there was no impact in BNP levels ($p = 0.66$). Moreover, compared to baseline, treatment with atorvastatin 10mg/d also improved FMD ($3.24 \pm 3.12\%$ vs. $4.20 \pm 2.09\%$, $p = 0.08$) and TNF α ($p = 0.01$) but had no impact on MMP9 ($p = 0.76$) and BNP ($p = 0.40$). The increase in FMD was greater with the dose of 40mg/d ($p = 0.001$). In the 40mg/d treatment group the increase in FMD was significantly associated with baseline TC levels ($r = 0.57$, $p = 0.004$) and with creatinine clearance ($r = 0.61$, $p = 0.002$). In the 40mg/d treatment group the association between creatinine clearance and FMD was also significant even after adjustment for confounders such as TC, age, ejection fraction smoking habits, the presence of diabetes mellitus and hypertension [$b = 0.09$, 95%CI: 0.02-0.16, $p = 0.01$].

Conclusions: In ischemic HF subjects atorvastatin treatment improved inflammatory status and endothelial function. Importantly, the greatest improvement in endothelial function was observed in patients receiving high dose atorvastatin treatment with elevated baseline TC levels and preserved renal function.

P1513

The role of inflammatory cytokines in submaximal exercise capacity of patients with chronic heart failure: does the left ventricular function matter?

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Background: The mechanisms underlying impairment of submaximal exercise capacity (SEC) in patients with chronic heart failure (CHF) are not completely known. Inflammatory cytokines have a definite role in the pathophysiology of CHF and in the mechanisms of muscle wasting in several chronic conditions. However, the potential impact of inflammatory cytokines such as interleukin 6 (IL6) or tumor necrosis factor alpha (TNF α) on SEC has not been completely elucidated in CHF.

Aims and Methods: To evaluate the hypothesis that serum cytokine levels may affect submaximal exercise capacity, we studied the association between serum IL6 and TNF α with the distance walked in the 6 minutes walking test (6MWT) in a cohort of 73 consecutive patients with CHF. Impaired SEC was defined as 6MWT distance <300 metres

Results: Baseline characteristics were: mean age 72 ± 11 , 71% were male, 25% were in NYHA class III or IV. Up to 63% of patients had LVEF ≤ 49 . Mean 6MWT distance was 302 ± 105 metres, median values and interquartile ranges [Q1-Q3] of IL6 and TNF α were 6.1 pg/mL [2.4-13.0] and 13.8 pg/mL [5.0-24.5] respectively. In unadjusted correlation analyses, log₁₀[IL6] was significantly associated with 6MWT distance as a measure of SEC ($r = -0.335$; p -value = 0.004) whereas log₁₀[TNF α] was not ($r = 0.026$; p -value = 0.835). In multivariable linear regression analyses adjusted for covariates associated with SEC, log₁₀[IL6] remained a significant predictor of 6MWT distance (standardized β coefficient = -0.266; p -value = 0.001) and this effect was independent from haemoglobin or iron status. In this regard, multivariate logistic regression models, greater levels of IL6 were significantly associated with impaired SEC (OR=7.2; 95%CI [1.8-29.0]; p -value = 0.005).

Although the impact of IL6 was independent of LVEF, further analyses revealed that there was a significant interaction between LVEF and IL6 levels (p -value = 0.023). In fact, among patients with LVEF $\leq 49\%$, the proportion of patients with impaired SEC was significantly higher in patients with high IL6 levels (>median) compared to those with low IL6 levels (\leq median, 87% vs. 45%, respectively, p -value < 0.001). This was not observed for patients with LVEF>49% ($p > 0.05$).

Conclusions: In patients with CHF, increased levels of IL6, but not TNF α , are associated with poorer submaximal exercise capacity and this association is independent from haemoglobin levels or iron status. In these patients, the negative impact imposed by IL6 in terms of the distance walked in 6MWT might be conditioned by the level of left ventricular systolic function.

P1514

Acute myocardial infarction induces atrial inflammation that can be prevented by c1-esterase inhibitor

This study was funded by a the Netherlands Forensic Institute (NFI, grant number 34) and an unrestricted grant from ViroPharma Inc. R Reindert Emmens¹; MPV Begieneman¹; L Woudstra¹; WJ Paulus²; AC Van Rossum³; D Wouters⁴; S Zeerleder⁴; M Van Ham⁴; JWM Niessen¹; PAJ Krijnen¹

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Purpose: Atrial fibrillation (AF) is a common complication in acute myocardial infarction (AMI). Inflammation plays an important role in the pathophysiology of AF. However, whether AMI induces atrial inflammation is unknown. In this study therefore, we analyzed atrial inflammation in AMI patients and in rats with experimentally induced AMI. In the rats, we also investigated the effects of the anti-inflammatory agent C1-esterase inhibitor (C1inh) on atrial inflammation.

Methods: In the hearts of patients who died at different timepoints after AMI (total n=24), neutrophils, lymphocytes and macrophages were stained immunohistochemically and quantified in the left and right atria, the infarcted left ventricle and non-infarcted right ventricle and compared to control patients who died of causes unrelated to cardiovascular disease (n=5). AMI was induced in 17 rats through coronary artery ligation. Ten of these rats were subsequently treated with C1-inh for 6 days. Forty-two days after AMI the hearts were examined for the presence of lymphocytes and macrophages and the endothelial inflammation marker CML in the myocardium of both the atria and ventricles.

Results: In all investigated areas of the human hearts increased lymphocytes and macrophages were observed to a varying extent. This increase was most pronounced from 12 hours to 5 days after AMI. Similar to patients, in rats AMI resulted in an increase of macrophages and CML in the atria. C1inh treatment in turn decreased the amount of inflammatory cells and CML in the atria.

Conclusions: AMI induces atrial inflammation in patients and in rats, which may provide a substrate that predisposes towards AF. As C1inh treatment could counteract this AMI-induced atrial inflammation in rats this may be a treatment option to prevent AMI-induced AF.

P1515

Early postoperative proinflammatory response in patients with severe heart failure

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Inpatients with severe heart failure (HF), coronary bypass grafting (CABG) remains an alternative method for therapy in absence of donor heart. The advantages are, however, still under discussion due to the intraoperative inflammatory response and energy depletion.

Aim: the estimation of the dynamics of interleukins (IL-6, receptors IL-6 (sIL-6R)) and fatty acid binding protein (H-FABP) in arterial and in coronary sinus blood during open heart surgery in patients with severe heart failure.

Patients (n32 pts) with LVEF<35% and NYHA class III-IV were included in the study. Patients with stable HF (n=24 pts, mean age 54.8 ± 11.6 yrs, LVEF 31.7 ± 3.3) had CABG and left ventricular plasty (CABG group), while 8 patients with unstable HF (mean age 56.9 ± 7.6 yrs, LVEF 25.3 ± 2.1 , at admission NYHA 3.1 ± 0.3 , PAPsyst 56.2 ± 7.4 mm Hg) had undergone CABG and left ventricular assist device implantation (VAD group). In-operating room central arterial and coronary sinus blood samples were taken for estimation of H-FABP, IL-6, IL-6 receptors three times: 1 - before cardiac arrest, 2 - after global ischemia period and 3 - after intraoperative controlled coronary reperfusion.

Results: H-FABP: before surgery patients of VAD group had higher H-FABP level ($p < 0.05$). After coronary reperfusion, a 7-fold increasing of H-FABP ($p < 0.000$) in patients of VAD group, but not in patients of CABG group ($p = 0.7$) were found. Multiple regression showed a correlation of H-FABP after reperfusion with basal right ventricle systolic function (FAC, $r = -0.54$, $p = 0.003$), preoperative PAPsyst ($r = 0.38$, $r = 0.037$), and with early postoperative death ($r = 0.47$, $p = 0.01$) in VAD group. IL-6: before surgery, a 6-fold increased IL-6 level was found in CABG patients ($p = 0.03$). VAD patients had normal range of IL-6. Cardiac arrest was followed by an increased IL-6 in both groups, but more significantly in the VAD group (arterial $p = 0.09$, coronary sinus $p = 0.03$). After surgery, IL-6 receptors rose dramatically in coronary sinus blood in the VAD group (OR 0.9-2.1, $p = 0.02$), but decreased in both arterial and coronary sinus in the CABG group ($p = 0.06$ and $p = 0.029$ respectively).

Conclusion: high H-FABP level in patients of VAD group before surgery could be used as a sign of significant cardiomyocytes damage and death as well as predictor of poor early postoperative prognosis. Different dynamics of IL-6 in patients of VAD and CABG group shows strong impact of artificial circulation support (VAD) on the myocardium, as a source of pro-inflammatory proteins, and should be more detailed estimated.

DEVICES/ARTIFICIAL HEART/CRT/ICD

P1516

Correlation between pacemaker electrode tip position in the heart right ventricle with left ventricle dyssynchrony evaluated with gated myocardial perfusion single-photon emission computed tomograph

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Objective: Observational studies have shown that the location of the electrode in apex of the right ventricle may result in impairment of left ventricular function and its pathological remodeling. This can lead to decline of the left ventricular ejection fraction and mechanical cardiac dyssynchrony.

Aim of the study was to assess the evaluation of myocardial perfusion, left ventricle ejection fraction value and degree of dyssynchrony in the GSPECT and to define the place of right ventricular pacing, which is associated with a lesser degree of left ventricular dyssynchrony heart and less severe heart failure.

Material and methods: 25 patients were enrolled to the study, 12 with RV outflow tract lead position and the RVA group of 13 patients, with RV apex lead position. Gated myocardial perfusion SPECT evaluation of left ventricular dyssynchrony by analyzing the systolic phase - the width of the histogram and the standard deviation were assessed in all patients. After 6 months of follow up comparison of the actual value of the left ventricular ejection fraction in echocardiography with its value before pacemaker implantation.

Results After 6 months of implantation in both groups the number of patients with third degree diastolic dysfunction increased and those with second degree diastolic dysfunction decreased. The worsening of diastolic function was significant only in the RV outflow tract group

Conclusion: In conclusion, the follow up observation of stimulation from RVOT, but not from RVA, led to progression of diastolic dysfunction in patients with normal LVEF as confirmed by GSPECT study.

P1517

Assessment of influence of levosimendan on the process of reverse heart remodelling in patients with dilated cardiomyopathy and implanted CRT

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Objective: to assess whether the 24-hour intravenous infusion of long acting positive inotropic agent levosimendan influences the heart remodeling process in patients after CRT implantation.

Methods: We included into study 14 patients with dilated cardiomyopathy, LBBB. All patients were evaluated with the use of contrast enhanced MRI of the heart to rule out presence of fibrous tissue on the lateral wall of the left ventricle. All 14 patients were undergone CRT implantation and subsequent random division into 2 groups. First group (n=7) received 24-hour IV infusion of levosimendan after CRT implantation. Second group patients were discharged from our hospital without levosimendan infusion. Both groups were comparable in terms of age, BMI, NYHA functional class, QOL scores, QRS duration, echocardiographic parameters, proBNP levels.

Results: Six months after implantation we observed improvements in all 14 patients of both groups. First group patients showed improvement in ejection fraction ($26,4 \pm 6,7$ to $31,3 \pm 9,3$, $p=0,035$) and quality of life 6 months after implantation. Patients of control group also demonstrated improvements in quality of life, but also in NYHA functional class, mitral regurgitation and proBNP and did not show improvement in ejection fraction. Comparison of 2 groups 6 months after device implantation did not show any differences in earlier described parameters.

Conclusion: Twenty four hour intravenous infusion of levosimendan seems to play no role in reverse remodeling of the heart in patients with dilated cardiomyopathy undergoing CRT implantation. These results might be related to small number of observations in our study.

P1518

The effect of biventricular stimulation in patients with severe chronic heart failure with QRS complex duration between 120 and 150 msec

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Objective: to assess the effectiveness of CRT implantation in patients with QRS complex duration between 120 and 150 msec one year after

Methods: 28 patients (pts) with ischemic or dilated cardiomyopathy complicated by CHF NYHA functional class (FC) III-IV, LV EF below 35%, QRS duration between 120 and 150 msec and with ECHO confirmed mechanic myocardial dyssynchrony were examined. 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 (TS-DS), 12 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 evidently decreased from $313,2 \pm 16,3$ ml to $255,2 \pm 24,7$ ml ($p < 0,05$), LVESV decreased from $249,8 \pm 13,6$ to $181,9 \pm 24,7$ ($p < 0,05$), LVEDD decreased from $78,0 \pm 3,8$ to $66,7 \pm 2,5$ mm, LVESD decreased from $70,9 \pm 1,9$ to $69,8 \pm 2,0$ mm, LVEF increased evidently from $25,1 \pm 1,2\%$ to $31,1 \pm 2,7\%$ ($p < 0,05$). In 96,2% of pts with CHF and QRS between 120 and 150

msec intraventricular delay was associated with interventricular delay, in 3,8% of patients signs of interventricular delay were absent but all these patients demonstrated impaired intraventricular conduction. Intracardiac hemodynamic changes were accompanied by decreased mechanic dyssynchrony event rate - there was trend to the evident decrease of interventricular delay from $50,5 \pm 5,6$ to $40,7 \pm 1,2$ msec. ($p < 0,05$), TS-DS- from $61,9 \pm 4,45$ to $47,5 \pm 5,1$ msec. ($p < 0,05$), 12 segments max delay from $142,1 \pm 7,9$ to $140 \pm 14,79$ msec ($p < 0,05$); improved LQ of patients: LQ evidently decreased from $45,4 \pm 3,0$ scores to $32,1 \pm 4,8$ scores ($p < 0,05$); 6 MWT increased from $162,8 \pm 0,4$ m to $310,0 \pm 0,4$ m; BNP decreased from $1239,3 \pm 220,7$ to $335,7 \pm 98,7$ ($p < 0,05$); HF FC decreased from $3,21 \pm 0,06$ to $2,3 \pm 0,13$ ($p < 0,05$).

Conclusions: At 12 months biventricular heart stimulation evidently enhances heart haemodynamics and the clinical conditions of pts, improving exercise tolerance in pts with QRS duration between 120 and 150 msec.

P1519

Right ventricle diameters and function changes during cardiac resynchronization therapy

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Purpose: To estimate the right ventricle diameters and function changes during cardiac resynchronization therapy (CRT).

Methods: 91 patient meeting European Society of Cardiology recommended CRT implantation indications were included into this study. Right ventricular end - diastolic chamber size was assessed according to the American Society of Echocardiography guidelines using apical four- chamber view, before starting CRT and after 12 months of treatment. We measured three RV dimensions: RVD1 - diameter of tricuspid valve annulus, RVD2 - the maximum dimension of the middle third of the RV and RVD3 - the distance between the RV apex to the mid - point of the tricuspid annulus. Right ventricular function was evaluated measuring tricuspid annular plane systolic excursion (TAPSE). Statistical analysis was performed using SPSS version 21.0.

Results: Mean initial RVD1 was 42.1 ± 5.6 mm., after 12 months of CRT in responders' and non - responders' group it was 37.4 ± 5.1 mm and 42.1 ± 5.7 mm ($p=0.01$) respectively. Mean initial RVD2 was 34.1 ± 6.5 mm., after 12 months of CRT in responders' and non - responders' group it was 29.1 ± 4.8 mm and 32.2 ± 4.2 mm ($p=0.02$) respectively. Mean initial RVD3 was 83.8 ± 11 mm., after 12 months of CRT in responders' and non - responders' group it was 77.9 ± 10.4 mm and 79.6 ± 7.4 mm ($p=0.6$) respectively.

Initial TAPSE was 13.9 ± 4.6 mm., after 12 months of CRT in responders' and non - responders' group it was 18.6 ± 5.0 mm and 15.3 ± 5.2 mm ($p=0.03$), respectively.

Conclusion: 1.The structure and function of the right ventricle does change after 12 months of CRT.

2.Severe dilation of the RV might be the prognostic sign of the absence of the response to CRT.

P1520

What can we expect from changes in QRS duration after CRT implantation?

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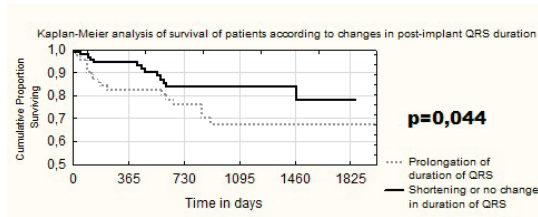
Background: The prolongation of QRS reflects the severity of electrical desynchronization and increases the risk of death. Implantation of CRT can eliminate this negative impact by electrical resynchronization which is accompanied by changes in the duration of stimulated QRS. These changes can be recorded by surface ECG however published studies bring controversial results.

Aim: Find out impact of the early post-implantation changes in QRS duration on survival.

Methods: The retrospective study included 155 patients with HF after CRT implantation according to guidelines. Patients were divided into two groups according to post-implantation changes in QRS.

Results: The prolongation of post-implant duration of QRS was in 40% of patients, shortening or no changes in 60% of them. The difference was statistically significant (150 vs 168 ms, $p < 0,001$). The survival of patients with prolongation of QRS was inferior ($HR=2,02$, $p=0,04$). The risk of post-implantation QRS prolongation reduced 3 pre-implantation factors: duration of QRS>155 ms($HR=0,2$, $p=0,001$), LBBB ($HR=0,26$, $p=0,006$) and chronic therapy without amiodarone ($HR=0,27$, $p=0,017$).

Conclusion: We demonstrated the negative impact of the prolongation of QRS induced by CRT on survival which increased risk of death about 2-fold. We identified also 3 pre-implantation factors that reduce the risk of post-implantation QRS prolongation.



P1521

Prognostic implication of functional mitral regurgitation in patients undergoing cardiac resynchronization therapy

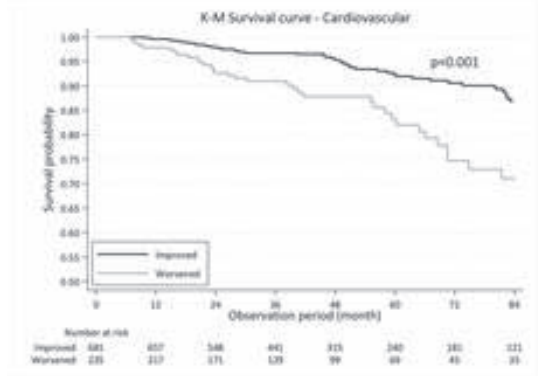
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Introduction: reduction of mitral regurgitation (MR) is one of the mechanisms by which cardiac resynchronization therapy (CRT) exerts its beneficial effects. We investigated the prognostic role of MR on outcomes in CRT patients (pts).

Methods: 1122 CRT pts (66 ± 10 years, 78% male), prospectively followed, were divided in 2 groups according to baseline MR grade: MR [-] (grade 0-1°): n=508 (45%) and MR [+] (grade 2°-3°-4°): n=614 (55%). The subgroup of 916 pts (82%), with MR data available at 1 year follow-up, was divided in 2 cohorts according to MR improvement: IMPROVED (MR Improved or MR [-] unchanged; n=681 (74%)) or WORSENE (MR Worsened or MR [+] unchanged; n=235 (26%)).

Results: all-cause mortality was lower in MR [-] group than MR [+] (respectively all-cause mortality annual rate: rate 100 pts/yr 3.4 (95% Confidence Interval (CI):2.7-4.3) vs 6.0 (CI:5.0-7.1); Incidence rate ratio (IRR) at 1 year: 1.76 (CI: 1.31-2.39) - p < .001). Similarly, cardiac mortality was lower in MR [-] group than MR [+] (1 year IRR: 1.72 (CI: 1.10-2.57) - p=.002). MR impact on prognosis was clearer when outcome was evaluated according to MR Improvement at FU: all-cause mortality was lower in IMPROVED than WORSENE (1 year IRR: 1.87 (CI: 1.31-2.66) - p < .001) as well as cardiac mortality (1 year IRR: 2.33 (CI: 1.5-3.6) - p < .001). Kaplan Meier analysis confirmed these results. Regression analysis showed that absence of significant MR, chronic AF and LVEF are independent predictors of MR improvement, meanwhile NYHA IV and worsening MR after CRT are independent predictors for cardiac death.

Conclusions: Hemodynamic significant MR as well as worsening MR after CRT are both independent predictors of poor prognosis at long term FU.



P1522

6-minute walk test or peak oxygen consumption is better to predict clinical response to resynchronization therapy?

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Background: Cardiac resynchronization therapy (CRT) is an established and recommended treatment for selected patients with symptomatic left ventricular systolic dysfunction who are under optimal medical therapy. An aim of this therapy is to improve functional capacity, clinical outcome and reduce mortality. However, many patients do not respond to CRT therapy.

Aim: This study investigated which of two functional capacity parameters - 6-minute walk test (6-MWT) or peak oxygen consumption (VO₂peak) is better to evaluate response for CRT therapy in patients after CRT-D (cardiac resynchronization therapy with defibrillator) implantation in 12-month follow-up.

Material and Methods: In this study 43 patients (mean age 63 ± 7 years; 77% males) after CRT-D implantation were included. In all patients a spirometry with VO₂peak measurement and 6-MWT were performed before CRT implantation and after 12-month follow-up. Responders to CRT therapy were clinically defined as patients who survived the observation's period, were not hospitalized for heart failure exacerbation and improved his physical efficiency at least by 1 class in NYHA.

Results: After 12-month observation there were 34 responders (f=0.79) to CRT therapy. In this group a distance in 6-MWT was 350,00 ± 70,05 m and VO₂peak - 14,34 ± 3,16 ml/kg/min. In the group of non-responders (f=0,21) analyzed parameters of functional capacity were: was 333,33 ± 83,27 m and 9,75 ± 2,06 ml/kg/min respectively. There was a statistical significance in VO₂ peak measurements in responders vs. non-responders (p=0,01). An analysis revealed no statistically significant relation between the distance in 6-MWT in both studied groups.

Conclusions: VO₂peak measurement in comparison to 6-MWT is a better parameter in evaluating the effectiveness of CRT therapy.

P1523

Real life results of cardiac resynchronization therapy in a regional prospective registry in Catalonia

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Abstract: Results of cardiac resynchronization therapy (CRT) have been reported in randomised studies and registries. However, there is limited data in unselected populations. The objective of the study was to analyse efficacy, safety and resource consumption of CRT in the population of Catalonia.

Methods: A prospective study of consecutive patients with CRT implant was performed on 7 university hospitals in Catalonia, which represent 90 % of the implanted patients in a year. Clinical data, device interrogation and complementary tests were collected. Survival was analysed at 6 and 12 months.

Results: Of the 200 patients included in the registry, 68 % received CRT- D. The rate of immediate complications was 12.5 %. The mortality rate at 12 months was lower than the European average. There was 52 % of clinical responders (figure 1) and 46 % of the population improve echocardiograph parameters. During follow-up there was a decrease in the number of hospital admissions due to heart failure; only 7% of the patients were admitted at least once, which resulted statistically significant when pre and post-implant periods were compared (P < 0.001).

Conclusions: In an unselected population, we observe similar results of efficacy in CRT and lower rate of hospitalizations and mortality in the Catalan registry than European registries. CRT initially increases the cost of treatment; but there is a decrease in hospitalizations during follow-up.

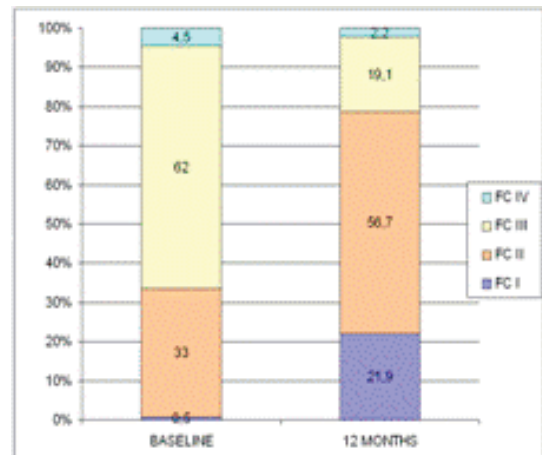


Figure 1: NYHA FC improvement during FU

P1525

Anti adrenergic receptor autoantibodies: a new way to identify responders to CRT

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Aim: Cardiac resynchronization therapy (CRT) non-response remains a major clinical problem. Antibodies specific for the β 1-adrenergic (β 1-AABs) and muscarinic (M2-AABs) receptors are found in patients with chronic heart failure (HF). The aim of our study was to evaluate if sera levels of β 1-AABs and M2-AABs may be useful to assess CRT response.

Methods: We retrospectively analyzed ninety HF patients [median age 67 yrs, 84% males, NYHA II-IV, in sinus rhythm, left ventricular ejection fraction (LVEF) <35%] who received CRT/defibrillator (CRT-D) from 2010 to 2013. β 1-AABs and M2-AABs were measured by ELISA assay. Echocardiography was used to assess CRT response (reduction >15% in left ventricular end-systolic volume at 6 months follow-up). Renal function parameters [creatinine, blood urea nitrogen (BUN), eGFR, cystatin C (cys-C) and neutrophil gelatinase associated lipocalin (NGAL)], were also evaluated.

Results: A significantly higher percentage of patients positive for β 1-AABs (OD sample/OD reference ratio > 2.1) in non-responders than in responder patients was observed (57% vs 27%, $p=0.004$). No influence of M2-AABs on CRT-D response was demonstrated (Table). β 1-AABs were predictive of a poor CRT-D response [OR (95%CI) 3.64 (1.49-8.88) $p=0.005$], also after adjustment for renal function parameters [OR (95%CI) 4.95 (1.51-16.26) $p=0.008$] observed to influence CRT-D response (creatinine $p=0.03$, BUN $p=0.009$, cys-C $p=0.02$). Patients exhibiting abnormal cys-C or NGAL levels showed higher percentage of β 1-AABs ($p=0.007$ and $p=0.03$, respectively).

Conclusions: Our study suggests that the evaluation of β 1-AAB is useful to identify responders to CRT-D.

Table

	Responders (n=41)	Nonresponders (n=49)	p^{\wedge}
β 1-AABs positive, n (%)	11 (26.8)	28 (57.1)	0.004
NT-proBNP (pg/mL)*	1228 (161-7438)	2287 (233-31990)	0.04
hs-CRP (mg/L)*	2.5 (0.3-110.0)	4.1 (0.2-203.0)	0.01
Creatinine (mg/dL)*	1.00 (0.70-1.87)	1.10 (0.34-4.15)	0.02
eGFR (MDRD) (mL/min/1.73m2)*	79 (38-121)	70 (15-232)	0.01
BUN (mg/dL)*	22.2 (15.4-42.5)	26.2 (8.4-70.6)	0.01

P1526

Effect of early post-implantation hemodynamic response to cardiac resynchronization therapy on stable functional mitral regurgitation improvement in idiopathic dilated cardiomyopathy

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Aims: Functional mitral regurgitation (FMR) is associated with reduced survival in dilated cardiomyopathy (DCM). We sought to identify the predictors of FMR improvement after CRT in DCM, then evaluating its impact on long-term outcome. **Methods and Results:** From January 2003 to December 2013, 388 DCM patients were consecutively enrolled. Among them, 44 cases (10% of the overall population) implanted with CRT in presence of conventional indications, had moderate-severe FMR at the time of procedure. Early echocardiographic evaluation after CRT-implantation (median 2.5 days) has been performed in each patient. FMR improvement (absent/mild) at mid-term (7 months; IQR 4-10) was considered as the primary study end-point. No pre-implantation variables predicted FMR evolution, but FMR improvement was strongly predicted by an acute favourable hemodynamic response (persistence/development of normal right ventricular function and 10 mmHg decrease or normalization of systolic pulmonary artery pressure) at post-implantation echocardiography. FMR improvement was stable in the long-term and was associated to a better transplant-free survival (OR 20.4; 95% CI 2.17-50.6; $p=0.008$).

Conclusions: FMR improvement frequently occurs after CRT-implantation in DCM and is associated with improved transplant-free survival. Echocardiographic evaluation of acute hemodynamic response to CRT is helpful to early identify a favourable FMR evolution.

P1527

The subcutaneous implantable cardioverter-defibrillator: first single-center experience with concomitant implantable pulse generators

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Background: Subcutaneous implantable cardioverter-defibrillator (S-ICD) is a device for antiarrhythmic therapy with no intravascular leads. The S-ICD does not have pacing functions. We describe the technical feasibility of combining the S-ICD with other implantable pulse generators (IPGs), including pacemakers with trans-venous or epicardial electrodes. For the first time, we describe how S-ICD can also co-work successfully with cardiac contractility modulation (CCM) and with vagus nerve stimulation (VNS).

Methods: Between 7/2011 and 11/2014 six patients had S-ICD in combination with CCM, three patients with single-chamber pacemakers with trans-venous or epicardial pacing electrodes received S-ICD, and one S-ICD patient received VNS. In all patients intraoperative S-ICD testing, crosstalk tests and postoperative ergometer testing were performed.

Results: In all 10 patients device implantations were successfully performed without complications. S-ICD therapy was shown to be technically feasible with concomitant IPGs including CCM, pacemaker and VNS. Mean follow up was nearly 17 months (in CCM 5 cases had up to 35 months of follow-up, mean 20.4 months). S-ICD testing and crosstalk check before and during exercise enable successful programming of the S-ICD for proper functioning with concomitant IPG. None of the devices had to be permanently inactivated and no patient received inadequate shock.

Conclusions: In select patients, S-ICD can be combined with a pacemaker. Combination of a S-ICD with CCM and with VNS may be practical for reducing the number of trans-vascular leads. S-ICD appeared safe with CCM over a long follow-up period. Additional reports on S-ICD co-work with IPGs are warranted.

P1528

WCD-utilisation for SCD-risk assessment in heart-failure-patients with reduced EF (<35%) during waiting time

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Introduction: Whilst a reduced EF is clearly an indication for the implantation of an ICD, the results of randomized trials and current guidelines demand a waiting period in which the patient might recover and has no longer an indication for an ICD. In this period of medical optimization the patient is usually at high risk for SCD thus needs protection. The wearable cardioverter defibrillator (WCD) allows us to safely discharge those patients knowing that they will be protected by a non invasive, reversible method. During this time the patients can be followed up and arrhythmic events will be recorded and delivers helpful insight when making the decision for further treatment strategy.

Methodology: Based on the recommendations of the HRS and the screening protocol of our institution we prescribed a WCD for heart-failure patients with an EF of 35% and lower. During the period of medical optimization patients were monitored by the device-own telemonitoring system. Reevaluation was initiated after a period of 10-12 weeks, when further strategy such as final ICD implantation was decided. We retrospectively analyzed the data of our heart failure patients 18 month after implementation.

Results: From the total 89 Patients having been fitted with the WCD 69 (78%) were heart-failure pts with a LVEF <35%. The average weartime exceeded 22h/d. In this subgroup the indication were divided as follows ICM 21 (30,4%) NICM 44 (63,8) others 3 (4,3%) N=69pts 30 pts (43,5%) showed no improvement or arrhythmic events, hence the decision was made to implant an ICD. 20 pts. showed EF improvement significant enough to no longer include them in the high risk group. 19 pts still wear the WCD or have been lost to follow up. In the ICM group the rate of ICD implants was highest with 55% (12/22) whereas in the NICM group 41% (18/44) received an ICD. No VT/VF termination was present in this subgroup, however in two patients, arrhythmic anomalies could be detected that lead to therapeutic interventions.

Summary: The usage of the WCD supported in determining candidates for an ICD and helped discover arrhythmic anomalies that would otherwise have gone undetected. When patients were reevaluated a significant number (43,5%) did not need an ICD after the waiting period due to significant improvement of the ejection fraction.

P1529

2014 national guidance will significantly increase device implant rates in regions of the UK

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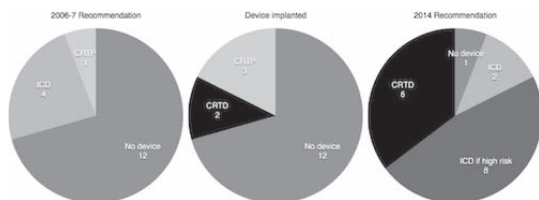
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Purpose: Implant rates for ICD therapy have been below target consistently in all UK regions. Considerable geographic variation is noted. Our region has the lowest ICD implant rate but well above target CRT rate. In 2014 national guidance was updated considerably extending the primary prevention indications for which devices can be offered. There has been debate about whether they will actually alter practice.

Methods: From a database of all referrals to our heart failure clinic in 2013 we identified those with an EF <35%. From their assessment NYHA class, ECG rhythm, QRS duration and morphology, and aetiology were identified. We followed to see which had device implanted and compared this with the national guidance at the time and what the new guidance would have suggested.

Results: Of 232 patients, 181 (78%) had an echocardiographic assessment and 18 (10%) of these had an EF <35%, assessment was not available for 1 patient. 5 went on to have CRT, 2 also with ICD. 1 patient was eligible for ICD under the old guidance but declined any procedure. 1 with ischaemic cardiomyopathy eligible for ICD underwent CRT after discussion with the patient. None eligible was not offered device and CRT was implanted beyond the guidance in 3, all in AF. Applying the 2014 guidance 16 of the 17 may have been eligible for a device; all including ICD. The 'if at high risk' group is sizeable: 5 of the 8 in our sample were of ischaemic aetiology.

Conclusions: This sample represents only part of our device referral population but shows even with low implant rates we were implanting beyond previous guidelines. Although a large proportion fall into the poorly defined 'if at high risk' group the 2014 guidance will lead to a large increase in implants, particularly of ICD, in our region and likely many others.



P1530

Role of 123-iodine metaiodobenzylguanidine (MIBG) imaging in managing reimplantation of icd in patients underwent device extraction

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Purpose: According to guidelines, implantable cardioverter defibrillator (ICD) is recommended for the prevention of sudden cardiac death (SCD) in heart failure (HF) patients (pts) with an ejection fraction (EF) ≤ 35%, a NYHA class II or III and in full medical therapy. Moreover, numerous patients treated with ICD experienced complications needing ICD removal. In this setting it is difficult to decide the timing or the indication to ICD re-implantation, especially in pts who never experienced a malignant arrhythmia, since EF has a low sensibility and specificity. Recently, 123-iodine metaiodobenzylguanidine (123-I MIBG) imaging has shown the possibility to identify, among pts who are candidates for ICD implantation and independently from EF, a cohort at high risk of SCD defined as: heart/ mediastinum (H/M) ratio ≤ 1.6 and a summed score at SPECT (SS) > 26. The aim of our study is to evaluate the role of 123 I-MIBG imaging in guiding re-implantation of ICD in patients who underwent device extraction.

Methods: We enrolled 24 pts consecutively admitted to our hospital with a diagnosis of HF and EF ≤ 35%, undergone ICD extraction for device infections. Patients were divided in two groups: group-1 (G1) patients who did not undergo ICD replacement, including pts who did not undergo appropriate shocks in the previous 5 years, H/M ratio >1.6 and SS <26; group-2 (G2) pts who underwent ICD replacement, including pts with ≥1 appropriate shock, H/M ratio ≤ 1.6 and SS > 26. All patients have been followed-up during 1 year. All patients signed an informed consensus to participate to the study and, for group 1, to not undergo ICD replacement.

Results: Eight pts in G1 and 16 pts in G2 were enrolled. No significant differences were observed between the groups in term of baseline characteristics. All patients were on optimal medical therapy according to current guidelines. In G1 the H/M ratio was 1.75 ± 0.15 vs 1.39 ± 0.14 in G2 (p < 0.001), SS was 13.5 ± 8.2 in G1 vs 25.4 ± 10.9 in G2 (p < 0.05) and EF was 30.44 ± 5.07 in G1 vs 25.94 ± 5.86 in G2 (p = 0.62). At 12 months follow-up all G1 pts were alive and without re-hospitalization episodes. In G2 6 pts have experienced episodes of appropriate shocks.

Conclusion: Our results showed that 123-I MIBG could be a useful tool to better identify patients who needs ICD replacement, independently from ejection fraction. Further studies, conducted in wider populations, are needed to confirm our findings.

P1531

The prevalence, predictors and prognostic implication of electrical storm in patients with an implantable cardioverter defibrillator and severe left ventricular systolic dysfunction

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Background: Electrical storm (ES) is an emergency complication in patients with an implantable cardioverter defibrillator (ICD). The multiple ICD shocks during ES represent a traumatic situation for patients and worsen their quality of life. The aim of this study was to determine the prevalence, predictors and prognostic implication of ES in patients with severe heart failure who had received an ICD in primary or secondary prevention.

Methods: 675 ICD-treated patients (562 men, mean age 62 ± 10 years) with severe left ventricular systolic dysfunction were enrolled in this study. ES was defined as ≥ 3 separated episodes of ventricular tachyarrhythmia resulting in device shock within 24 hours. The mean follow-up was 923 692 days.

Results: During the follow-up ES occurred in 54 patients. Cox regression analysis showed that secondary prevention (p = 0.002) and diabetes mellitus (p = 0.044) were risk factors of ES. Kaplan-Meier analysis showed that electrical storm was not associated with survival of patients (Log Rank p = 0.07).

Conclusion: In the present study ES occurred in 8 % patients and was more frequently in patients with ICD implanted for secondary prevention and with diabetes mellitus. The development of ES was not accompanied with increased mortality.

P1532

Inappropriate shocks analysis in a spanish ICD primary prevention population

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Purpose: To analyse inappropriate shocks and identify clinical predictors and prognostic implications in a real world primary prevention ICD population.

Methods: Multicentre retrospective study performed in 13 centres in Spain with experience in the field of the ICD implantation (at least 30 per year) and ICD follow-up. All consecutive patients who underwent an ICD implantation for primary prevention between January 2008 and May 2014.

Results: 1016 patients were included of which 4 (0,39%) were lost in the follow-up. 217 (21,4%) patients suffered any shock of which 69 (6,8%) were inappropriate shock (IS) and 156 (15,4%) were appropriate shocks (AS). Age <65 years (hazard ratio (HR) 2,588 [95% CI 1,282-5,225]; p = 0.008), history of atrial fibrillation (HR 2,252 [95% CI 1,230-4,115]; p = 0.009), non-ischemic myocardiopathy (HR 2,258 [95% CI 1,090-4,479]; p = 0.028), and cardiac resynchronization therapy (HR 0,385 [95% CI 0.200-0.740]; p = 0.004), were identified as IS predictors after a multivariate analysis. IS were not associated either with rehospitalisation due to heart failure, myocardial infarction, cardiovascular mortality or all-cause mortality (table 1).

Conclusions: This analysis of our national registry identifies known independent IS predictors as age, atrial fibrillation history or cardiac resynchronization therapy and suggest that IS are not linked to poorer clinical endpoints.

Table 1.

	Inappropriate shocks			p
	No IS (n=943)	IS (n=69)	HR (95% CI)	
Total	12,3% (116)	8,7% (6)	1,537 [0,676-3,494]	0.305
CV	8,3% (72)	5,3% (3)	1,661 [0,506-5,434]	0.617

Inappropriate shock effect on cardiovascular and all cause mortality

P1533

The impact of levosimendan on cerebral hemodynamics in patients with acute myocardial infarction complicated by heart failure

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Purpose: To study the impact of levosimendan (LS) on the indices of cerebral hemodynamics in patients with myocardial infarction.

Materials and methods: 182 with ST-elevated myocardial infarction of 60,4 (53;69) mean age complicated with left ventricular failure Killip II - III were randomized in 2

groups. Group I - 49 patients of mean age 59,6 (52;69) received standard therapy, group II - 133 patients of mean age 60,6 (54;69) in addition to standard therapy on the second day of MI received LS according to conventional scheme. Standard therapy included PCI (32 (65,3%) and 69 (51,9%) in groups I and II correspondingly, $p=0,105$), (TLT 8 (16,3%) and 19 (14,3%) in groups I and II correspondingly, $p=0,749$), medication which was comparable in both groups. On the first and the tenth day of MI all the patients were performed a diagnostic ultrasonic of heart and extracranial cerebral vessels by "Sonos 250" a transcranial doppler examination by "ANGIODINE-2". All the included patients had signs of carotid arteries atherosclerosis: thickening of the intima-media complex more than 0,9 (subgroup 1) or plaques obliterating vascular lumen not more than 60% (subgroup 2).

Results: After administration of LS in group II as opposed to group I cross-sectional area, blood peak flow and volumetric blood flow velocity were authentically increased; a resistance index of extracranial arteries were decreased in both subgroups. The blood peak flow in medial cerebral artery was increased by 5,6% and in anterior cerebral artery - by 8,6% ($p<0,001$) in patients without stenosis and by 8,3% and 8,4% correspondingly ($p<0,001$) in patients with stenosis of extracranial arteries, while the velocity indices in group I didn't change.

Conclusion: Administration of LS in patients with myocardial infarction complicated with left ventricular failure not only improves myocardial systolic function, but also has a positive impact on cerebral hemodynamics.

P1534

What is the survival of patients with EF less than 35% after ICD implantation in secondary prevention compared to patients with implanted ICD in primary prevention?

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Background: The ejection fraction below 35% or surviving ventricular tachycardia or fibrillation increase the risk of sudden cardiac death. Both are the indication criteria for defibrillator implantation. ICD improves survival and reduces the risk of cardiac death in these high-risk patients compared to antiarrhythmic therapy. However we still miss data about the survival of patients after ICD implantation with EF below 35% who survived ventricular tachycardia/fibrillation.

Methods: The retrospective study included 675 patients with HF, NYHA II-IV, EF \leq 35% who were divided into two groups according to type of prevention (primary-secondary). Primary end-point was death from any cause.

Results: A total of 451 patients underwent implantation of ICD in primary prevention and 224 patients in secondary prevention after surviving ventricular tachycardia/fibrillation. In the group of patients after ICD implantation in primary prevention died 21% and in secondary prevention 46% of them. Kaplan-Meier analysis showed worse survival of patients after implantation of ICD in secondary prevention compared to patients in primary prevention ($p=0,0006$).

Conclusion: In our study we showed that survival of patients with EF below 35% after ICD implantation is worse if the ICD is implanted in secondary prevention. In our opinion, ventricular tachycardia/fibrillation are signs of progression of disease (heart failure).

P1535

Long-term prognosis of patients with arrhythmogenic right ventricular dysplasia and implantable defibrillator

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Purpose: Arrhythmogenic right ventricular dysplasia (ARVD) is a cardiomyopathy with structural and functional abnormalities of the right ventricle attributable to diffuse replacement of myocytes by fatty and fibrous tissue.

The implantation of an ICD is recommended (class I) in patients with documented TVMS. The implantation of an ICD is reasonable (class IIa) in patients with ARVD and extensive disease, including those with an affection of the left ventricle, one or more affected relatives of sudden cardiac death or undiagnosed syncope.

The purpose of our study was to determine the incidence of events in our series of patients with ARVD.

Methods: We reviewed the electrograms of 31 patients with definite diagnosis of DAVD and ICD. All stored electrograms of arrhythmic events that triggered ICD therapy were classified as appropriate or inappropriate intervention.

Results: 25 patients (80.65%) had ICD as secondary prevention and 6 (19.35%) as primary prevention (3 because of unexplained syncope, 2 because of a family history of sudden death and one because affected left ventricle).

Respect to patients for secondary prevention, 19 presented appropriate therapies (76%), with an average of 11.11 ± 13.4 months to receive the first one; and 3 of them received inappropriate therapies (12%). None of the 6 patients in primary prevention had an appropriate event and one of them had an inappropriate one. Survival free of life-threatening arrhythmic events showed a statistically significant

difference between patients treated in primary and secondary prevention, evaluated in Kaplan Meier curve ($p<0.01$) (Figure 1).

Conclusions: Patients with ARVD have a high number of appropriate events and these appear soon. We need to improve the selection of asymptomatic patients who will benefit from ICD implantation.

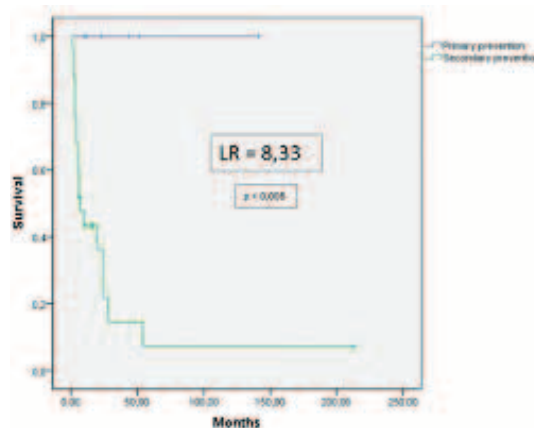


Figure 1

P1536

Effect of early treatment with ivabradine plus beta-blockers versus only beta-blockers in patients hospitalized with systolic heart failure: a randomized study

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Introduction and Objectives: Heart rate (HR) has prognostic value in patients with heart failure and depressed ejection fraction (HF-dEF) in sinus rhythm, having shown that the value of HR at 28 days of initiation of treatment predicts long-term mortality. HF-guidelines recommend to obtain a HR<70 bpm, but controversy exists about whether to first reach the maximum dose of beta-blockers or input can start associating beta-blocker plus ivabradine. We analyzed the effect on HR at 28 days after discharge of two different protocols, ivabradine plus betablocker (lv+BB) or only BB during admission, in patients with HF-dEF, sinus rhythm, HR>70bpm and ejection fraction <40%.

Methods: Comparative, randomized study comparing treatment with lv+BB versus BB only at the usual dose titration regimen, from 24 hours after admission.

Results: 43 consecutive patients who met the inclusion criteria (22 BB, 21 lv+BB) were included. Both groups were homogeneous with respect to age, sex, blood pressure levels and heart rate, BNP, renal function, comorbidities and treatment with diuretics, ACE inhibitors or ARB and MRA. HR at admission was 89 ± 14 in BB and 92 ± 23 bpm in lv+BB group (NS). HR at discharge was slightly lower in the lv+BB group (70 ± 10 vs 72 ± 10 , NS). HR at 28 days was lower in the lv+BB group (63 ± 5 vs 72 ± 8 bpm, $p=0.02$), and 12.5% in BB group and 62.5% in lv+BB group had HR<70bpm, $p<0.001$. There were no adverse effects associated with drugs or had to reduce their dose. There were two decompensated heart failure readmissions in BB group versus none in group BB+lv, with no deaths.

Conclusions: Co-administration of lv+BB early after admission in patients with HF-dEF, sinus rhythm and HR>70 bpm is feasible, safe and significantly decreases 28 days-HR as compared to only BB, looking even reduce readmissions for heart failure in the short term. Increased monitoring is necessary to show whether early reduction of HR is associated with a lower morbidity and mortality in the long term.

P1537

The role of cardiovascular magnetic resonance in appropriate selection of implantable cardioverter defibrillator therapy

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Introduction: A significantly reduced left ventricular ejection fraction (LVEF) is an indication for implantable cardioverter defibrillator (ICD) placement for the primary prevention of sudden cardiac death. However, LVEF as measured by transthoracic echocardiography (TTE) is inferior to that of cardiovascular magnetic resonance

(CMR), which is considered to be the gold standard for LVEF assessment. In this study we wished to examine the role of CMR for assessment of left LVEF in determining eligibility for ICD implantation when compared with echocardiography.

Method: In this prospective cohort study, patients under consideration for ICD implantation underwent LVEF assessment by both TTE and CMR. LVEF was assessed on echocardiography using Simpson's biplane method. LVEF was determined from CMR based on manual planimetry of SSFP cine images of contiguous left ventricular short axis slices.

Result: Fifty-one patients (9 female, mean age 62.2 +/- 5.7 years) were enrolled over a twelve-month period. The mean LVEF by CMR and TTE was 30 +/- 18 %, and 33 +/- 20%, respectively, ($p=0.01$), with a correlation coefficient between the two of 0.83. CMR resulted in reclassification regarding ICD eligibility in 7 (13%) patients, while 8 patients (15%) were deemed inappropriate for ICD insertion.

Conclusion: In this study, CMR changed the eligibility for ICD in a substantial proportion of patients. Given the significant economic implications of ICD insertion, absolute appropriateness of this therapy is vital. Thus, given that CMR is the gold standard for LV functional assessment, and the clear discrepancies between CMR and TTE in this patient population, we would advise all patients undergo CMR assessment in order to determine eligibility for ICD insertion.

P1538

Extracorporeal life support as a bridge to ventricular assist device in cardiogenic shock

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Purpose: Patients receiving long-term ventricular assist devices (VADs) for refractory cardiogenic shock (rCS) with multi-organ failure present substantial postoperative mortality and morbidity. Conditioning these patients preoperatively with extracorporeal life support (ECLS) could offer an improved outcome.

Methods: Data of patients who underwent ECLS prior to VAD implantation between 01/2013 and 10/2014 were analyzed retrospectively.

Results: Twenty-two patients (15 male, 7 female) were supported by ECLS prior to VAD implantation.

In 12 patients rCS was caused by dilative cardiomyopathy, in four by ischemic cardiomyopathy and in four by myocarditis. Two patients suffered from acute myocardial infarction. In 10 patients cardiopulmonary resuscitation (CPR) was necessary at least once before VAD implantation.

The femoral artery and vein were accessed in all but one case. Antegrade leg perfusion was established in 20 patients. Median time on ECLS was 4 days with a range from 1 to 31 days.

Thirty-day mortality after VAD implantation was 45%; six patients survived to hospital discharge. No differences in clinical parameters were noted between survivors and non-survivors.

Conclusion: In treatment of refractory cardiogenic shock ECLS is a valid initial treatment option. If weaning is not possible VAD implantation can be performed, yielding improved outcome as compared to primary VAD implantation. Preceding CPR or prolonged duration of ECLS does not preclude successful VAD implantation.

P1539

Optimizing pump speed promotes synergy between left ventricular assist device and right ventricular function in patients on long-term mechanical assistance

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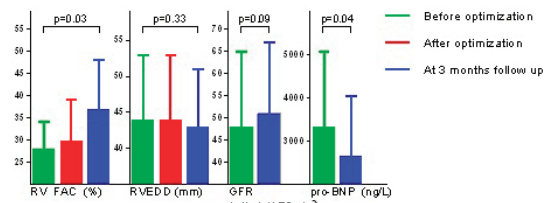
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Background: Optimal interaction between Left Ventricular Assist Device (LVAD) and right ventricular (RV) function is paramount for survival in patients receiving mechanical assistance as destination therapy (DT). Assessment of adequate LVAD pump speed is recommended before hospital discharge. However, the role of systematic re-assessment of optimal speed setting in ambulatory patients at long-term follow-up is unclear.

Methods: Ambulatory HeartWare DT-LVAD patients underwent speed optimization at least 6 months after implantation. Left and right ventricular performance was echocardiographically assessed for incremental speed settings with steps of 100 rotations per minute to determine optimal hemodynamics. Evaluation at 3 months follow-up included laboratory and echocardiographic measurements.

Results: Assessment of optimal pump speed was performed in 14 patients (11 male, 58 ± 13 years, 19 [IQR 10-32] months on LVAD support). In 7 patients (50%) pump speed was adjusted (increase 171 ± 111 RPM, $p < 0.01$). Three months after optimization RV fractional area change (RV FAC) was improved (28 ± 6 to 37 ± 11%) without RV dilatation (RV EDD 44 ± 9 to 43 ± 8 mm). Furthermore, pro-brain natriuretic peptide level (pro-BNP) had decreased (3349 ± 1732 to 2658 ± 1386 ng/L), while glomerular filtration rate (GFR) tended to improve (48 ± 17 to 51 ± 16 ml/min/1.73m²) (figure 1).

Conclusion: Systematic assessment of LVAD speed setting reveals the need for optimization in a substantial proportion of patients on long-term support, resulting in enhancement of RV function, a decline in pro-BNP and a tendency towards improved GFR.



Effect of LVAD pump speed optimization

P1540

Biventricular assist device utilization for patients with morbid congestive heart failure as a bridge to heart transplantation in a low organ donation environment

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Background: Heart transplantation remains the gold standard treatment for patients with end stage heart failure. Low organ donation combined with delayed referral of advanced-stage cardiomyopathy patients necessitates biventricular assist device (BiVAD) support for extended periods of time.

Methods: We retrospectively reviewed the records of the patients treated with this paracorporeal device between June 2004 and August 2014 at our institution. Sixty-nine patients (mean age 41.9 ± 13.3 years, range: 11 to 59 years) were supported as a bridge to transplantation. Sixty out of 69 (87%) patients were in INTERMACS 1 Level while 15 of them had survived after a successful resuscitation (intravenous inotropes, 60; ventilated, 10; mean: CI 1.9 L/min/m²; CVP 19 mmHg; total bilirubin 3.75 mg/dl; NT-proBNP, 35,500 pg/ml). Various short-term devices were used as a bridge to bridge (IABP:52, Impella:2, Levitronix:4 and ECMO:2). Two patients needed a BiVAD after left ventricular assist device support of 439 and 295 days, respectively.

Results: Thirty day, 180 day, and 1 year survival after implantation (excluding transplanted patients) was 78%, 87% and 80% respectively. Thirty-seven of them were transplanted and seven are ongoing. Mean time on support was 781 days and 61 out of 69 patients with adult-sized pumps were discharged home with a mobile driver. Thirty patients exceeded 2 years of uncomplicated support before they were transplanted. One of our patients was successfully transplanted after 1460 days of support. One patient with renal failure and dialysis dependence lived at home 3.5 years after implantation. Complications included infection (n=15), bleeding requiring reexploration (n=12), and thromboembolic events (n=20). Twenty five patients died during support due to different reasons. Early mortality was due to multiorgan failure while late mortality regarded mostly cerebrovascular complications.

Conclusions: Support with BiVAD offers an acceptable rate of survival to heart transplantation. Furthermore, the use of a BiVAD itself does not confer an increased morbidity or mortality, and overall outcomes with this device are comparable to that of implantable LVADs if used strategically in severe congestive heart failure. With the institution of meticulous wound care, morbidity has been significantly reduced, and management as an outpatient is achievable, however readmissions are still frequent.

P1541

Patient selection for left ventricular assist device implantation and prevention of post implant right ventricular dysfunction: role of echocardiography

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Patient selection for implantation of Left Ventricular Assist Device (LVAD) is complicated and challenging. Post operative RV failure (RVF) may occur after Left Ventricular Assist Device (LVAD) implant. Preoperative identification of risks factors for RVF should lead to improved selection of patients. Aim of the present study is to observe whether right ventricular longitudinal strain (RVLS) evaluation may have clinical implications in patient selection and after LVAD implantation.

Methods: Clinical features and comprehensive transthoracic echocardiography for the evaluation of RV function was prospectively collected in 37 males patients (mean age 58 years ± 5) before LVAD implantation. Echocardiographic studies were performed using a Vivid E9 (GE Vingmed, Horten, Norway); the tricuspid annular plane systolic excursion (TAPSE), the pulsed tissue Doppler imaging on the tricuspid lateral annulus (S'), and the RV fractional area change (FAC) were calculated in accordance with the current recommendations of American Society of Echocardiography. For a subgroup of 17 patient was possible, according to imagines adequacy, to

analyze images off-line to calculate the free wall RVLS using a commercially available semi-automated 2D strain software (EchoPac, GE). During the post-operative period we recorded the need and the duration of intravenous inotrope support and inhaled nitric oxide. Correlation between variables was performed by Spearman's test.

Results: Concerning clinical features only 2 patients were subject to urgent LVAD implantation.

Based on standard echocardiographic criteria 86% of entire population had RV dysfunction (RVD), (73% only TAPSE <15 mm, 75% FAC<30% and 86% S TDI S <0,10 cm/sec). Median RVLS was -16% (IQ:-13.5%; -18%).

To better evaluate importance of RVLS in patient selection, entire population was divided in 2 subgroup of 20 and 17 patient respectively according to have or not available RVLS before LVAD implantation.

A post analysis of those 2 group, based on guidelines criteria for RVD post LVAD implantation (> 15 days of inotropes infusion, >2 days NO inhalation) was calculated. In No RVLS group 17% developed RVD for inotropic support (8,2 ± 5,2) and 57% for NO infusion (3,7 ± 3,4), in RVLS group no one had RVD for inotropic support (4,2 ± 2,7) and 12% for NO infusion (1,5 ± 1,1), with a statistical difference between two group, respectively p 0,01 and p 0,03.

Discussion: In Our experience RVLS, provide a precise estimation of RV systolic performance and permitted a better selection of patient before LVAD implantation reducing risk of RVF in post operative period.

P1542

Early assessment of renal parameters after long-term ventricular assist device implantation as predictors of acute renal failure requiring renal replacement therapy

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Purpose: Long-term ventricular assist device (VAD) implantation is widely used treatment modality in patients with end-stage heart failure as a bridge to heart transplant or destination therapy. Acute renal failure (ARF) requiring renal replacement therapy (RRT) remain one of the main causes worsening both short-term and long-term prognosis. In this prospective study we review whether early assessment of renal parameters after VAD implantation can distinguish patients in high-risk of ARF requiring RRT.

Methods: 24 patients indicated to VAD implantation without RRT before surgery were enrolled into study. Levels of blood urea nitrogen (BUN), serum creatinine, cystatin C, both serum and urinary neutrophil gelatinase-associated lipocalin (NGAL) and urinary alpha-1-microglobulin were assessed before and within 2 hours after VAD implantation. Data were compared according to presence of post-operative ARF requiring RRT. Values are presented as median with interquartile range.

Results: Post-operative acute renal failure requiring renal replacement therapy occurred in 7 of 24 patients - RRT was initiated between 1st and 7th day after surgery. There was no significant difference in renal parameters before VAD implantation between subjects with or without ARF requiring RRT after operation. Within 2 hours after surgery only serum creatinine was significantly increased in patients with ARF requiring RRT (143,0, 133,4-156,6 vs. 100,1, 92,4-123,1 μmol/l; p = 0,010). Optimal threshold value of serum creatinine within 2 hours after VAD implantation for patients in high-risk of ARF with RRT was 123,7 μmol/l (sensitivity 85,7%, specificity 82,4%) or it's increase more than -0,3% compared to pre-operative value (sensitivity 85,7%, specificity 70,6%). Other renal parameters showed no significant difference both in absolute levels and dynamics.

Conclusion: Acute renal failure requiring renal replacement therapy remains common and serious issue after VAD implantation. Based on our results patients with high-risk of this complication can be early distinguished according to levels of serum creatinine after surgery and it's dynamics compared to pre-operative levels. Interestingly other renal parameters including new biomarkers as NGAL bring no additional information in our subjects. However, this assumption need to be confirmed with larger population research.

P1543

Prognostic factors for exit-site infections in patients with LVADs

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Introduction: Left ventricular assist devices (LVADs) are increasingly used as a definite treatment for end stage HF, leading to significant improvement of patients' survival.

However exit-site infections remain a serious complication of prolonged mechanical support associated with significant morbidity and mortality.

Purpose: Our purpose was to identify risk factors for late exit-site infections

Methods: Thirty two patients who underwent an LVAD implantation in our center

with detailed medical charts with clinical, laboratory, echocardiography and hemodynamic data were included in the study

Results: Late driveline infections developed in 9/32 patients (28%), 16 infections total at a median of 13 months after implantation. Almost all patients that developed an exit site infection during the first year of implantation (3/4) presented with repeated infections in the long term.

Baseline characteristics of patients presented with a late driveline infection were (etiology of Heart Failure [7 ischemic, 2 non-ischemic], gender [8 male, 1 female], age: 53.4 ± 11.8, weight: 71.6 ± 12.2, duration of Heart Failure: 8.2 ± 4.9 years, diabetes 4/9, mean duration of support: 17.2 ± 15.3) months.

Ischemic etiology (95%, p = 0.03) and high preoperative systemic vascular resistance (1344 ± 285 [without infection] vs 1804 ± 600 [infection], p = 0.02) were identified as independent prognostic factors for late exit site LVAD infection

Patients were more likely to be diabetic 4/9 (infection) vs 6/23 (without infection) (p:0.4), with coronary artery disease as the underlying cause of HF 2/9 (infection) vs 16/23 (no infection) (p:0.02) and supported with Heartmate II 9/9 (infection) vs 14/23 (no infection) (p: 0.03).

Conclusions: In our study exit site infections is a more frequent complication of LVAD support in diabetic patients and in those with ischemic cardiomyopathy and high pre-operative systemic vascular resistance. Repeated infections will more likely occur to patients that developed an exit site infection after the first year of implantation.

P1544

Progression of aortic regurgitation after continuous-flow left ventricular assist device implantation

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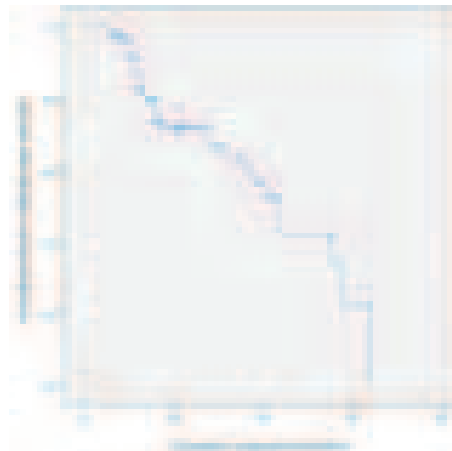
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Purpose: Aortic regurgitation (AR) is a complication following left ventricular assist device (LVAD) implantation that can cause clinical symptoms. The aim of this study was to examine AR progression after continuous-flow LVAD implantation.

Methods: This study included patients with no or less than severe AR who underwent HeartMate II (no=21) or HeartWare (no=69) implantation in a single center between 12/2010 and 6/2014. Serial echocardiograms were obtained preoperatively, at a minimum of 3-months and most recent evaluation. AR was graded as none, mild, moderate and severe and the change in AR at follow-up was analyzed with significance tests. Kaplan-Meier estimates for freedom from moderate or worse AR at follow-up were generated.

Results: Mean age was 51.7 ± 10.9 years, 85.6% were male and 48.9% had dilated cardiomyopathy. Median duration of LVAD support was 415 ± 206 days and 46.6% of patients were supported for more than a year. AR progression was seen in 24% of patients from none to mild or moderate AR and in 16% from mild to moderate or severe AR. Duration of support was a significant predictor for AR development (p=0.006) whereas aortic valve opening pattern was not significant (p=0.063). No statistically significant differences were noted in age, sex, body surface area, postoperative left ventricular end-diastolic diameter, hypertension, etiology of heart failure and implanted device type (HMII vs. HW). Only 2 patients had progression from preoperative none-mild AR to severe AR and were listed for urgent cardiac transplantation.

Conclusion: AR development risk is associated with longer duration of CF-LVAD support. However, only 2 patients were clinically symptomatic due to severe AR. Pump speed optimization to adjust aortic valve opening and early transplantation have to be considered.



SURGERY

P1545

What is the optimal choice of grafts in patients with severely impaired left ventricular function?

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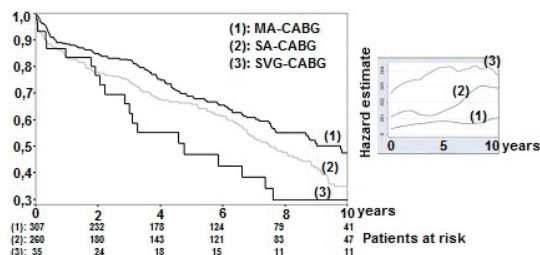
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Purpose: There is a paucity of long-term results after multiple arterial CABG (MA-CABG) in patients with low left ventricular ejection fraction (LVEF) $\leq 25\%$. The purpose of the present study is to determine whether superior long-term survival in such patients may render obsolete single artery CABG plus vein grafts (SA-CABG) and/or only saphenous vein grafts (SVG-CABG).

Methods: We retrospectively evaluated 602 consecutive patients with LVEF $\leq 25\%$ who underwent CABG (307 MA-CABG, 260 SA-CABG and 35 SVG-CABG). The mean follow-up was 5.3 ± 4.1 years. Multivariate logistic regression analysis was performed for in-hospital mortality and multivariate Cox regression analysis for long-term mortality, adjusting for all available preoperative, intraoperative and post-operative risk factors. Risk-adjusted Kaplan-Meier survival curves were constructed and adjusted hazard estimates were determined.

Results: There were 13 (4.2%) in-hospital deaths in MA-CABG (reference group), 21 (8.1%) in SA-CABG (OR 1.64, 95%CI 0.71-3.78) and 4 (11.4%) in SVG-CABG (OR 2.77, 95%CI 0.69-11.16). MA-CABG improved long-term survival compared to SA-CABG (HR 1.41, 95%CI 1.10-1.81, $P=0.007$) and SVG-CABG (HR 1.89, 95%CI 1.19-3.01, $P=0.007$). Risk-adjusted Kaplan-Meier survival curves of the three groups as well as adjusted hazard estimates are shown in figure.

Conclusion: Vein grafts in patients with LVEF $\leq 25\%$ result in worse in-hospital mortality and significantly worse long-term survival either alone (SVG-CABG) or in combination with a single artery (SA-CABG) when compared to MA-CABG. Conversely, the long-term hazard of MA-CABG remains low and stable and is superior when compared to groups with more vein grafts (SVG-CABG and SA-CABG), thus putting in question the wisdom of using any vein graft in these patients with low LVEF.



P1546

Hybrid coronary revascularization in 100 patients with multivessel disease: what can we expect?

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Introduction: Hybrid coronary revascularization (HCR) arises as a combined approach of surgical and percutaneous coronary intervention (PCI). This strategy joins the best of two traditionally isolated treatment options in multivessel coronary artery disease (CAD). We aim to assess the safety and clinical outcomes of patients submitted to HCR.

Methods: From May 2008 to December 2014 one-hundred consecutive patients underwent two-staged coronary revascularization (PCI after coronary artery bypass grafting), in our hospital, after Heart Team evaluation. Death, myocardial infarction and repeated target vessel revascularization (MACE) were analyzed in index hospitalization and at follow-up.

Results: Mean age was 67 ± 10 years and 66% of patients were male. HCR was performed after an acute coronary syndrome in 47% of the population and two-thirds of the patients had preserved left ventricular ejection fraction. In all cases an arterial graft to the left main was performed. Forty-nine percent of patients also underwent other arterial or veins grafts. CABG was carried out off-pump in 76% of patients. PCI occurred 5 ± 3 days after surgery, with 100% of angiographic success and using drug-eluting stents (67%), bare-metal stents (32%) or both (1%). No intra-operative or in-hospital deaths were reported. At a mean follow-up of 22 ± 14

months, eighty-three patients were evaluated and overall population freedom from MACE was 97%: one case died from pneumonia and two had non-STEMI, treated with conservative approach. No cardiac death occurred.

Conclusions: Hybrid coronary revascularization may be considered a viable option in patients with multivessel CAD. In our experience HCR has a good outcome at short and mid-term follow up. In spite of the lack of large randomized controlled trials with long term follow-up, it seems reasonable to consider that this strategy can have an important role in CAD treatment.

P1547

Perioperative changes in cardiac autonomic innervation following coronary artery bypass grafting

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Purpose: Surgical revascularization is the most commonly performed cardiac intervention and it is recommended when two or more branches (vascular systems) are affected. The decision for surgical revascularization determines the currently growing interest in methods for finding informative features for cardiac surgery indication, prognosis and follow-up of the intervention. Objective of this study is to propose a method to assess the status of autonomic nervous regulation (ANR) and adaptation reserves of the body in patients with multivessel coronary artery disease (MCAD) in the preoperative and early postoperative period after CABG.

Methods: Rest ECG of 20 CABG patients with MCAD (2-4 coronary arteries shunting) was recorded before the intervention and on 3 to 7 days following. All patients were in sinus rhythm pre- and postoperative. Each ECG recording contains the conventional 12 leads. All ECGs have been digitized at 1000 samples per second, with 16 bit resolution over a range of ± 16.384 mV. A modified Indicator of the Activity of ANR (IAANR) has been used, whose value is determined by the estimated 5 heart rate variability (HRV) indices: heart rate (HR), standard deviation of examined normal RR interval (SDNN), geometrical HRV index, low frequency (LF) and very low frequency (VLF) bands of total HRV spectrum.

Results: i. Significantly higher sympathetic tone towards the parasympathetic contour preoperative ($p < 0.001$) and postoperative ($p < 0.0001$), and this prevalence increases postoperative; ii. Parasympathetic tone is moderately suppressed preoperative and to a greater extend postoperative ($p < 0.05$); iii. Compared to the moderate stress of the regulatory systems preoperative (IAANR = 4.07), in the early postoperative period, they are in a state of high tone (IAANR = 5.36; $p < 0.05$), with increased activity of renin-angiotensin-aldosterone system to provide a higher adaptability of the organism.

Conclusion. The results show: i. Significant higher sympathetic versus parasympathetic tone contours pre- and postoperative, and this dominance increases postoperative; ii. The parasympathetic tone is strongly suppressed preoperative and to even greater extend postoperative; iii. In the early postoperative period ANR are in highly increased state of, with an increased activity of sympatho-adrenal and pituitary-adrenal systems to provide a higher adaptability of the organism. The ability of the ANR to respond to myocardial ischemia by increased activity of the efferent and afferent contours makes it a valuable informational source for prognosis of the results of CABG.

P1548

Intracardiac hemodynamics in patients with coronary heart disease after coronary artery bypass grafting

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Purpose: To examine the intracardiac hemodynamics in patients with coronary artery disease (CAD) before and 4 months after coronary artery bypass grafting.

Materials and methods: We examined a total of 55 patients (25 women and 30 men) with coronary artery disease from 39 to 76 years, with obstruction of two (5 patients), three (15 patients), more than four (35 patients) coronary arteries (CA). All patients had hemodynamically significant CA obstruction; 37 patients had obstruction of different CA, 8 - had more than 80% obstruction of left main CA, 53% of patients had a myocardial infarction (MI). All patients underwent coronary artery surgery (CABG) or mammary coronary artery bypass surgery (MCABG) resulted in two (9 patients), three (21 patients) and more than 4 grafts (25 patients). We performed a 4 months observation of 55 patients with (CAD) who underwent (CABG). Patients were divided into two groups: group 1 included 25 people with CAD without a history (MI) and the 2-nd group consisted of 30 patients with postinfarction atherosclerosis (PICS). The groups matched by age and sex. We assessed parameters of cardiovascular hemodynamics by volume compression oscillometry before and 4 months after CABG.

Results: Analysis of hemodynamic parameters showed that patients from the first group had increased all the examined parameters: cardiac output (CO) (13.6%), cardiac index (CI) - 13.1%, stroke volume (SV) - 8.5%, stroke index (SI) - 8.6%, the volume rate of cardiac output - 4.5% LV contracting power - 12% after 4 months

of CABG. The second group, after 4 months after the operation, on the contrary, demonstrated a decrease of CO (5.2%), CI - 5.32%, CV - 10.7%, the volume rate of cardiac output - 22.6%, LV contracting power - 22.1%.

Conclusion: Thus, the analysis of cardiovascular hemodynamic parameters obtained by the volume compression oscillometry showed that CABG in patients without a history of MI, led to an improvement in ventricular function after 4 months after surgery. Whereas in the group of patients with PICS even after successful surgical myocardial revascularization in the first 4 months there has been a deterioration in hemodynamic parameters caused more pronounced initially negative remodeling of the heart and symptoms of heart failure, which was confirmed by a decrease in almost all indicators.

P1549

Analysis of inotropic function of the heart of patients with ischemic heart disease after coronary artery bypass surgery

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Aim: To study and compare rates' changes of inotropic function of the heart of patients with ischemic heart disease after coronary artery bypass surgery (CABG) in early postoperative period.

Materials and methods. 30 patients suffering from ischemic heart disease (IHD) were examined (6 women and 24 men), aged from 39 to 76 years, who have two (2 people), three (10 people) and more than four (18 people) coronary arteries (CA) damaged. Hemodynamically significant artery stenosis were diagnosed at all patients, at that 17 patients had vascular occlusion of different localization, 4 patients had stenosis of the trunk of the left coronary artery for more than 80%, 53% of patients had myocardial infarction. All patients had coronary artery bypass surgery (CABG) or mammo-coronary bypass surgery (MCBS) with the imposition of two (9 people), three (11 people) and more than four (10 people) shunts. In the 1-st group of patients (20 people) CABG was done in the conditions of cardiopulmonary bypass (CPB) and pharmacologic cold cardioplegia (PCC). In the 2-d it was done on the beating heart (off-pump coronary artery bypass, OPCAB). We assessed parameters of cardiovascular hemodynamics by volume compression oscillometry before and 7 days after CABG.

Results: The analysis of hemodynamic parameters showed that in the 1-st group in 7 days after the surgery cardiac output (CO) decreased for 11%, heart index (HI) - for 6.1%, stroke volume (SV) - for 23%, stroke volume index (SVI) - for 25%, volume rate of output (VRO) - for 26.5%, power of contraction of the left ventricle (LV) - for 30.2%. In the 2-d group by the 7-th day after the surgery CO vice versa increased more than in 1.5 time, HI - for 11.3%, VRO - for 26%, power of contraction of the left ventricle (LV) - for 24.4%.

Conclusions: Thus, preliminary analysis of cardiovascular hemodynamic parameters that were obtained by VCO method in dynamics of CABG showed that patients with IHD already in 7 days after the off-pump coronary artery bypass had an improvement of inotropic function of the heart, while those patients who had CABG in the conditions of CPB and PCC in early postoperative period had a decrease almost of all parameters; this probably may testify to cardio depressive effect of this surgical intervention for recovery of cardiovascular hemodynamics in total.

P1550

Differential expression of S100A1 in patients undergoing on-pump and off-pump coronary artery bypass grafting

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Purpose: S100A1 is a protein of the S100 family which is involved in a variety of cellular processes such as contraction, apoptosis and gene expression. Apart of these properties S100A1 potentiates cardiac function which is an important feature in heart failure. The present study aimed to examine the fold change of S100A1 mRNA levels during CABG.

Methods: We examined atrial tissue biopsies from patients taken before aortic occlusion and after reperfusion after on-pump CABG (ONCAB, n=37, 29 male, 17 on statin therapy, aged 63.3[1.3] mean [S.E.]) and at the beginning of the first anastomosis and the end of the final anastomosis after off-pump CABG (OPCAB, n=30, 27 male, 22 on statin therapy, aged 64 [1.5] mean [S.E.]). S100A1 mRNA levels were determined by real-time RT-PCR.

Results: S100A1 showed 3.21-fold change (95% CIs 2.34-4.05) in ONCAB group as compared to 1.39-fold change (95% CIs 0.42-2.35) in OPCAB group (P=0.0068). In patients on chronic statin therapy prior to surgery S100A1 mRNA levels were increased 216% in the ONCAB group (3.35 mean (0.63 S.E.)) -fold change vs. 1.55 mean (0.56 S.E.) -fold change in OPCAB patients on statin, P=0.04 **Conclusion:** The ability of S100A1 to restore myocardial cellular homeostasis in patients undergoing ONCAB may explain the superiority in midterm and long-term results of this

conventional surgical method in comparison to OPCAB in certain published clinical series. Furthermore, statins may facilitate the overexpression of S100A1 in the group of ONCAB.

P1551

In patients undergoing on-pump coronary artery bypass grafting (CABG), increased atrial Farnesoid X receptor signaling is associated with atrial myocyte apoptosis compared to off-pump CABG

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The Farnesoid X receptor (FXR) a member of the nuclear receptor superfamily of ligand-activated transcription factors that functions as an endogenous sensor for bile acids, is expressed mainly in the liver, adipose tissue and intestine. Recent evidence suggests that FXR also acts as a novel functional receptor in murine myocardium, regulating apoptosis and contributing to ischaemia/reperfusion injury. The potential expression and possible function of FXR in the diseased human heart remains largely unknown. The present study aimed to examine the levels of FXR, its target small heterodimer protein (SHP) at the mRNA and protein levels and parameters of apoptosis (pro-apoptotic BAX/anti-apoptotic BCL2 mRNA ratio) in 44 patients undergoing on-pump CABG and 31 patients off-pump CABG. The on-pump group consisted of 13 women and 32 men with a mean ± S.E. age of 64.31 ± 1.55 and 68.23 ± 1.54 years respectively, and the off-pump patients consisted of 3 women and 28 men with a mean ± S.E. age of 69.00 ± 2.08 and 63.46 ± 1.66 years respectively. We analyzed FXR, SHP, BAX and BCL2 mRNA expression by quantitative Real Time PCR using 18s as an internal control for standardization in right atrial biopsies taken before aortic occlusion and after reperfusion during CABG. FXR and SHP protein was determined by Western blot. FXR mRNA (fold change) post CABG was significantly (p < 0.05) higher in on-pump (2.75 ± 0.63) vs. off-pump (1.60 ± 0.22) [mean ± s.e.]. SHP mRNA was also significantly (p < 0.05) higher on-pump (4.58 ± 0.60) vs. off-pump (2.06 ± 0.31) post CABG. FXR and SHP protein paralleled mRNA levels. The BAX/BCL2 ratio a measure of apoptosis, was significantly (p < 0.05) increased in on-pump (3.50 ± 0.44) vs. off-pump patients (1.44 ± 0.24) post CABG. Of all the possible correlations tested, there was a positive correlation between FXR and BAX/BCL2 ratio (p = 0.015, r = 0.685) in on-pump patients post CABG. These results suggest that FXR and its target protein SHP are expressed in aortic tissue and are differentially regulated depending on on-pump vs. off-pump CABG. Increased FXR and apoptotic signaling in on-pump CABG vs off-pump CABG and the demonstration of a positive correlation between FXR and the BAX/BCL2 ratio with on-pump CABG, suggests a potential benefit of off-pump CABG.

P1552

A comparison of different methods of heart muscle preconditioning. A preliminary study of patients with heart failure, undergoing elective off-pump coronary artery bypass graft surgery

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Background: Cardiac damage after cardiac surgery can lead to prolonged hospitalization for patients with heart failure (PwHF) as well as an increased perioperative mortality rate. The concept of pharmacological preconditioning by volatile anesthetics has recently gained widespread interest.

Aim: The aim of this study was to compare different methods of heart muscle preconditioning in PwHF, undergoing elective off-pump coronary artery bypass graft surgery (OPCAB).

Methods: The randomized controlled study was performed to compare cardiac troponin I release in PwHF receiving different methods of anesthesia with a combination of remote ischemic preconditioning (RIPC) during OPCAB. 31 pts. (51-79) mean age 63 yrs (75% male), NYHA (II) were randomly assigned: 9 pts to combined desflurane anaesthesia (CDa) and RIPC (group 1), 10 pts to desflurane anaesthesia (Da) (group 2) and 12 pts to total intravenous anesthesia (TIVA) (group 3). RIPC was performed during general anesthesia before surgery in three 5 min cycles of transient upper limb ischaemia/reperfusion. In addition, all patients were anesthetised with a standardised protocol. Depth of anesthesia was evaluated by bispectral index. Troponin I release was measured as a marker of myocardial necrosis before surgery, 6, 12 and 24 hours after surgery.

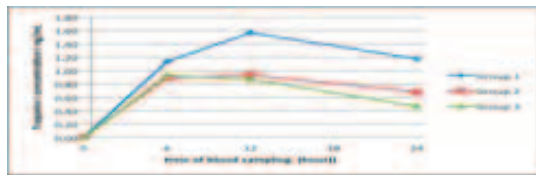
Results: In PwHF there was a trend of reduction in postoperative median peak of troponin I in patients' Da (group 2) and in patients receiving TIVA (group 3) compared to patients anesthetised with CDa and received RIPC (group 1). Ryc 1.

Conclusions: Using two methods of heart preconditioning simultaneously resulted in a higher peak troponin I release.

Table P1553.

Group No	Group Content	n	Transesophageal Echocardiographic Mean ADIDs vs. RMS					
3D EED (mm)	RMS (mm)	p	3D HHD (mm)	RMS (mm)	p			
1	(31+33 ATS)	13	25.3±0.4	26.8	<0.001	25.2±0.4	26.8	<0.001
2	(31+33 CM)	11	23.6±0.2	24.2	<0.001	22.1±0.9	24.2	<0.001
3	(31+33 SJM)	10	25.2±0.7	26.8	<0.001	25.1±0.8	26.8	<0.001
4	(29 ATS)	10	23.5±0.6	24.8	<0.001	23.3±0.6	24.8	<0.001
5	(29 CM)	12	23.3±0.4	24.2	<0.001	22.4±0.6	24.2	<0.001
6	(29 SJM)	17	23.7±0.4	24.2	<0.001	23.3±0.7	24.2	<0.001
7	(27 ATS)	7	21.7±0.4	22.8	0.001	21.4±0.7	22.8	0.003
8	(27 CM)	13	21.9±0.4	22.5	0.001	20.7±0.7	22.5	<0.001
9	(27 SJM)	11	21.7±0.7	22.5	0.009	21.3±0.6	22.5	<0.001
10	(25 ATS)	8	19.5±1	20.8	0.014	19.4±1	20.8	0.009
11	(25 CM)	6	19.4±0.4	20.5	0.003	18.3±0.9	20.5	0.003
12	(25 SJM)	8	20.2±0.8	20.4	0.62	20.0±0.9	20.4	0.36

ADID: Anatomic Diastolic Internal Diameter, ATS: ATS Medical, CM: Carbomedics, SJM:St. Jude Medical, 3D:Three Dimensional, EED: edge to edge diameter HHD: hinge to hinge diameter, RMS: Reported manufacturer Size



Ryc 1. Troponin release in time function

P1553

Quantitative assessment of normal mitral mechanical valves by real time three dimensional transesophageal echocardiography: a reference study

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Background: Hemodynamic performance of mitral mechanical valves (MMV) is primarily determined by the anatomic diastolic internal diameter (ADID). Since in both invitro and in vivo studies it was observed that the echocardiographic ADIDs are smaller than the reported manufacturer sizes it may be helpful to know the reference ADIDs of the MMVs for future evaluation. This prospective, study aimed to assess the reference ADIDs of MMVs.

Methods: Patients with recent bileaflet MMV replacement were examined by real-time three-dimensional transesophageal echocardiography (RT-3D TEE) in the early postoperative period when presence of pannus overgrowth was unlikely. Patients with MMV thrombosis were excluded. Hinge to hinge and edge to edge ADIDs were measured.

Results: 128 patients with MMVs (38 ATS, 44 Carbomedics, 46 St. Jude Medical, all bileaflet) were evaluated. The mean ADIDs measured by RT-3D TEE for each valve size are presented in Table 1. 3D ADIDs were smaller as compared to the reported manufacturer sizes.

Conclusion: This RT-3D TEE-guided study provides mean ADIDs for all sizes in 3 most commonly used MMV brands worldwide. These ADIDs could be a basal reference and therefore may be an important adjunct to the clinical follow-up of MMVs.

P1554

Usefulness of impedance cardiography in optimisation of diagnosis and treatment of asymptomatic aortic stenosis

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Exercise stress test is routinely used in clinical assessment in patients with asymptomatic aortic stenosis (AAS) but the only hemodynamic parameter that is measured is arterial blood pressure. We implement noninvasive cardiac output measurement during exercise to monitor hemodynamics more precisely in pts with AAS.

Patients and Methods: In this preliminary study we analyzed data of 40 pts (mean age 58 ±12yrs) with diagnosed AAS - mean transvalvular gradient>40mmHg. All pts underwent symptom limited exercise stress test (EST) with noninvasive hemodynamics measurement (PhysioFlow). We analyzed stroke volume and cardiac index (continuous measurements averaged every 15 second) before exercise, at 3 minutes of exercise, at maximal heart rate and 1 minute after exercise.

Results: All EST were finished because of pts fatigue (8/10 in Borg scale). No symptoms were reported by pts, maximum heart rate was >85% of maximal heart rate adjusted for age and gender in all pts. We did not observe blood pressure decrease on the top of effort in any case. During 6 month of follow up 2 pts became symptomatic and were qualified for aortic valve replacement.

At rest mean cardiac index was 2,2±0,2 l/min/m². In 5 pts we recorded CI<2l/mim/m² - one of them became symptomatic during this short follow up. After 3 minutes of exercise CI increased in all pts - mean 3,75 ± 0,99l/min/m², and achieve at maximal exercise mean value 5,2 ± 1,1l/min/m². Generally in this AAS pts during exercise CI increased 134 ± 52% from rest value. In 7 pts this increase was below 100% - two of them became symptomatic during 6 monts of observation.

Conclusion: Noninvasive hemodynamics monitoring during rest and exercise in pts with AAS is safe and possibly can improve the clinical assessment.

P1555

Therapeutic strategies in prosthetic valve endocarditis in patients with prior valvular heart failure

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Background: Early surgery represents the current trend in the treatment of prosthetic valve endocarditis (PVE) with new onset aggravated heart failure (HF). However, there are limited data about this indication in patients with prior HF.

Objective: To demonstrate that medical therapy with antibiotics (MTA) remains effective in PVE patients with prior stable heart failure (HF) without complications.

Method: Retrospective analysis of 247 patients discharged with established endocarditis. 56 patients had possible or definite PVE (modified Duke criteria) and were divided in two groups: early and late PVE (12 month after surgery cut off). All patients had prior the infectious event valvular heart failure (HF). We evaluate the role of MTA on PVE course. Variables: demographic data, microbial etiology, comorbidities, clinical, biological and echocardiography parameters, MTA regimens and side effects. MTA duration: 6 weeks.

Results: Early PVE: 51.78%, mean age: 54.64 years old, male 64%. Ejection fraction (EF) was preserved in ~ 85% of studied patients in both groups. PVE Etiology (%Early vs Late): Negative blood cultures (BC) 55.2 vs 48.2; S. Aureus 3.5 vs 14.8; Coagulase-negative Staphylococci 20.7 vs 11.1; Viridans 3.45 vs 7.41; grup D Streptococci 0 vs 14.9. In our patients late PVE was frequently found on biologic valves (p = 0.001), while early PVE appear immediately after placement of mechanical valves. MTA regimens were frequently changed due to renal or skin side effects (Oxacillin p = 0.035, Vancomycin p = 0.005). The regimen Impipenem + Amikacin was safe and effective in both groups with few side effects and with the shorter duration

Table P1557.

Pre-operative	1 groupe (Gal-3 \leq 18.2 ng/ml)	2 groupe (Gal-3 $>$ 18.2 ng/ml)	Pre-operative	1 month	6 month
	1 month	6 month			
LA (mm)	57.1 \pm 6.9*	52.1 \pm 6.2	44.5 \pm 5.3*	48.8 \pm 7.1*	47.4 \pm 7.9
LVESD (mm)	47.3 \pm 5.8*	48.6 \pm 5.8	34.5 \pm 3.9*	45.0 \pm 4.6 ⁸	40.9 \pm 4.3
LVEDD (mm)	65.4 \pm 8.0*	64.5 \pm 7.7	50.8 \pm 5.1*	63.8 \pm 7.7 ⁸	58.3 \pm 6.6
EF (%)	52.4 \pm 6.7*	48.1 \pm 6.8	59.3 \pm 4.6*	55.5 \pm 7.5	55.7 \pm 4.4
LVM (g)	183.4 \pm 46.1	186.3 \pm 43.2	181.5 \pm 47.5	184.5 \pm 42.0	188.6 \pm 46.9
					175.3 \pm 38.0

*,& - p < 0.05

up to fever remission ($p = 0.004$), irrespective of causative organism. MTA responders show no difference of outcome between regimens (multivariate analysis). EF does not influence mortality per se. Patients outcome: favorable 71%, in hospital death 2%, transferred due to complications 27%, out of which 79% necessitate early valve surgery. Early surgery, irrespective of PVE type, was due to perivalvular extension of infection ($p = 0.0025$); systemic embolism ($p = 0.007$); persistent fever ($p = 0.03$). In-hospital mortality was related to prosthesis dehiscence favored by annular abscesses ($p = 0.008$). Perioperative mortality was 33%.

Conclusions: MTA was effective and safe in two third of PVE patients with prior heart failure, irrespective of antibiotic regimen, in both, early and late, PVE without complications. Study limitation: a small number of patients, high number of patients with preserved EF, high percentage of negative blood cultures.

P1556

Evaluation of endothelial functions in patients with paravalvular leakage in early postoperative period

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Purpose: Micro-defects around the prosthetic valvular annulus may cause small paravalvular leakages (PVL) in the very early postoperative period, but these defect are closed by tissue healing and fibrosis in a few days. Endothelin which is secreted by endothelial cells has a major role in wound healing including mitogenesis, fibrosis, vascular hypertrophy and inflammation. Persistence and progression of small defects which cause paravalvular leakage in early postoperative period may be a result of endothelial dysfunction. The aim of this study to investigate endothelial dysfunction in patients who have PVL in early postoperative period.

Methods: Prosthetic valve functions in patients who had recently (in 3 months) undergone prosthetic valve replacement were evaluated by 2-dimensional and real-time 3-dimensional transesophageal echocardiography. Patients who had PVL were included in the study as PVL group and patients who had normally functioning prosthetic valves were included as control group. Endothelial function was evaluated by the noninvasive measurement of flow mediated dilatation (FMD) of brachial artery. High resolution ultrasound was used to measure brachial artery diameter at rest, during reactive hyperemia (endothelium-dependent, FMD).

Results: Between January 2010 and December 2013 33 patients (mean age: 47,9 \pm 10,4 years, 14(42.4%) female, 24 mitral, 6 aortic ve 3 aortic and mitral) were included in PVL group and 40 patients (mean age: 49,9 \pm 13,0 years, 19 (47.5%) female, 28 mitral, 7 aortic ve 5 aortic and mitral) were included in control group. The maximum gradients were significantly higher in PVL group than the controls for both aortic and mitral valves (49,86 \pm 7,2 ; 39,8 \pm 9,6, $p = 0,037$, 20,6 \pm 2,3 ; 12,3 \pm 2,4, $p < 0,001$ respectively). The FMD value was significantly lower in PVL group (12,9 \pm 1,8 vs 13,8 \pm 1,6 ; $p = 0,022$). FMD level of <12.8 predicted PVL with an 55% sensitivity and 31% specificity (area under curve:0.355, $p = 0.034$). There was no correlation between FMD and PVL severity but a mild negative correlation was observed between FMD and paravalvular defect counts ($r = -0,246$; $p = 0,036$).

Conclusion: According the results of this study, endothelial dysfunction may play a role in the pathogenesis of PVL in patients with aortic and mitral prosthetic valves.

P1557

Influence of galectin-3 level on heart remodelling at patients with mitral valve insufficiency

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Objectives: To evaluate correlation galectin-3 level as defined before surgery with the echocardiographic parameters in patients with mitral insufficiency who underwent heart valve replacement after 6 months follow-up period.

Methods and Results: 48 patients (mean (SD) age 57.5 \pm 12.4 years) who underwent heart valve replacement with and mitral valve insufficiency were included. 32 were male and 16 were female. 22 patients has atrial fibrillation (AF), 15 has arterial hypertension (AH) and 20 has severe pulmonary hypertension (PH). Before operative treatment 8 patients has NYHA class I-II heart failure and 40 patients has NYHA class III-IV heart failure. Plasma galectin-3 levels were assessed pre-operatively. Two-dimensional echocardiographic parameters were measured at baseline, 1 month and at 6 months after surgery. Depending on the level of Gal-3 the patients were divided into 2 groups: the level-3 Gal \leq 18.2 ng / ml (group 1) and over 18.2 ng / ml (group 2).

In group 1 at 6 months after surgery it was observed significant reduction in the size of the left ventricle. LVESD with 47.3 \pm 5.8 mm decreased to 34.5 \pm 3.9 mm ($p < 0.05$), and the LVEDD with 65.4 \pm 8.0 mm to 50.8 \pm 5.1 mm ($p < 0.05$). Accordingly, in this group increased and EF: from 52.4 \pm 6.7% to 59.3 \pm 4.6%. In the group 2 positive dynamics was also observed, but it was less pronounced. Since reliable data are obtained only when estimating the size of the LA, while the size of the LVESD with 45.0 \pm 4.6 mm decreased to 39.3 \pm 3.5 mm ($p < 0.01$), and the LVEDD with 63.8 \pm 7.7 mm to 56.0 \pm 6.2 mm ($p < 0.01$). Ejection fraction was unchanged.

Conclusions: The preoperative level of galectin-3 at patients with mitral insufficiency affects the intensity of the positive changes - a reduction of the heart chambers. At patients with preoperative high level of Gal-3 normalization of LV and LA size is less significant.

P1558

Percutaneous mitral dilatation: always a first-line indication

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Various techniques of mitral valve dilatation balloon catheters have been proposed as an alternative to surgical commissurotomy until the introduction of percutaneous mitral dilatation in 1984. The results provided for this purpose have proved efficacy in the short and long term.

The aim of the study is to report the descriptive statistics and to assess the efficacy and safety of the procedure.

This is a retrospective study, conducted between January 2011 and December 2014. 141 patients have been collected in the cardiology department of our CHU.

The mean age was 36 years with female predominance (85%). 130 patients (92%) were symptomatic class functional II or III. the mean Wilkins score was 7,22.

After percutaneous mitral dilatation, the mean mitral surface increased from 0,87 cm² to 1,84cm², the mean transmittal gradient decrease from 13,8mmHg to 5,4mmHg, the mean systolic pulmonary pressure decrease from 42mmHg to 28mmHg.

A good immediate result was obtained in 134 patients (95%). In 2 patients, mitral regurgitation worsened, becoming grade IV. 3 patients had presented a mitral leaflet rupture, and 2 patients had presented a tamponade.

In the light of these findings, percutaneous mitral dilatation has proved the efficacy and safety of the procedure, its indication remains in first intention.

P1559

Aortic stenosis operated in the octogenarian: predictors of a worse prognosis in the medium-term

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Purpose: Aortic valve stenosis is increasingly prevalent in agreement with the aging population. So it becomes important to characterize this group of patients in its various forms.

Aims: To analyze the clinical profile, ECG patterns, and echocardiographic predictors of poor prognosis (death and / or hospitalization for HF to 12 months) of a population of octogenarians with severe aortic stenosis who underwent valve replacement surgery.

Methods: analysis of 40 patients with severe aortic (Ao) stenosis undergoing valve replacement surgery. The severity of stenosis was established by echocardiographic criteria and TTE was performed pre- and postoperatively. The predictors associated with worse prognosis were determined by univariate and multivariate analysis, about 1 year after surgery.

Results: Female gender accounts for 52% of the study population. The average age is 82 years (min 80 and max 85 years). All patients received aortic bioprosthesis. In 80% of cases the indication for surgery was the presence of symptoms. In the remaining 20% of cases was the presence of LV dysfunction or trigger symptoms with exercise testing. The moderate to severe mitral insufficiency is associated with a worse prognosis ($p < 0.05$). Co-morbidities were present in 95% of cases, DM was associated with a worse prognosis ($P = 0.04$). Dyspnea is the most frequent symptom in females ($p < 0.01$) and is associated with greater ventricular hypertrophy ($p < 0.05$). The absence of angina was not a predictor of the absence of significant coronary artery disease ($p = 0.02$). 50% of patients without ECG criteria for LVH, had severe LVH in TTE ($p = 0.03$). The males has a higher degree of LV dysfunction ($p = 0.04$). The smallest variation of transvalvular gradient pressure was associated with worse prognosis ($p = 0.03$). The concomitant coronary artery bypass grafting was 24%. The mortality rate was 14% and event rate of 24% in the post-operative follow-up. After multivariate analysis, the best predictor of events was the association of coronary artery bypass surgery with Ao valve replacement ($p = 0.03$), independently whether was complete or incomplete revascularization.

Conclusions: The difference in symptoms between the sexes and ejection fraction in men may suggest that the mechanisms of ventricular adaptation to aortic stenosis may differ between the sexes. The ejection fraction in most patients was higher than 50%, which emphasizes the value of diastolic ventricular dysfunction in the development of symptoms of pulmonary congestion in the elderly. The best predictor of events per year was the concomitant CABG.

P1560

Percutaneous mitral valve repair improves left ventricular hemodynamics assessed by echocardiographic single beat analysis

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Purpose: The aim of this study was to investigate the early hemodynamic changes in patients with heart failure and mitral regurgitation after successful percutaneous mitral valve repair with catheter-based clip implantation.

Methods and Results: 24 consecutive patients (mean age 73 years, 63 % men) with reduced left ventricular (LV) systolic function (mean ejection fraction 35 %) and secondary mitral regurgitation were studied with echocardiography. Pressure-volume loops were reconstructed by non-invasive single-beat analysis with simultaneous blood pressure measurements during echocardiographic examination, before and 2 days after successful percutaneous mitral valve (MV) repair.

Percutaneous MV repair reduced LV end-diastolic volume from (mean) 192 mL to 175 mL ($p = 0.001$), LV end-systolic volume was 129 mL before vs. 122 mL after repair ($p = 0.061$). Total stroke volume decreased following successful MV repair from 64 mL to 54 mL ($p = 0.012$), but forward stroke volume and forward cardiac output remained constant, 42 mL vs. 39 mL ($p = 0.331$) and 3.1 L/min vs. 3.2 L/min ($p = 0.579$), respectively. Mean early myocardial relaxation velocity (E') decreased from 5.7 cm/s to 4.3 cm/s ($p < 0.0001$). End-systolic elastance (Ees = contractility) and arterial elastance (Ea = afterload burden) were unchanged, examined at similar blood pressures after MV repair (1.2 vs. 1.3, $p = 0.218$, and 2.9 vs. 3.0, $p = 0.509$, respectively). Preload recruitable stroke work (52 mmHg vs. 45 mmHg, $p = 0.023$) decreased due to a reduced stroke work (5729 mmHg*mL vs. 4748 mmHg*mL, $p = 0.004$). Total mechanical energy assessed as calculated pressure-volume area decreased from 12356 mmHg*mL to 10138 mmHg*mL ($p = 0.043$).

Conclusions: Percutaneous mitral valve repair rapidly induces reverse LV remodeling and maintains contractility and cardiac output in heart failure patients. This indicates a leftward shift of the reconstructed pressure volume loop. Since the regurgitation volume and, thereby, total stroke volume are reduced, percutaneous mitral valve repair is associated with reduced myocardial work and economized cardiac function.

P1561

Value of combined circumferential and longitudinal left ventricular systolic dysfunction to predict adverse outcome in patients with asymptomatic aortic stenosis

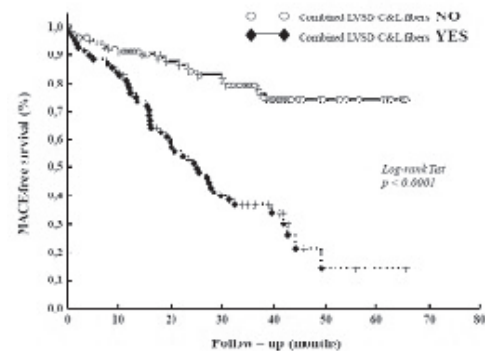
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Background: Patients with asymptomatic aortic stenosis (AS) may have left ventricular systolic dysfunction (LVSD) defined as impairment of circumferential and/or longitudinal (C&L) myocardial fibers, despite a preserved LV ejection fraction. We assessed whether combined LVSD of C&L fibers has a prognostic impact in asymptomatic AS.

Methods: 200 asymptomatic patients with any degree of AS (aortic peak flow velocity > 2.5 m/sec) were analyzed. Midwall shortening and mitral annular peak systolic velocity were considered as indexes of C&L function and classified low if $< 16.5\%$ and < 8.5 cm/sec, respectively. Primary outcome was a composite of major cardiovascular events (MACE) including aortic valve-related and ischemic cardiovascular-related events. Results- During 25 months of follow-up MACE occurred in 69 patients (35%): 46 of 72 subjects (64%) who had C&L-LVSD and 23 of 128 (18%) subjects who had not ($p < 0.001$). Cox analysis identified C&L-LVSD as an independent MACE predictor together with aortic trans-valvular peak gradient, E/E' ratio and excessive LV mass. C&L-LVSD also predicted the occurrence of aortic valve-related events and ischemic cardiovascular-related events analysed separately. ROC curve analysis showed that AUC for C&L-LVSD in predicting MACE was 0.77, significantly higher ($p = 0.002$, z-statistic) than AUCs of C&L fibers considered individually (0.64 and 0.63, respectively).

Conclusions: C&L-LVSD provides additional prognostic information into traditional risk factors for patients with asymptomatic AS



Event free survival and C & L LVSD

P1562

Characterization and clinical outcomes of patients with infective endocarditis: a single-center experience

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Background: Epidemiologic profile of patients (pts) with infective endocarditis (IE) has changed in recent years with fewer cases associated with rheumatic disease and a higher incidence in elderly people due to degenerative valvular disease.

Purpose: Describe epidemiology, microbiologic profile, outcomes during hospitalization and predictors of adverse events in pts with IE.

Methods: Retrospective study including consecutive pts admitted to our centre with IE during a 6 years period. Data on demographics, past medical history, clinical presentation, isolated microorganisms and echocardiogram were evaluated, as well as hospitalization outcomes. Predictors of intra-hospital death were analyzed.

Results: We studied 78pts, 76.9% males, age 59 ± 17 (22-89) years old; 53% had previous valvulopathy and 15% were current IV drug consumers. Diagnosis of left sided prosthetic valve in 30.1%, device-related IE in 2.6% and IE of native valve in the remaining pts. Aortic valve was the most often involved valve; right-side valves involvement was present in 15.4%. Infection was considered to be nosocomial in 15% cases. Staphylococcus aureus was the most frequent isolated microorganism (24.4%), followed by Enterococcus faecalis (11.5%). Adverse outcomes during hospitalization occurred in 85% of pts: 55% evolved with heart failure (HF), 22% with septic shock, 45% had evidence of locally uncontrolled infection or periannular complication, and 44% showed embolic events. Twenty-four pts (31%) underwent surgery and 3 of them died after the intervention. Intra-hospital death rate was 29.5%. Predictors of intra-hospital death were: previous HF ($p = 0.001$), evidence of paravalvular abscess ($p = 0.008$), clinical evolution with HF ($p = 0.006$) or septic shock ($p = 0.019$).

Conclusions: As reported in the literature, in our serie *S. aureus* and *E. faecalis*, were the most frequent isolated microorganisms. We found a relative high number of IE in iv drugs abusers, which could justify an average age lower than previously reported. Infective endocarditis is still associated with major intra-hospitalar complications; in our population the predictors of death were medical history HF, presence of paravalvular abscess, clinical evolution with HF and/or septic shock.

P1563

Extracorporeal membrane oxygenation as bridge therapy in urgent heart transplant: a single center initial experience

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Purpose: Urgent Heart Transplant (HTx) is increasing in Spain (39.1% in period 2009-2013; 49% of HTx in 2013 were urgent). This expansion is due probably to the parallel increase of use of short-term assist device as bridge to HTx in cardiogenic shock, mainly venous-arterial Extracorporeal Membrane Oxygenation (ECMO): 11.7% of all HTx were bridged with this device in 2013 in Spain. Moreover urgent HTx has worse prognosis than elective or even non-assisted urgent HTx. However, our experience with ECMO in urgent HTx is still limited. The aim of this study is to describe our initial experience in urgent HTx bridged with ECMO.

Methods: Descriptive observational study where we analyze retrospectively all consecutive patients that underwent urgent HTx supported with ECMO in our center from 1-Dec-2012 to 19-Jan-2015. We describe the baseline characteristics, comorbidities and heart disease. We have explored ECMO-related complications, ECMO support time, Inotropic Index before ECMO and before HTx, length of stay in Intensive Care Unit (ICU) and mortality.

Results: 7 patients (71% male, n=5) with a mean age of 44.8 ± 8.9 years old underwent urgent HTx supported with ECMO. All presented cardiogenic shock (INTERMACS class I-II) related to myocardial infarction (n=4), idiopathic dilated cardiomyopathy (n=2) and giant cells myocarditis (n=1). There were three patients with diabetes and one with chronic kidney disease. Mean Inotropic Index before ECMO implant and HTx were 77.2 ± 47.6 and 43.8 ± 36.3 respectively. 28,5% (n=2) of patients had inserted intra-aortic counterpulsation balloon. Median ECMO support time was 6 days (range 1-11 days). All patients required mechanical ventilation during circulatory support. Overall survival was 57.1% (n=4) with a median follow-up of 228 days (Range 43-716). Three patients died: two due to acute graft failure and one due to ICU related complications (n=1), with a median survival of 2 days after HTx (range 1-30). Survivors stayed in ICU for a median of 24 days (range 6-91). 42,8% patients presented ECMO related complications (25% in survivors group and 66,6% in non-survivors): cannula related complications (n=1), thrombosis/bleeding complications (n=3) and infections (n=2).

Conclusions: Assuming the study limitations given the low number of patients included, our overall survival rate (57.1%) and ECMO related complication rate (42,8%) is comparable with other published series. ECMO support ≥ 6 days and the presence of ECMO related complications seems to be linked to death outcome. ECMO as bridge to HTx is associated with poor survival and significant associated morbidity although can improve survival of patients with cardiogenic shock.

P1564

Diastolic pulmonary gradient in advanced heart failure: does it make a difference?

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Pulmonary hypertension (PH) is a frequent complication in advanced heart failure (HF) with negative impact in prognosis and may counterindicate heart transplantation (HTx). Pulmonary vascular resistance (PVR) & mean transpulmonary gradient (mTPG) have been considered markers of risk after HTx guiding management. Recently (Nice 2013) diastolic pulmonary gradient was proposed to classify group 2 PH in combined PH (wedge pressure > 15 mmHg + DPG ≥ 7 mmHg) and isolated post-capillary PH (DPG < 7 mmHg) which may have prognostic value according to recent publications. Aim: to assess the impact of DPG in short-term survival in a cohort of HTx.

Methods: observational study of HTx performed in our center (Jan 1991-Sept 2008). Right heart catheterisation was performed at baseline. Patients were divided in combined PH and isolated PH. SV data were obtained from the Spanish National Registry of HTx. T Student test was used to compare variables and Kaplan-Meier test to analyze SV at 24m. Log rank test was used to compare SV.

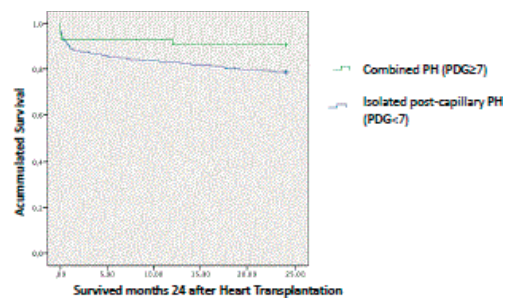
Results: we included 398 patients, 84.4% male, mean age 50.85 ± 11 years and 44.5% ischemic aetiology. No statistical difference was found in SV at 24m.

Conclusion: In our cohort of patients with advanced HF with moderate Group 2 PH who underwent HTx DPG ≥ 7 mmHg does not show to impact in short-term SV

Baseline Hemodynamic profile & Survival

	Post-capillary PH n=54	Combined PH (n=42)	p value
mPAP (mmHg)	29,76 \pm 11,33	42,18 \pm 11,01	>0,05
PVR (UW)	2,38 \pm 1,64	5,63 \pm 2,57	<0,001
SV at 24 m (%)	78,5	90,5	p = 0,08

mPAP: mean pulmonary arterial pressure; UW: wood units; SV: survival; m: months.



Survival ROC curves

P1565

Single centre experience on monitoring circulating antibody and C4d staining

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Introduction: Humoral immune response after heart transplantation is a complex entity with increasing interest. There is a strong recommendation for monitoring circulating antibody (CA) and staining myocardial biopsies for its diagnosis. We present our center's experience.

Material and Methods: In 2010 we started monitoring CA at 3, 6, 9, 12 months post-transplant, and then annually. We also started to stain follow-up biopsies for C4d. We included patients transplanted between July 2010 to April 2014, except those who died 30 days post-transplant. We collected, prospectively, basal characteristics, new CA and C4d+ biopsies. New CA and C4d+ biopsies relation with first year rejection, CMV infection and coronary allograft vasculopathy (CAV) have also been analyzed.

Results: 38 patients were included. Basal characteristics: Age 55.06 ± 12.5 , 65.8% male, 26.3% diabetes, 29% urgent transplantation. During follow up (median 27.5 months, IQR 13.7-37.9), de novo CA appeared in 4 patients (10.5%). Three of them (75%) were against HLA II (MFI maximum 7850+5142). The other patient presented antibodies against HLA I and II (MFI maximum 22000 and 14000 respectively). Three of them were donor specific antibodies (DSA). All de novo CA appeared during first year post-transplantation (median 8.6 months [3.4-11.5]) (figure 1). 429 biopsies were obtained (media 11.3 biopsies per patient), 10.3% were C4d+. Median time for a positive biopsy was 2.5 months (0.7- 7.7) (figure 1). 20 patients (52.6%) had one or more positive biopsies. Analysis on circulating antibodies or any positive biopsy association with rejection, CMV infection and CAV were run without statistical significance.

Conclusion: Immune events associated with AMR seem to be frequent (10.5% circulating antibody y 52.6% C4d+ biopsy), however we did not find a significant relation with rejection, CAV or CMV infection in short term follow-up.

P1566

Analysis of the risk factors related to the mortality in the cohort of heart transplantation in Brazil

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Table P1568.

Patient N.	Baseline RHC		Pulmonary vasodilators RHC		LVAD RHC		LVAD Support (weeks)				
	sPAP	TPG	PVR	sPAP	TPG	PVR	sPAP	TPG	PVR		
1	100		32	6.6	86	24	5.0	44	13	2.4	7.0
2	75		19	4.8	71	15	3.1	44	7	1.2	6.9
3	60		20	7.4	73	29	4.8	32	12	1.9	4.1
4	75		25	7.1	62	16	5.9	24	10	2.0	8.3
5	80		27	7.5	68	20	6.1	53	13	1.9	7.9
All	78		25	6.7	72	21	4.7	39	11	1.9	6.8±1.6

RHC: Right heart catheterization, LVAD: left ventricular assist device, sPAP: systolic pulmonary artery pressure, TPG: transpulmonary gradient, PVR: Pulmonary vascular resistance (Wood units)

Introduction: Heart failure is the final pathway of most diseases that involve the heart, as a challenge in health management. Heart transplantation is a viable strategy for patients with end-stage heart disease. The donor shortage requires a process to ensure the appropriate selection of the recipient. In Brazil, there is a single list of candidates in chronological order of arrival. Analysis of the risk factor related to the mortality in the local population is essential for the allocation processes of this scarce resource.

Objective: The purpose of this study is to assess the risk factors exclusively with the receptor related to the one-year mortality. **Methodology:** This research is a cohort from all the transplanted patient between 2008 and 2013 at our National Institute in Brazil. General variables were collected from files of the patient, including laboratory results obtained and summaries pre-transplant filed. The variables pre-transplant of each patient collected were: color (white or black); use of beta-blocker; hypertension; diabetes mellitus; dyslipidemia smoking alcohol consumption previous cardiac surgery; weight; creatinine clearance; total bilirubin. We also analyzed the IMPACT score that congregate almost all the variable that we analyzed independently. The Research Ethics Committee of the Instituto Nacional de Cardiologia project approved this project, in compliance with the recommendations of the National Health Council. Forty-two patients were included from both sex in our cohort. None of our variables was found related in the univariate analyzes to the mortality. However, an exploratory analysis of the IMPACT score, found that the IMPACT score > 6 could be used to differentiate the risk of death. It was observed that the subgroup, who died, had Impact Score ≥ 6 points (42.1%) significantly ($p = 0.014$) greater than that subgroup who lived (8.7%). **Discussion:** In the heart transplant patient population From this institute single variables were not able to predict mortality at one year. However, the IMPACT score did. We suggest future research may use the hypothesis that the IMPACT score may also be used as an allocation variable prioritizing candidates to be transplanted.

P1567

Value of troponin T high sensitivity as a prognostic factor in primary graft dysfunction after heart transplantation

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The primary graft failure is a major cause of morbidity and mortality in the immediately post-transplantation (HT). Early diagnosis is the key to reducing mortality. Their presence is due to several factors: donor characteristics, surgical technique, and features of the receiver. The score RADIAL recently published proposed six predictors factors for diagnosis.

To analyze the value of the determination of high-sensitivity troponin T (TnT-hs) to predict acute graft dysfunction and prognosis, the concentration of TnT-hs in first 24 hours post-HT was prospectively analyzed in 51 TC in the last two years, RADIAL score was also calculated.

A total of 27 patients (53%) had ventricular dysfunction post-TC, of these, 9 (18%) had left ventricular dysfunction (LVD) (7 biventricular and 2 pure LVD) and 25 right ventricular dysfunction (RVD). Four patients with LVD died (44%) compared to one with RVD (8%). The ROC curve of the TnT-hs in the first 24 hours to detect LVD was 0.83 ($p < 0.003$) and radial score of 0.47 (NS). The ROC curve for detecting TnT hs-RVD was 0.68 ($p < 0.03$) and Radial score of 0.65 ($p = 0.07$). The multivariate analysis to identify independent predictors of LVD were TnT-hs ($p < 0.04$) and CPB time ($p = 0.01$). The LVD was correlated with longer CPB time ($r = 0.49$; $p < 0.001$). The ROC curve identified a cutoff of TnT-hs of 1650 ng/L with a sensitivity of 89% and specificity of 77% for diagnosing LVD.

Conclusions: LVD postTC has a high mortality. The elevated value of hs-TnT determined in the first 24 hours of HT is an independent predictor of LVD. More studies are needed to determine the value of TnT-hs in the management of these patients in the immediate post-HT.

P1568

Left ventricular assist device for treatment of severe pulmonary hypertension in heart transplantation candidates

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Pulmonary hypertension (PH) refractory to pharmacologic therapy is a major limitation for heart transplant (HTx) in patients with end-stage left heart disease. Attempts to reduce left atrial pressure, the driving force of this type of PH, with the use of left ventricular assist devices (LVAD) have been reported with occasional success. The probability of substantial PH reduction and the time required for it is largely unknown.

Methods: Patients with refractory heart failure and PH preventing HTx listing defined by systolic pulmonary artery pressure (SPAP) >60 mmHg, transpulmonary gradient (TPG) >15 mmHg and pulmonary vascular resistance (PVR) >3.5 Wood units who showed no response to acute (nitric oxide, milrinone, nitroprusside) and chronic (sildenafil, bosentan or both) pulmonary vasodilators received a Berlin Heart Excor LVAD as "bridge to candidacy". Repeated right heart catheterization (RHC) were performed in order to investigate degree and timing of reductions in PH.

Results: In our center, 25 patients have been bridged to HTx with an LVAD. In five cases (20%) the indication was refractory PH. Baseline RHC, last RHC under pulmonary vasodilator therapy and RHC post LVAD are shown in the table 1. All patients showed marked reduction in their PH parameters, thus allowing listing for HTx. Time to reduction of PH ranged from 4 to 8 weeks. Four of the 5 patients have undergone successful HTx. The other patient is still waiting for HTx.

Conclusion: In this small series, implantation of a pulsatile Excor LVAD has been systematically successful in reducing refractory PH to a degree that allows HTx. This approach took 4-8 weeks to show its benefit.

P1569

Surveillance of acute cellular rejection after heart transplantation: reducing the need for endomyocardial biopsies

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Background and Purpose: Surveillance of AR after heart transplantation (HTx) has been traditionally based in frequent endomyocardial biopsies (EMB) that are both invasive and costly. Typically, 10-14 EMB are performed during the first post-HTx year. Improvement in echocardiographic techniques (including speckle-tracking analysis) for the detection of AR may allow a reduction in the number of EMB without compromising overall results. We evaluate the effectiveness of a new echo-based protocol for AR monitoring, and compare it with previous EMB-based results.

Methods: We compared AR diagnosis and clinical outcomes in a sample of 70 recipients from the historical cohort (Group 1, HTx from 2005 to 2009) with those of 70 patients transplanted from 2010 to 2014 (Group 2). AR surveillance during the first post-HTx year was based in 11 scheduled EMB in group 1 and 7 EMB + 11 echocardiography studies in group 2. Main end-points were significant AR ($\geq 2R$ of ISHLT classification) requiring treatment and death. Immunosuppressive therapy

in both groups included induction therapy (basiliximab) and triple therapy with calcineurin inhibitor, mycophenolate mofetil and steroids.

Results: Baseline characteristics were similar between groups. The mean number of EMB/patient in group 1 was 12.8 ± 1.2 . Acute rejection requiring treatment ($\geq 2R$) was diagnosed in 35% (25/70). In 24 of the 25 patients, AR occurred during the first 6 months after HTx. Ten patients (14%) showed more than 1 episodes of AR. After 6.6 ± 2 years of follow-up, there were 2 deaths (3%, 1 heart failure and 1 septic shock). The mean number of EMB/patient in group 2 was 8 ± 0.5 , and 12 ± 0.5 echocardiograms were performed in this group ($p < 0.01$, for the comparison with group 1). AR $\geq 2R$ was diagnosed in 14 (20%) of the 70 patients ($p = 0.04$, for the comparison with group 1), with 13/14 episodes occurring during the first 6 post-HTx months. Mean left ventricular ejection fraction at the end of the first year was $62 \pm 10\%$ ($p = NS$ for the comparison with group 1). Five HTx recipients (7%) had more than 1 episode of AR. During a mean follow-up of 2.4 ± 1.3 years, there were two deaths: 1 sudden death (necropsy not performed) and 1 septic shock.

Conclusion: The new protocol resulted in a reduction of 38% in the number of EMB, with a lower number of diagnoses of AR episodes. This reduction in the number of EMB did not result in an increase of deaths or other complications related to AR.

P1570

Usefulness of 2d strain parameters to diagnose acute rejection after heart transplantation

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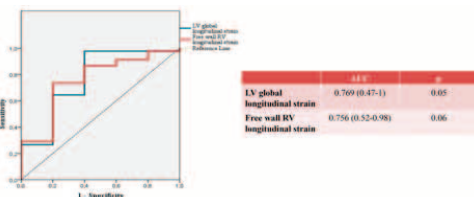
Introduction: Acute allograft rejection (AAR) is a relevant complication after orthotopic heart transplantation (OHT) and its diagnose is based on endomyocardial biopsy (EMB). Recent advances in 2D-strain imaging may allow an early non-invasive detection of AAR.

Objective: to analyze the usefulness of echocardiographic parameters to detect AAR after OHT

Methods: We prospectively included 34 consecutive recipients admitted between 2010 and 2012 for an OHT. 235 pairs of EMB and echocardiograms were performed. A median of 7 (IQR 6-8) studies per patient were performed along the first year of follow-up. We analyzed classic parameters, speckle-tracking derived left ventricular (LV) longitudinal, radial and circumferential strain, and global and free wall right ventricular (RV) longitudinal strain.

Results: AAR was detected in 26.4% of EMBs (n=62), 5.1% (n=12) required specific treatment (AAR $\geq 2R$). Lower absolute values of global LV longitudinal strain and Free Wall RV longitudinal strain were present in the cases of AAR $\geq 2R$ compared with those without AAR ($13.7 \pm 2.7\%$ vs. $17.8 \pm 3.4\%$ and $16.6 \pm 3.6\%$ vs. $23.3 \pm 5.2\%$ respectively). An average LV longitudinal strain $< 15.5\%$ presented 85.7% sensitivity (Se), 81.4% specificity (Sp), 98.8% negative predictive value (NPV), 25% positive predictive value (PPV) and 81.7% accuracy (Acc) for the presence of AAR $\geq 2R$. Free wall RV longitudinal strain $< 17\%$ presented 85.7% Se, 91.1% Sp, 98.8% NPV, 42.9% PPV and 90.7% Acc for AAR $\geq 2R$. Both variables were normal in 106 echocardiograms (57.6%), none of them presented with AAR $\geq 2R$

Conclusions: We propose the combination of two new echocardiographic measures (global LV and free wall RV longitudinal strain) to detect AAR after OHT. If validated, its routine measure could be a reliable tool to non-invasively diagnose AAR.



ROC curves and areas under the curve

P1571

Utility of sAxI and Lp-PLA2 biomarkers in early detection of cardiac allograft vasculopathy

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Purpose: Cardiac allograft vasculopathy (CAV) remains one of the major limitations in long-term survival in Heart Transplantation patients (TC). Its diagnosis requires

invasive methods and often is done in advanced stages of the disease. The aim of this work is to study the utility of two biomarkers in the early detection of CAV, in particular sAxI (protein involved in vascular remodeling) and Lp-PLA2 (marker of atherosclerosis).

Methods: We studied 96 TC. We obtained peripheral blood samples to analyze sAxI and Lp-PLA2 levels at the time that the coronary angiography was done for the diagnosis of CAV. Cardiac allograft vasculopathy was classified according to the recommendations of the ISHLT.

Results: Study population included 96 patients, aged 48 +/- 15 years old, 77 % male. In 45 patients the angiographic study did not show CAV (CAV0), in 27 CAV was mild (CAV1), in 5 moderate (CAV2) and in 19 severe (CAV3). We found no significant differences in Lp-PLA2 levels ($p = 0.8$) in patients with or without CAV. In contrast, sAxI levels were significantly higher (64.7 vs 79.3 , $p = 0.03$) in patients with CAV (CAV 1,2,3) compared to patients without CAV (CAV0). In the logistic regression analysis sAxI levels > 74 were associated with increased risk of CAV (Odds Ratio = 2.367; 95% 1015-5520; $p = 0.04$)

Conclusion: Monitoring the levels of sAxI could be useful for identifying patients with CAV development. Conversely, Lp-PLA2 levels don't seem to be useful in early detection of CAV. Further studies with larger number of patients may provide more information on the utility of these biomarkers in the early detection of CAV

P1572

Beta-adrenergic receptor polymorphism and maximal exercise capacity after orthotopic heart transplantation

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Background: Single nucleotide polymorphism (SNP) of β -adrenergic receptors (β -AR) expressed in the human heart changes the physiological response to agonist binding. Orthotopic heart transplantation (HTx) results in denervation of the cardiac allograft entailing the dependence of β -AR activation on circulating catecholamines. We investigated whether $\beta 1$ - and $\beta 2$ -AR SNP in the cardiac allograft correlates with maximal exercise capacity as measured by cardiopulmonary exercise testing in HTx recipients > 1 year after transplant.

Methods and Results: Donor hearts were genotyped for different β -AR SNPs known for their association with physiologically different response to agonist binding ($\beta 1$ -AR: Ser49Gly, Arg389Gly; $\beta 2$ -AR: Arg16Gly, Gln27Glu). The recipient genome was analyzed for the presence of the Del322-325 of the $\alpha 2c$ -AR which is part of the negative feedback loop controlling noradrenaline sequestration in the synaptic cleft. Univariable analysis was used to identify demographic, biological, and clinical variables associated with peak VO₂. Univariate variables with a $p < 0.1$ were tested for their independent correlation with peak VO₂ using multivariate regression.

Results: The $\alpha 2c$ -AR Del322-325 SNP was present in 12% (n=5/41) of the study population and without correlation to blood pressure, heart rate at rest and during exercise, and peak VO₂. The overall peak VO₂ of the 41 HTx recipients was 57 ± 14.8 % of the age and gender matched predicted value. The $\beta 1$ -AR Gly49 allele was associated with a decrease of peak VO₂ when compared with homozygotes Ser49Ser ($47.3 \pm 10\%$ vs. $60.2 \pm 14.9\%$; $p = 0.015$). By trend, peak VO₂ was increased in $\beta 1$ -AR Gly389 carriers as compared to homozygotes Arg389Arg ($61.4 \pm 14.9\%$ vs. $53.6 \pm 14.1\%$, $p = 0.093$). $\beta 1$ -AR Glu27Glu tended to lower peak VO₂ when compared to Gln27 carriers ($50.9 \pm 13.6\%$ vs. $58.5 \pm 14.9\%$, $p = 0.193$). Multivariate analysis identified as independent predictors of peak VO₂ (adjusted R² = 0.55) $\beta 1$ -AR Ser49Gly SNP ($p = 0.005$), chronotropic reserve ($p = 0.016$), and peak systolic blood pressure ($p = 0.031$).

Conclusion: In a study collective with representative peak VO₂, the recipient $\alpha 2c$ -AR Del322-325 allele was rare and not correlated with physiological variables. The $\beta 1$ -AR Gly49 SNP is associated with a lower peak VO₂ after HTx which is in accordance with higher desensitization and lower intracellular cAMP levels reported for $\beta 1$ -AR Gly49 expressing HEK cells exposed to sustained $\beta 1$ -AR receptor activation when compared to $\beta 1$ -AR Ser49 expressing cells.

DIURETICS AND FLUID STATUS MANAGEMENT

P1573

The efficacy of tolvaptan in congestive heart failure patients with and without hypoalbuminemia: a pilot study

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Purpose: Heart failure (HF) with hypoalbuminemia is refractory to conventional therapy. We investigated whether tolvaptan, a potent aquaretic agent, might be of benefit in HF patients with hypoalbuminemia.

Methods: We prospectively enrolled 40 patients hospitalized for HF. Patients received conventional therapy. We subsequently added tolvaptan in the range of 3.75 mg to 15 mg daily and it was discontinued after improvement of HF symptoms. We compared clinical and laboratory data in HF patients with and without hypoalbuminemia (defined as serum albumin ≤ 3.0 g/dL).

Results: Tolvaptan was administered in 18 HF patients with hypoalbuminemia (Group A) and 22 HF patients without hypoalbuminemia (Group B). The mean serum albumin was 2.63 ± 0.27 g/L and 3.46 ± 0.25 g/L, respectively. The average urine output on tolvaptan increased significantly in both groups (1644.4 ± 797.6 mL/day to 3011.6 ± 1453.8 mL/day, $P=0.004$; 1459 ± 612.7 mL/day to 2112.2 ± 724.5 mL/day, $P=0.008$; respectively). In addition, we observed higher urine output on therapy in Group A than in Group B ($P=0.015$). There was a moderate negative correlation between serum albumin and average urine output on tolvaptan ($r=-0.42$, $P=0.007$).

Conclusions: Tolvaptan was effective in HF patients with and without hypoalbuminemia. Tolvaptan might become a promising treatment option for HF patients with hypoalbuminemia.

P1574

Efficiency of torasemide in heart failure in patients with ischemic heart disease and chronic obstructive pulmonary disease

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The purpose of the study was to assess the impact of torasemide on the systemic and pulmonary hemodynamics, respiratory function, systolic and diastolic function of the left and right ventricle in chronic heart failure (CHF) in patients (pts) with ischemic heart disease (IHD) associated with chronic obstructive pulmonary disease (COPD).

Materials and methods: 64 pts (18 men and 46 women, mean age 61.9 ± 3.9 years) with NYHA II-III with IHD and COPD of II-III st. Group 1 consisted of 30 pts treated with combined therapy of CHF and torasemide (20 mg/day), the group 2 were administered furosemide (40 mg after 2 days) before the disappearance of edema syndrome and pulmonary congestion with subsequent transfer of pts on a maintenance dose of furosemide 20 mg after 2 days and torasemide - 10 mg/day. Control group consisted of 20 healthy subjects matched for age and sex. Before the beginning of the study, after 4 and 16 weeks all the patients obtained echocardiography, spirometry and Holter ECG monitoring. The study was conducted at baseline, after 4 and 16 weeks.

Results: After 16 weeks of treatment, there was a significant improvement in clinical course of CHF according to the six-minute walk test in both groups. The improvement in systolic (Δ ejection fraction (EF) 8,2% in group 1 compared with 6,1% in group 2, $p=0,02$) and diastolic function of the left ventricle (LV) (Δ E/A 9,3 and 6,2%, respectively, $p=0,016$) was found. This corresponded to a decrease in LV end-diastolic volume and left atrium which was more pronounced in group 1 in all phases of observation. In addition, the right ventricle (RV) EF was significantly higher in group 1 compared with group 2 (Δ EF 7,2% against 4,1%, $p=0,016$). More pronounced decrease in RV and systolic pulmonary artery pressure in group 1 compared with group 2 (Δ -10,3% against 8,1%, $p=0,03$) was noted. Negative dynamics of forced expiratory volume in 1 second (FEV1) in both groups of pts wasn't observed. Research has shown that the long-term use of furosemide and torasemide has no negative effect on renal function in pts with CHF associated with IHD and COPD. There was a trend for an increase in glomerular filtration rate in pts treated with torasemide.

Thus, the 16-week therapy with torasemide in patients with CHF associated with IHD and COPD is accompanied by improvement of systolic and diastolic left ventricular function, reducing sizes of the left and right chambers of the heart, decrease in pulmonary artery pressure and has no effect on lung function, along with the safety and well tolerance.

P1575

Peritoneal ultrafiltration in end-stage chronic heart failure

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Background: Cardiorenal syndrome type 2 (CRS-2) is common in end-stage chronic heart failure (CHF). Peritoneal ultrafiltration (pUF) may entail clinical functional improvement and a reduction in hospitalizations.

Methods: 39 consecutive end-stage CHF patients with stable CRS-2 were initiated on ambulatory pUF after interdisciplinary cardiological/ nephrological evaluation

and prospectively followed for one year. All-cause hospitalization was the primary endpoint. Secondary endpoints included mortality, treatment alteration and change in weight, NYHA functional class, or quality of life (QoL). Outcomes were compared both within the pUF cohort (365 prior to initiation) and to 39 matched CHF patients receiving standard medical treatment.

Results: Compared to pre-treatment, there was a trend to a reduction in one-year hospitalization days in the pUF group ($P=0.07$). One-year mortality was 33% in the pUF group and 23% in the matched control cohort. pUF was stopped in 8 patients (18%) due to recurrent peritonitis ($n=3$), insufficient ultrafiltration ($n=3$), or cardiac recompensation ($n=1$). As compared to standard medical treatment, pUF significantly improved volume overload ($P<0.05$), NYHA functional class ($P<0.001$), and mental health ($P<0.05$). Moreover, hospitalization days for all causes as well as cardiovascular hospitalization days were significantly reduced between periods in the pUF group ($P<0.05$ and $P<0.001$, respectively).

Conclusion: Peritoneal ultrafiltration is effective in improving the clinical condition of end-stage CHF patients suffering from CRS-2. Randomized controlled trials are needed to clarify the effects of pUF on hospitalization and mortality in these patients.

P1576

Hypertonic saline improves furosemide dose response curve in heart failure

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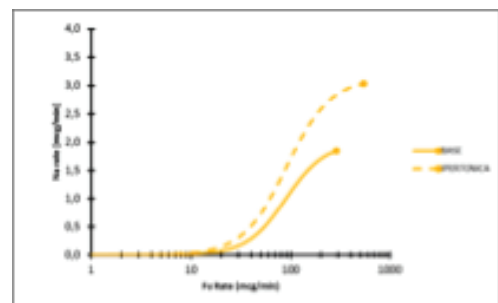
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Aims: Loop diuretics remains a mainstay of heart failure (HF) therapy. The chief indicator to evaluate diuretic responsiveness is the urine production per unit dose of diuretic rather than the absolute urine output or diuretic dose. In many patients, sodium and water excretion plateau over time before adequate fluid elimination, a phenomenon termed as diuretic resistance, which may be overcome by the administration of hypertonic saline solution (HSS) plus high dose furosemide (Fur).

Method: Urine sample of 36 consecutive patients hospitalized for acute HF were collected at 30, 60, and 90 minutes and 3,4,5,6,8 and 24 hours after infusion of fur 125 mg (14 pts.), fur 250 mg (13 pts.) and fur 500 mg (9 pts.). Fur diluted in 150 ml of normal saline (initial) and hypertonic saline (after 24 hrs) was infused over 20 minutes. Diuresis, natriuresis, urinary osmolality and Fur concentration were evaluated for each collected urine sample.

Results: HSS addition to Fur significantly increased urine output, natriuresis, urinary osmolality and fur urine delivery in all patients and at all detected times. The total amount of furosemide (mcg) into urine was greater after i.v administration of HSS plus furosemide both for 125 mg (15.673,24 vs 12.026,88), 250 mg (36.252,24 vs 26.301,20) and for 500 mg (82.000,61 vs 52.677,78). In 31 patients (86%) curves fit with sigmoid function assigned automatically by computer program (ALLFIT) confirming that the addition of HSS to Furosemide have positive effects on diuresis and natriuresis.

Conclusion: This study demonstrates that addition of HSS to high dose furosemide improves furosemide dose response curves, total diuresis, and natriuresis in acute HF. These results serve as pathophysiological basis of an innovative approach to manage acute HF.



Patient PF: dose response curves

P1577

Chronic intermittent renal replacement therapy in end-stage heart failure patients: a randomized study- one year results

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Purpose: Chronic intermittent renal replacement therapy as an efficient method of decongestion has not been evaluated yet in end-stage heart failure patients, refractory to standard treatment. Assessment of chronic renal replacement therapy's safety and efficacy in advanced heart failure patients with peripheral congestion and resistance to loop diuretics.

Methods: Twenty (20) patients with advanced stage (NYHA III and IV) heart failure due to left ventricular systolic dysfunction and peripheral congestion associated with resistance to per os diuretics were randomized to renal replacement therapy versus standard heart failure treatment. Renal replacement therapy patients (Group A, n=9) after implantation of a permanent internal jugular double lumen catheter underwent renal replacement therapy sessions 1-3 per week, aiming at maintenance of a stable body weight without symptoms and signs of systemic or peripheral congestion. Patients in the control group (Group B, n=11) received standard treatment, including intravenous diuretics and inotropes, as needed. Patients were followed for 12 months in the outpatient heart failure clinic. Endpoint was the composite of death from any cause or need for crossover on the opposite therapeutic arm.

Results: Baseline characteristics were similar in both groups: Age 71.7 ± 6 vs 67 ± 8 years ($p=0.2$), NYHA class 3.3 ± 0.5 vs 3.4 ± 0.5 ($p=0.6$), creatinine 2 ± 0.7 vs 2 ± 0.6 mg/dl ($p=0.9$), sodium 138 ± 5 vs 139 ± 3 mEq/L ($p=0.5$), systolic blood pressure 103 ± 19 vs 106 ± 12 mmHg, ($p=0.7$), LV Ejection Fraction $23\% \pm 6\%$ vs $28\% \pm 7\%$ ($p=0.2$), right atrial pressure 16 ± 4 vs 13 ± 6 mmHg ($p=0.3$), wedge pressure 23 ± 5 vs 20 ± 11 mmHg ($p=0.6$), BNP 1225 ± 916 vs 903 ± 600 pg/ml ($p=0.6$), oral furosemide dose 377 ± 116 vs 432 ± 233 mg/day ($p=0.6$), for groups α and β respectively. At 12 months follow up, 5/9 Group A patients died (4) or had to cross over to standard medical treatment plus inotrope infusions (1) while 9/11 Group B patients died (5) or had to cross over (4) to renal replacement therapy due to their clinical needs, which included worsening renal function or worsening heart failure with hospital admission (mean time to endpoint 43 weeks vs 20 weeks for group A and B patients respectively, $p=0.02$).

Conclusions: In this small randomized study, renal replacement therapy showed an outcome benefit compared to standard treatment, including the intravenous ones.

P1578

Lack of consistency between different methods for assessing hemodynamic congestion on the basis of the inferior vena cava echographic indexes.

A retrospective study

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Introduction Among the indices able to replace invasive CVP measurement for patients with acute decompensated heart failure (ADHF) the diameters of the inferior vena cava (IVC) and their respiratory fluctuations (so-called IVC collapsibility index) measured by echocardiography have recently gained ground as a quite reliable proxy of CVP. The aim of our study was to evaluate the inter-method agreement by comparing three different ways of assessing congestion through the IVC echographic exploration.

Methods Medical records of patients hospitalized for ADHF since 1 July to 31 December 2013 with right or bi-ventricular heart failure in NYHA class III-IV were retrospectively evaluated. The measurements of the IVC expiratory diameter and IVC collapsibility index (IVCCI) were noted and their diagnostic significance was analyzed using three different keys of interpretation. These were: a) the criteria for the indirect estimate of right atrial pressure, b) the categorization into three IVCCI classes, indicating different ranges of CVP and c) the subdivision into three classes according to the values of the maximum IVC diameter.

Results. 47 patients were enrolled. Among them, the patients classified as affected by persistent congestion were 22 (46.8%), using Rudski's criteria, or 13 (27.6%), using Stawicki's criteria, or 13 again, using the criteria of Pellicori. The inter-rater agreement (Cohen's kappa) turned out rather poor, by comparing the Rudski's criteria with those of Stawicki (Cohen's kappa = 0.369; 95% CI 0.197 to 0.540), as well as by comparing the Rudski's criteria with those of Pellicori (Cohen's kappa = 0.299; 95% CI 0.135 to 0.462). Besides, even in the comparison between the criteria of Stawicki and those of Pellicori, a substantially unsatisfactory concordance was found (Cohen's kappa = 0.468; 95% CI 0.187 to 0.750).

Conclusions The three IVC ultrasonographic criteria of hemodynamic congestion that we tested appeared to be inconsistent or clearly contradictory. Alternatively, in patients with history of ADHF and suspected latent congestion, a well-calibrated combination of multiple indicators of hemodynamic overload would be warranted, by means of the sequential or simultaneous use of clinical scores of congestion, IVC ultrasonographic indices and circulating levels of natriuretic peptides.

P1579

Different definitions of worsening renal function in patients with acute cardiac decompensation: a retrospective study showing poor concordance between them

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Introduction: Approximately one third of patients with acute decompensated heart failure (ADHF) treated with an intravenous (iv) loop diuretic at a relatively high dose (>80 mg/day of furosemide, or an equivalent dose of another loop diuretic), exhibit worsening renal function (WRF) after a single course of iv infusions or iv bolus injections maintained for several days. WRF is currently defined as an increase in serum creatinine > 0.3 mg/dl (WRF-Cr) or a decrease in the glomerular filtration rate of $\geq 20\%$ (WRF-GFR) compared to baseline values. Furthermore, small increases in serum creatinine in the normal or near-normal range of its values are indicative of significant reductions in estimated glomerular filtration rate (eGFR) due to the nonlinear exponential relationship between serum creatinine and eGFR. Therefore, underestimating this relationship could lead to an erroneous quantitative estimate of new-onset renal dysfunction, diuretic-related.

Methods: The relationship between baseline serum creatinine (exposure variable) and the risk of diuretic-related WRF (dichotomous outcome variable), expressed either as WRF-Cr or as WRF-GFR, was assessed by logistic regression analysis. For this purpose, medical records with a diagnosis of previous ADHF were retrospectively analyzed. The eGFR was calculated using the equation "Modification of Diet in Renal Disease" (MDRD). The WRF was inferred from measurements of serum creatinine that had been made daily during the scheduled courses of iv diuretic therapy.

Results: Thirty-eight patients with chronic heart failure (CHF) and history of a previous episode of ADHF were enrolled in the study. An increase higher than 0.3 mg/dl of serum creatinine (WRF-Cr) was detected in 14 of 38 patients (36.8%). In addition, a decrease of $\geq 20\%$ in GFR (WRF-GFR) was detected in 14 of 38 patients (36.8%). However, a poor concordance between the two criteria was found (Cohen's Kappa = 0.208, 95% CI: -0.110 to 0.526). WRF-Cr and WRF-GFR showed opposing relations with baseline serum creatinine. In fact, the risk of WRF-Cr appeared positively associated with baseline serum creatinine (odds ratio = 33.56; 95% CI: 2.93-384.18 $p=0.0047$), while the risk of WRF-GFR was inversely associated with the same analyte (odds ratio = 0.0393; 95% CI: 0.0039 to 0.3966 $p=0.0061$).

Conclusions: The criterion to discontinue or reduce the iv diuretic in the presence of WRF-Cr for patients with ADHF or resistance to oral diuretic should include the notion that this finding indicates a significant reduction of eGFR only for values of serum creatinine in the normal or near-normal range.

DRUG THERAPY, OTHER

P1580

Digoxin in patients with heart failure and atrial fibrillation: a retrospective study

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Digoxin is a drug frequently used to achieve rate control in atrial fibrillation. It's use in patients with heart failure, with or without atrial fibrillation, is controversial, some studies showing decreased rates in readmissions and others showing an increase in mortality. Many patients have heart failure and atrial fibrillation, we tried to access the impact of the use of Digoxin in this population.

The purpose of this study was to evaluate, in a period of two years, the effect of Digoxin on the rates of mortality and readmissions in a population with both atrial fibrillation and heart failure.

The study population was composed by all patients discharged from our hospital with both diagnosis in 2011, data was retrieved by reviewing medical charts and by telephonic interview.

We found a population composed by 205 patients, 44.4% male, with an average age of 76.5 years old. At discharge, 76 patients (37.1%) were prescribed Digoxin and 109 (53.1%) were medicated with beta-blockers, 49 (23.9%) were discharged with both therapies.

In the entire population, for the two years of follow-up, the mortality rate was 39% and the rate of hospital admission for any cause was 62%. There was no significant increase in mortality in patients medicated with Digoxin (46.1% against 34.9% in the patients under other therapies, $p=0.11$). However, in the group of patients medicated with beta-blockers, the use of Digoxin was associated with a significant increase (25% to 42.9%, $p < 0.05$) in mortality.

Digoxin prescription was associated with a significant increase in the percentage of patients with hospital admissions (from 56.6% to 72.4% in the, $p > 0.05$) during the

two years of follow-up. It was also associated with an increase in the average number of hospital admissions in the first year of follow-up (from 0.75 to 1.12, $p > 0.05$) and in the two year period (from 1.15 to 1.67, $p < 0.05$). Unlike mortality there was no increase in hospital admissions associated with the use of Digoxin in the patients also medicated with beta-blockers.

In conclusion, this study suggest caution in the use of Digoxin in patients with both atrial fibrillation and heart failure.

P1581

Early ivabradine initiation in patients hospitalized for decompensated chronic heart failure

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Premises and Purpose: Patients hospitalized for heart failure decompensation have a postdischarge vulnerable period associated with increased risk of readmission and death. Ivabradine has been shown to be effective in stable chronic heart failure patients. The purpose of this study was to examine the tolerance and effectiveness of ivabradine administered early in patients hospitalized for decompensated heart failure.

Material and Methods: This prospective study included 47 consecutive patients (P) (37 males, 10 females) admitted for decompensated heart failure, with LV systolic dysfunction (LVEF < 40%) and sinus rhythm (heart rate > 70 b/min). Ivabradine was initiated in the hospital (2-3 days before discharge), or in the first 2 weeks after discharge. At baseline and after 6 months clinical characteristics, ECG, echocardiographic parameters and laboratory data were recorded. During follow-up readmissions and deaths were recorded. Data are expressed as mean \pm SD or percentages, comparisons were done with Student's paired t test.

Results: Mean age was 60 \pm 12 years, heart failure etiology was ischemic in 22 P and nonischemic in 25 P. 17 P (36%) had diabetes, 20 P (42%) had left bundle branch block, 9 P (19%) had COPD. At baseline NYHA class was 3.4 \pm 0.5, systolic BP was 131 \pm 24 mmHg, diastolic BP was 83 \pm 16 mmHg, while mean resting heart rate was 96 \pm 12 b/min. Left ventricular ejection fraction was 25.8 \pm 7%, mean serum creatinine was 1.1 \pm 0.3 mg/dl. Ivabradine initial dose was 10 mg/day in 40 P (85%) and 5 mg/day in 7 P (15%). Ivabradine was initiated in the hospital in 33 P (70%) and early after discharge in 14 P (30%). Associated heart failure therapy consisted of ACE inhibitors/ARBs in 37 P (78%), betablockers in 43 P (91%), furosemide in 47 P (100%), spironolactone in 37 P (78%), digoxin in 4 P (8%). After 6 months NYHA class improved significantly (2.3 \pm 0.4, $p < 0.0001$), heart rate decreased (73 \pm 12 b/min, $p < 0.0001$) and LVEF increased by 5% (31 \pm 8%, $p = 0.007$). Mean ivabradine dose at 6 months was 11 \pm 3 mg/day (14 P received 15 mg/day - 32.5%). Ivabradine treatment had to be stopped due to intolerance in 3 P (6%), bradycardia needing dose reduction was noted in 4 P (8.5%) and atrial fibrillation during follow-up occurred in 1 P (2.1%). Readmissions due to heart failure aggravation were noted in 9 P (19%), 2 deaths were recorded (4.7%).

Conclusions: Initiation of ivabradine therapy in patients hospitalized for decompensated heart failure, with sinus rhythm and heart rate > 70 b/min before discharge or early after discharge is well tolerated and seems to improve clinical evolution.

P1582

Effectiveness and safety of bivalirudin versus heparin and glycoprotein IIb/IIIa inhibition among patients with ST-elevation myocardial infarction

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Background: The evidence of benefit and safety provided by bivalirudin in the treatment of ST-segment elevation myocardial infarction (STEMI) is controversial. We aimed to compare the effectiveness and safety of bivalirudin versus abciximab plus unfractionated heparin (UFH) in STEMI patients undergoing primary percutaneous coronary intervention (PPCI).

Methods: Retrospective study of 75 consecutive patients treated with abciximab plus HNF (Group I), recruited between January to December 2010, that were compared with 111 consecutive patients treated with bivalirudin (Group II), recruited between July 2012 to July 2013, in the setting of PPCI.

Results: There were no significant differences in age, sex, vascular access, diabetes, creatinine clearance, PPCI of left coronary artery, number of stents used, left ventricle systolic function and admission Killip class between the two groups. We did not have any case of major bleeding or red cell transfusion. There were 6 cases of femoral hematoma (4 in Group I and 2 in Group II). Medium hemoglobin drop at 48 h after PPCI was 1.4 \pm 0.1g/dL in Group I and 1.2 \pm 0.1g/dL in Group II ($p = 0.27$). Hemoglobin drop of at least 2g/dl were observed in 47 cases, without significant differences between groups (39.2% in Group II vs 21.3% in Group I,

$p = 0.29$), even after adjusting for potential confounder (OR 1.47; 95% CI: 0.71-3.04). Group I had a reduction of 55x10⁹ in platelet count at 48 h while the Group II had 30x10⁹ ($p < 0.001$). This difference was still significant after adjusting for potential confounders in multivariate analysis ($p < 0.001$). During hospitalization and 30-day afterwards we observed 2 deaths (one due to cardiogenic shock and other due to ischemic stroke) and 1 stent thrombosis in Group II; none of these events occurred in Group I (this differences has no statically significance between the Groups).

Conclusions: During hospitalization and 30-day afterwards there were no significant differences in the mortality and stent thrombosis of bivalirudin vs abciximab+UFH in STEMI patients who had PPCI. We did not find differences in hemoglobin drop and major hemorrhagic complications between the 2 Groups. Platelet count was more stable in patients treated with bivalirudin. We did not find any significant difference (except platelet count) between these two strategies.

P1583

Clinical characteristics of preterm infants with low birth weight and patent ductus arteriosus treated with ibuprofen

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Ibuprofen is used as a treatment for closure of Patent Ductus Arteriosus (PDA), however, is not without side effects. The aim of this study was to analyze the clinical characteristics, efficacy and safety of preterm with low birth weight infants and PDA treated with ibuprofen. Between January-2011 and November-2012 were included 81 preterm infants at our center with ≤ 32 week's gestation. The hemodynamic instability was considered when precise inotropic therapy. Echocardiographic analysis was used to diagnose a PDA, to determine the magnitude of the transductal shunt and to ascertain its hemodynamic significance. The hemodynamically significant ductus was considered when the target Doppler echocardiography there was a shunt from left to right through the important ductus. The birth weight of infants was defined as: extremely low ≤ 1000 g (ELBW), very low 1001-1500g (VLBW) and low weight 1501-2000g (LBW).

Results: Of 29 DAP detected, in 9 preterm infants with hemodynamically significant PDA were treated with ibuprofen. In 88.9% were <1000 g at birth, with an average birth weight of 873.3 \pm 249 g vs. 1192 \pm 2367 of those not treated with ibuprofen, $p = 0.027$ and 66.7 % were gestational age < 28 weeks, with a mean of 26.7 \pm 2.12 vs. 28.5 \pm 2.1, $p = 0.44$. Of those who received ibuprofen in 4 patients required only one cycle.

In the echo was characterized by have higher chamber dilation versus those who were not treated 85.7 % vs. 23.5%, $p = 0.005$, flow pattern 71.4 % vs. 13.3%, $p = 0.006$, and increased ductal diameter 2.25 \pm 0.4 vs. 1.62 \pm 0.6, $p = 0.019$. Hemodynamically was characterized by a slightly lower diastolic BP 20.8 \pm 7.1 vs. 27.4 \pm 8.7 mmHg, $p = 0.083$ and lower oxygen saturation 92 \pm 8.7 vs. 96.8 \pm 2.9 %, $p = 0.055$. We found not differences in the need for vasoactive drugs 55.6 % vs. 36.8 %, $p = 0.350$, although there was a greater need for blood transfusions 87.5 % vs. 66.7 %, $p = 0.269$, and a lower incidence of cerebral hemorrhage 11.1% vs. 31.6 %, $p = 0.243$, but not statistically significant. Note that two preterm were complicated by necrotizing enterocolitis [22.2% vs. 0 %, OR 0.269 (95% CI 0.143 to 0.507), $p = 0.033$]. In 55.6 % was preserved diuresis. Of the 9 preterm treated, 4 died with persistent ductus, in the rest, two were performed by surgical closure refractoriness and three were ductal closure. **Conclusions:** Treatment with ibuprofen in preterm infants with patent ductus arteriosus may be a therapeutic alternative, but appears to increase the risk of necrotizing enterocolitis

P1584

Trends in hospital management of heart failure and patient profiles in Romania in the past 15 years

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Purpose: Heart failure (HF) management in hospitalized patients in the past 2 decades has changed due to development of new guidelines and some new drugs. In the same time the patient profile was different due to population aging and higher prevalence of comorbidities such diabetes mellitus (DM), hypertension (HT) and atrial fibrillation (AF). This study analysed the characteristics of hospitalized patients for HF in 2000 and 2014 in one cardiac center from Romania.

Methods: The study represents a retrospective subgroup analysis of Timisoara Heart Failure Registry (2000) and analysis of hospitalized patients for HF in 2014 in our center. The data recorded included: demographics, etiology of HF, comorbidities, clinical characteristics, drug therapy and duration of hospitalization. It included

360 consecutive, hospitalized HF patients (P). The patients were divided into 2 groups: group 1 (n=240) hospitalized in 2000 and group 2 (n=120) in 2014. At discharge demographic and clinical characteristics (age, underlying heart disease, heart rhythm, blood pressure, heart rate, NYHA class, LV ejection fraction (EF) and duration of hospitalization) were recorded. Statistical analysis was done with Student's t test, Fisher's exact test.

Results: In both groups most of the patients were males (137 P - 57% in group 1, 78 P - 65% in group 2), mean age was 66 ± 10 y in group 1 and 69 ± 10 y in group 2 ($p=0.01$). At baseline in group 2 there was a higher NYHA class (3.3 ± 0.7 vs. 2.8 ± 0.7 , $p < 0.0001$). LVEF was higher in group 1 ($39 \pm 10\%$) than in group 2 ($36 \pm 10\%$) $p=0.01$. The patients in group 2 had higher prevalence of HT (78% vs 59%, $p=0.01$), DM (27% vs 16%, $p=0.03$) and AF (51% vs 60%, $p=0.1$). Duration of hospitalization (days) was higher in group 1 (11.7 ± 6.8 vs 9.2 ± 4.3 , $p=0.001$). In group 2 P received more often betablockers (59% vs 38%, $p=0.003$), spironolactone (63% vs 39%, $p=0.0001$) and oral anticoagulation (45% vs 28%, $p=0.003$). **Conclusions:** In 2014 the patients hospitalized for heart failure were older than 14 years ago, with higher NYHA class and more severe LV dysfunction. DM, AF and HT have increased in prevalence. The higher use of betablockers, spironolactone, and anticoagulation reflected the results of large clinical trials and guidelines. The duration of hospitalization has shortened as a consequence of a better treatment with positive economical aspects.

P1585

Tolvaptan in patients with heart failure and hyponatremia: a single center experience

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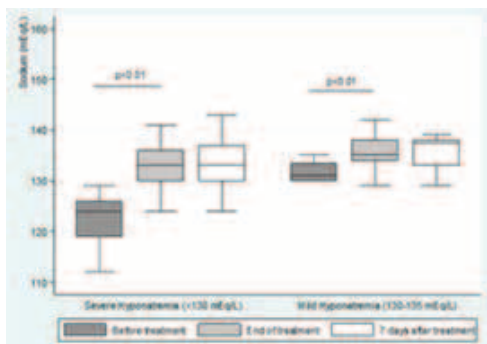
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Background: Hyponatremia in the context of heart failure (HF) is a common condition that worsens the prognosis and for which there is no specific treatment. Tolvaptan has shown some promising results in these patients.

Methods: We analyse the effectiveness and safety of tolvaptan in 58 patients with HF and hyponatremia, identifying possible conditions affecting response. Patients were considered as responders if they reached sodium values of 135 mEq/L and differences in 24h-urine volume at least +500 mL, partial responders if they do not reached the sodium objective but they increased the 24h urine volume and nonresponders if they do not achieve any of these **Objectives:**

Results: Tolvaptan was associated with a mean increase in sodium levels of 8.6 (IC95%=6.1-10.1) mEq/L. Urine volume was increased in patients with mild and severe hyponatremia [Mean(SD): 751.7(218.6) mg/dL and 1,301.2(205.7) mg/dL]. 55.5% of patients were categorized as responders, 27.8% as partial responders and 16.7% as non responders. Previous dose of furosemide lower than 100 mg was associated with tolvaptan response.

Conclusion: Tolvaptan in patients with decompensated HF and refractory hyponatremia significantly increases sodium and rhythm diuresis with a good safety profile. Patients with high previous dose of furosemide could have worse treatment response.



Variation in sodium levels after to

P1586

Xanthine oxidase inhibition in chronic heart failure: effects on diastolic function and NT-proBNP levels in a double-blind, randomised, placebo-controlled study

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Purpose: Diastolic dysfunction is frequently observed in patients with dilated cardiomyopathy, and is associated with poor prognosis. It has been previously shown that parameters of diastolic function significantly relate to serum uric acid levels, reflection of the degree of oxidative stress. We hypothesised that inhibition of xanthine oxidase with allopurinol may therefore improve diastolic function in chronic heart failure (CHF) patients.

Methods: fifty-three stable CHF outpatients with left ventricular systolic dysfunction on optimal background therapy and clinically stable for at least three months, were randomly assigned to receive allopurinol, 300 mg/day, or placebo for three months, in a double-blind trial.

Results: mean age was 66 ± 10 years and mean NYHA class was 2.2 ± 0.6 ; mean serum uric acid levels were 400 ± 100 mmol/L. At follow-up, in the allopurinol group there was a significant reduction in NT-proBNP levels compared with baseline (-191 ± 583 mmol/L, $p=0.0004$), while no significant difference was observed in the placebo group, with a significant treatment effect ($p=0.0033$). In the allopurinol group we found a significant reduction of mitral E wave velocity (E) (0.6 ± 0.2 vs. 0.7 ± 0.2 m/s, $p=0.01$), and of the ratio between E and the velocity of early myocardial lengthening (E') (10.7 ± 6.7 vs. 15.1 ± 11.8), but no significant changes of these two parameters in the placebo group, with a significant treatment effect for both ($p=0.01$ and $p=0.02$, respectively).

Conclusions: in CHF patients, the addition of allopurinol on top of optimal medical therapy for three months significantly improves echocardiographic parameters of diastolic function and lowers NT-proBNP levels.

P1587

Combined antianemic therapy and its impact on prognosis in patients with dilated cardiomyopathy with concomitant anemia

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The Aim: To analyze the effect of antianemic therapy on clinical and functional status and life prognosis of patients with dilated cardiomyopathy associated with anemia at the end of 1 month and 1 - a one-year follow-up.

Methods: 28 patients with dilated cardiomyopathy with anemia (mean age 54.6 ± 16.3 years, m/w, 12/14, mean Hb level 102.58 ± 17.26 g / L, mean Ht $33 \pm 4\%$) were divided into two groups: I (n=14) included pts with oral iron preparation with standard therapy of CHF) and gr II (n=14), which was represented by antianemic therapy with combination of the preparation of oral iron (Fe3+ -polymaltoze complex) and erythropoietin alfa 2000ME dose / week. The control group was selected on the basis of retrospective data analysis of pts that were previously under the supervision of the our department (n=14). Pts in the intervention group received antianemic therapy for 1 month with control of Hb. It was studied 1-year survival prognosis. Analyzed the incidence and cause of death.

Results: After 1 month of observation it has shown that pts in both grps showed an increase in hemoglobin level, without significant intergroup differences (up to 114.3 ± 9.3 g / l and 117.7 ± 11.2 g / l, respectively, in groups I and II, $p < 0.05$). At the same time, the reduction of hemoglobin 105.28 ± 9.11 g / l to 101.19 ± 11.11 g / l in the control group was determined. The results showed approximately the same FC by 6MWT in all, the differences were not significant (260 ± 36.4 m, 280 ± 46.3 , 3100 ± 66.4 m $p > 0.05$). Hemodynamic parameters showed an increase in systolic blood pressure to 100 ± 12.6 mm.r.t.st in group II, and 96 ± 8.4 mm.r.t.st in group I (originally 89.5 ± 14.3 and 92.3 ± 12.7 mmHg, respectively). In the control group changes of central hemodynamics were observed.

After 1 year in general, the death was observed in 8 cases (19% overall): I gr- 2 pts (15.7%), II gr- in 3 pts (21.5%) the control gr - 3 pts (29%) ($\chi^2 = 0.009$, $p > 0.05$). At the same time, the progression of heart failure as a possible cause of death was seen in 62% of cases, pulmonary thromboembolism - 25% and SCD- in 13% without significant differences between groups ($\chi^2 = 1.58$; $p = 0.909$)

Thus, the results of our investigation within 1 month marked increase in hemoglobin during treatment with iron supplementation and its combination with EPO, accompanied by the positive dynamics of the general condition. 1 year forecast of life showed 19% mortality due to various reasons, the differences between the groups in the cause of death could not be found.

P1588

Warfarin and/or dual antiplatelet therapy for chronic heart failure with atrial fibrillation and recent coronary angioplasty plus stent: analysis of three antithrombotic regimens

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Table P1589.

Medication	PR in men	PR in women	Average Age of pts not receiving medication	Average Age of pts not receiving medication		
Angiotensin-converting enzyme-inhibitors (ACE-I) %	77	53	0,04	67,6	61,6	0,08
Angiotensin receptor blockers (ARB) %	16	26	0,29	63,0	63,9	0,81
ACE-I or ARB %	91	79	0,13	73,7	62,1	0,027
Beta-blockers %	93	85	0,30	75,5	61,9	0,009
Spirolactone/eplerenone (MRA) %	71	50	0,09	68,1	60,6	0,016
Digitalis %	29	10	0,04	62,1	67,2	0,14
Ivabradine %	3	11	0,16	64,0	53,2	0,09
Diuretics %	68	40	0,03	64,7	62,2	0,44

Introduction: Among patients(pts) with or without chronic heart failure the indication for oral anticoagulation with warfarin (OAC) plus dual antiplatelet therapy (DAPT) is typically represented by a persistent or chronic atrial fibrillation(AF) coexisting with a history of recent coronary angioplasty with stent (PCI-S).

Methods: Within a population with chronic ischaemic heart failure(NYHA class II-III) collected from January 2010 to December 2013, we made a retrospective cohort study to determine the respective impacts on cardiovascular outcomes of three different pharmacologic regimens, i.e., triple therapy (TT) with warfarin + clopidogrel and acetylsalicylic acid(ASA), dual therapy (DT) with warfarin +clopidogrel or ASA, dual antiplatelet therapy (DAPT)with clopidogrel + ASA. Outcomes of interest were a) death from all causes, b) cardiac ischemic events (which included the exertional angina and the acute coronary syndromes, as well as the need for percutaneous or surgical myocardial revascularization), c) heart failure hospitalizations (worsening heart failure), d) cerebral ischemic events (transient ischemic attack, or ischemic stroke, e) bleeding events (divided into intra- and extra-cranial bleeding events). The inclusion criterion was the coexistence of an indication for OAC (persistent or chronic AF, mechanical heart valve prosthesis, etc) with an indication for dual antiplatelet therapy due to recent PCI-S.

Results: 98 pts were included in the study. Among them, 48 (49%), 31 (31.6%), and 19(19.4%) pts were prescribed TT, DT, and DAPT, respectively. Throughout a mean follow-up of 378± 15.7days, there were no significant differences by comparing the three pharmacologic regimens for all of the abovementioned outcomes.

In particular, the total frequency of major bleedings was similar in the three groups: 5 cases(10.4%) in TT, one case (3.22%) in DT and no case in DAPT groups (p [chi-square test]= 0.1987).

Conclusions: In our retrospective study, TT, DT and DAPT displayed similar efficacy and safety. Although the superiority of OAC vs. DAPT for stroke prevention in AF pts has been demonstrated by previous randomized trials, a smaller frequency of high thromboembolic risks' features in DAPT group of the present study may have prevented the observation of a higher incidence of ischemic stroke in this group. Likewise, the observational nature of the study and its limited sample size may have caused lack of significant differences among the three groups as regards the rate of bleeding events, although a 2- to 3-fold higher risk of bleeding has been usually reported with TT compared to DAPT

P1589

Prescription rates and dosage of heart failure medication varies dramatically in woman, with age and comorbidities

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Purpose: The Heart Failure (HF) guidelines of the European Society of Cardiology (ESC) recommend an up-titration to a target dosage of HF medication in patients (pts) with chronic HF. However, underprescription is often seen in practice. The aim of this study was to evaluate Prescription Rates (PR) of HF medications in different pts populations and different comorbidities.

Methods: Over a period of one year pts who were either hospitalized for congestive HF or admitted to a HF specialist at the outpatient clinic at the hospital, were asked to join the prospective observational study. Amongst others, demographic data, co-morbidities and medical prescription information were collected.

Results: The study recruited 90 pts with a mean age of 63,4 SD±14,0 years. Comorbidities were common among the heart failure patients (81,1%). Overall prescription rate were high for Angiotensin-converting enzyme-inhibitors (ACE-I) or Angiotensin receptor Blockers (ARB) (90,9%), Beta-blockers (91%), but low for mineralocorticoid receptor antagonists (MRA) (66%), Ivabradine (6%) and Digitalis (26%). However PRs in woman were significantly lower for ACE-I, digitalis and diuretics than in men. Furthermore, older patients were less likely to receive recommended HF medication. ACE-I or ARB, MRA and Beta-blockers were less likely prescribed. Most common

comorbidities preventing prescription of recommended HF medication was severe renal dysfunction (8,9%).

Conclusions: Prescription rates of the recommended HF medications are lower in woman than in men admitted to a hospital for congestive HF. Furthermore older patients are less likely received recommended HF medication.

P1590

Collaborative care with a pharmacist improves optimisation of secondary prevention medication after discharge in patients with left ventricular systolic dysfunction due to acute myocardial infarction

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Purpose: Angiotensin converting enzyme inhibitors (ACEIs), beta-blockers (β Bs) and mineralocorticoid receptor antagonists (MRAs) improve outcomes in patients with left ventricular systolic dysfunction post acute myocardial infarction (MI). We aimed to optimise the use of these drugs in such patients using a strategy of collaborating with a pharmacist at the time of hospital discharge.

Methods: Controlled before-and-after study. Patients with incident MI and echocardiographic left ventricular ejection fraction <40% were included. Patients unable to return for cardiac rehabilitation (CR) after MI were excluded. Two groups; 1) Retrospective 'usual care' patients identified through a database of admissions 08/2012 to 08/2013, 2) Prospective 'intervention' patients identified during admission by CR nurses 08/2013 to 08/2014 and referred at the time of hospital discharge to CR in addition to a pharmacist clinic. The pharmacist prescribed in line with European Society of Cardiology (ESC) guidelines. Consultant Cardiologists provided clinical support.

Endpoints: % of patients treated with, mean % target dose achieved of and % of patients on full ESC target dose of ACEI, β B and MRA four months after index MI discharge. Statistical significance was tested by CHI-squared and Mann-Whitney U tests.

Results: 57 'usual care' and 51 'intervention' patients were identified. There was no statistical difference in systolic blood pressure, heart rate or creatinine between groups however 'usual care' patients were significantly older than 'intervention' patients (67 vs 60 yrs, p=0.014). The pharmacist reviewed 'intervention' patients a mean 4.6 times. Significantly more 'intervention' patients were treated with β B or MRA compared to 'usual care'; 96.1% vs 82.5% (p=0.025) and 49.0% vs 24.6% (p=0.008) respectively. More 'intervention' compared to 'usual care' patients were treated with ACEI, this was not statistically significant; 94.1% vs 89.5% (p=0.383). The mean dose of ACEI, β B and MRA (expressed as a % of ESC guideline target dose) was significantly higher in the 'intervention' compared to 'usual care' patients: 71.7% vs 43.8% (p<0.0001), 55.9% vs 30.9% (p<0.0001) and 35.3% vs 15.8% (p=0.006) respectively. As was the proportion achieving full target dose of ACEI, β B and MRA: 56.9% vs 21.1% (p<0.0001), 29.4% vs 7.0% (p=0.002) and 21.6% vs 7.0% (p=0.029) respectively.

Conclusion: Use of life-saving therapy was improved significantly by the addition of collaborative care with a pharmacist. A randomised clinical trial is needed to assess the impact of such a service on patient outcomes.

P1591

Early effects of Ivabradin-b-blocker combination compared to b-blocker up-titration on LV and pulsatile arterial functions in postinfarction patients with mild CHF and EF lowering

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Table 60508.

Group	Time	EDI, ml/m ²	EF, %	E/E'	ASBP, mmHg	aPP, mmHg	AP, mmHg	PWVcf, m/s	Ea, mmHg/ml	Ees, mmHg/ml	TAC, ml/mmHg
1	M0	83,9±3,7	42,0±1,90	9,5±0,50	129,3±6,10	46,7±2,13	7,6±0,44	8,6±0,41	1,91±0,08	4,42±0,24	1,14±0,05
	M2	84,0±3,7	44,1±2,30	8,2±0,38 ## **	115,0±5,10#	36,1±2,4###	5,6±0,29 ###***	6,6±0,22###**	1,61±0,06##	4,17±0,20	1,44±0,08###*
2	M0	83,9±3,8	41,7±2,00	9,5±0,50	125,0±5,40	42,2±2,0	7,3±0,20	8,5±0,27	1,85±0,07	4,21±0,21	1,17±0,05
	M2	84,8±3,9	44,6±2,30	9,4±0,48	117,1±5,20	37,5±1,7	7,4±0,25	8,8±0,30	1,68±0,06	4,12±0,18	1,34±0,07#

- p < 0,05, ## - p < 0,01, ### - p < 0,001 compared to M0; * - p < 0,05, ** - p < 0,01, *** - p < 0,001 compared to Group 2.

Purpose: To compare the effects of heart rate (HR) control achieved with ivabradine (lv) and bisoprolol (Bs) combination versus that of Bs uptitration on LV systolic function, mitral E/E', pulsatile arterial hemodynamics assessed by pulse wave analysis (PWA) in postinfarction patients with mild CHF and EF lowering.

Methods: In single-blind, parallel-group study 78 patients NYHA 1-2 <60 years (54±2,3) in sinus rhythm >70 bpm with documented MI>3 months, controlled mild hypertension and EF of 38-45% without mitral regurgitation treated eg with ACE inhibitors, Bs 2,5 mg od or b-blocker naive, were randomized into 2 groups. In Group 1 (n=40; 9 women) Bs was uptitrated to 5mg pd and lv was added and uptitrated to 7,5 mg bid (12,4±0,49 mg pd). In Group 2 (n=38; 9 women) Bs was uptitrated to 9,1±0,35 mg. At baseline (M0) and 2 months (M2), mitral E/E' was assessed by TDI and aortic systolic, pulse and augmentation blood pressures (ASBP, aPP, AP) and carotid-femoral pulse wave velocity (PWVcf) - with SphygmoCor. End-systolic elastance (Ees) was calculated as ratio of LV end-systolic pressure (ESP) and volume, ESP = 0.9*brachial SBP (oscillometry method), arterial elastance (Ea) - as ESP/stroke volume (SV), total arterial compliance (TAC) - as ratio of SV to aPP.

Results: Resting HR was similar in both groups at M0 (78,6±3,59 vs 81,4±3,7 bpm) and M2 (66,4±2,93 vs 64,9±2,91 bpm) as well as brachial SBP (135,4±5,8 vs 132,4±5,8 and 124,2±5,4 vs 125,2±5,7 mm Hg, all p > 0,05). Other results see in table.

Conclusion: In postinfarction pts with moderate CHF and EF lowering, equivalent HR control with lv+Bs, but not with Bs uptitration, produced early mitral E/E' reduction associated with arterial pulsatile unloading assessed by PWA and Ea, yet unchanged LV systolic function indexes.

P1592

Effect of sodium zirconium cyclosilicate (ZS-9) on aldosterone from the phase 3 randomized, double-blind, placebo-controlled HARMONIZE study

Supported by ZS Pharma, Inc., Coppell TX Zannad¹; HS Rasmussen²; PT Lavins³; A Yang²; B Singh²; SD Anker⁴

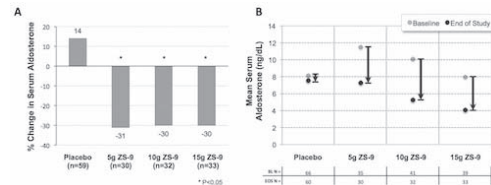
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Purpose: Hyperkalaemia (HK; K⁺ ≥5.1mmol/L) is a common electrolyte disorder in patients (pts) with heart failure (HF) and chronic kidney disease; it increases risk of mortality and limits RAAS inhibitor use. K⁺ drives secretion of aldosterone, which contributes to progression of renal disease, left ventricular hypertrophy, perivascular/interstitial fibrosis and vascular inflammation. Sodium zirconium cyclosilicate (ZS-9) is a nonabsorbed cation exchanger that selectively traps K⁺ in the GI tract. ZS-9 rapidly controlled normal serum K⁺ in 2 Phase 3 trials (Packham NEJM 2014; Kosiborod JAMA 2014). Here we present a prospectively predefined analysis on the effect of ZS-9 on aldosterone in pts from HARMONIZE.

Methods: HARMONIZE was a Phase 3, multicenter, randomized, double-blind, placebo (PBO)-controlled trial evaluating long-term safety/efficacy of ZS-9 in pts with HK. Pts received 10g of ZS-9 3x/day for 48h in the open-label acute phase (N=258). Pts achieving normal K⁺ (3.5-5.0 mmol/L) were randomized to ZS-9 (5, 10 or 15 g) or PBO 1x/day in the 28-day randomized phase. Primary endpoint was mean K⁺, days 8-29, of the randomized phase. Aldosterone change from acute phase baseline was analyzed from US sites (n=181).

Results: ZS-9 reduced aldosterone by -31%, -30%, and -30% in the 5g, 10g and 15g ZS-9 groups, respectively, compared with a +14% increase with PBO (P < 0.05). ZS-9 was well tolerated with a low adverse event rate.

Conclusions: Significant decreases in serum aldosterone were observed with ZS-9, suggesting its role in restoring normal K⁺ may be accompanied by correction of elevated aldosterone. These findings may have implications for delaying progression of HF and cardiorenal disease, both of which are frequently managed with RAAS inhibitors, and should be confirmed in future studies.



HEART FAILURE IMAGING

P1593

Association between left ventricular size and coronary artery calcium score

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Objective: Increased left ventricular (LV) size is associated with cardiovascular mortality and morbidity. The purpose of this study was to evaluate the relationship between cardiac echocardiography-derived parameters of LV end diastolic dimension (LVEDd) and coronary artery calcium score

Subjects and Methods: We studied 1137 male subjects. LV area was quantified from 2-demesional echocardiography, end-diastolic images at a mid-ventricular slice in individuals who underwent a comprehensive health examination in 2010 at our Hospital in South Korea, free of known cardiovascular disease. LVEDd was measured and LV index (LVI) was calculated by the quotient of LV area and body surface area (BSA). Crude and adjusted regression analyses were used to determine the association of LVEDd with risk factors and coronary artery calcification (CAC). Cox proportional hazards models were used to estimate hazard ratios (HRs) (and 95% CIs) for prevalence of CAC>0 using lowest quartiles of LVEDd as the reference groups

Results: Overall, 1137 subjects (age 44.2±9.3 years, mean BMI 24.8±2.98, mean systolic blood pressure 118.9±11.3) were included in this analysis. LVEDd was strongly correlated body mass index (r=0.240, p < 0.001) and systolic blood pressure (r=0.109, p < 0.001). Prevalence of CAC>0 according to LVEDd quartiles were 66/294(22.4%), 62/314(27.6%), 66/314(27.6%) and 39/215(18.9%). Increasing LVEDd quartiles were not associated with prevalence of CAC>0 (adjusted HR for highest quartile 0.763 (95%CI 0.463, 1.259), p value for the trend across quartiles 0.290).

Conclusion: Cardiac echocardiography-derived LVEDd is associated with body size and hypertension but was not associated with prevalence of CAC>0 in relatively healthy and young men. Further studies need to evaluate whether assessment of LVEDd helps identifying subjects with increased cardiovascular risk in this kinds of subjects.

P1595

Dynamics of global left ventricular two dimensional strain in primary anterior STEMI patients

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Purpose: to study the dynamics of global longitudinal strain (GLS) assessed by two-dimensional speckle tracking echocardiography in patients (pts) with primary anterior STEMI.

Methods: The study included 24 pts with primary anterior STEMI (mean age 58.46±10.2). Echocardiography with 2-dimensional speckle tracking imaging was performed on the 1st (T1), 7th (T2), 14th days (T3) after STEMI (<Vivid 9>). Analysis of echocardiographic images was performed offline by the two independent observers (EchoPac). Depending on value of GLS on T1 pts were divided into

2 groups: 5 pts with GLS < -15 and 19 pts with GLS > -15 (1st and 2nd group respectively).

Results: 23 pts had urgent reperfusion therapy, 6 pts underwent primary PCI, 16 pts - PCI after successful fibrinolysis (68.5%). 25 % pts had patency of IRCA achieved during the first 3 h. Average reperfusion time was 4.21 ± 0.94 h. Dynamics of EDV LV was following: 95.88 ± 21.71 ml (T1), 96.73 ± 16.95 (T2), 98.27 ± 12.6 (T3); of ESV LV 42.1 ± 13.5 ml (T1), 42.5 ± 13.76 (T2), 40.53 ± 13.66 (T3); of EF LV $55.7 \pm 9.8\%$ (T1), 56.1 ± 9.6 (T2), 58.8 ± 9.62 (T3) without significant differences. Nevertheless, it was found positive dynamic of GLS: -12.65 ± 3.53 (T1), -13.61 ± 3.81 (T2), -14.27 ± 4.1 (T3), $p < 0.05$. GLS reduced 11.35% ($p = 0.0048$) from T1 to T3. There were no dynamics in GLS between T1 and T2, T2 and T3 ($p > 0.05$). In the 1st group GLS to T3 was reduced ($p = 0.038$), whereas in the 2nd group there was no observed.

Conclusion: The modern management of STEMI pts limits adverse postinfarction remodelling and preserves of global left ventricular contractility detected by the EF LV. Meanwhile GLS was decreased in STEMI pts. We found the nonlinear dynamics of this parameter. There was strain improvement to T3 in pts with GLS < -15 on T1. In contrast, pts with GLS > -15 on T1 had no any dynamics. Thus, GLS is a new tool for the accurate diagnostics of left ventricular contractility.

P1596

Early prediction of myocardial viability after AMI by 2-Dimensional speckle tracking imaging

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Background: Identifying the transmural extent of myocardial necrosis and the degree of myocardial viability in acute myocardial infarction (AMI) is important clinically. The aim of this study was to assess myocardial viability using two-dimensional speckle tracking imaging (2-D STI) in patients with AMI.

Methods: Two-dimensional STI was performed at initial presentation, 3 days, and 6 months after primary percutaneous coronary intervention (PCI) in 30 patients with AMI whom had a left anterior descending coronary artery (LAD) culprit lesion. In addition, 20 patients who had minimal stenotic lesions (< 30% stenosis) on coronary angiography were also included in the control group. At 6 months dobutamine echocardiography was performed for viability assessment in seven segments of the LAD territory. According to the recovery of wall motion abnormality, segments were classified as viable or non-viable.

Results: A total of 131 segments were viable, and 44 were nonviable. Multivariate analysis revealed significant differences between the viable and nonviable segments in the peak systolic strain, the peak systolic strain rate at initial presentation, and peak systolic strain rate 3 days after primary PCI. Among these, the initial peak systolic strain rate had the highest predictive value for myocardial viability (hazard ratio 31.22, $p < 0.01$).

Conclusions: Two-dimensional STI is feasible for assessing myocardial viability, and the peak systolic strain rate might be the most reliable predictor of myocardial viability in patients with AMI.

P1597

Relationship of left atrial global peak systolic strain with left ventricular diastolic dysfunction and brain natriuretic peptide levels in hemodialysis patients

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Background: We investigated the relationship of left atrial deformational parameters evaluated by 2-dimensional speckle tracking imaging (2D-STI) with conventional echocardiographic diastolic dysfunction parameters and brain natriuretic peptide levels in end-stage renal disease (ESRD) patients on maintenance hemodialysis (HD).

Methods: We enrolled 30 hemodialysis (HD) patients. All patients had echocardiographic examination immediately before and after hemodialysis and venous blood samples were drawn simultaneously. In addition to conventional echocardiographic parameters, left atrial strain curves were obtained for each patient. Average peak left atrial strain values during left ventricular systole were measured.

Results: BNP values were higher before hemodialysis. The left atrial ejection fraction (LAEF) and peak LA strain during LV systole (LAGS) increased significantly after HD.

Before HD, there were significant inverse correlations between LAGS and BNP levels ($r = -0.482$, $p = 0.007$), E/E' ($r = -0.33$, $p = 0.049$), left atrium volume maximum ($r = -0.366$, $p = 0.047$) and left atrium volume maximum ($r = -0.579$, $p = 0.001$). LAGS had significant correlation with E' velocity ($r = 0.557$, $p = 0.001$) and LAEF ($r = 0.58$, $p = 0.001$). After HD, LAGS was significantly correlated with left ventricular ejection fraction ($r = 0.417$, $p = 0.022$). There were also significant correlations between LAGS and echocardiographic parameters diastolic LV function after HD.

Conclusion: Left atrium peak systolic global longitudinal strain values decreased

consistently with deteriorating systolic and diastolic function in hemodialysis patients. Left atrium peak systolic global longitudinal strain measurements may be helpful as a complimentary method to evaluate diastolic function in this patient population.

P1598

The prognostic value of echocardiography in patients with heart failure

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Background: Echocardiographic indices of cardiac structure and function and are strong predictors of mortality and morbidity in patients with heart failure; therefore, echocardiography is an important tool in the evaluation of patients with heart failure. The aim of this study was to identify high-risk echocardiographic parameters associated with adverse outcomes, which are useful to guide therapy and follow-up management of heart failure patients.

Methods: This retrospective study including 1841 patients (65 years, 1146 were male) admitted in the therapeutic unit of heart failure from 2006 to 2014. Cardiac parameters was performed in all patients We compared 2 groups: with and without acute heart failure.

Results: Among those patients, 497(27%) patients (mean age=65) had acute heart failure.

Cardiac decompensation correlated with end-diastolic volume of the left ventricle ($P = 0.006$), left ventricular filling pressures, right systolic dysfunction, mitral regurgitation > grade II, pulmonary artery systolic pressure ($p = 0.0004$).

There was no correlation between decompensation and left ventricular systolic dysfunction.

Conclusion: Echocardiography is an important tool in the evaluation of patients with heart failure; also Doppler echocardiography may assist in monitoring and optimization of therapy.

P1599

Failing on top--time to look up ?

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Introduction: The structure of the left atrium is complex. The assessment of left atrial volumes was traditionally based on estimates of volume measured by M-mode and two dimensional echocardiography. These methods, however, rely on geometric assumptions on the shape of the left atrium and are potentially fraught with error, due to the variation in the shape of the left atrium, especially when the chamber is enlarged.

Objective: The purpose of this study was to measure the total left atrial emptying fraction (LAEF) in a group of patients with a variety of diagnoses in a cardiology clinic.

Patients with a variety of risk factors for cardiac failure were chosen in order to determine the average total LAEF in the average, ambulant and asymptomatic attendee to the local cardiology clinic. All of these patients were in sinus rhythm.

Methods: Left atrial volumes were measured with the use of real time 3 dimensional echocardiography (RT3DE), as left atrial enlargement can occur asymmetrically in an anteroposterior, transverse or superoinferior dimension, thus flawing 2D techniques.

Results: See Table 1

Discussion: The normal LAEF has been shown to be quite consistent at $63 \pm 7\%$. With aging passive emptying accounts for greater and active emptying less of the total emptying of the left atrium.

The normal mean LA volume is reported to be 22 ± 6 ml/m² 9, 17. Left atrial dilatation (enlargement) can be defined as mild to moderate (32-40 ml/m²) or severe (> 40ml/m²).

The average total LAEF of 41% is far below the published normal value of $63\% \pm 7\%$. Of note only one subject had left atrial dilatation (with a left atrial volume of 34.47 ml/m²) and a severely depressed LAEF of 8.6 %.

It is suggested that depressed LAEF is common in the population of patients with cardiovascular risk factors, even though left atrial size and volumes may still be in the normal range. Whether this reflects a primary atrial myopathy which may be innocent, may progress to atrial fibrillation and/or may be a precursor of systolic and/or diastolic ventricular dysfunction merits further study.

Table 1

Cases:	Average age:	Average LA max:	Average LAmin:	Average LAEF:
60	50 years	18.52 ml/m ²	11.00 ml/m ²	41%

LAmax: Maximal left atrial volume, measured at left ventricular end systole LAmin: Minimal left atrial volume, measured at left ventricular end diastole LAEF: Left atrial emptying fraction

P1600**An integrated approach to the evaluation of the systolic function and remodeling of the right ventricular in patients with dilated cardiomyopathy and ischemic cardiomyopathy**

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Purpose: The important prognostic value in patients with cardiomyopathy, as potential responders to CRT, is the safety contractile reserve the right ventricular (RV). The aim of this work was to develop a complex evaluation of the systolic function and remodeling of RV on the basis of comparison of some parameters by cardiac ultrasound that can serve as a differential diagnosis of dilated cardiomyopathy(DCM) and ischemic cardiomyopathy.

Methods: All patients were divided into two groups: group 1-patients with DCM (28 men and 11 women; aged 55,2 ± 7,5) and group 2-patients with ischemic cardiomyopathy (49 men and 5 women; aged 57,6 ± 6,4) and chronic heart failure (CHF) were included in the study. In the first group, patients with CHF NYHA functional class III-IV were 78.2%, in the second group 86.1%. All patients were fully comply with the requirements of CRT recommended ESC (2013). We compared the values of the fractional area change of RV (2D RV FAC), tissue Doppler-derived tricuspid lateral annular systolic velocity (S'), Right ventricular index of myocardial performance (RIMP), RV basal diameter, Pulmonary artery dimension between valve and the bifurcation point (PA), the level of systolic pulmonary artery pressure (SPAP), correlation analysis S', 2D RV FAC, SPAP and RV basal diameter in the groups.

Results: A significant difference was revealed in the values S', 2D RV FAC and level SPAP 1.2 times the patients with DCM(p < 0.05). In the first group S' (cm/s) and 2D RV FAC (%) were 12.6 ± 3.2 and 37.3 ± 7.0, respectively. In the second group 10.5 ± 2.1 and 30 ± 6.7, respectively. We received reverse moderate correlation S' and RV basal diameter, as well as 2D RV FAC size and RV basal diameter, coefficient Spearman R = -0.33 and R = -0.36, respectively. We received a strong direct correlation level SPAP and RV basal diameter, coefficient Spearman R = 0.76. RIMP in the first group was 0.78 ± 0.12, in the second 0.73 ± 0.13, which was not significant difference.

Conclusions: The patients with DCM have the normal values 2D RV FAC, and S' that create preconditions to use these parameters in the differential diagnosis of DCM and ischemic cardiomyopathy. Comprehensive pre-operative assessment of contractility of RV by echocardiography using DTI in the clinic for cardiac surgery allows to evaluate systolic function RV for selection of promising response rate to CRT. Remodeling RV in patients with cardiomyopathy with higher functional class of CHF affects both RV basal diameter and the dimension of PA.

P1601**Global longitudinal strain, ejection fraction and wall motion score in patients with acute coronary syndrome**

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Introduction: The global longitudinal strain (GLS) allows the evaluation of left ventricular (LV) longitudinal function and discerning about the global deformation and regional segments. Multiple studies in the context of acute coronary syndrome (ACS) report it's value predicting the infarcted area or coronary occlusion in the setting of acute myocardial infarction (AMI). It's prognosis is not yet established.

Purpose: This study is intended to obtain data on the GLS utility in evaluating the prognosis of patients with ACS, comparing it to other ventricular function measurements, as the wall motion score (WMS) or the ejection fraction (EF).

Methods: Revised echocardiograms in the last year of hospitalized patients with ACS. Examinations were selected with conditions that allowed the realization of longitudinal strain by speckle tracking in 3 apical windows (4C, 2C and 3C). We excluded patients with 3 or more segments of the LV not amenable to analysis by ST-E. This selection resulted in a sample of 80 patients. We conducted follow up to 6 months and one year and defined as death and cardiovascular hospitalization and the combined endpoint of both. Statistical analysis in SPSS.

Results: In the study the average age was 66,23 anos, 81.1% were males. Patients with ST elevated myocardial infarction were 41.8% as well as patients with AMI without ST segment elevation, 3.8% were patients with unstable angina. Angiographically 11% had disease of the left main, 69.9% of the anterior descending, circumflex 45.2% and 65.8% of the right coronary artery. The average EF was 54.28%, the average GLS was -13.67 and the average WMS was 1,286. The EF and the WMS were not related to any of the endpoints at 6 months or 1 year. It was possible to relate the GLS with mortality (p = 0.023), although unrelated to cardiovascular hospitalization (p = 0.528) or the combined endpoint of 6 months (p = 0.201) or 1 year (p = 0.97). The sample was divided into 2 groups according to the value of the GLS (GLS ≤ -13: Group A [GA], GLS > -13 Group B [GB]) according to the ROC curve. There was an association between death and the GLS (GA 0%, WG 18.2%, p = 0.21) and regarding the events at 1 year (14.8% GA, GB 40.9% p = 0.40; odds ratio 3.981).

Although the events at 6 months (7.5% GA, GB, 14.7%, p = 0.32, odds ratio 2.126) and cardiovascular hospitalization (14.8% GA, GB, 22.7%, p = 0.477 ; odds ratio 1.691) were higher in GB there was no statistically significant difference.

Conclusion: In this study the GLS showed an association with mortality and events 1 year unlike EF and WMS.

P1602**Beyond systole: analysis of the prognostic value of diastolic function in patients with acute coronary syndrome**

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Background: Multiple studies validated the importance of clinical, imaging and analytical data in determining the prognosis of patients with acute coronary syndrome (ACS). Among these systolic ventricular function is validated as a crucial prognosis marker, with therapeutic implications. However diastolic dysfunction parameters also demonstrate prognostic correlation.

PURPOSE: This study aims to obtain data on the usefulness of diastolic function measurements in assessing the prognosis of patients with ACS.

Methods: Revised echocardiograms in the last year of hospitalized patients with ACS, selected those with image quality to quantify radial and longitudinal systolic function measurements and diastolic dysfunction. This selection resulted in a sample of 80 patients. Diastolic dysfunction was measured by measuring the transmural flow rates and speeds the doppler tissue to the mitral annulus. We conducted follow up to 6 months and one year and defined as endpoints death and cardiovascular hospitalization and the combined endpoint of both, defined as "events." Statistical analysis in SPSS.

Results: The average age was 66,23 years, 81.1% were males. Patients with ACS with ST elevation (STE) were 41.8%, the remaining were patients with ACS without STE (3.8% had unstable angina). Angiographically 11% had disease of the left main artery, 69.9% of the anterior descending, 45.2% of the circumflex and 65.8% of the right coronary artery. The mean ejection fraction was 54.28%, average global longitudinal strain was -13.67, average wall motion score was 1,286, average E was 0.7404, average E' was 0.0697 and average E/E' was 11,4281. The E values were different in patients who died (p = 0.001) and had events at 1 year (p = 0.046). The values of E' were different only in the deceased (p = 0.043). Values of E/E' were different in the deceased (p < 0.001) and in those with events at 6 months (p = 0.008) or 1 year (p = 0.005). None of the variables correlated with cardiovascular hospitalization. Linear regression showed that E/E' was able to predict mortality (p < 0.001) and 6 months events (p = 0.046). ROC curve selected the cutoff E/E' 17 as the best predictor of mortality and events at 1 year, but it wasn't possible to estimate odds ratios (OR). Selecting a cutoff E/E' 16 (GA <16; GB ≤16) are achieved to predict mortality (0.0% GA, GB, 57.1%, p < 0.001) and 6 months events (GA 8.7%, GB 37.5%, p = 0.022; OR 6.12) and one year (17.1% GA, GB 87.5%, p < 0.001; OR 29.0).

Conclusion: In this study, diastolic dysfunction parameters showed usefulness in predicting prognosis, particularly E/E' which was an independent predictor.

BIOMARKERS**P1603****Prognostic biomarkers of cardiovascular events in patients with regression of chronic lymphocytic leukemia**

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Purpose: evaluate the prognostic value of galectin-3 (Gal-3) and N-terminal of pro-hormone brain natriuretic peptide (NT-proBNP) for cumulative survival in patients with regression of chronic lymphocytic leukemia.

Methods: One hundred fifty six subjects with regression of chronic lymphocytic leukemia. Observation period was up to 12 months. Blood samples for biomarkers measurements were collected. ELISA method for measurements of circulating level of Gal-3 was used. Concentrations of Gal-3 and NT-pro-brain natriuretic peptide (BNP) for cumulative survival cases due to advanced chronic heart failure (CHF) were tested.

Results: Two hundred sixteen cumulative clinical events occurred in 51 patients (32.7%) within the follow-up, with their distribution being as follows: 7 cardiovascular deaths, 122 cardiac arrhythmias, 16 cardiac ischemic events, 3 strokes, 30 chronic heart failures and 38 hospital admissions for cardiovascular reasons. Medians of circulating levels of Gal-3 in subjects without and with cardiovascular events were 5.16 ng/ml (95% confidence interval [CI] = 4.74-5.56 ng/ml) and 16.4 ng/ml (95% CI = 14.80-18.01 ng/ml) (p < 0.001) respectively. Medians of circulating levels of NT-proBNP in subjects without and with cardiovascular events were 13.14 fmol/ml (95% confidence interval [CI] = 10.94-15.35 fmol/ml) and 22.19 fmol/ml (95% CI = 12.00-33.38 fmol/ml) (p = 0.07) respectively. The results of regression

analysis showed directly related circulating Gal-3 with E/Am ($r=0.35$, $P=0.002$), E/Em ($r=0.35$, $P=0.002$), NT-pro-BNP ($r=0.31$, $p=0.017$), hypertension ($r=0.37$, $P=0.001$), obesity ($r=0.41$, $p=0.003$), T2DM ($r=0.39$, $P=0.001$), TC ($r=0.34$, $P=0.003$), LVEF ($r=-0.38$, $P=0.001$). Gal-3, NT-pro-BNP, GFR, E/Em, LVEF, T2DM, hypertension, and multi-vessel lesion of coronary artery were selected as predictors in the univariate logistic regression analysis. Multivariate logistic regression revealed independent predictive value of circulating Gal-3 for one-year cumulative cardiovascular events (odds ratio [OR] = 1.13; 95% CI = 1.07-1.25; $P=0.003$). In fact, Gal-3, NT-pro-BNP, E/Em, and LVEF remained statistically significant predictors for cumulative cardiovascular events, whereas T2DM, hypertension, obesity, and multi-vessel lesion did not.

Conclusions: Increased circulating Gal-3 and NT-proBNP associate with increased one-year cumulative cardiovascular events among patients with documented chronic lymphocytic leukemia.

P1604

NT-proBNP predict progression of subclinical coronary atherosclerosis at CT scan in an asymptomatic middle-aged population

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Background: Coronary calcium score (CCS) is a well validated index of subclinical atherosclerosis with high negative predictive value in patients with intermediate risk and low/absent CCS. Predictors of CCS progression are not well understood, as traditional coronary risk factors show a low relation with CCS progression. Cardiac natriuretic peptides have been recently indicated as possible biomarkers of vascular remodeling beyond the presence of cardiac anomalies and have been associated with the amount of CCS. We analyzed the hypothesis that NT-proBNP could be a predictor of CCS progression.

Methods: We analyzed 601 middle aged asymptomatic subjects without previous cardiovascular events and a baseline value of CCS < 100 Agatston Unit (A.U.) from the screening program of the Montignoso Heart and Lung Project. These subjects underwent a second computed tomography (CT) scan 3 years after basal CT, risk factor assessment, laboratory testing comprehensive of NT-proBNP, echocardiography. Glomerular filtration rate (GFR) was estimated with the Cockcroft Gault formula. To evaluate predictors of CCS progression, subjects were divided according to CCS > or < 100 at the follow-up CT.

Results: Mean age of our population was 64 ± 6 (range 45-77) with a mean 10 years Framingham risk score of $8.39 \pm 3.1\%$ configuring an intermediate risk population. CCS progression occurred in 51 subjects (8%). Compared to participants without progression, those with CCS progression were older (66 ± 6 y.o. vs. 63 ± 6 y.o.) and had lower glomerular filtration rate (89.63 ± 22.2 ml/min vs. 89.6 ± 22.2 ml/min $p < 0.05$) and higher NT-proBNP ($94; 49-117$ ng/L vs. $59; 31-111$ ng/L, $p < 0.05$), without significant differences in mean Framingham risk score ($9.14 \pm 3.4\%$ vs. $8.3 \pm 3.1\%$, $p = 0.103$). At multivariate analysis NT-proBNP predicted CCS (O.R. 1.613, 95% C.I. 1.060-2.60) independently by GFR, age, Framingham risk score and cardiac left ventricular indexed mass at echocardiography. The area under the curve for NT-proBNP at the ROC curve for CCS prediction was 0.610 (95% C.I. 0.54-0.71).

Conclusion: Among middle-aged asymptomatic subjects, NT-proBNP appears as significant predictor of CCS progression over 3 years, beyond traditional risk factors, reinforcing the hypothesis of cardiac natriuretic peptides as biomarkers of vascular remodeling.

P1605

Role of natriuretic peptides in medium cardiovascular complications risk formation among hypertensive railway employers

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Research objective: Evaluation of influence of general risk factors for hypertension (smoking, heredity, obesity) onto natriuretic peptides values among hypertensive railway employers with associated medium cardiovascular risk.

Research methods: Fifty eight male railway employers were included into this research, with mean age 40.93 ± 1.48 suffering from hypertension of 1 and 2 degree with medium cardiovascular risk. All patients were examined according to the obligatory diagnostic standards of European Society of Cardiology (ESC). Hypertension was determined as BP level $\geq 140/90$ mmHg (ESC, 2013). Examined patients had 1-2 risk factors for cardiovascular diseases. There were 58.2% smokers, 58.6% had hereditary tainted and obesity was revealed in 10%. Average hypertension duration was 2.0 years. Control group consisted from 30 almost healthy volunteers. All patients underwent determination of body mass index (BMI), examination of blood lipid profile (cholesterol, triglycerides, low density lipoproteins and high density lipoproteins), serum BNP levels, echocardiography.

Results: Comparative analysis of antropometric parameters of healthy volunteers and patients indicated that, aorta, LV mass index, right ventricle, systolic and diastolic myocardial stress, carotid intima-media thickness of common carotid artery in

hypertensive patients with medium cardiovascular risk were higher in comparison to the same values in control group ($p < 0.01$). BMI, lipids (cholesterol, HDLP) did not significantly differ in both groups.

Hypertensive patients with medium cardiovascular risk showed significant decrease in BNP level by 52% in comparison to the control group. Smoking and hereditary tainted did not influence content of BNP in examined patients. Following multifactorial correlation analysis negative correlation of BNP with low density lipoproteins ($r = -0.248$), systolic blood pressure ($r = -0.418$), diastolic blood pressure ($r = -0.371$), systolic ($r = -0.377$) and diastolic myocardial stress ($r = -0.326$) was revealed, as well as positive correlation between left atrium ($r = 0.278$).

Conclusion: Revealed fluctuations of BNP in hypertensive patients with medium cardiovascular risk are connected with there correspondent blood pressure, myocardial stress and allow us to consider natriuretic peptides as markers of unloading of the myocardium. Damage of left atrium as target organ in hypertension is a consistent manifestation of cardiovascular continuum and left atrium size measurement met be considered as early sign of heart involvement in hypertension.

P1606

A score of risk of events in elderly patients with acute myocardial infarction without ST elevation

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Purpose: given the aging of the population and taking into account that age is a risk factor for cardiovascular disease, particularly for coronary heart disease, it is important to evaluate risk for early invasive treatment.

Aims: to establish an affordable score for event risk stratification at 12 months of follow-up and validate their score.

Methods: analysis of 241 patients aged over 75 years with AMI without ST elevation (NSTEMI) admitted to a UCIC 2007-2010.

Identified the predictors of events (death and / or readmissions for ACS / IC) at 12 months by logistic regression. -are assigned 1 or 2 points (p.) According to the obtained OR ($p < 0.05$) and cut-off points established by ROC curve: Killip class > 2 (2p); BNP > 318 ng / ml (2p); a history of ACS / previous coronary heart disease (1p.); no prescription ACEI / ARA at discharge date (1 p.). The predictive accuracy of the score events was evaluated by ROC curves. Two groups were constituted (G): A < 2.5p. and B > 2.5 p. and compared the clinical, echocardiographic, analytical parameters and event rate. The potential prognostic score at 12 months was translated by Kaplan-Meier survival analysis. The score was subsequently validated in 160 elderly patients admitted in 2012. statistical significance at $p < 0.05$.

Results: The mean age was 82 ± 4.5 years (min 75 and max 95 years). The men represent 57 % of the population ($n = 137$). In-hospital mortality rate was 10% and the event rate at 12 months was 22%.

The risk score > 2.5 p. has a predictive accuracy of events defined by a sensitivity of 76 % and a specificity of 80% (AUC = 0.782, $p < 0.001$).

For admission the GB is most often present with dyspnea ($p < 0.001$) and less with chest pain ($p = 0.02$). As for the ECG analysis, group B has a higher prevalence of intraventricular conduction disturbances ($p = 0.04$). As for the TTE analysis, the group with score > 2.5 presents lower values of E/Em (48 vs 55% ; $p < 0.001$). The GB presents more often mitral regurgitation ($p < 0.01$) and complication rate ($p < 0.01$), especially worsening renal function ($p = 0.02$). This group has a higher prevalence of 3 vessels coronary disease. GB has a higher event rate at 12 months (OR = 5.4; $p < 0.001$). After validating the score found that group B shows higher event rates at 12 M (OR = 2.25; $p = 0.03$)

Conclusions: This score proved to be a simple method to stratify the severity of NSTEMI in the elderly, enhancing the link between clinical and analytical factors to which they have recognized individually, an important prognostic value.

P1607

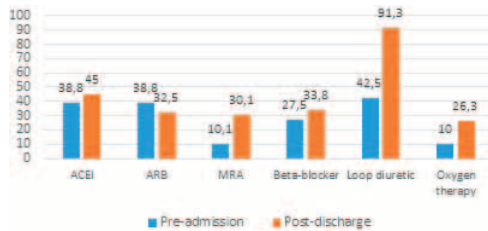
Plasma NT proBNP at first hospitalization predicts readmission for heart failure in elderly patients with heart failure and preserved ejection fraction. A prospective study in a secondary hospital

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The aim of this study was to evaluate the prognostic factors related to readmission for heart failure and preserved ejection fraction (HF PEF) in a selected sample of elderly patients without a prior history of HF. METHODS Data from 221 consecutive patients admitted to a secondary hospital were prospectively collected. Patients with end-stage renal disease, high output HF, valvular prosthesis, severe

mitral or aortic native valve disease and those with a decreased left ventricular ejection fraction (<50%) were excluded. Finally, 82 patients constituted our study group. All patients were followed during one year after hospital discharge. RESULTS Mean age was 79.7 years (SD 8.4) and 58.8% were female. 95% of them accomplished the Paulus diagnostic criteria. Hypertension (83.8%), atrial fibrillation (70%), and anaemia (47.5%) were the most prevalent comorbidities. Fig. 1 shows pre-admission and post-discharge distribution of the main pharmacological groups classically used in HF patients. Loop diuretics was the most common treatment prescribed at discharge. Remarkably, oxygen therapy was recommended in 26.3%. During the follow-up period, 29 patients were readmitted to the hospital. The leading cause of rehospitalization was decompensated HF (25%). Cox regression model identified plasma level of NTproBNP higher than 1822.6 ng/l (HR 3.67; 1.22-11.05 CI 95%, $p=0.021$) as the single most important independent predictor of readmission for HF. In the univariate analysis, treatment with loop diuretics at hospital discharge was associated to a reduction of readmission for HF at follow-up (HR 0.30, 0.10-0.92 CI 95%, $p=0.035$). CONCLUSIONS Plasma NT proBNP was the main predictor of readmission for HF. Loop diuretics at hospital discharge may result in a long term reduction of rehospitalization for HF.



Pre-admission & post-discharge treatment

P1608

Pronouncedly elevated pericardial fluid levels of n-terminal probrain natriuretic peptide are involved in left ventricular dysfunction with ischemic heart disease

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Background: Increasing evidence suggests that N-terminal probrain natriuretic peptide (NT-proBNP) may be a more discriminable marker for the detection and evaluation of heart failure than BNP. However, fundamental mechanisms that contribute to the heart failure in ischemic heart disease (IHD) via NT-proBNP remain unclear.

Objectives: The purpose of this study was to investigate whether NT-proBNP represents autocrine/paracrine factors and are accumulated in pericardial fluid (PF) in patients with IHD.

Methods: With an electrochemiluminescent immunoassay, we measured the concentrations of NT-proBNP in serum and pericardial fluid simultaneously in 101 patients undergoing coronary artery bypass grafting. We investigated the correlation of NT-proBNP levels in serum or PF with hemodynamic variables.

Results: The PF levels of NT-proBNP were markedly elevated compared with serum levels (7224 ± 16345 pg/ml vs. 764 ± 1199 pg/ml, $p=0.0001$). NT-proBNP levels in PF but not in serum had closer relations with left ventricular (LV) end-diastolic ($r=0.493$, $p<0.0001$) and systolic volume indexes ($r=0.582$, $p<0.0001$). NT-proBNP levels in PF but not in serum inversely correlated with LV ejection fraction (EF) ($r=-0.406$, $p<0.0001$). Given a cutoff value of 1465pg/ml for the NT-proBNP in PF, it can discriminate between patients with and without LVEF<55% in IHD, and showed 86.5% sensitivity and 83.7% specificity for the diagnosis.

Conclusion: Increased PF concentrations of NT-proBNP reflects the direct actions as a local mediator against cardiac remodelling in IHD patients with left ventricular systolic dysfunction.

P1609

Is there a correlation between B-type natriuretic peptide and 6-minute walking test in heart failure patients?

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B-type natriuretic peptide (BNP) and the 6-minute walking test (6MWT) are both related to the severity and prognosis in chronic heart failure (HF) patients.

Aim: to assess the correlation between NTproBNP and 6MWT in patients with HF in NYHA III-IV class.

Materials and Methods: Plasma NT-proBNP, 6MWT, demographics, creatinine level and glomerular filtration rate were measured at discharge in 38 patients, within the program for outpatient HF clinic. Pearson's and Spearman's bivariate coefficients

and multiple linear regression analysis with 6MWT as dependent variable were used. **Results:** The majority of the patients were males - 24 (63%) and mean age was 71 ± 10.8 years. The mean ejection fraction was $42.47 \pm 14.31\%$. Atrial fibrillation was present in 37% and 52% were in sinus rhythm. The median NTproBNP was 2415.5 pmol/l. The average 6MWT was 194.82 ± 123.58 m. There was a mild insignificant correlation between NTproBNP and 6MWT - Spearman's $\rho=-0.245$, $p=0.138$. Age was found as the only predictor of decrease in functional capacity, $\beta=-3.99$ (95%CI-7.95;-0.39) $p=0.031$, while NTproBNP values failed to do so ($\beta=-33.52$, $p=0.108$).

Conclusions: There is no significant correlation between BNP and 6MWT. Both tests are in different aspects important for the diagnosis of HF. The BNP levels are related to the hemodynamics, while 6MWT reflects age and functional capacity.

P1610

Cardiac biomarkers as evidence of heart failure progress

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Aim: To evaluate the diagnostic potential of apelin-12, galektin-3, high-sensitivity cardiac troponin-T (hs-cTnT) as predictors of heart failure (HF) severity.

Methods: We studied 108 patients (77 men and 32 women, mean age 56.5 ± 13.9) with HF due to dilated cardiomyopathy (DCM, $n=47$) or ischemic cardiomyopathy (ICM, $n=61$). According to NYHA classification, there were following functional classes: I ($n=21$), II ($n=32$), III ($n=34$), and IV ($n=21$). The average left ventricular ejection fraction (LV EF) was $32.2 \pm 8.6\%$. Blood samples in these patients were collected at the first day of hospitalization before medical therapy initiation. Commercially available ELISA Kits for detection of the plasma levels of Apelin-12, Galektin-3, hs-cTnT and NT-proBNP, have been used.

Results: Mean plasma levels of apelin-12, galektin-3 and hs-cTnT were 0.77 ± 0.35 ng/ml; $10.7 [3; 30]$ pg/ml; 10.4 ± 4.76 ng/ml, respectively. Patients with I-IV functional classes of HF had the follow mean biomarkers concentrations: Apelin-12 - 0.8 ± 0.35 ; 0.81 ± 0.29 ; 0.68 ± 0.38 ; 0.82 ± 0.35 ng/ml; hs-cTnT - $5.1 [3; 5.3]$; $3 [3; 12]$; $16.7 [7.6; 39]$; $33 [16; 39]$ pg/ml; Galektin-3 - 12.5 ± 4.08 ; 9.9 ± 3.7 ; 10.67 ± 5.1 ; 9.2 ± 4.0 ng/ml respectively. The only levels of hs-cTnT in patients with I-II and III-IV functional classes were significantly different between the groups ($p<0.01$). Levels of other biomarkers were comparable in patients with different degree of HF severity ($p>0.05$). As it was expected, mean concentrations of NT-proBNP progressively increased with an increase in NYHA functional class: 1002 ± 688 ; 1367 ± 992 ; 3365 ± 2176 ; 6572 ± 4334 pg/ml, respectively, $p<0.001$. There was no correlation between levels of Apelin-12, hs-cTnT, Galektin-3 and LV EF ($r=0.16$, $p=0.13$; $r=-0.003$, $p=0.98$; $r=0.12$, $p=0.24$) respectively.

Conclusion: There was no correlation between such biomarkers as Apelin-12 and Galektin-3 and HF. Although hs-cTnT and NT-proBNP should be considered as predictors of HF severity independently from the underlying cause of the disease.

P1611

Low plasma albumin at admission is associated with worse outcomes in cardiogenic shock

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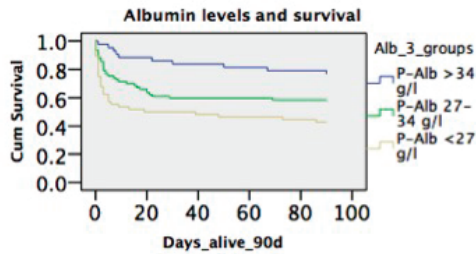
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Purpose: To assess the prevalence of low plasma albumin levels and the associated clinical profile and outcome(s) in cardiogenic shock patients. Low albumin is known to be associated with excess mortality in critically ill patients. However, prevalence and outcome data from a broad contemporary cohort of cardiogenic shock patients has not been available.

Methods: Albumin levels were determined at enrollment in 178 patients with cardiogenic shock in the prospective multicenter CardShock study. All samples were analysed at ISLAB, Kuopio. Albumin levels, clinical data and outcomes were analysed using SPSS statistics software.

Results: The in-hospital mortality in the cohort was 37,6%. Low plasma albumin (P-Alb <34 g/l) at admission was observed in 134/178 patients (75%) and was more frequent in patients with lower body weight, history of ischemic heart disease or left ventricular ejection fraction <40%. Patients with low P-Alb more often presented with pulmonary oedema on chest X-ray. Low P-Alb was associated with higher in-hospital mortality (42,5% vs. 22,7%, $p=0,02$). 90-day mortality also increased further with lower albumin levels; 23,3% for P-Alb >34 g/L, 41,6% for P-Alb 27-34 g/L and 57,1 % for P-Alb <27 g/l (pairwise comparisons between all groups log rank $p<0.05$) (Figure 1).

Conclusions: A low albumin (<34g/l) at presentation is associated with higher mortality in a setting of cardiogenic shock. The prevalence of low plasma albumin in the cohort was marked, with 90-day mortality increasing with lower albumin levels.



Albumin levels and 90-d survival

P1612

Elevated ALT values predict mortality in cardiogenic shock: the CARDSHOCK study

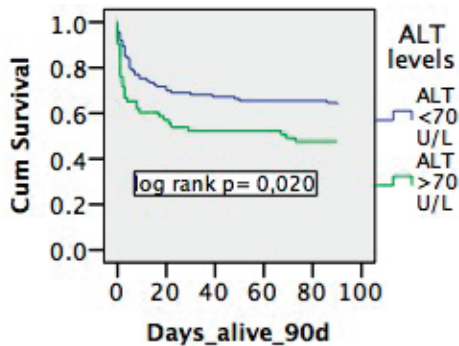
T Jantti¹; J Lassus¹; J Parissis²; J Tolonen¹; A Sionis³; J Spinar⁴; M Banaszewski⁵; K Pulkki⁶; A Mebazaa⁷; V-P Harjola¹
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Purpose: To assess the prevalence of abnormal liver function tests and the associated clinical profile and outcome(s) in cardiogenic shock patients. Alterations in liver function tests are a recognized feature of acute heart failure, but prevalence and outcome data from a broad contemporary cohort of cardiogenic shock patients has not been available.

Methods: Alanine aminotransferase (ALT) levels were determined at enrollment in 178 patients with cardiogenic shock in the prospective multicenter CardShock study. All samples were analysed at ISLAB, Kuopio. ALT levels, clinical data and outcomes were analysed using SPSS statistics software.

Results: In this cohort of cardiogenic shock, the prevalence of elevated ALT (>70 Units/L) at enrollment was 64/178 patients (35.9%). The overall in-hospital mortality was 37.6%. Elevated ALT was associated with higher in-hospital mortality (50.0% vs. 30.7%, $p=0.01$). The effect was also seen with 90-day mortality (90-day mortality 52.4% vs. 46.3%, log rank $p=0.020$ for the differences in Kaplan-Meier survival curves, Figure 1). An elevated ALT was also more frequently associated with signs of hypoperfusion (lactate >2 mmol/l, oliguria) at presentation (p -values of 0.001 and 0.03, respectively).

Conclusions: Elevated ALT-values at presentation are associated with signs of hypoperfusion and higher mortality in a setting of cardiogenic shock.



ALT and 90-day mortality

P1613

Prognostic value of galectin-3 in adult patients with congenital heart disease

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Aim: Galectin-3 is a β -galactoside-binding lectin and is best known for its role as a mediator of tumor growth and metastasis. In addition galectin-3 plays a role in inflammatory and immune-mediated disorders as well as in fibrogenesis, mechanisms involved in the progression of heart failure and cardiac remodelling. It has an important and significant prognostic value in identifying patients with heart failure at

elevated risk for subsequent morbidity and mortality. However, no efficient data exist regarding the relationship of plasma galectin-3 levels and cardiorenal abnormalities in congenital heart disease.

Aim of this study was to examine the prognostic value of plasma galectin-3 in adult patients with congenital heart disease.

Methods: Patients were divided according to their diagnosis in patients with simple ($n=15$), complex ($n=24$) and cyanotic congenital heart disease ($n=3$). Plasma levels of galectin-3 were measured in 42 consecutive adult patients (28 men, mean age 30.37 ± 20 yrs) with congenital heart disease by immunoassay.

Patients were monitored for long-term major cardiovascular events: death, hospitalization, NYHA class worsening, new onset of arrhythmias, surgical or percutaneous intervention.

Results: Median values, with 25th and 75th quartiles positions, of galectin were 72.5ng/ml (55.75 - 112.50 ng/ml) for patients with simple congenital heart disease, 104 ng/ml (72.50 -126.50 ng/ml) for patients with complex congenital heart disease and 116.50 ng/ml (37 - 131.50 ng/ml) for patients with cyanotic congenital heart disease.

Patients were followed for 1144 \pm 353 days. During the follow up period, 3 patients died due to cardiovascular causes, 5 underwent intervention, 2 were hospitalized for cardiovascular reasons, 2 deteriorated clinically and 1 presented with ventricular or supra-ventricular arrhythmias. Plasma galectin-3 levels could predict all events ($HR=1.012$, $p=0.006$) as well as cardiovascular death alone ($HR=1.023$, $p=0.026$)

Conclusion: Plasma galectin-3 seems to be predictor of cardiovascular mortality and major cardiovascular events in adult patients with congenital heart disease.

P1614

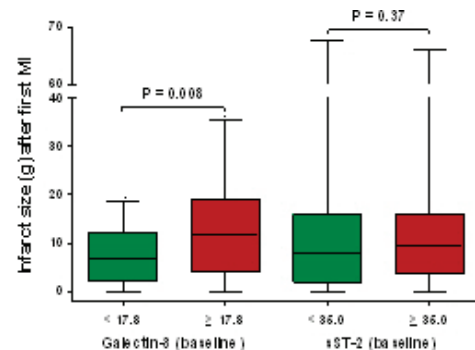
Fibrotic biomarkers and prediction of cardiac remodeling after myocardial infarction

The GIPS-III trial was funded by grant 95103007 from ZonMw, the Netherlands Organization for Health Research and Development (the Hague, the Netherlands) Rogier Van Der Velde¹; CPH Lexis¹; WC Meijers¹; IC Van Der Horst¹; E Lipsic¹; MM Dokter¹; DJ Van Veldhuisen¹; P Van Der Harst¹; RA De Boer¹
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Background: Fibrosis is a pivotal event in infarct repair and progressive remodeling after myocardial infarction (MI). New fibrotic biomarkers may be used to monitor fibrosis, and therefore we evaluated the predictive value of fibrotic biomarkers for cardiac remodeling after acute MI.

Methods and Results: Plasma galectin-3 and sST2 were measured in 380 patients admitted with primary percutaneous coronary intervention (PCI) for acute myocardial infarction (MI), at baseline and at 4 months. Cardiac MRI (CMR) was performed after 4 months to measure left ventricular ejection fraction (LVEF) and infarct size. In total, 262 patients had blood samples and CMR data available (mean age 57.8 ± 11.6 years; 78.2% male). Median (IQR) galectin-3 levels did not differ between baseline and follow-up (13.4 ng/mL vs. 13.9 ng/mL; $P=0.26$), whereas sST2 levels differed (30.5 ng/mL vs 29.5 mL; $P<0.001$). Increased baseline galectin-3 (>17.8 ng/mL) identified patients with lower LVEF: 49.8% (± 9.3) vs. non-elevated galectin-3: 54.8% (± 8.2); $P<0.001$, and larger infarct size: 13.8% (± 12.4) vs. 8.7% (± 8.8); $P=0.002$ after 4 months. Elevated sST2 (>35.0 ng/mL) did not predict decreased LVEF or larger infarct size. Furthermore we showed that at baseline, galectin-3 was an independent predictor for LVEF ($\beta = -0.17$; $P=0.006$) and infarct size ($\beta = 0.16$; $P=0.01$). However, at 4 months after MI, galectin-3 lost its value. Increasing galectin-3 levels over time were associated with better LVEF ($\beta = 0.19$; $P=0.003$) after MI, whereas change in sST2 was not associated with LVEF ($\beta = 0.04$; $P=0.57$).

Conclusion: The fibrosis biomarker galectin-3, but not sST2, taken immediately after MI, predicts LVEF and infarct size after 4 months. We hypothesize that galectin-3 may play a role in the pathophysiology of cardiac remodeling after acute MI.



P1615

Predictors of prognosis in patients surviving out-of-hospital cardiac arrestK Ablasser¹; A Lecher¹; F Fruhwald¹¹Medical University of Graz, Department of Cardiology, Graz, Austria

Introduction: Out-of-hospital cardiac arrest is associated with very high mortality even after successful resuscitation with return of spontaneous circulation. Outcome predictions are often difficult. Goal of this study was to look at biomarkers to predict mortality within 60 days after cardiac arrest.

Methods: A retrospective analysis of all consecutive post-cardiac arrest (CA) patients admitted to your cardiac care unit (CCU) in the time March 2013 till July 2014 who had return of spontaneous circulation (ROSC) was performed.

Results: Overall 50 consecutive patients with out-of-hospital cardiac arrest were admitted to the CCU with ROSC in the studied time period. Overall 60-day mortality was 60% with a mortality on the CCU of 52%. Baseline characteristics show 20% woman, average age of 62.6 and 54% ventricular fibrillation (VF) to 46% non-shockable primary rhythm.

Initial documented non-shockable rhythms have a sig. worse prognosis compared to patients in VF (76% vs. 48% mortality, $p=0.044$). Initial systolic or diastolic blood pressure does not predict mortality, in contrast to heart rate (HR). HR below the median of 70/min was associated with a highly significant better outcome in the subgroup of patients with VF (33.3% vs 64.3% mortality, $p=0.04$). Lactate as well as pH correlate highly significant with mortality at day 60. Patients with a pH over the median (7.2565) have a 60-day survival of 65% vs. 22% ($p=0.006$). Similar significant results are observed for patients above and below the lactate median (3.2) (62% vs. 25% survival; $p=0.002$). Initial (68.2 $\mu\text{g/l}$ vs. 41.3 $\mu\text{g/l}$, $p=0.05$) as well as maximum (123.8 $\mu\text{g/l}$ vs. 49 $\mu\text{g/l}$, $p=0.001$) Neuron-specific enolase (NSE) concentration was significantly increased in patients with poor outcome. However s100 did not correlated with mortality.

Conclusions: Mortality of patients who retained ROSC arriving on the CCU after out-of-hospital cardiac arrest is very high. High initial serum lactate levels, low pH and low HR were predictive of worse outcome. As indicators of neurological damage only initial and maximum NSE levels, but not S100, were markers of poor outcome.

P1616

The role of modern markers in prognosis heart failure at 1 year with different etiology in patient-residents of the north-west region of russiaLV Prokopova¹; MY Sitnikova¹; VV Dorofeykov¹; BI Smirnov²; EV Shlyakhto¹¹Federal North-West Medical Research Centre, Saint Petersburg, RussianFederation; ²Saint Petersburg Electrotechnical University "LETI", Saint Petersburg, Russian Federation

HF- public health problem worldwide. Etiological factors of HF varied. Thus, one may mix the patient for several reasons. The **Aim:** Assess current prognostic indicators in terms of their significance, depending on the etiology of heart failure among residents of the North-West region of Russia. **Materials and methods.** A prospective study of 212 patients: 176 men and 36 women with chronic heart failure II - IV functional class (FC) c left ventricular EF less than 35%. Predictive value 200 parameters, including the concentration of NT-proBNP, ST2), myeloperoxidase (MPO) (Roche, USA), a high-sensitivity troponin (Roche, USA) in the blood plasma. All-cause mortality was assessed at 1 year. **The Results.** LVEF averaged 24,8 \pm 7,4%; ME-24%. Etiological factors in 102 patients - CHD (48%) in 47 patients (22%) - dilated cardiomyopathy (DCM), 53 (25%) - myocarditis, 10 patients (5%) - a combination of hypertension and damage to the alcohol infarction. Within 1 year, 64% of patients survived (135 people). Patients with coronary artery disease differed from other groups: older age (55,1 \pm 0,7 and 42,5 \pm 1,3 years, $p=0,000$), late age debut CHF (51,9 \pm 0,7 and 39,4 \pm 1,2 years; $p=0,000$); low levels of NT-proBNP (3757,5 \pm 381,1 and 4920,8 \pm 602,2 pg / ml; $p=0,017$); high erythrocyte sedimentation rate (16,8 \pm 1,2 and 12,7 \pm 1,3 mm / h; $p=0,003$); smaller end-diastolic volume of LV (126,7 \pm 3,6 and 274,5 \pm 9,7 ml / m²; $p=0,08$) and end-systolic volume of the left ventricle (182,9 \pm 6,3 and 208.8 4 ml; $p=0,01$). Patients with dilated cardiomyopathy characterized by early-onset heart failure (43,5 \pm 1,6let; $p=0,013$); large end-systolic volume of the left ventricle (209,9 \pm 9,1ml); high levels of NT-proBNP (6096,37 \pm 1043,7 pg / ml; $p=0,026$), urea (11,2 \pm 0,8 and 9,3 \pm 0,4 mmol / l; $p=0,005$) and total bilirubin (26,7 \pm 2,0 and 19,4 \pm 0,9 mmol / l; $p=0,001$). In the group of patients with myocarditis - a higher index of end-diastolic volume of LV (142,4 \pm 6,8 ml / m²; $p=0,048$); ESR minimal content (12,0 \pm 1,5 mm / h; $p=0,03$). Confirmed the prognostic significance of the studied parameters ST2 ($p=0,018$), MPO ($p=0,008$), NT-proBNP ($p=0,000$), high-sensitivity troponin ($p=0,000$) without regard to the etiologic factor.

Conclusions: NT-proBNP, MPO, ST2, high-sensitivity troponin are highly significant in determining the short-term prognosis in patients with HF and etiology as ischemic heart disease, myocarditis, dilated cardiomyopathy, a combination of alcohol myocardial damage and hypertension among residents of the North-West region of Russia.

P1617

Heart failure with preserved ejection fraction: conventional and emerging prognostic biomarkers in daily clinical practiceP Paula Martinez Santos¹; E Batlle Lopez²; I Vilacosta³; B Sanchez Sauce²;J Jimenez Valtierra²; E Espana Barrio²; A De La Rosa Riestra²; F PerezGonzalez²; J Alonso Bello²; MD Martin Rios⁴¹Hospital de Fuenlabrada, Cardiology, Madrid, Spain; ²University Hospital AlcorconFoundation, Cardiology, Madrid, Spain; ³Hospital Clinic San Carlos, Cardiology,Madrid, Spain; ⁴Foundation Jimenez Diaz, Madrid, Spain

Purpose: Albumin serum levels and N-terminal brain natriuretic peptide (NT proBNP) have shown to be useful in predicting outcome in patients with heart failure and systolic dysfunction. Carbohydrate antigen 125 (CA 125) has also been associated to a higher risk of mortality and rehospitalization in patients with HF and reduced left ventricular systolic function. The role of these biomarkers for stratifying prognosis in patients with HF and preserved ejection fraction (PEF) is not so well established. The aim of this study was to evaluate the prognostic role of these biomarkers among acute decompensated HF PEF patients. **METHODS** Data were collected prospectively from 221 consecutive patients with HF admitted to a secondary hospital from 2011 to 2012. Patients with advanced chronic renal disease, high output HF, history of a congenital heart disease, patients with mitral or aortic prosthesis, severe mitral or aortic native valve disease, and patients with a LVEF < 50% were excluded. All patients were followed during one year after discharge. **RESULTS** Finally, 154 patients with HF PEF were enrolled. The average age was 81 years (SD 9). 63 % were female. During follow-up, 37 patients died (mortality rate: 24%). The cause of death could be ascertained in 25 of these 37 subjects. Median plasma concentration of NT proBNP at baseline was 1965 ng/l, (IQR 4016). In a multivariable analysis, NT proBNP, higher than the median (OR 5,36; 1. 84-15.65, CI 95%, $p=0,002$) was associated with an increased risk of mortality. Average serum albumin value was 3,7 (SD 0,4) g/dl. Hypoalbuminaemia was defined as a plasmatic concentration <3.5 g/dl. No association was found between albuminaemia and advances stages of liver disease or malnutrition. Hypoalbuminaemia was associated to a higher risk of death (RR 2.57, 1.46-4.52 CI 95%, $p=0,001$). The median plasma concentration of CA 125 at baseline was 28.9 U/ml (IQR: 65.2). No gender differences were found. There was no significant association between a previous history of autoimmune disease or malignancy and CA 125 concentrations. Increased CA 125 levels were related to congestive radiologic signs, such as pleural effusion. ($p=0.001$). CA 125 > 31 U/ml was related to a significant increase risk of death (RR 4.72, 95% CI 1.09-20.37; $p=0.017$) in male patients, but not among women. CA 125 >31.4 U/ml was also identified as an independent predictor of mortality among octogenarians (OR 4.32, 95%CI 1.10-16.94; $p=0,036$). **CONCLUSION** NT proBNP, albuminaemia, and CA 125 could be used as filtering tools to select those cases with the highest clinical risk among hospitalized HF PEF patients.

P1618

Hs-CRP in ambulatory type 2 diabetic patients with heart failure lacks prognostic valueM De Antonio¹; J Lupon¹; N Alonso¹; J Santesmases¹; E Zamora¹; MDomingo¹; M Boldo¹; A Galan¹; B Gonzalez¹; A Bayes-Genis¹¹Germans Trias i Pujol University Hospital, Badalona, Spain

Background: Type 2 diabetes mellitus (T2D) is a pathological situation that is usually associated with low grade systemic inflammation and elevated circulating high-sensitivity C reactive protein (hs-CRP). Heart failure (HF) is also a low-level inflammatory condition, and high hs-CRP levels were associated with prognosis in HF patients.

Objective: To assess inflammation in T2D HF patients relative to non-T2D HF patients estimated by hs-CRP levels, and to ascertain the relationship with outcomes of hs-CRP according to the presence or absence of T2D.

Patients and Method: hs-CRP was available in 852 consecutive outpatients (71.5% men; mean age 68 \pm 12.4 years). Diabetes mellitus was present in 308 (36.2%) patients. Aetiology of HF was ischemic heart disease in 52% and non-ischemic in 48% of patients. Mean LVEF was 35.9 \pm 13.6%. Most patients were in NYHA class II (66%) or III (25.7%).

Results: hs-CRP did not statistically differ between T2D (median 4.3 mg/L (Q1-Q3 1.5-9.1) and non-T2D patients (median 3.3 mg/L (Q1-Q3 1.1-8.9), $p=0.14$). After a mean follow-up of 4.7 \pm 2.5 years 424 (49.5%) patients died and 192 were admitted due to HF. All-cause mortality and the composite end-point (all cause mortality + HF hospitalisation; n=466) were more frequent in T2D HF patients ($p<0.001$). After adjusting by age, sex, NYHA functional class, ischaemic aetiology, eGFR, body mass index, NTproBNP, and treatment with beta-blockers and ACEI or ARB, hs-CRP remained independently and statistically associated with all-cause mortality (hazard ratio (HR) 1.23 [95%CI 1.06-1.43], $p=0.006$) and the composite end-point (HR 1.25 [95%CI 1.09-1.45], $p=0.002$) in non-T2D patients, but not in T2D patients (HR 1.03 [95%CI 0.88-1.20], $p=0.71$; and HR 1.08 [95%CI 0.94-1.25], $p=0.28$, respectively).

Conclusion: hs-CRP serum levels did not differ in T2D vs. non-T2D patients with HF, probably because HF patients are already inflamed. hs-CRP was independently

associated with mortality and with the composite end-point of death + HF hospitalization in non-T2D HF diabetic patients, but not in T2D HF.

P1619

The role of GDF-15, a marker of fibrosis, in cardiogenic shock

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Purpose: To investigate circulating levels of Growth-differentiation factor 15 (GDF-15) in cardiogenic shock (CS) and their associations with etiology, markers of myocardial injury and all-cause mortality.

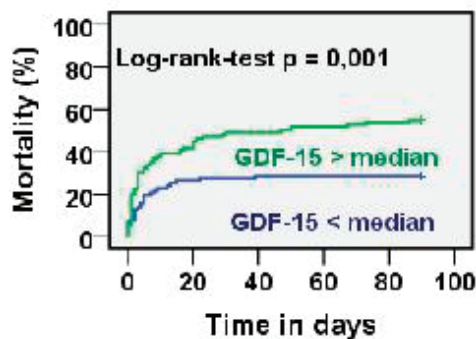
Methods: GDF-15, TnT and NT-proBNP was determined at baseline in 178 patients with CS of various etiologies in the prospective European multi-center CardShock study. Differences in GDF-15 levels between groups of CS etiology [acute coronary syndrome (ACS) (n=143) and non-ACS (n=35)] were assessed and the influence of GDF-15 on 90-day mortality.

Results: Mean age was 67 years, 26% were women and 42% of the patients died. Median levels of GDF-15 in the study population was 9577 pg/ml (interquartile range (IQR) 4502 - 19115), with no significant difference between ACS and non-ACS groups (9647 pg/ml [IQR 4497 - 18232] vs. 9171 pg/ml [IQR 4617 - 29825]; p=1.0). The correlation of GDF-15 with hsTnT (rs 0.137, p=0.07) or NT-proBNP (rs 0.37, p<0.001) was moderate at most.

Mortality at 90 days was higher in patients with GDF-15 levels above median (all 55% vs. 29%, p<0.001; ACS group 59% vs. 31%, p=0.001; non-ACS group 41% vs. 17%, p=0.11).

In univariate analysis GDF-15 above median was significantly associated with 90-day mortality (OR 3.0; 95%CI 1.6-5.7; p<0.001). On a multivariable analysis GDF-15 above median still seemed to be associated with a doubling of 90-day mortality risk (OR 2.4; 95%CI 0.9-6.3; p=0.07).

Conclusions: GDF-15 levels are markedly elevated on admission in CS of both ACS and non-ACS etiology. There is no relevant correlation between levels of GDF-15 and TnT, a measure of myocardial injury. GDF-15 levels above median are associated with increased mortality in CS, but the clinical utility of GDF-15 in this population with very high overall mortality remains to be determined.



NURSING

P1620

Anticoagulation therapeutic range fulfilment in patients with heart failure

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Background: Oral anticoagulation treatment (OAT) with vitamin K antagonists, such as warfarin or acenocumarol, are standard treatments for stroke prophylaxis in patients with atrial fibrillation and in patients carrying cardiac prosthesis. Such patients are quite common in heart failure (HF) Units, where nurses display an important clinical role. Patient outcomes depend on quality of warfarin management, which includes regular monitoring and dose adjustments. Currently,

these controls and dose adjustments are performed in Primary Care by General Practitioners.

Objective: To assess the time on therapeutic range (TTR) in consecutive patients attended in a multidisciplinary HF Unit.

Methods: Direct TTR and percentage of days on TR (Rosendaal method) were calculated using a specific web-site, based in the 4-6 last international normalized ratio (INR) determinations (mean 5.2 ± 0.6) and according to the target INR by medical indication.

Results: From October 3 to December 31, 2014, 94 patients have been evaluated (mean age 73.1 ± 9.4 years, 75.5% men). Twelve patients were cardiac prosthesis carriers. Prescribed INR was 2-3 in 95% of patients. Mean TTR was 64.3% ± 22.4 and mean percentage of days in TR was 61.2% ± 27.2. Only 43.6% of patients had direct TTR ≥ 70%. This figure was 74.5% for TTR ≥ 50%. The proportion of patients with percentage of days on TR ≥ 70% and ≥ 50 was 42.6% and 66% respectively. As adjustments of OAT are performed mainly in Primary Care, a report for General Practitioners was performed when appropriate in order to try to improve TTR.

Conclusions: A non-negligible number of patients on OAT from a real-world HF Unit are far from optimal TTR, although mean TTR was similar to that observed in randomized OAT trials. Nurses at HF Units can perform additional monitoring of INR and then help patients and General Practitioners in being aware of such circumstance and improve TTR with closer controls.

P1621

Effectiveness of independent heart failure nurse and heart failure specialist pharmacist managing acute heart failure in hospital

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Heart Failure Nurses (HFN) reduce heart failure (HF) readmissions, length of stay (LOS) and mortality. Pharmacists have additional roles due to specialist knowledge. In our hospital HFN previously had part-time advisory and education role. By improving specialist assessment we aimed to improve prescribing and reduce readmission rates.

Methods: Full-time HFN re-trained as independent prescriber and new prescribing Heart Failure Specialist Pharmacist (HFSP) role was developed (8 hours per week). HFSP re-trained to independently examine and prescribe HF medication. Electronic nursing care plans were developed providing prompts to monitor diuretics, renal function and provide HF education. Patient LOS and re-admission rates were compared during two 9 month periods a year apart. This was collated from hospital information system and analysed by third party to exclude bias.

Results: There was 77% reduction in patients being discharged without ACE inhibitor or ARB and 57% reduction without beta-blocker. There was 29% decrease in readmission rates. LOS was slightly higher in line with national data. HFSP accounted for 69% of prescribing by HF team and reduced potential interactions. The team also provided specialist cardiology advice hospital-wide to doctors and nurses and identified acute coronary syndromes, arrhythmias and valve disease liaising with Cardiologists to ensure appropriate urgent review.

Conclusions: Expansion of a HFN role to include independent prescribing and addition of a clinical part-time HFSP led to a marked improvement in prescribing and readmission rates.

P1622

Effectiveness of cardiac telemonitoring in a patient with advanced heart failure and psycho-social issues

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PURPOSE

Cardiac telemonitoring (CTLM) strives to become a valid tool to support the care of patients with heart failure (HF). However, the precise components that make CTLM effective together with the type of patient who could potentially benefit from it still remain unknown. This case analyses the effectiveness of a CTLM programme in a context of advanced HF and psychosocial issues

CLINICAL DESCRIPTION

Main problems: Male, 55 years old. NYHA III-IV. Cardiovascular risk factors: ex-smoker, alcohol abuse, malnutrition. Psycho-social factors: inadequate self hygiene, inadequate management of his HF. Married, lives with one daughter. Unemployed. Past history: cardiovascular: HF, dilated cardiomyopathy, EF 15% alcohol induced, MI, AF, PHT, ICD in situ, not suitable for cardiac transplant. Non cardiovascular: hepatopathology. Under cardiology, endocrinology and digestive specialists. Probable underlying issues: psycho-social issues, uncoordinated assistance of care

Management: Cardiologist review: outpatient clinical assessment prior to commencement of CTLM. CTLM programme: for 5 months, daily reviews of transmitting data: BP, HR, SatO2, WEIGHT and an associated 7 item questionnaire related to signs/symptoms, adherence to treatment, exercise. Monthly/ fortnightly: - telephone calls, checking patient's condition, reinforcing education on diet, exercise, treatment - order of blood samples - telephone titration of medications - all done by

Table 60905. Benefits of HFN and HFSP

Outcome from In-Patient Data	Pre service expansion	Post service expansion	Change
Patients referred with LVSD	252	187	25% decrease
Patients with LVSD and no contraindications discharged without ACE Inhibitors/ARBs (%)	5.6	1.3	77% decrease
Patients with LVSD and no contraindications discharged without beta-blockers (%)	10	4.3	57% decrease
Patients receiving heart failure education (%)	66	72	8% increase
Median Length of stay (days)	11	12	8% increase
All cause readmission rates (%)	15.5	11	29% decrease
Initiation of medications by HF team (no.)	0	101	-
Titration of medications by HF team (no.)	0	178	-
Total number of HF medications (% by HFSP vs % by HFN)	0	279	69% vs 31%
Additional Pharmacist interventions (no.) excluding HF medication	0	149	-

cardiologist. In the last call, alcohol intake noticed and patient referred to GP. Two days later seen by endocrinologist as an outpatient, same alcohol issue evidenced and strong recommendations given to give up alcohol for good. Two days later patient was readmitted to hospital

Results: After 3 months of CTLM vs hospital discharge: Barthel 100 vs 85, EHfBS 19 vs 25, Euroqol 90 vs 55. Clinical progress: 5 months admission free: blood results, observations, questionnaires maintained. SBP 85-100mmHg, DBP 50-75mmHg, HR 60-75x¹, Sat 02 94-98%, WEIGHT +- 1.5kg. Patient referred routine of daily transmissions self motivating

Conclusions: Enrolling such profile patient in a CTLM may have provided some help in terms of self motivation and routine follow up. Variables designed to be measured seemed to offer positive clinical progress. On the other hand, this case shows the limitations of CTLM to assess, evaluate, detect and act upon any psycho-social issues. CTLM could have probably been complemented with an integrated care plan within a multidisciplinary approach, following clinical guidelines with set nursing and medical face to face assessments

P1623

Comorbidities of patients attended in a heart failure clinic, including advanced HF patients

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Abstract

Introduction: Heart failure (HF) is often accompanied by a number of comorbidities, defined as coexisting chronic conditions with HF who plays a key role in its development, progression, response to treatment and prognosis. Comorbidities' burden has implications on patient's costs, resources (multidisciplinary team). The prevalence of comorbidities may vary among countries, centers and organization of HF unit.

Aim: To evaluate the prevalence of comorbidities in patients attended in a HF clinic of a tertiary center, including advanced HF patients.

Methods: Single-center retrospective study of HF patients attended from January 2011 to December 2014. Medical records were reviewed and a database of the HF research unit. Epidemiological data, hospitalizations and comorbidities screened were: age, sex, underlying heart disease (ischemic, dilated and others), previous hospitalization for HF, hypertension, diabetes mellitus (DM), dyslipidemia (DL), thyroid dysfunction, smoking, COPD/asthma, malignancy, peripheral artery disease, obesity and cerebrovascular accident (CVA).

Results: 615 patients (average age 61.4 years, women 28%) were included in the study. Main underlying heart disease was: dilated cardiomyopathy 38.9%, followed by ischemic with 37.2%. Previous HF hospitalization was 55%. Comorbidities were: smoking (55.9%), dyslipidemia (47.6%), hypertension (53.5%) and DM (28.8%), neoplasia (12.5%), COPD/asthma (9.1%), CVA (8.1%), thyroid dysfunction (6.1%), obesity (37%) and peripheral arterial disease (5.9%).

Conclusions: HF patients evaluated in this study have a high prevalence of comorbidities. Knowing the prevalence of comorbidities is mandatory for organizing a successful multidisciplinary approach in each center.

P1624

The impact of advanced nurse practitioners in the care of people with heart failure: a systematic review

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The aim of this systematic review (SR) was to assess the impact of advanced nurse practitioners (ANPs) on the care of patients with heart failure, with a primary objective of impact on hospital admissions. Secondary objectives included impact on mortality, length of hospital stay, emergency department visits, quality of life and self care behaviours.

This SR involved an extensive search of the literature. A rigorous search of electronic databases was performed for studies reporting on ANP led care of patients with heart failure. Studies must have reported on the primary outcome of hospitalizations to be included. 13 studies met the inclusion criteria and data was extracted and assessed for quality using a validated tool.

In 13 studies which included 13,383 patients with a mean age of 68.6 years; ANP led care had statistically significant reductions in all-cause and heart failure hospitalizations in 5 and 3 studies respectively. Mortality, length of stay, emergency department visits and costs were also decreased while increases in quality of life and self care were observed. Meta-analysis was not possible due to the heterogeneity of the studies.

This SR demonstrated that ANP led care reduced all cause and heart failure admissions, along with the majority of the secondary outcomes. There was not always statistical significance and many studies were not of a high quality. None of the included studies were from Europe and further research with rigorous methodology is required to validate these findings.

Results

Reduction	All admissions (11)	HF admissions (8)	Reductions	Mortality (5)	Length of stay (7)
p < 0.05	5	3	p < 0.05	1	2
p > 0.05	1	3	0 > 0.05	1	3
No p value	4	2	No p value	3	2
NS increase	1	0			

Reductions	Costs (7)	ED visits (3)	Improvements	QOL (5)	Self care (2)
p < 0.05	2	0	p < 0.05	1	1
p > 0.05	0	2	p > 0.05	3	0
No p value	4	1	No p value	1	1
NS increase	1	0			

P1625

The relationship between self-concept and coping strategies in patients with heart failure

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Background and Research Objective: Cardiovascular diseases are the primary cause of death in Iran, and currently, heart failure (HF) has a prevalence of 3500 in 100,000 people. A patient's psychological adaptation to heart failure can influence its impact on his or her life. Living with chronic heart diseases is comfortable for the patients, who must adapt to this discomfort. Failure of adjusting one's behaviour to the heart failure results in disadaptive coping which implies dissatisfaction, uncertainty, anxiety, passivity, feelings of helplessness and depression, all of which have an unfavorable effect on disease, mortality and quality of life. The purpose of this study is the relationship between self-concept and coping strategies in patients with heart failure.

Subjects and Methods: Using a descriptive correlational design, a convenience sample of 117 HF patients were selected from a major medical and academic centers, affiliated with our University of Medical Sciences in Iran. Two validated and reliable questionnaires including Cognitive Perception of Cardiovascular Healthy Lifestyles and Coping Strategies Scale (CSS) were completed by each patient.

RESULTS: A direct relationship between threat to self-concept and Coping Strategies in form of Emotion-focused and Avoidant centered Strategies was noted ($P < .05$). Threat to body sensation and self constant had a direct relationship to Coping Strategies in form of Emotion-focused and Avoidant centered Strategies ($P < .05$). In other words, patients who faced more threat to self-concept more use of Coping Strategies in form of Emotion-focused and Avoidant centered Strategies. But no relationship was found between challenge to self concept and coping strategies ($P > .05$).

Conclusions: In our study patients who faced more threat to self-concept more use of Coping Strategies in form of Emotion-focused and Avoidant centered Strategies. Emotion-focused coping occurs when an individual perceives a demand or stress to be impossible to change and tries to alter the way he/she thinks or feels about the situation. Examples are avoidance, denial, and venting of feelings, which have an unfavorable effect on disease, mortality and quality of life. Alternatively, problem-focused coping occurs when an individual interprets a situation or stressor as modifiable. Examples include active coping (such as better adherence of medical regimens), problem solving, and information seeking. Through education and counseling, nurses can empower their patients to perceive HF not as a threat and use of problem-focused coping strategies to better treatments results.

P1626

Low vitamin D levels is associated with depressive symptoms in patients with heart failure

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Introduction: Depressive symptoms are common in patients with heart failure (HF). Low vitamin D levels have been associated with depression, but this has not been studied in HF.

Aim: To investigate the depressive symptoms and vitamin D levels in a population of HF patients.

Method: We studied a population of HF patients who had been enrolled in multi-center trial. Depressive symptoms were measured with the Centre for Epidemiological Studies Depression Scale (CES-D) and 25-hydroxy-vitamin D was measured in blood samples.

Results In 506 patients, both depressive symptoms and Vit D levels were recorded. Their mean age was 71 years and 38 % were women. At baseline, 39% of patients had depressive symptoms (CES-D >16). At discharge, a significant association between 25-hydroxy-vitamin D levels and depressive symptoms was found ($p = 0.02$). Patients with a vitamin D level in the lowest vitamin D tertile (<29.6 nmol/l) had significantly more often depressive symptoms (47%), compared to 32% of patients with vitamin D levels in the 2nd tertile (29.6-43.9 nmol/l) ($p = 0.005$). After adjustment for baseline depression, age, gender, NT-proBNP, CRP, diabetes, hypertension, eGFR and COPD, the lowest tertile of 25-hydroxy-vitamin D was associated to an increased probability (Odds ratio 2.5 $p = 0.017$) to report depressive symptoms at 18 month follow-up. However after adding physical performance to the model the odds attenuated and become non significant (Odds ratio 2.1, $p = 0.06$).

Conclusion: In patients with HF, low levels of D-vitamin at discharge were associated with depressive symptoms at discharge and at 18 months follow-up. However, HF patients' physical performance status may modify this association.

P1627

Challenges in discussing prognosis and end-of-life care with heart failure patients

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Purpose: One important part of the clinical work at nurse-led heart failure (HF) clinics is to provide patient education that explains the progression of HF and establishes goals for the end-of-life care. The objective of this study was to expand on the knowledge of the practice of such discussions at nurse-led HF clinics, and compare this between Sweden and the Netherlands.

Methods: A survey with open-ended questions was performed including 279 nurses from 81 Swedish and 91 Dutch HF clinics. The nurses registered 1 809 patient conversations (mean age 71 years (± 12), 62% men, 88% in NYHA class II-III) and were asked to report why or why not they discussed prognosis and end-of-life care with each patient during the visit. Data was analysed using content analysis.

Results: Prognosis was discussed with 687 patients (38%) and end-of-life care with 179 patients (10%). In the content analysis three categories were identified, describing the nurses' reasons for discussing or not discussing prognosis and end-of-life care.

1) Prognosis and end-of-life care discussions are guided by clinical routines throughout an anticipated HF trajectory. This category describes the idea of an anticipated course of HF, indicating that there are specific occasions during the course of HF that are more suitable for these discussions. The nurses discuss mostly when the patient is believed to be approaching the end-of-life or when they are deteriorating.

2) Prognosis and end-of-life care discussions should be tailored to the specific patient's situation. This category describes that the nurses discuss these topics according to each individual patient's situation. Nurses described that other matters are of greater importance than prognosis and end-of-life care, such as improving self-care or titration of medication.

3) Prognosis and end-of-life care discussions are directed by professional responsibilities. This category describes that the nurses did not perceive these discussions as a part of their role as a nurse, indicating that they perceive these discussions to be beyond their responsibility and authority.

Conclusions: HF nurses expressed reasons for discussing or not discussing prognosis and end-of-life care with the patient as depending on external circumstances outside their professional role, several factors related to the patient, or to factors in the course of the disease. HF nurses have a key position within the HF team to assess HF patients' needs and preferences for care. Thus, they could take more responsibility for discussing prognosis and end-of-life care with HF patients.

P1628

Physical activity in daily life in heart failure patients living in two european countries

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Purpose: To assess physical activity levels in HF patients, to describe the different types of physical activity these patients do and explore the differences between patients from the Spain and Sweden

Method: The short International Physical Activity Questionnaire (IPAQ) was used to assess the level of physical activity during the previous week. Data was collected during April-July 2014 in Swedish and Spanish HF patients. Difference were analysed using Pearson's chi-square or Mann-Whitney U test.

Results: In total, 154 Swedish and 548 Spanish HF patients (29% female, mean age 69 ± 12 years, 75% NYHA class II/19% NYHA III) participated. No differences were found in gender, age NYHA class between the two countries. Of these 702 HF patients, 16% had a high physical activity (at least one hour per day of moderate-intensity activity or half an hour of vigorous-intensity activity); 49% had moderate physical activity (at least 30 minutes of moderate intensity physical activity on most days) and 30% of the patients had low physical activity. More patients in Sweden had a high physical activity level compared to patients in Spain (26 vs 15%, $p < 0.001$).

Swedish patients reported to do more vigorous activities (lifting, digging, aerobics, or fast bicycling) (68 ± 192 min/week) compared to Spanish patients (22 ± 128 min/week, p -value = .01). Swedish patients also did more moderate activities (carrying light loads, bicycling at a regular pace, or doubles tennis) 207 ± 362 min/week) compared to Spanish patients (56 ± 239 min/week, p -value < 0,001). Spanish patients did more walking (walking at work and at home, walking to travel from place to place, and any other walking that might be done solely for recreation, sport, exercise, or leisure) (434 ± 442 min/week) compared to Swedish patients (244 ± 346 min/week, p -value < 0,001).

Conclusions: Despite that most of the patients were in NYHA class II and not symptomatic even at moderate to high level of activity, one third of them had a low physical activity level in their daily life. We found differences in the kind of physical activities

Table 1 P1629.

Results	Means (%)		p
	0Month	9Months	
BMI Overweight	25,22 ± 2,7 86 (51,2%)	25,37 ± 2,41 96 (57,3%)	(p = 0,259)
Weight (Kg)	77,61 ± 9,22	78,51 ± 913	(p = 0,034)
% Fat mass % Muscle Mass	27,53 ± 32,53 40,22 ± 24,45	19,60 ± 5,00 39,67 ± 3,40	(p = 0,002) (p = 0,771)
Waist circumference (cm)	91,05 ± 6,09	92,41 ± 5,69	(p < 0,001)
HR (bpm)	68,66 ± 11,43	65,62 ± 10,14	(p = 0,004)
sBP (mmHg) dBP (mmHg)	132,9 ± 13,47 73,69 ± 11,56	107,7 ± 12,40 63,38 ± 9,06	(p < 0,001) (p < 0,001)
IPAQ High Moderate Low MET (Metabolic Equivalent Task)	13 (7,92%) 143 (87,20%) 8 (4,88%) 1041±295	1 (0,61%) 47 (47,56%) 85 (51,83%) 1462±413	(p < 0,001)
Blood Sugar (mg/dL)	88,56 ± 8,22	76,15 ± 8,45	(p < 0,001)

Results before and after the mission

between Spain and Sweden, which could be due to cultural and regional differences. It is for example less common to bike in Spain and therefore people walk, while in Sweden it is quite common that also elderly persons bike. Specific differences and consequences need to be further explored.

POPULATION STUDIES/EPIDEMIOLOGY

P1629

Benefits of exercise in a military force

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Physical activity (PhA) can contribute to prevention of cardiovascular risk factors (CVRf). This study aimed to verify that PhA plan (military gymnastics program application - MGPA) established by the Portuguese Army, objectively relates to health gains, particularly in relation to CVRF, such as hypertension (HTN), dyslipidemia and obesity.

Prospective study of 164 soldiers of the Portuguese Army, 98% men, 28.8 ± 7.4 years old, who joined a NATO Force outside the country, were evaluated for 9 months: blood pressure levels, heart rate, analytical parameters and biometrics. The MGPA consists of 1h PhA protocol aerobic and anaerobic, 5 times/week. Diet and rest period have not changed. The PhA was quantified by the International Physical Activity Questionnaire (IPAQ) score, classifying them as low, moderate or high.

The results are presented in Table 1. After applying the MGPA we found some statistical differences: systolic blood pressure (sBP) [132mmHg ± 13. vs. 107mmHg ± 12 (p < 0.001)] and diastolic blood pressure (dBP) [73mmHg ± 11 vs. 63mmHg ± 9 (p < 0.001)]; % fat mass [27.5% ± 32.7 vs. 19.6% ± 5.0 (p = 0.002)]; waist circumference [91,1cm ± 6.1 vs. 92,4cm ± 5.7 (p < 0.001)]; and values of 6 hours fasting blood glucose [88,6mg / dL ± 8.2 vs. 76,2mg / dL ± 8.5 (p < 0.001)]. To highlight that 22% (n = 4) of hypertensive no longer need anti hypertensive medication. There were no major cardiovascular events.

MGPA, despite its short duration had a positive impact on sBP and dBP, % fat mass, waist circumference and in glycemic profile. The study should be tested and validated in larger cohorts to be able to withdraw more definitive conclusions

P1630

CHF therapy in the russian federation, which is used in patients, can improve the prognosis?

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Objective: To investigated the frequency of use the recommended drugs for the treatment of patients with chronic heart failure, according to the urban settlements.

Methods: 19503 respondents were included in the representative sample from the nine regions in the European part of Russia. CHF patients were divided into groups: patients living in urban areas (over 50,000 population) and rural (less than 25 000 population) community.

Results: CHF patients were significantly higher in urban areas (7.4%) than the agriculture community (6.8%) (p = 0.013). Patients taking any drug significantly more

often in urban areas (95.6%) than in rural areas (91.9%) (p = 0.003). ACE inhibitors have proved the main drug treatment in patients with chronic heart failure (78.2% in urban areas and 77.9% in rural areas). No significant differences were detected (p = 0.83). Beta-blockers are taken in groups of patients with chronic heart failure (45.5% vs. 44.6, p = 0.68) is much smaller these ACE inhibitors. Aldosterone antagonists have not been accepted patients (5.9% vs 3.5%, p = 0.043). Diuretics are often taken in urban areas (38.8%) and in rural areas (42.6%) (p = 0.3), but the loop diuretics are rare in the treatment of patients. Classic symptoms decompensation (edema, cardiac asthma, pulmonary cracking) was found less than 10% of patients with CHF and ankle swelling - in 23.9% of cases. Only 7% of this patients received loop diuretics. Tachycardia was detected in 68.9% of patients who received beta-blockers. Only 13.1% of patients have blood pressure below 140/90 mm Hg. Analysis of drug doses showed that 85.3% of CHF patients using small doses of medicaments. 21.3% of urban patients and 34.6% of rural patients take non-recommended combination of ACE inhibitors and beta-blockers (metoprolol tartrate) (p = 0.001). Only 18.4% of CHF patients take a combination of two recommended drugs.

Conclusion: Patients with heart failure used ACE inhibitors in 78% cases, but often in very small doses. Therapy in patients with CHF in Russia does not control the hemodynamic parameters, which significantly worsens the prognosis of these patients.

P1631

Do we need heart failure clinics in Russia: meaningful findings of russian hospital heart failure registry (RUS-HFR)

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Purpose: The economic and social burden of managing CHF is increasing in all countries, Russia is not exception. National, local registries are helpful in solving this problem. Methods. The RUS-HFR was a prospective, multicentre, observational study conducted in 3 Cardiology Centers in Russia (-1-center with HF service-Federal Medical Research Center, St.Petersburg, -2- cardiology hospital.Orenburg, -3- cardiology clinic,Samara). Inclusion criteria: CHF I-IVfc, LVEF ≤ 40%, age 18-75 yrs. From Oct 2012 to Jan 2014, 524 patients were enrolled in all centers (-1-259/-2-135/-3-130). Age 60.0 ± 9.6 yrs. 80.5% men, IHD 63.3-74.8%, hypertension- 69.5-88.9 %, DCM 4.6-5.2%. LVEF 28.5 ± 7.2%. Patients were comparable in clinical parameters. FU period was 6-18 months after discharge.

Results: On admission patients had CHF fc II-39,8/ 17,8/20,0%, fc III-44,6/56,3/58,5%, fc IV-1,5/23,7/20,0%. NT-proBNP was checked in a 6% of patients in center -1.On admission 11-70% were on beta-blockers,12-58% ACEI/ARB, 6-55% diuretics, 4-53% spironolacton,5-13% digoxin, as at discharge: 87% ACEI/ARB, 76-95% beta-blockers,80-94% diuretics, 65-81% spironolacton, 4-53% digoxin. Nearly target doses of main CHF drugs were titrated in center -1, rate control in AF was on higher doses of beta-blockers,less with digoxin, in compare to centers -1,2. In center -1 indications to cardiac surgery were found in 61,8% of patients. With HF decompensation patients spent 26 ± 14/15 ± 10/13 ± 5 days,largest value in center -1.At discharge CHF fc decreased: 64,3/41,5/36,3 %-fc II, 20,1/50,4/56,9-fc III, 0/3,0/5,4%- c IV, better results in center -1. In 1,5years of FU 76,8/67,4/82,3% of patients were contacted by telephone calls, 47,2/29,2/ 12,7%-felt better, 20,5/25,0/6,3-worse, 30,1/48,6/77,2%-the same. In center

-1 CHF fc IV-2,3%,fc III-23,9%, fc II-59,7%, fc I-12,5%, in centers -2 and -3 there was tendency to increase group with fc III. The all-cause death and hospitalization for HF decompensation in 1,5 years FU were 11.6/20,9/26.2% and 16.1/21/47.3% respectively in centers.

Conclusions: Local RUS-HFR provided in 3 cardiology centers of Russia demonstrated that treatment of patients with CHF in clinics with HF service had many advantages over cardiology clinics. Optimization of main drug groups, patient compliance, reasonable surgical approach, lower rates of all-cause death and hospitalization for HF decompensation in FU evidently showed the necessity of organizing HF service in Russia with consulting clinics to improve the welfare of the CHF patients and benefit of the national health care system.

P1632

Predictors of optimal pharmacological treatment in patients with heart failure and depressed ejection fraction. Results of the VIDA-IC study

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Introduction and Objectives: Many studies have demonstrated prognostic benefits of evidence-based drug therapy, but rate of use of these drugs remains less than optimal. We analyzed rates of optimal drug therapy in a "real-word" population of patients with heart failure and depressed ejection fraction (HF-dEF), as well as factors associated with its use.

Methods: VIDA-IC study included 1037 patients with EF<40% in 2012 in Spain. For analysis, concomitant use of ACE inhibitors (or ARB), betablockers and MRA was considered to be optimal treatment.

Results: Mean age was 71 ± 11 years, 30% women. Mean EF 33 ± 7%. ACEI/ARB was used in 92% of patients, beta-blockers in 77%, MRA in 66%, Ivabradine in 7%. Optimal treatment was used in 55%. Independent predictors for non using betablockers were age (OR:1.025;95% CI 1.009-1.041;p=0.002), lower blood pressure (OR:1.106, 95%CI 1.007-1.024;p<0.001) and lower heart rate (OR:1.105;95%CI 1.006-1.025;p=0.002). For MRA were age (OR:1.047;95%CI 1.012-1.084;p=0.009), higher EF (OR:1.079;95%CI 1.021-1.139;p=0.007) and betablockers use (OR:0.381,95%CI 0.166-0.875;p=0.002). Age (OR:1.061,95%CI 1.030-1.094;p<0.001) and lower HR (OR:1.019;95%CI 1.002-1.037;p=0.027) was associated with no of optimal treatment.

Conclusions: Half of patients with HF-dEF are still not receiving optimal drug therapy, mainly due to low MRA prescription and to a lesser extent beta-blockers. Factors associated with non-optimal therapy were older age and lower heart rate.

P1633

Sex-specific differences in temporal trends in the incidence of acute decompensated heart failure with reduced and preserved ejection fraction

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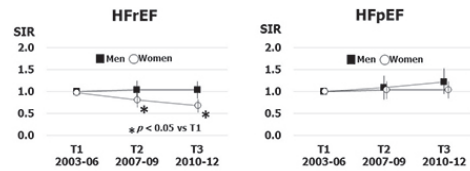
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Background: Although it is assumed that the incidence of acute decompensated heart failure (HF) is rising with the increasing proportion of elderly in the population, sex-specific temporal trends in the incidence of HF, especially with reduced or preserved left ventricular ejection fraction (EF), in the general population remain unclear.

Methods: We conducted a population based HF registration study over a 10 year period in a district with a high proportion of elderly in the population (n = 119 × 10³; age over 60 years = 40%). Medical charts were prospectively reviewed at all hospitals located within the area, and cases were then registered in accordance with the Framingham criteria.

Results: A total of 2,598 cases of onset of HF were registered, with 55% of these being new onset (n=1,413), during the 10 year survey period. The study period was divided into three terms (T1, 2003-2006; T2, 2007-2009; T3, 2010-2012), and data were compared among the three time periods. Age adjusted incidence (per 10⁵ person-year) remained unchanged in men (from 90 in T1 to 90 in T3), but decreased in women (from 107 in T1 to 80 in T3; p<0.01). Among patients who underwent echocardiography (> 90%), the age-adjusted standardized incidence ratio (SIR) of HF cases with reduced EF (HFREF) was stable in men (1.00 in T1 as the reference, 0.95 in T2; 1.0 in T3). However, the ratio decreased gradually in women (1.00 in T1, 0.84 in T2; 0.71 in T3; p<0.05). Whereas the SIR for HF with preserved EF (HFPEF) remained unchanged in both sexes (Figure).

Conclusion: In an aging population, although the incidence of HFREF declined in women over time, the incidence of HFPEF was sustained over the recent decade in both genders. These trends suggest a future pandemic of HFPEF rather HFREF in the aging population.



Temporal trend of SIR in 2 types of HF

P1634

Heart failure: one syndrome with two clinical entities. Differences in efficiency and quality parameters between heart failure with preserved and depressed ejection fraction

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Acute Heart Failure (AHF) is one of the most common causes of admission in a hospital. We distinguish patients with preserved (HFpEF) and depressed ejection fraction (HFdEF)

Purpose: We tried to study the features that could make difference between HFpEF and HFdEF in efficiency parameters (cost, mean stay) and quality parameters (mortality, readmission).

Methods: 600 discharges were analyzed in 2013 with main diagnose as Heart Failure (CIE9 428). Costs per patient were calculated throughout analytic accountability. Rest of parameters were obtained from the discharge document.

Results: They appear in the table number one. You can see that HFpEF is more usual than HFdEF. Besides, HFpEF is more common in women, and HFdEF in men. In addition, HFpEF is more frequent in older people.

Conclusions: It seems that HFdEF unitary cost is higher, in a probable relation to its longer stay. Nevertheless, the global cost is higher in FEPEF because it is twice more common. Men are more likely to suffer from HFdEF and it occurs at younger ages. There is no difference in mortality and readmission between them.

Table 1

	HFdEF	HFpEF	P value
Average Cost (€)	3660,01	2623,77	0,0052
Mean Stay (Days)	9,19	7,71	0,0112
Men (%)	57,87	42,13	<0,0001
Mean age (years)	76,85	81,69	<0,0001
AHF discharge (%)	37,42	62,58	<0,0001
Readmission (%)	11,17	9,97	NS
Mortality (%)	4,26	4,23	NS

P1635

Atrial fibrillation is associated with worse clinical profile in heart failure: aata from REALITY HF Study

This study is supported by ServierY Cavusoglu¹; O Kozan²; S Kucukoglu³; A Temizhan⁴

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Purpose: Atrial fibrillation (AF) is the most common arrhythmia in heart failure (HF) and associated with the severity of HF. The aim of this analysis of the REALITY HF (Resting Heart Rate and Real Life Treatment Modality in Outpatients with Left Ventricular Systolic Dysfunction) study was to evaluate clinical profile of HF patients with AF as compared to those in sinus rhythm.

Methods: REALITY HF was a multicenter, prospective, national registry designed to evaluate HF patients' clinical characteristics, current treatment modalities and enrolled 1251 patients from 16 centers who were admitted to the outpatient clinic with the diagnosis of chronic HF, LVEF <40% and >18 years of age. 822 patients (76.2%) in sinus rhythm and 258 patients (23.8%) with persistent AF were included in this analysis.

Results: When compared to the patients in sinus rhythm, patients with AF were older (60 ± 12 vs 66 ± 10 years, p < 0.001), have lower EF (30 ± 6.6 vs 28 ± 7.6, p < 0.001), higher heart rate (76 ± 13 vs 84 ± 21 bpm, p < 0.001), lower body weight

(79 ± 14 vs 77 ± 14 kg, $p=0.025$), lower systolic blood pressure (125 ± 21 vs 119 ± 20 mmHg, $p=0.001$), lower HDL cholesterol level (43 ± 12 vs 38 ± 12, $p=0.007$), higher creatinine levels (1.20 ± 0.8 vs 1.29 ± 0.5 mg/dL, $p<0.001$), higher uric acid levels (7.0 ± 5.5 vs 7.8 ± 2.0 mg/dL, $p=0.008$), lower haemoglobin level (13.6 ± 1.9 vs 13.1 ± 1.9 gr/dL, $p=0.002$), lower haematocrit levels (41.2 ± 5.7 vs 40.2 ± 5.5 %, $p=0.031$). More patients with AF had valvular heart disease (13.6 vs 2.7%, $p<0.001$). Although the use of beta blockers, ACEI/ARB, MRA were similar, more patients with AF were on diuretic therapy (87.7 vs 65.4%, $p<0.001$) and digoxin treatment (44.1 vs 12.5%, $p<0.001$). More patients with sinus rhythm showed better NYHA functional capacity as compared with those in AF (NYHA I: 24.8 vs 14.2%; NYHA II: 41.6 vs 35.4%; NYHA III: 27.8 vs 35% and NYHA IV: 5.9 vs 15.4%, $p<0.001$). When patients with AF were classified into 3 groups according to the tertiles of heart rate: <70 bpm ($n=52$), 71-82 bpm ($n=87$) and >82 bpm ($n=113$), more patients in lowest heart rate tertile tend to have better NYHA class (NYHA I: 32.4, 32.4 and 35.1%; NYHA II: 20, 38.9 and 41.1%; NYHA III: 17.4, 30.2 and 52.3% and NYHA IV: 17.4, 35.9 and 46.2% respectively, $p<0.043$).

Conclusions: These results suggest that in real life clinical practice, HF patients with AF are associated with worse clinical profile, more likely to need diuretic therapy, more likely to have impaired functional capacity and better rate control in AF tend to link better NYHA class.

P1636

Comparative performance of two predictive methods for death in patients with chronic heart failure: Cox regression and decision trees (CART)

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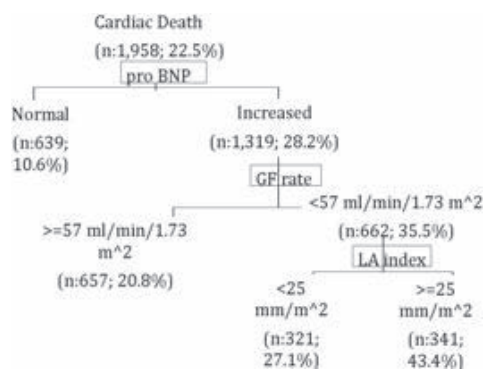
Introduction: Prediction of clinical events is highly relevant in the clinical management of chronic diseases. Nowadays, we have several statistical tools for this **Purpose:** However, few studies have evaluated the performance of the different methodologies currently available.

Objective: To compare the predictive ability and discrimination power of two different methods -Cox and Classification and Regression Tree (CART)- for the analysis of cardiac mortality in patients with chronic heart failure (CHF).

Method: Cox models and the CART analysis were applied to a prospective cohort of 2,507 outpatients with CHF to identify the best prediction model of 5-year cardiac mortality. Discrimination ability was compared using Harrell's C index for Cox and the area under the ROC curve. The models were internally validated using the technique of "bootstrap" ($n=500$).

Results: The overall 5-year cardiac mortality was 22.5% (565 events). The best Cox model for cardiac death was based on 9 variables (diabetes, left ventricular ejection fraction, age, decompensated HF according to the Framingham criteria, indexed left atrial size, anemia, glomerular filtration rate, elevated plasma proBNP and NYHA class). By contrast, the CART analysis found a simple algorithm combining only three variables (ProBNP elevated, glomerular filtration rate and indexed left atrial size) that differentiated 4 risk groups for the endpoint (figure). Discriminatory ability for cardiac death was similar (loss prediction <10%) between the two methods: 0.73 vs 0.67 (Cox vs CART), and internal validation showed acceptable stability: 0.72 and 0.67 (Cox vs CART).

Conclusions: Although the Cox method yields to more discriminative models, the CART method appears to be a valid alternative tool for its simplicity in outpatients with CHF.



5-year cardiac death CART model

EXERCISE TESTING & TRAINING

P1637

Post myocardial infarction patients with severe left ventricular systolic dysfunction: functional capacity and factors associated with recovery after a cardiac rehabilitation program

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Background: Cardiac rehabilitation improves outcomes after myocardial infarction (MI). We analyzed the functional capacity and factors associated with recovery in post ST segment elevation MI patients with severe left ventricular systolic dysfunction after a cardiac rehabilitation program.

Methods: We retrospectively reviewed 70 patients (88.6% male) with severe left ventricular systolic dysfunction (Left Ventricular Ejection Fraction LVEF<35%) post ST segment elevation myocardial infarction, who were referred to a cardiac rehabilitation program. The program included physical training, dietary and pharmacotherapy counseling and a specific smoking cessation follow-up when needed, lasting for about 8-10 weeks. The functional capacity was assessed with a treadmill stress test before and after the program. Exercise capacity was reported in terms of estimated metabolic equivalents of task (METs) and a significant recovery was considered if the exercise capacity before the program was ≤6 METs and ≥8 METs after.

Results: Mean age was 58.2 years (SD=10.5), 61.4% were hypertensive, 35.7% diabetic, 72.9% dislipidaemic, 25.7% obese, 65.7% were current smokers and 12.9% had been previously diagnosed with coronary heart disease. The mean LVEF at the beginning of the program was 30.2% (SD=5.3). The functional capacity mean before the program was 5.7 METs (SD=2.5) and at the end was 9.8 METs (SD=2.6). 20 patients (28.6%) had a significant recovery in their functional capacity. Following an univariate analysis, the factors associated with functional capacity recovery were not being a current smoker at the time of admission for the Acute Coronary Syndrome (ACS), with an odds ratio OR of 0.23 (95% confidence interval CI 0.06-0.9, $p=0.02$) and lower LDL levels at the beginning of the program, with a mean difference of 28.6 mg/dL (95% confidence interval CI 1.23 - 55.9, $p=0.04$).

Conclusions: Cardiac rehabilitation is effective improving functional capacity in post myocardial infarction patients with severe left ventricular systolic dysfunction. Not being a current smoker at the time of admission for the ACS and lower LDL levels at the beginning of the program were factors associated with a significant recovery in functional capacity.

P1638

The effects of aerobic exercise training with vascular occlusion in patients with chronic heart failure

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Background: Aerobic exercise training is an important adjunct to medical therapy in patients with chronic heart failure (CHF), but the effect that aerobic exercise training with vascular occlusion in patients with CHF improves exercise capacity is unknown. The aim of this study was to evaluate the impact of aerobic exercise training with vascular occlusion in patients with CHF.

Methods: Twenty patients with CHF due to Ischemic cardiomyopathy (New York Heart Association functional class I to II) were randomized to an interventional exercise group (IG, $n=10$) or a control exercise group (CG, $n=10$). Exercise was performed at an intensity of 40 to 60% of maximum Peak VO₂/W for 15 min three times per week for 6 months. In IG, patients remained seated on the cycle ergometer saddle with their feet on the pedals, and the proximal end of thighs were applied by pneumatic tourniquets (width: 90mm, length 700mm) with appropriate pressure which was added 20-40 mmHg to the systolic pressure (209 ± 8.0mmHg). We evaluated safety and effect of the intervention on exercise capacity and serum levels of Brain natriuretic peptide (BNP).

Results: There were no differences between two groups at study entry. (Age: 55.0 ± 4.7 vs 55.5 ± 4.5 years; Height: 153.6 ± 7.2 vs 152.6 ± 7.1 cm; Weight: 66.1 ± 4.9 vs 66.3 ± 4.9 kg; Ejection Fraction: 51.5 ± 4.7 vs 48.4 ± 4.7%; Peak VO₂/W: 16.0 ± 6.5 vs 13.8 ± 5.4 ml/kg/min; BNP: 92.9 ± 10.0 vs 88.5 ± 9.3 pg/ml; Circumference of right thigh: 43.0 ± 4.7 vs 42.8 ± 4.3 cm; Circumference of left thigh: 43.2 ± 4.7 vs 42.7 ± 4.3 cm) Change of peak VO₂/W was significantly larger in IG than in CG (29.1% vs 12.4%, $p<0.05$). Change of serum levels of BNP was significantly larger in IG than in CG (-31.0 ± 7.6 vs 5.0 ± 6.4 pg/ml, $p<0.05$).

Conclusion: These results suggest that aerobic exercise training with vascular occlusion can improve, without serious adverse events, exercise capacity and BNP in patients with CHF.

P1639

Cardiac rehabilitation in heart failure with reduced left ventricular ejection fraction due to ischaemic cardiomyopathy: effect on all-cause mortality and cardiac mortality

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Purpose: Although numerous studies have reported that cardiac rehabilitation (CR) confers important improvements in health-related quality of life in heart failure, there are few studies that have examined its effects on mortality.

The aim of our study was to assess the effect of a CR program on long term all- cause mortality and cardiac mortality in heart failure with reduced left ventricular ejection fraction due to coronary artery disease.

Methods: We performed a retrospective cohort study of 252 patients with heart failure and reduced left ventricular ejection fraction (EF < 40%) due to coronary artery disease who underwent percutaneous coronary intervention in our hospital, from March 2004 to July 2009. We compared the outcomes of patients included in a CR program (n = 72) with patients who did not follow such program (n = 180).

Results: Over an individual follow-up of two years, participation in CR program was associated with a significant reduction in all-cause mortality (RR 0.344, 95% confidence interval [95%CI], 0.154- 0.769, p=0.007) and cardiac mortality (RR 0.123, [95%CI] 0.029-0.525, p=0.001). Findings were similar for men and women, for NYHA I-II and NYHA III-IV and for patients with left ventricular ejection fraction lower and higher than 30%.

Conclusion: Our study demonstrates that CR in heart failure with reduced left ventricular ejection fraction due to coronary artery disease is associated with a significant reduction in all-cause mortality and cardiac mortality rates.

Descriptive characteristics

Variables n (%)	No CR(n=180)	CR(n=72)	P
Age, y < 65 65-75 >75	50(27,8%) 75 (41,7%) 55 (30,6%)	51 (71,8%) 17(23,9%) 4,2%)	<0.001
Male,sex n (%)	132(73,3%)	59(81,9%)	0.193
Hypertension, n (%)	118(65,6%)	36(50%)	0.031
Diabetes mellitus, n (%)	87(48,3%)	26(36,1%)	0.093
Hypercholesterolemia, n (%)	109(60,6%)	44(61,6%)	0.935
Smoking n (%)	102(56,7%)	52(72,2%)	0.023
Prior MI n(%)	42 (23,3%)	17(23,6%)	0.923
LV Ejection fraction (%) 40% - 30% < 30%	76(42%) 105(58%)	42(58,3%) 30(41,7%)	0.025
NYHA I-II III-IV	148(83,1%) 30(16,9%)	64 (90,1%) 6(8,5%)	0.071
Multivessel disease	128(71,1%)	47(65,3%)	0.368

Descriptive characteristics of the entire cohort by participation in cardiac rehabilitation

P1640

High intensity interval training attenuates endothelial dysfunction in heart failure with preserved ejection fraction (HFpEF)

Support for this study was provided by the European Commission, Framework Program 7, grant number: EU 602405-2V Volker Adams¹; T Fischer¹; M Alves²; N Rolim²; S Werner¹; TS Bowen¹; U Wisloff²; G Schuler¹

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Background: More than 14 million Europeans suffer from heart failure (HF), with 50% characterized to have a preserved ejection fraction (HFpEF). Morbidity and mortality remains high in HFpEF, with limited benefits observed following large-trial pharmacological interventions. HFpEF patients demonstrate endothelial dysfunction, which is an independent risk factor for future cardiovascular events. At least in HF with reduced ejection fraction (HFrEF), exercise training is known to be a beneficial therapeutic intervention that reduces endothelial dysfunction, but whether the same also occurs in HFpEF is unclear. The present study therefore examined, in an animal model of HFpEF, the impact of high intensity interval exercise training (HIT) on endothelial function whilst identifying possible molecular mechanisms.

Methods: Seven week old female Dahl salt-sensitive rats were randomized into the following groups: (1) control: animals fed with a diet containing 0.3% NaCl, n=10; (2) HFpEF: animals fed with a diet containing 8% NaCl, n=11; (3) HFpEF-HIT: animals fed with a diet containing 8% NaCl who performed treadmill exercise 3x38 min/week, at a maximum heart rate of 60% with 4 intervals of 4 min at 90%, n=11. At 28 weeks, echocardiography and invasive hemodynamic measurements

confirmed HFpEF was developed, and the aorta was removed and endothelial depended and independent vasodilation measured in vitro. Expression of eNOS and AGE (advanced glycation end product)-modified proteins were quantified by western blot, and MMP-2 and 9 activities were measured by zymography. Data are presented as arbitrary units.

Results: HFpEF significantly reduced both endothelium-dependent and endothelium-independent vasodilation, but HIT prevented these impairments. HFpEF significantly reduced protein expression of eNOS compared to controls and HFpEF-HIT rats (0.60 ± 0.09 vs. 1.12 ± 0.20 and 1.00 ± 0.12, respectively). MMP-2 and MMP-9 activity significantly increased in HFpEF compared to controls (MMP-2: 0.82 ± 0.05 vs. 2.35 ± 0.16; MMP-9: 0.25 ± 0.07 vs. 0.42 ± 0.04), but this was not observed following HIT (MMP-2: 1.84 ± 0.15; MMP-9: 0.26 ± 0.03). Expression of AGE-modified proteins was increased in HFpEF compared to controls (0.86 ± 0.08 vs. 1.78 ± 0.36), however this was prevented by HIT.

Conclusion: Endothelial dependent and endothelial-independent vasodilation is impaired in HFpEF, which is associated with reduced expression of eNOS, increased MMP activity, and increased AGE mediated protein crosslinking. HIT, however, was able to prevent endothelial dysfunction and the associated molecular alterations observed in HFpEF.

P1641

Could the 2-minute step test be an alternative to the 6-minute walk test for the assessment of exercise tolerance of patients with systolic heart failure?

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The consequence of exercise intolerance, of patients with heart failure is the difficulty climbing stairs. This form of locomotion is the most difficult and tiring for patients. The walk in place (2 min step test: 2MST) is a test that reflects the activity of climbing stairs.**Aim:** To evaluate the safety and applicability of 2MST in an assessment of exercise tolerance in patients with heart failure.

Methods: The study comprised 168 men with stable systolic HF (age 59 ± 12, mean LVEF 32 ± 8%, NYHA class I/II/III/IV - 28/85/49/6).All participants underwent a 2MST (walk in place, lifting their knees to target midway between their kneecap and the crest of the iliac) that measures the number of knee raises that the individual can perform in 2 minutes, a 6-minute walk test (6MWT), and a cardiopulmonary exercise test (CPX). The quadriceps strength was assessed.

Results: The 2MST was safe and well tolerated in all participants. The number of knee raises obtained in the 2MST correlated with the 6MWT (r=0.45, p<0.05) and the CPX result. Fatigue and leg fatigue were greater after the 2MST than the 6MWT whereas dyspnea and HR and BP responses were similar. Of note, the 2MST results did not correlated to patients' height. The whole relationships of the 2MST and 6MWT with CPX results, quadriceps strength, and clinical and demographic parameters are presented in table 1.

Conclusion: The 2MST is well tolerated by patients with HF. Exercise tolerance assessed by 2MST is connected with measures of exercise capacity evaluated by CPX and are in concordance with those of 6MWT. The 2MST may thus be considered as an alternative for 6MWT.

Relationships of the 6MWT and the 2-MST

Variable	6-minute walk test [m]	2-minute step test [number]
age [years]	-0.47*	-0.21*
height [cm]	0.30*	0.11
exercise time [s]	0.60*	0.34*
exercise time [s]	0.58*	0.33*
VE/CO2 slope	-0.34*	-0.17*
quadriceps strength[Nm]	0.48*	0.61*

*p < 0,05

P1642

Effects of exercise training after an acute coronary syndrome on echocardiography evaluation and health status

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Despite the role of both diastolic and systolic function in prognosis after acute coronary syndrome (ACS), diastolic function is often overlooked in comparison to

improvement of ventricular systolic function and health status. An adequate cardiac rehabilitation program (CRP) after ACS can improve global and cardiac mortality. We studied echocardiography parameters and EuroQoL5D scale, before and after CRP, in patients who had ACS and were included on CRP.

Methods: Study of 121 patients who completed a two month CRP consisting of biweekly exercise training sessions, nutrition counseling and psycho-educational group intervention. Patients were enrolled between January 2011 and December 2012. All subjects underwent echocardiography and EuroQoL5D scale before and at the end of the CRP.

Results: Mean age was 53.8 years (SD 9.1) and 81.8 % were male. ACS with ST-segment elevation occurred in 53.8% of cases while 36.8% were admitted with ACS without ST-segment elevation. The majority of patients had one vessel coronary disease (63.2%), with 18.8% having 2-vessel disease, and most underwent percutaneous revascularization (90.6%). Most patients were medicated with angiotensin-converting - enzyme inhibitor(80.3%) and beta blockers (90.6%). The EuroQoL5D scale improved after CRP ($p=0.000$). The mean of left ventricular systolic function (LVSF) before CRP was 58.5% (DP 8.5) and after 60.5% (DP 8.0), $p<0.001$. When we analyzed separately the patients with reduction of LVSF (Ejection Fraction (EF) $<55\%$) ($n=26$), mean was 46.1% (DP 7.6) before CRP and improved for 51.1% (DP 10.4) after CRP, $p=0.000$ as well as patients with normal LVSF ($EF\geq 55\%$) ($n=95$), mean before CRP was 62.1% (DP 4.5) and after 63.3% (DP 4.5), $p=0.021$. At the end of CRP there was no significant differences on echocardiography diastolic parameters like E/A [1.21(DP 0.3) versus 1.23(DP 0.3); before and after CRP, respectively; $p=0.123$], deceleration time [215.1 msec (DP 44.9) versus 215.6 msec (DP 56.8); $p=0.935$], E/E' [8.46 (DP 2.8) versus 8.36(DP 2.5); $p=0.616$], left auricular diameter [38.9 mm (DP 3.9) versus 39.2 mm (DP 3.6); $p=0.194$]. There was also no significant improved on right ventricular systolic function (RVSF) after CRP: peak systolic velocity [13.4 cm/s (DP 1.9) versus 13.3 cm/s (DP 2.0); $p=0.884$] and TAPSE [23.2 mm (DP 4.3) versus 23.8 mm (DP 3.6); $p=0.582$].

Conclusion: Diastolic function and RVSF did not change significantly after CRP on patients who had ACS, but the program improved health status and LVSF. So, cardiac rehabilitation can be of value and should be implemented after ACS.

P1643

Physical exercises at an early stage of cardiac rehabilitation in coronary artery disease patients with incomplete myocardial revascularization

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Objective: To compare cardioprotective effect of controlled physical exercises (CPE) of high (based on the phenomenon of ischemic preconditioning (IP)) and moderate intensity in early rehabilitation in coronary artery disease (CAD) patients with incomplete myocardial revascularization (IMR) after percutaneous coronary intervention (PCI).

Material and Methods: We examined 65 CAD patients (men and women) aged 39-65 (median 54.6 \pm 9.2 y.o.) with IMR after PCI. Verification was performed in the first 10 days after PCI. Paired diagnostic stress-test showed the phenomenon of ischemic preconditioning (IP) in 23 patients. These patients were randomized in 2 groups and performed 10-days course of daily CPE of different intensity. I group patients ($n=11$) participated in high intensive CPE (80% of supreme threshold exercise intensity) with the aim of IP phenomenon preservation. Duration of basic period in daily CPE was determined by time to ST depression and/or angina pectoris development (19-43 min, median 29.8 min). II group patients ($n=12$) performed daily CPE of moderate intensity (60% of supreme threshold exercise intensity) with duration of 30 minutes. CPE were carried out under the results of ECG, blood pressure and heart rate monitoring, markers of myocardial necrosis (myoglobin, troponin, MB-CK, BNP). This confirmed the safety of CPE and formation of IP. The results of coronary angiography were comparable in patients of both groups. Results. Compare of effectiveness of 10-days CPE courses with high and moderate intensity in parallel groups showed that exercise duration in the I group increased by 16.1 \pm 3.6%, and in the II group - by 4.1 \pm 1.2% ($p<0.05$), metabolic equivalent increased by 9.3 \pm 2.6% and 2.4 \pm 1.1% ($p<0.05$), respectively, maximum ST depression in I group was decreased by 46.3 \pm 6.8% and in II group - by 9.8 \pm 1.6% ($p<0.001$). Results of Holter ECG monitoring in I group patients showed decreasing of ectopic activity by 23.6%, in II group patients - by 10.3%. Overall duration of ST depression per calendar day significantly decreased in I group - by 31.8%, in II group - by 9.9%. Values of myocardial necrosis stayed within reference ranges. Conclusion. 10-days courses of 80% intensity CPE in CAD patients with IMR were more effective in adaptation to ischemia and cardioprotective effect formation as compared to 60% intensity CPE. Short courses of daily PE of high intensity form cardioprotective effect in CAD patients with IMR and reduce the time for rehabilitation.

P1644

Influence of home-based telemonitored Nordic walking training on autonomic nervous system balance in heart failure patients

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Rehabilitation positively affects the modulation of autonomic nervous system (ANS). There are no papers evaluating the influence of Nordic walking training (NW) on ANS activity among heart failure (HF) patients. **Purpose:** To assess the influence of NW on ANS activity measured by heart rate variability (HRV) and heart rate turbulence (HRT) in HF patients and its correlation with physical capacity improvement measured by peak oxygen consumption (peak VO₂ [ml/kg/min]) in cardiopulmonary exercise test (CPET). **Methods.** The study group comprised 111 HF patients (NYHA II-III; EF $\leq 40\%$). Patients were randomized (2:1) to 8-week NW (five times weekly) at 40-70% of maximal heart rate, training group (TG) $n=77$, or to control group (CG) $n=34$. The effectiveness of NW was assessed by changes-delta (Δ) in peakVO₂, HRV and HRT as a result of comparing these parameters from the beginning and the end of the program. Results Eventually, 36 TG patients and 15 CG patients were eligible for HRV and HRT analysis. Only in TG low/high frequency ratio (LF/HF) decreased 1.9 \pm 1.1 vs 1.7 \pm 0.63 ($p=0.0001$) and peakVO₂ increased 16.98 \pm 4.02 vs 19.70 \pm 4.36 ($p<0.0001$). Favorable results in CG were not observed. The differences between TG and CG were significant: Δ peakVO₂ ($p=0.0081$); Δ LF/HF ($p=0.0038$). An inverse correlation was found between the decrease in Δ LF/HF and the increase in Δ peakVO₂ $R=-0.3830$, ($p=0.0211$) only in TG. HRT did not change significantly in both groups. Conclusion. NW positively affects the parasympathetic-sympathetic balance in HF patients, which correlates with the improvement in Δ peakVO₂. No significant influence of NW on HRT has been proven.

P1645

Supervised exercise programme in primary care to improve quality of life and functional capacity for heart failure patients

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Purpose: Evaluate the effectiveness of a supervised progressive exercise programme (SPEP), for people with heart failure in addition to optimal treatments, to improve the quality of life (QoL) and their functional capacity.

Methods: Randomized clinical trial 1:1 into two groups: EFICAR (SPEP + optimised usual care) and control group (optimised usual care). Inclusion criteria: age <80 years, LVEF $<50\%$, stable NYHA class II-IV, physically and mentally able to attend the exercise programme. Therapy titration and stress test (ST) were performed before randomization. SPEP included 36 sessions of progressive exercise program (3 hours/week for 3 months) with an aerobic and a strength component. The outcome measures were the change in QoL measured by the SF-36 and the Minnesota Living with Heart Failure Questionnaires (MLHFQ) and changes in functional capacity measured by the 6-Minute Walking Test at baseline and 3 months.

Results: 150 patients were randomized into two well-balanced groups (mean age 67.4 \pm 10.1 years; 77.3% men; 46.7% ischemic etiology; mean LVEF 37.4 \pm 7.9%). During follow up, 6 patients of the control group (8%) and 16 patients (21.3%) of the EFICAR group abandoned the SPEP (5 for musculoskeletal problems, 3 for work reasons, 2 were not interested after they started the sessions, 6 for other causes). There were no serious adverse events in all exercise programme (2031 completed sessions, 83400 minutes). At 3 months, the quality of life improvement in the exercise group was -2.37 (95% CI, -5.60 to 0.84) vs -3.56 (95% CI -6.69 to -0.44) in the control group for the MLHFQ (p:n.s) and 0.42 (95% CI -1.31 to 2.16) vs 1.31 (95% CI -0.35 to 2.98) for SF-36 in physical component (p:n.s) and 0.93 (95% CI -1.17 to 3.04) vs 0.24 (95% CI -1.78 to 2.27) for SF-36 mental component (p:n.s). The functional capacity improvement in the exercise group was 27.90 m (95% CI (16.83 to 38.97) vs -0.11m (95% CI -10.91 to 10.69) in the control group ($p<0.05$).

Conclusions: Supervised exercise program in primary care is safe and the adherence of the exercise group was optimal. Exercise training conferred improvements in physical capacity in the limit of clinical significance but there were no significant changes in the quality of life questionnaires compared with usual care at 3 months.

PROGNOSIS

P1646

Poor prognosis factors in medically treated patients with prosthetic valve endocarditis and prior heart failure

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Background: Valvular prostheses are known as predisposing factors for endocarditis. By cost and mortality, prosthetic valve endocarditis (PVE) represents a serious complication.

Objective: To determine factors that influence the prognosis during hospitalization in patients with prior valvular heart failure (HF) receiving medical therapy with antibiotics (MTA) for PVE.

Method: Retrospective analysis over 5 years (2000-2004) of 56 patients with possible or definite PVE (modified Duke criteria). All patients had prior HF. Those patients were divided in two groups: early and late PVE (12 month after surgery cut off). PVE course under MTA was evaluated. The following variables were analyzed: demographic data, comorbidities, microbial etiology, clinical, biological and echocardiography parameters, in hospital death and other complications. MTA duration was 6 weeks.

Results: Early PVE: 51.78%, mean age: 54.6 years old, male 64%. PVE type was independent of prostheses position but related to prostheses type. Comorbidities related to in-hospital death: diabetes (OR=9.33) and the presence of ischemic heart disease (IHD). About 85% of studied patients in both groups had prior HF with preserved ejection fraction (EF) and 15% decreased EF. Responders to MTA have not been influenced by the type of MTA (multivariate analysis). One third of patients had adverse outcome linked to PVE related complication: persistent fever, perivalvular extension of infection with annular abscesses ($p=0.002$). Prostheses dysfunction due to dehiscence was related to annular abscesses ($p=0.01$) and was independent by the etiology and the type and position of prosthesis determining a worse outcome ($p=0.00009$). Those patients developed hemodynamic instability irrespective of PVE type and baseline EF or NYHA class. Left ventricular systolic dysfunction influenced prognosis only in patients with ischemic heart disease IHD ($p=0.0002$). Systemic embolism was related to etiology ($p=0.005$) and worse outcome ($p=0.007$). There were no differences between factors of bad prognosis between two groups. In-hospital death was 2% and 27% of subjects were transferred due to complications. **Conclusions:** Persistent fever, perivalvular extension of infection, prosthesis dysfunction, systemic embolism, ischemic LV systolic dysfunction and diabetes determined a worse outcome in our patients. Those factors need to be determined by sequential echocardiography and clinical evaluation in order to establish those patients that may benefit for dual therapy: medical and early surgery.

P1647

Prognosis of elderly patients in a heart failure management program depending on their left ventricular ejection fraction

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Objective: to compare the clinical profile and prognosis of patients included in the Congestive Heart Failure Management Program (UMIPIC) from our University Hospital depending on their Left Ventricular Ejection Fraction (LVEF).

Methods: patients were included in the UMIPIC from June 2011 until July 2012. Epidemiological, clinical, analytical, functional and echocardiographical data at inclusion were recorded in an electronic formulary. Tracking of these patients was made through consult visits and phone interviews until January 2014, inclusive.

Results: 74 patients were included in the Congestive Heart Failure Program during the referred period. Their mean age was 79.83 years (SD=7,812). 80% were women. Echocardiography was performed by a Cardiologist in 81% of these patients. Left ventricular ejection fraction was higher than 45% in 80% of the patients tested. In 20% patients with LVEF<45%, 50% were males, with a mean age of 80.75 years; 16.7% were in atrial fibrillation (AF) and there was left ventricle hypertrophy (LVH) in 16.7%. On the other hand, patients with LVEF>45% were women in 87.5% of the cases, 60% were in AF and 52.1% had echocardiographical criteria for LVH. Amongst quantitative parameters, there were statistically significant differences between groups at albuminaemia, sideraemia and serum transferrin (lower mean levels in the LVEF<45%), and also higher mean levels of NT-proBNP in the LVEF<45% group. There were not significant differences in age, heart rate, body mass index, functional capacity (measured with the Barthel test), comorbidity (measured with the Charlson test) and cognitive impairment (measured with Pfeiffer test). Neither in haemoglobin mean levels, red blood cell width, pulmonary hypertension, nor in number of patients with chronic respiratory insufficiency. Survival, defined as number of tracking days, was significantly lower in the group LVEF<45% ($p=0,001$), with a mean of 313,75 days (CI95% 175,24 - 472,21). However, patients with a LVEF>45% had a mean follow up of 607,48 days, (CI95% 529,46 - 685,50). Patients with LVEF<45% had a Relative Risk of dying of 6,784, compared with patients with LVEF>45%.

Conclusions: mortality was significantly higher amongst elderly patients with

LVEF<45%, usually males, in sinus rhythm, without left ventricle hypertrophy. This high risk group of patients also has lower sideraemia, transferrin saturation and albuminaemia, and higher mean levels of NT-proBNP, but there were no significant differences in age, BMI, functional capacity, comorbidity or cognitive impairment with patients with LVEF>45%.

P1648

Outcomes of patients with degenerated bioprosthetic surgical valves undergoing transcatheter aortic valve implantation

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Most surgical heart valves currently implanted are bioprosthetic tissue valves. Such valves deteriorate with time, eventually presenting with either stenosis or regurgitation. Reoperation, the current standard of care for failed valves, carries significant risk in terms of both morbidity and mortality. 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 the CoreValve prosthesis in patients with degenerated bioprosthetic surgical valves and comparing them with patients with aortic stenosis.

Methods: The CoreValve prosthesis was implanted in 14 patients with symptomatic degenerated surgical aortic valves (SAV) and in 427 patients with aortic stenosis (AS).

Results: The mean age was similar in both groups (SAV vs. AS) 77.6 ± 11 vs. 79.2 ± 6.8 years, $p=0.439$ and logistic EuroSCORE was higher by SAV $30.1 \pm 18\%$ vs. 17.2 ± 5 , $p=0.001$. TAVI procedure was successful in all patients with degenerated bioprostheses.

In two patients required to implant a second valve prosthesis. After procedure the mean gradient was higher than in patients with AS 17.5 ± 8 mmHg vs. 8.9 ± 4.9 mmHg, $p < 0.001$, and 100% of patients had ≤ 2 degree of aortic regurgitation. There were no complications after procedure including mortality at 30 days.

There were more moderate and severe prosthesis-patient mismatch when compare with the rest of patients treated (81.8% vs. 40.5%, $p=0.024$ and 35.5% vs. 9.5%, $p=0.001$, respectively). There were tend to lower requiring pacemaker after procedure (7.7% vs. 26.8%, $p=0.105$). In the follow-up, after 30.5 ± 20 months all-cause mortality was 14.3% and 80% of patients was at New York Heart Association functional class I-II

Conclusions: The valve-in-valve procedure is clinically effective in patients with degenerated bioprosthetic aortic valves. The procedure and outcomes are similar in some aspects to TAVI in the setting of native aortic valve stenosis, there are some differences that deserve special consideration.

P1649

Frailty syndrome is a part of life in aged patients with heart failure qualified for cardiac resynchronization

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Cardiac resynchronization therapy (CRT) is a method for treatment of advanced heart failure (HF). The method more frequently is detectable in a elder patients (> 65 y) and probably frailty syndrome is most often recognized in this group. Frailty is a common geriatric syndrome that embodies an elevated risk of catastrophic declines in health and function among older adults. Some of those patients had previously implanted standard pacing system and need upgrade for CRT, the others need CRT de novo implantation. We hypothesized that patients with de novo CRT implantation had frailty syndrome more intense.

Methods: 106 pts aged > 65 years qualified for CRT were included. All patients had EF<35%, left bundle branch block and NYHA ≥ 2 . Patients were divided into 2 examined group: de novo CRT implantation - 74 pts; and upgrade from classic pacing system (DDD or VVI) - 32 pts. In all CRT-P or CRT-D was finally implanted. In all frailty was evaluated by using Canadian Study of Health and Aging Clinical Frailty Scale (CSHA-CFS). Values > 5 are recognize as frailty syndrome; value = 4 describe pts exposed on frailty syndrome. Obtained data were statistically analyzed.

Results: Average values in CSHA-CFS was statistically higher (5.26 ± 0.81) in de novo pts if compare to the upgrade pts (4.88 ± 0.79); $p=0.0273$. Frailty syndrome was recognized in 81.08% in de novo group and in 68.75% in upgrade group. Patients exposed on frailty was identifiable as follow: de novo - 18.9% vs. upgrade - 28.1%. Statistical correlations were observed between NYHA class and level of frailty syndrome ($r=0.28$). None of the following echocardiographical parameters including ejection fraction ($r=-0.18$), left ventricular end-diastolic dimension

($r=0.07$) and left ventricular end-systolic dimension ($r=0.03$) didn't statistically correlated with level of frailty syndrome. Only 1 patients out of 106 had no attributes of frailty (or exposed on) syndrome.

Conclusions: Frailty syndrome is a significant part of life patient with heart failure over 65 years. It is most often recognized in patients de novo qualified for cardiac resynchronization - it can be caused by the fact of professional medical care patients qualified for upgrade for CRT from standard pacing.

P1650

Five-years outcome after transcatheter aortic valve implantation with the corevalve prosthesis

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Little is known about long-term outcomes following TAVI. Previous reports of transcatheter aortic valve implantation (TAVI) have focused on short- and mid-term outcomes; however, long-term durability of transcatheter heart valves and long-term clinical outcomes are unknown. The aim of this study was to evaluate clinical and hemodynamic outcomes 5 years after TAVI.

Methods: Between April 2008 and January 2010, 100 patients underwent TAVI for the treatment of severe symptomatic aortic stenosis with the CoreValve prosthesis

Results: the mean age and euroSCORE were 79.7 ± 6.5 years and $20.9 \pm 15\%$ respectively. Mean aortic valve gradient decreased from 50.7 ± 15 mm Hg to 9.03 ± 4.2 mmHg after TAVI and 11.3 ± 9.4 mm Hg at 5 years (p for post-TAVI trend 0.03). Mean aortic valve area increased from 0.63 ± 0.2 cm² to 1.64 ± 0.41 cm² after TAVI and 1.47 ± 0.27 cm² at 5 years (p for post-TAVI trend 0.01). Mean left ventricular ejection fraction increased from 62.9 ± 14 mmHg to 66.8 ± 12 mmHg after TAVI and 60.7 ± 8 mmHg at 5 years (p for post-TAVI trend 0.001)

In-hospital mortality was 4%. Late mortality after a mean of 48.8 ± 23 months was 29.2% and in only 7 p was cardiovascular mortality. Survival rates at 1 to 6 years were at %, 78%, 70%, 65%, 63.5% and 57.1% respectively. At 5 years, 2 patients had severe prosthetic valve dysfunction (severe stenosis and moderate transvalvular regurgitation). Survival rates at 1 to 5 years were 83%, 74%, 53%, 42%, and 35%, respectively.

Median survival time after TAVI was 3.6 years (95% confidence interval [CI]: 3.24 to 4), and the risk of death was significantly increased in patients with acute kidney injury (adjusted hazard ratio [HR]: 4.3; 95% CI: 1.3 to 14.1), p=0.016, severe Prosthesis-patient mismatch (P-PM) HR 6.99; 95% CI 2.33 to 20.9) p<0.001 and subclavian approach HR 19.5; 95% CI 3.46 to 10), p<0.001.

Conclusions: Our study demonstrated favorable long-term outcomes after TAVI. Signs of prosthetic valve failure were observed in 2% of patients. Complications after procedure, notably acute kidney injury and severe P-PM, were associated with reduced long-term survival.

P1651

Impact of new-onset persistent left bundle branch block on late clinical outcomes in patients undergoing transcatheter aortic valve implantation with corevalve prosthesis

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Cardiac conduction disturbances, including a left bundle branch block (LBBB), occur frequently following transcatheter aortic valve replacement (TAVR) and may be associated with adverse clinical events. The impact of new-onset persistent left bundle branch block (N-LBBB) after TAVI remains controversial. The aim of this study was to determine the impact of new-onset persistent left bundle branch block (on late outcomes after transcatheter aortic valve implantation (TAVI)). Methods A total of 341 consecutive patients who underwent TAVI with a balloon-expandable valve without pre-existing LBBB or permanent pacemaker implantation (PPI) were included. Electrocardiograms were obtained at baseline, immediately after the procedure, and daily until hospital discharge. Patients were followed at 1, 6, and 12 months and yearly thereafter. **Results:** New-onset LBBB occurred in 178 patients (54.8%) immediately after TAVI and persisted at hospital discharge. At a median follow-up of 28 months (range 1 to 84 months), there were no differences in mortality rate between the N-LBBB and no N-LBBB groups (16.9% vs. 14.3%; adjusted-hazard ratio: 1.23 [95% confidence interval (CI): 0.704 to 2.113]; p=0.47. There were no differences between groups regarding cardiovascular mortality HR=0.49 (95% CI 0.168-1.456), p=0.201, rehospitalizations for heart failure

HR=1.06 (95% 0.380-2.945), p=0.9. Only 3 patients with N-LBBB required PPI during the follow-up period. There were 3 cases of unexpected (sudden or unknown) death was observed in 2 patients with N-LBBB. Patients with N-LBBB not showed a poorer evolution of left ventricular ejection fraction over time (1, 2 and 3 years) than no N-LBBB group: 62.3 ± 9 vs. 64.5 ± 8.7 , p=0.072; 62.3 ± 9 vs. 63.5 ± 9 , p=0.536 and 62.5 ± 4.7 vs. $60.3 \pm 7\%$, p=0.367, respectively). N-LBBB was also not associated with a poorer New York Heart Association functional class at follow-up (1.75 ± 0.6 vs. 1.68 ± 0.7 , p=0.502). Conclusions N-LBBB was a frequent complication of transcatheter aortic valve implantation, but it was not associated with any increase in overall or cardiovascular death or rehospitalization for heart failure after a mean follow-up of 2 years.

P1652

Prevalence of frailty and impact on survival in elderly patients hospitalized for heart failure

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Therole of frailty --a geriatric syndrome characterized by increased vulnerability to stressors due to the decline of physiologic systems, reflecting biologic rather than chronologic age-- is not well known in patients with heart failure (HF).

Aim: To analyze the prevalence of frailty, characteristics of frail patients and its influence on survival after hospitalization in older patients hospitalized for HF.

METHODS. FRAIL-HF is a prospective cohort study of 450 non-dependent patients ≥ 70 years old admitted for HF with 1-year follow-up. Frailty was diagnosed according to Fried criteria described in the Cardiovascular Health Study (at least three of these components: exhaustion, weight loss, low activity, slow walk and poor grip strength) and measured before discharge. HF characteristics, chronic comorbidities, coexistent acute diseases and HF drug prescription were also measured. Survival analysis and Cox proportional-hazards model were used to assess the independent impact of frailty on mortality.

RESULTS. Among 416 patients with complete information on frailty status, 76% fulfilled frailty criteria. Mean age was 80 ± 6 years. Frail patients were older, more often female, and presented with HF of hypertensive (32%) or valvular (28%) origin, and less ischaemic (31%) (19%, 21% and 48%, respectively). There were no differences in chronic comorbidity index, LVEF, blood pressure, and NT-proBNP levels between the two groups. Frail subjects were less often prescribed ACE Inhibitors or ARB (67% vs 83%, p=0.002) and beta blockers (62% vs 77%, p=0.009) than non-frail patients.

Overall survival at 12 months was 89% (95% CI: 81-94) in the non-frail group and 75% (95% CI: 70-79) in frail subjects (log-rank test: p=0.003). After adjusting for age and presence of a coexisting acute disease, frail patients showed a higher all-cause mortality risk (HR 2.36; 95% CI, 1.21-4.60). Additional adjustment for LVEF, NT-proBNP levels and Charlson index did not alter results significantly. No positive interaction between frailty and HF drugs effect on survival was found.

CONCLUSION. Frailty is very prevalent even among nondependent elderly patients hospitalized for HF. Frailty is not due to more severe disease, and is independently associated with increased mortality risk. Frailty does not modify the effect of ACEI, ARB and beta blockers on survival.

P1653

A new strategy in the prediction of long-term events in infective endocarditis

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Purpose: predictors of poor prognosis in infective endocarditis (IE) are identified. However, there are limited data on the simultaneous application of several predictors. The clinical profile and prognosis of prosthetic valve endocarditis (PVE) are not well defined.

Aims: Establish a "score" for low risk stratification of events in the medium - long term defined endpoint death and / or readmission (M / R) for heart failure or reinfection at 12, 36 and 60 months of follow-up.

Methods: Retrospective study of 100 patients (P), 23 with prosthetic valve endocarditis was definite (defined by modified Duke criteria) from May 2000 to August 2012. We identified clinical, analytical variables (at baseline) and the existence of complications associated with a higher event rate and attributed by 1 or 2 points (p) according to the OR obtained (p<0.05) in univariate analysis: anemia of chronic disease (2p); presence of refractory heart failure (2p); prosthesis endocarditis (1 p.)

; existence of *Candida albicans* in blood cultures (1 p.) and diabetic patients (1 p.). We established a score with cut-off (ROC): 2.5 p.

Subsequently it was found that if the score is predictor of events at 12, 36 and 60 M of follow-up (survival analysis-Kaplan-Meier). We evaluated predictors of mortality in relation to prosthetic valve endocarditis (PVE) by multivariate analysis.

Results: The study population consisted of 73 % men and 27 % women. The average age is 59.18 ± 18.77 years (minimum 1 year and maximum 96 years). The event rate was 37 % (20 % of mortality, 14 % of readmissions for HF and 3 % of recurrent IE).

A score > 2.5 proved to be an independent predictor of M / R to 12M (OR 2.2; [CI 0.4 to 3, 4], $p < 0.01$), 36M (OR 3.2; [CI 1.5-4.4], $p < 0.01$) and 60M (OR 3.7; [CI 1.7 to 5.9], $p < 0.01$), translated linearly in the survival curves (Kaplan - Meier log rank: $p < 0.001$). Predictors of Events in the medium - long term in PVE were early infection of valvular prosthesis implanted for less than one year, $p = 0.04$, anemia of chronic disease ($p = 0.01$) and in-hospital complications in particular, the refractory HF ($p = 0.02$) and the presence of peri-valvular abscess ($p = 0.04$).

Conclusions: The score proved to be an independent predictor of morbidity / mortality in the long term, enhancing the connection between analytical and clinical factors to which must be recognized individually, an important prognostic value.

P1654

T(-786)C polymorphism of endothelial nitric oxide synthase is associated with worse clinical prognosis in chronic systolic heart failure

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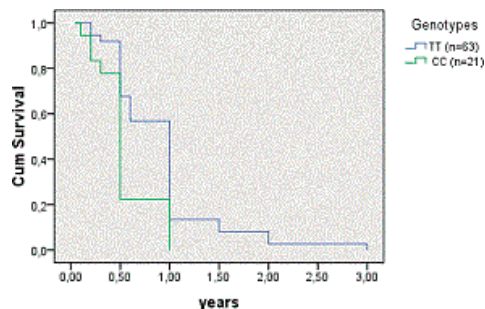
Background: Previous studies demonstrated the link between low endothelium-dependent vasodilatory response and high mortality risk in chronic heart failure (CHF). But it's unknown whether endothelial nitric oxide synthase (eNOS) gene polymorphism is associated with survival in CHF patients (pts).

Aim: To evaluate long-term prognosis in systolic CHF in relation to eNOS T(-786)C gene polymorphism.

Methods: 145 stable ischemic CHF pts with left ventricular (LV) systolic dysfunction (LV ejection fraction $\leq 45\%$). Smokers, pts with diabetes and those on carvedilol or nebivolol (nitric oxide bioavailability modulators) treatment were excluded. 5 years prognosis (heart failure hospitalization data only and both death/heart failure hospitalization data) was evaluated by Kaplan-Meier method.

Results: The frequency of T(-786)C genotypes was: TT - 43,5% (n=63), TC - 42,0% (n=61), CC - 14,5% (n=21). The pts with CC genotype demonstrated significantly worse heart failure hospitalization rate at 5 years follow-up as compared with TT homozygote group (log-rank = 8,761, $p = 0,003$), (Fig.). Simultaneously, combined outcome had no significant differences between TT and CC group (log-rank = 1,271, $p = 0,260$). There were no significant differences in above-mentioned heart failure hospitalization rate and combined outcome between TT and TC groups.

Conclusion: In stable ischemic systolic CHF CC T(-786)C eNOS genotype is associated worse long-term outcome versus TT T(-786)C eNOS genotype.



Kaplan-Meier curves

P1655

Predicting early-medium term adverse events in patients with infective endocarditis

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Infective endocarditis (IE) is associated with high mortality and morbidity rates; complications occurring in the initial infection can contribute to the poor prognosis.

Following in-hospital treatment, the main complications include recurrence of infection, heart failure, need for valve surgery and death.

Purpose: Identify prognostic factors of early-medium term adverse events and establish a "Score" for risk stratification in pts with IE.

Methods: Retrospective study including consecutive patients (pts) admitted to our centre with IE during a 6 years period. We identified the variables associated with higher adverse events at 90 days (end-point: death or reinfection) and attributed 1 or 2 points (p) according to the OR obtained ($p < 0.05$) in univariate analysis: previous history of valvulopathy (1p) and heart failure (HF) (1p); septic shock (2p), presence of local complications (defined as valve destruction or periannular complication) (2p) and clinical evolution with HF (1p). We established a Score cut-off (ROC curve) of 2.5p and then we analyzed if the score was predictor of defined endpoint (using survival analysis Kaplan-Meier).

Results: We studied 78pts, 76.9% males, age 59 ± 17 (22-89) years old. Diagnosis of left sided prosthetic valve in 30.1%, device-related IE in 2.6% and IE of native valve in the remaining pts. Aortic valve was the most often involved valve and *Staphylococcus aureus* was the most frequent isolated microorganism. Twenty-four pts (31%) underwent surgery and 3 of them died after the intervention. The defined end-point occurred in 34.7% of pts. Although associated with septic shock ($p = 0.002$) the infection with *S. aureus* was not a predictor of death. Local complications were diagnosed using transesophageal echocardiogram, and of them the best predictor of the end-point was the presence of paravalvular abscess ($p = 0.015$). A Score >2.5 proved to be predictor of adverse events at 90 days ($p < 0.01$).

Conclusion: In our population the predictors of adverse events were previous history of valvulopathy and/or HF, septic shock, presence of local complications and clinical evolution with HF. The proposed Score proved to be an independent predictor of early death in patients with IE.

P1656

Prognostic value of functional mitral regurgitation in patients with heart failure

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Background: Functional mitral regurgitation (FMR) is a common finding in patients with heart failure but its effect on outcome is still uncertain.

The aim of this study is to evaluate the prognostic value of FMR in patients with heart failure.

Methods: We enrolled 893 (67 years, 530 were male) patients admitted to the therapeutic unit of chronic heart failure from as follow: group 1 : no/mild FMR (n=403, 45%), group 2 : moderate FMR (n=466, 52%) and group 3 : severe FMR (n=24, 3%) and compared the results from their demographic, clinical data and echocardiography. FMR was quantitatively determined by measuring vena contracta (VC) or effective regurgitate orifice (ERO) or regurgitate volume (RV). Severe FMR was defined as ERO >0.2 cm² or RV >30 ml or VC >0.4 cm.

Results: Patients with HF with severe FMR had more hospitalization for cardiac decompensation ($p = 0.0002$), more Ischemic heart disease ($p = 0.001$), were more likely to have atrial fibrillation ($p = 0.04$), to be treated with high doses of diuretics ($p = 0.00001$); had higher pulmonary pressures ($p = 0.00004$) and right ventricular systolic dysfunction ($p = 0.00001$). There was a good correlation with NYHA functional class ($p = 0.009$) and diastolic dysfunction ($p = 0.0001$). However male sex, diabetes, hypertension stroke attack did not differ among the groups.

Conclusion: Mitral regurgitation has a negative effect on prognosis of patients with heart failure.

P1657

Prognostic value of global longitudinal peak systolic strain in comparison with nt-proBNP in chronic heart failure patients

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Purpose: NT-proBNP level is a well-known predictor of unfavorable outcome in patients with chronic heart failure (CHF). Global longitudinal peak systolic strain (GLPSS) likewise has recently been reported as a prognostic marker for major adverse cardiac events, especially in patients with sinus rhythm (SR). The aim of the study was to compare prognostic value of GLPSS and NT-proBNP level in CHF patients with SR.

Methods: 43 patients (14 female, mean age $58,8 \pm 13,3$ years) with stable CHF NYHA class I-III of various etiologies (58,1% ischemic) and SR were enrolled in the study. All patients received optimal medical treatment. 14 patients (32,6%) had preserved LVEF. All patients underwent estimation of GLPSS ($-9,4 \pm 4,7\%$ in average) using two-dimensional speckle tracking echocardiography and NT-proBNP level (mean value $1640,0 \pm 1842,6$ pg/ml). Average period of observation amounted $25,1 \pm 9,7$ months. Cardiovascular mortality (CVM) was considered the primary

end-point.

Results: CVM due to sudden cardiac death (n=4) and progression of CHF (n=3) amounted 16,3%. Receiver-operating characteristic (ROC) analysis showed superiority in prognostic value of GLPSS (area under curve (AUC)=0,837; 95% confidence interval (CI) 0,693-0,932, $p < 0,0001$) over NT-proBNP (AUC=0,754, 95% CI 0,559-0,872, $p = 0,04$) for predicting CVM. Cox regression analysis showed that GLPSS with a best cut-off = -6,6% received from ROC-analysis was predictive for CVM as well (hazard ratio=13,4; CI=1,6-112,1, $p = 0,0026$).

Conclusions: GLPSS is a strong predictor of a two-year cardiovascular mortality in chronic heart failure patients with sinus rhythm with a cut-off point = -6,6%. The prognostic accuracy of GLPSS was better than of NT-proBNP level.

P1658

Cardiopulmonary exercise testing parameters with highest prognostic value in chronic heart failure patients receiving optimal medical treatment

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Objectives: to identify the most significant predictors of cardiovascular mortality (CVM) among cardiopulmonary exercise testing (CPET) indices in optimally treated chronic heart failure (CHF) patients.

Methods: 111 patients (83 men, 28 women, mean age 60,6±12,8 years) with chronic HF NYHA class I-III of various etiologies, mean left ventricular ejection fraction (LVEF) =37,7±13,6% and average NT-proBNP level=1979,6±1776,2 pg/ml were enrolled in the study. 34 patients (30,6%) had preserved LVEF. All patients performed CPET being in stable state on optimal medical treatment. Average follow-up was 25,1±9,7 months. Cardiovascular mortality (CVM) was considered the primary end-point. The prognostic value of multiple CPET parameters was analyzed including peak oxygen uptake (VO₂peak) and its derivatives (% from predicted VO₂ peak, Weber class, oxygen uptake efficiency slope), ventilatory indices (ventilatory equivalent for carbon dioxide VE/VCO₂, ventilatory class derived from VE/VCO₂, end-tidal carbon dioxide partial pressure at rest and at the peak load, exercise oscillatory ventilation), exercise blood pressure (BP) and ECG dynamics, heart rate (HR) recovery in 1 minute after test termination and reason for test termination. The prognostic value of combined Heart Failure Survival Score (HFSS) model (VO₂peak+LVEF+mean BP+serum sodium+coronary heart disease+QRS≥120ms+resting HR) was also evaluated.

Results: During follow-up 20 (18,0%) patients died of cardiac causes: 7 of sudden cardiac death and 13 of progression of CHF. In step-wise Cox regression analysis HFSS (hazard ratio [HR]=0,297; 95% confidence interval [CI]=0,159-0,556, $p = 0,002$) and ventilatory class (HR=4,517, 95% CI = 1,372-14,864, $p = 0,014$) had the highest predictive value for CVM. Addition of other CPET indices didn't further refine the prognosis based on these two parameters.

Conclusions: In patients with CHF, Heart Failure Survival Score based on VO₂ peak and ventilatory class have the highest prognostic value for cardiovascular mortality. Adding of other currently used CPET parameters does not qualify the prognosis.

PULMONARY HYPERTENSION

P1659

Non-invasive parameters vs right heart catheterization assessment in patients with pulmonary hypertension

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Diagnosis of pulmonary hypertension (PH) usually requires invasive assessment by right heart catheterization (RHC), but screening and monitoring of the disease are performed with the use of non-invasive

Methods: echocardiography and cardiopulmonary exercise testing (CPET). Here we aimed to assess the correlations between parameters obtained in non-invasive testing and RHC in patients with PH.

We retrospectively analyzed medical records of 49 patients with PH (30 women) aged 29-81 years (mean 61.1±14), hospitalized from 2008 to 2013, who underwent a total of 61 RHC procedures. Correlations between echocardiographic parameters: tricuspid annular plane systolic excursion (TAPSE), systolic, diastolic and mean pulmonary artery pressures (sPAP, dPAP, mPAP), right atrial pressure (RAP) and RHC parameters: pulmonary vascular resistance (PVR), cardiac output (CO), sPAP, dPAP, mPAP, were assessed in 56 cases. Associations between CPET parameters: end-tidal partial pressure of oxygen (PetO₂), end-tidal partial pressure of carbon dioxide (PetCO₂), peak oxygen uptake (VO₂peak) and RHC parameters - in 23 cases. RAP in echo was estimated based on diameter and respiratory variation

of inferior vena cava. Non-invasive CO assessment was calculated from equation: CO=VO₂peak/0.16.

Of various echocardiographic variables only TAPSE correlated with RHC parameters: PVR ($r = -0,62$, $p < 0,001$) and CO ($r = 0,62$, $p < 0,001$) estimated by the Fick method and measurements of sPAP, dPAP, mPAP ($r = -0,53$, $p < 0,001$, $r = -0,63$, $p < 0,001$, $r = -0,57$, $p < 0,001$, respectively). No correlation was found between RAP assessed in echocardiography and RHC. Only modest correlation existed between mPAP estimated in echocardiography and in RHC ($r = 0,54$, $p = 0,003$). The average deviation of echocardiographic mPAP measurement from actual in RHC was 11.61±12.99 mmHg (21.3% of the average RHC measurement of mPAP). CO calculated on the basis of peak VO₂ correlated with CO measured by Fick ($r = 0,64$, $p < 0,001$) and thermodilution method ($r = 0,56$, $p < 0,001$). PVR estimated by thermodilution and Fick method showed a positive correlation with PetO₂ ($r = 0,66$, $p = 0,014$ and $r = 0,65$, $p = 0,009$) and negative with PetCO₂ ($r = -0,58$, $p = 0,016$ and $r = -0,61$, $p = 0,02$) for measurements at the anaerobic threshold.

Conclusions: Simple indicators of cardiac function obtained by commonly used non-invasive methods allow only for approximate estimation of main hemodynamic RHC-derived parameters: mPAP, CO and PVR. The biggest challenge remains in proper evaluation of RAP by echocardiography. Alterations in PetO₂ and PetCO₂ may serve as a non-invasive indicator of increased PVR.

P1660

Evaluation of total pulmonary vascular resistance during exercise in patients with pulmonary hypertension

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Background: The total pulmonary vascular resistance (TPVR) contribute to afterload of the right ventricle (RV), significantly influencing its performance.

Purpose: Assess the behavior of TPVR with treadmill exercise (SE) in healthy subjects (controls) and in patients with pulmonary hypertension (PH) (cases).

Methods: Prospective study of 10 cases and 10 controls "age and sex-matched". They went SE, symptom-limited, using the modified Bruce protocol. We analysed at rest (R) and at peak exercise (E) the following parameters: heart rate (HR), diameter of left ventricle outflow tract (LVOT), velocity time integral (VTI) of LVOT, gradient between the right ventricle and right atrium (gradRV/RA), diameter of inferior vena cava and its collapsibility.

To determine the total pulmonary vascular resistance (TPVR) we calculated: cardiac output (CO), in L/min, using the formula - CO=stroke volume (SV)×HR, where SV=area×VTI of LVOT; mean pulmonary artery pressure (MPAP), in mmHg, using the formula of Chemla - MPAP = systolic pulmonary artery pressure (SPAP) × 0.6 + 2, where SPAP = gradVD/AD + the estimated right atrial pressure (RAP). We calculated the TPVR, in UWood, with the formula TPVR = MPAP/CO.

We analyzed the change in TPVR between rest and exercise for cases and controls.

Results: In cases there was a non significant increase in TPVR (R-11,8±5,0 to E-16,4±12,0 UWood ($p = 0,285$); in controls we verified an almost significant decrease in TPVR with exercise (R-2,4±0,6 to E-1,7±0,8 UWood ($p = 0,056$)).

Conclusions: The determination of the behavior of TPVR with exercise is feasible by treadmill exercise echocardiography. With exercise the TPVR in controls decrease, whereas in cases they do not decrease.

P1661

Role of ACE2 in pathomechanism of pulmonary hypertension

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Introduction: Pulmonary hypertension (PH) is a rare disease with mixed etiology caused by enlargement of the pulmonary arterial wall, reduction of the lumen, increasing of pulmonary vascular resistance and right heart failure. Mortality rate is higher than 59% in 5 year.

Aim: We wanted to evaluate the role of two important enzymes of RAAS (ACE, ACE2) in pathomechanism of pulmonary hypertension.

Materials and Methods: Clinical data and serum samples of 25 patients with pulmonary and 25 patients with systemic hypertension (as control) cured in our clinic were collected. We determined the amount of ACE in sera (by ELISA) and the activity of ACE and ACE2 (by synthetic fluorescence substrates).

Results: We could detect significantly higher ACE2 activity values (40.4±6U/l) compared with control group (22.6±2U/l, $p = 0,01$). This parameter is inversely proportional both to ejection fraction of left ventricle ($p < 0,05$) and to the tricuspid annular plane systolic excursion (TAPSE, $p = 0,019$) showing good correlation with right ventricular ejection fraction. We found significant, linear correlation between invasively measured right ventricular pressure values such as systolic (sPAP), mid (mPAP), and diastolic (dPAP) pulmonary arterial pressure and ACE activity in PH group (pmPAP=0.0262, n=9, psPAP=0.0104, n=11, pdPAP=0.0011, n=11). The

ACE activity linearly decreased with increasing of right ventricular pressure values. The activity of ACE2 increased parallel in direct ration with mPAP ($p = 0.0099$, $n=13$). There was no significant connection in amount of ACE and ACE activity between the two groups. There was no correlation with echocardiographic parameters such as diameter of left atrium, left ventricle, wall thickening, calculated right ventricular pressure and activity of ACE, ACE2 and amount of ACE.

Conclusion: Our data show an important role of ACE2 shedding in pathomechanism of pulmonary hypertension. Paralell with progression of PH circulating ACE2 level increases, the tissue level may decrease. Nevertheless ACE2 might be an important biomarker in diagnostic procedure or evaluation of PH progression.

P1662

Description of the clinical, functional and hemodynamic characteristics of patients with pulmonary arterial hypertension group 1 secondary to grown-up congenital heart disease at 2600 meters above sea

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Introduction: There is a scarce knowledge about the characteristics of patients with pulmonary arterial hypertension (PAH) secondary to grown-up congenital heart disease residing in Bogotá (2.640 meters above sea level). The description of a selected population, not necessarily a representative, can be an approach to the behavior of PAH in our environment.

Objective: To describe the clinical, functional, and hemodynamic characteristics in a selected population of patients diagnosed with PAH (WHO group 1) secondary to grown-up congenital heart disease belonging to institutional HAP programs in five reference centers in Colombia at 2600 meters.

Material and Methods: The study was observational, retrospective, and included patients aged 18 and over with diagnosis of PAH by right hearth catheterization (R.H.C), between January of 2008 and June of 2014. Demographic, clinical, functional, and hemodynamic variables were analyzed, qualitative variables were described by absolute and relative frequencies, quantitative variables were analyzed with measures of central tendency and dispersion. Data were collected through a questionnaire, using the medical records of patients registered in each of the participating institutions.

Results: From a cohort of 107 patients who met the diagnosis of PAH type 1, 24,3% had a diagnosis of PAH secondary to grown-up congenital heart disease (n26), 72% where women (48 ± 16 years). The most common etiologies were atrial septal defect and patent ductus arteriosus. At the moment of diagnosis, 87% were in functional classes II and III (NYHA), with a distance on the six-minute walk test of $414 \text{ m} \pm 110 \text{ m}$ and mean pulmonary arterial pressure (mPAP) severely increased ($73 \pm 20 \text{ mmHg}$). Pulmonary vascular resistance of 8.9 ± 6.8 woods units and cardiac index $8 \pm 3 \text{ min/m}^2$. 27% were on supplemental oxygen and 15% on anticoagulants, specific treatment was initiated in the 95% of patients, as monotherapy in 23%, in double combination therapy 23% and triple therapy 25%.

Conclusion: This research is one of the first performed in our city, to know the clinical characteristics of grown-up congenital heart disease PAH patients at 2600 mts above the sea level. It was identified that there are many gaps in our knowledge about the disease, reflected in the late diagnosis and initiation of treatment. One limitation found in this study is the total sample obtained. It is suggested to conduct research at this height above sea level in patients with PAH to consolidate data and learn more about the characteristics and behavior in our population.

P1663

Pulmonary artery systolic pressure and heart failure: effect on prognosis

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Purposes: Pulmonary hypertension in heart failure (HF) is associated with a worse prognosis. The estimated value of pulmonary artery systolic pressure (PSAP), determined by transthoracic echocardiogram, seems to be an acceptable alternative to right ventricle catheterization. The objective of this study is to evaluate the prognostic impact of PSAP in patients admitted for HF, when accessing mortality/hospital readmission rate (M/Ra) at 3, 6, 12, 18 and 24 months (M).

Methods: A retrospective study was performed on patients admitted for HF. Clinical symptoms along with vital signs, blood work and echocardiogram imaging were evaluated. Patient follow-up was maintained for 24 months. The study population was divided into 2 groups: Group A (GA) with PSAP < 40mmHg vs Group B (GB) $\geq 40 \text{ mmHg}$. Statistical analysis was performed using SPSS and considered significant if $p < 0.05$.

Results: A study population included 638 patients, 49.2% men, mean age 76 ± 10 years. No statistical difference was found when comparing age, sex and patient medical history.

Higher hemoglobin and sodium values, as well as a superior creatinine clearance,

was noted in GA patients. GB patients presented greater brain natriuretic peptide (BNP) values. On echocardiogram evaluation, GB patients presented with more severe diastolic dysfunction.

A statistical difference was found when determining the cause of heart failure, particularly heart failure due to valve disease (33.2% vs 46.6%, $p < 0.001$). Mitral valve insufficiency was found to be statistically relevant (48.6% vs 70.2%, $p < 0.001$), more frequently severe in GB patients (10.0% vs 36.6%, $p = 0.021$).

No statistically difference was found when comparing worsening renal function. During hospital-stay, complications were more prevalent in GB subjects (8.1% vs. 12.0%, $p = 0.044$), most notably nosocomial infections (3.1% vs 6.0%). GB had a statistically longer hospital-stay (7.7 vs 9.9 days, $p < 0.001$).

Endpoint evaluation confirmed a greater M/Ra rate in GB consistent during the 24 month follow-up (19.6% vs 28.4%, $p = 0.020$, log rank 0.017 at 3M; 30.2% vs 39.8%, $p = 0.041$, log rank 0.026 at 6M; 42.3% vs 53.1%, $p = 0.015$, log rank 0.008 at 12M; 51.6% vs 62.4%, $p = 0.015$, log rank 0.009 at 18M; 54.9% vs 66.3%, $p = 0.009$, log rank 0.005 at 24M). Multivariable statistical analysis proved these differences where independent of mitral valve insufficiency.

Conclusion: Pulmonary hypertension, determined by PSAP value, in patients with HF is associated with a worse short-term, as well as long-term, prognosis.

P1664

NT-proBNP and six minute walk test predict mortality in patients with precapillary pulmonary hypertension

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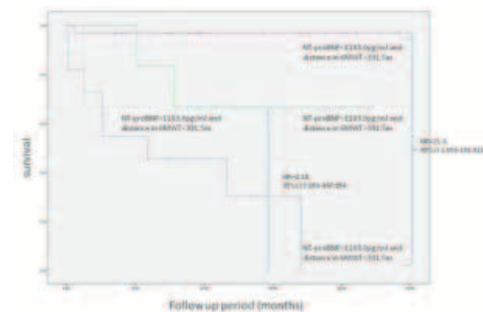
Purpose: NT-proBNP plasma levels and distance walked in six minute walking test (6MWT) are recognized predictive parameters in patients with precapillary pulmonary hypertension (pPH). The aim of our study is to explore the additive role of 6MWT in the prognostic significance of NT-proBNP in patients with pPH.

Methods: This is a prospective study. All patients underwent 6MWT, while NT-proBNP plasma levels were determined during the same clinical assessment.

Results: Our study included 50 patients (34 women, mean age 50.6 ± 16.2 years) with pPH that walked $403.4 \pm 153.9 \text{ m}$ in 6MWT. Baseline NT-proBNP levels were 520.0 pg/ml (IQR 369.5-2774.1). Over a median follow up period of 18.2 months (IQR 4.9-41.3 months) 12 patients died. Cox proportional hazard analysis demonstrated that NT-proBNP plasma levels and distance walked in 6MWT were independent predictors of mortality. ROC curve analysis showed that the optimal cut-off value to predict mortality was 1183.0 pg/ml for NT-proBNP and 331.5 m for 6MWT. Kaplan-Meier survival analysis showed that patients with NT-proBNP $> 1183.0 \text{ pg/ml}$ had 8.8-fold increased risk of death compared with patients with lower NT-proBNP levels, as well as that patients that walked $< 331.5 \text{ m}$ in 6MWT had 7.7-fold increased risk of death compared with those that walked more.

When combining both NT-proBNP and 6MWT distance, Kaplan-Meier survival analysis showed that patients with NT-proBNP $> 1183.0 \text{ pg/ml}$ and 6MWD $< 331.5 \text{ m}$ have 2-fold (95%CI 7.053-847.954) increase in the risk of death compared to patients with NT-proBNP $> 1183.0 \text{ pg/ml}$ and 6MWD $> 331.5 \text{ m}$ and 21-fold (95%CI 1.058-198.812) increase in the risk of death when compared to patients with NT-proBNP $< 1183.0 \text{ pg/ml}$ and 6MWD $> 331.5 \text{ m}$ (figure).

Conclusions: The combination of NT-proBNP and 6MWT is a strong predictive tool in patients with pPH.



Kaplan-Meier curve

P1665**The prognostic significance of the interaction between serum albumin levels and pulmonary hypertension secondary to heart failure**R Robert Dragu¹; M Habib¹; S Rispler¹; R Zukerman¹; D Aronson¹¹Rambam Health Care Center, Haifa, Israel

Purpose: Hypoalbuminemia is frequently observed in patients with established left heart failure (LHF) and is independently associated with increased mortality risk. The aim of the present study is to determine the impact of pulmonary hypertension (PH) secondary to LHF, on hepatic synthetic function, and the relationship between serum albumin levels and survival.

Methods and Results: Of 431 patients with chronic LHF who underwent right heart catheterization, 292 presented with PH. Right atrial pressure (RAP) was higher (13.3 ± 6.6 mmHg vs. 5.8 ± 3.1 mmHg, $p=0.0001$), while albumin serum levels were lower (3.55 ± 0.53 mg/dl vs. 3.75 ± 0.52 mg/dl, $p=0.009$) in patients with PH as compared with those without PH.

During the follow-up (median 33.9 months), 41.7% of patients with PH died, as compared with only 18.4% in the HF and no-PH group. The nonlinear relationship between albumin levels and likelihood of mortality was detected using restricted cubic spline transformations. In an univariate Cox proportional model, the hazard ratio (HR) for all-cause mortality for serum albumin, as a continuous variable, was 0.54 (95% confidence interval (95%CI) 0.38-0.78, $p=0.001$). In multivariate analysis, after adjustment for age, gender, RAP, pulmonary capillary wedge pressure, estimated GFR and pulmonary hypertension, the HR was 0.57 (95%CI 0.38-0.87, $p=0.001$), indicating a 43% increase in all-cause mortality for every 1 gm/dl reduction in serum albumin level.

Conclusion: In patients with chronic left heart failure and pulmonary hypertension, elevated right heart filling pressures may affect the hepatic synthetic function. Albumin serum level is a strong independent marker for mortality in LHF and may contribute to the increased mortality associated with PH.

HYPERTENSION/LV HYPERTROPHY**P1666****Salivary alpha-amylase levels and heart rate variability in hypertensive patients with left ventricle diastolic dysfunction**This study was supported by research internal grant (n°29234/2013) from "Grigore T. Popa" University of Medicine and Pharmacy Iasi, Romania. L. C. Dima Cozma¹; F. Mitu¹; C. M. Ghiciuc¹; F. R. Patacchioli²¹Gr. T. Popa University of Medicine and Pharmacy, Iasi, Romania; ²Sapienza University of Rome, Rome, Italy

Purpose: At this stage of research, evaluation of diurnal trajectory of salivary alpha-amylase (SAA) could be useful as a new noninvasive index of autonomic nervous system (ANS) dysregulation in different clinical conditions. The aim of this study was to describe the profile of SAA in hypertensive patients with left ventricle diastolic dysfunction and to establish the possible correlations with heart rate variability (HRV) parameters.

Methods: 10 male patients (mean age 57 ± 2.4 years) with documented hypertension (24 h mean systolic blood pressure - SBP, 164 ± 4.1 mmHg and 24 h mean diastolic blood pressure - DBP, 90 ± 2.1 mmHg) and 7 male controls (mean age 57 ± 1.7 years, 24 h mean SBP 125 ± 1.3 mmHg and 24 h mean DBP 78 ± 0.7) were investigated. To estimate left ventricle diastolic function an analysis of transmitral flow pattern by Doppler method was used. HRV parameters were measured with patients in the sinus rhythm (standard deviation of RR-intervals, SDNN, SDANN, and the standard deviation of RR-intervals, rMSSD).

Results: Mean heart rate was higher in hypertensive patients (81 ± 1.6 vs 70 ± 1.7 bpm, $t=-4.701$, $p<0.001$). The AUC 7-20 for SAA was 35414 ± 1467 ng/ml/min in control males and 38354 ± 1382 ng/ml/min in hypertensive patients. E/A ratio (1.2 ± 0.05 vs 0.85 ± 0.15 in hypertensives) and isovolumic relaxation time (IVRT) (164.77 ± 33.77 vs 230.43 ± 35.9 in hypertensives) had significantly variations between groups. SDNN was significantly higher in hypertensive patients (120 ± 16 vs 92 ± 24 ms, $p=0.001$), as well as SDANN (104 ± 20 vs 76 ± 23 ms, $p=0.01$). There was correlation between IVRT and SDNN ($r=0.51$, $p<0.005$) and between SAA AUC and SDANN in hypertensive patients ($r=0.42$, $p=0.004$).

Conclusions: Parameters of HRV sympathetic activity are correlated with diastolic dysfunction and SAA in hypertensive patients.

P1667**Ramadan fasting induces modifications on ambulatory blood pressure in treated hypertensives?**I Ichraq Nassiri¹; M Abellhad¹; I Nouamou¹; R Habbal¹¹Ibn Rochd University Hospital, Department of Cardiology, Casablanca, Morocco

Introduction: Fasting of Ramadan is a religious obligation that is practiced by the Muslim population in the world. However, there is a lack of scientific literature regarding the effects on cardiovascular disorders such as hypertension.

Objective: This study was conducted to assess the impact of Ramadan fasting on blood pressure in treated hypertensive patients.

Materials and Methods: This prospective observational trial was conducted on 18 patients treated for hypertension, who were determined to end the fast of Ramadan. All subjects were on antihypertensive therapy. Measurements of blood pressure was performed by Holter blood pressure (24 hours) before and after the month of Ramadan.

Results: The mean age of subjects was 57.61 ± 12.64 years; with a female predominance. There was a significant decrease in average diastolic 24-h ambulatory blood pressure, as well as average diastolic awake ambulatory blood pressure after Ramadan (70.72 ± 9.24 mmHg vs 65.06 ± 8.23 mmHg, $P=0.01$ et 73.72 ± 10.10 mmHg vs 70.06 ± 9.43 mmHg, $P=0.01$). Average systolic 24-h ambulatory blood pressure, as well as average awake systolic and average asleep systolic and diastolic ambulatory blood pressure was similar before and after Ramadan (125.50 ± 11.62 mmHg vs 122.94 ± 10.09 mmHg, $P=0.08$; 128.44 ± 12.19 mmHg vs 126.11 ± 10.80 mmHg, $P=0.06$; 120.67 ± 13.20 mmHg vs 119.83 ± 13.76 mmHg, $P=0.73$; 65.72 ± 8.84 mmHg vs 65.72 ± 8.84 mmHg, $P=0.81$)

Conclusion: We conclude that, according to our results, hypertensive patients can continue their treatment as the traditional fasting during Ramadan can be performed safely.

P1668**Endothelial dysfunction in hypertensive patients with chronic obstructive pulmonary disease or bronchial asthma**OV Olena Soya¹; OV Kuryata¹¹Dnipropetrovsk State Medical Academy, Dnipropetrovsk, Ukraine

Background: The question concerning influence chronic obstructive pulmonary disease (COPD) and bronchial asthma (BA) on cardiovascular risk factors remain debatable. The aim of study - to assess serum lipid levels and endothelial function in comorbid patients with hypertension and COPD or BA.

Methods: Were observed 28 hypertensive patients (23 male) with COPD (mean age 57.3 ± 4.5 years; forced expiratory volume (FEV1) = $61.7 \pm 4.9\%$) and 30 patients (21 mail) with BA (mean age 55.2 ± 5.0 , FEV1 = $69.6 \pm 5.1\%$). There was studied endothelial dysfunction by methodics of D. Celermajer with duplex ultrasound scanning of the right brachial artery. The patients in both groups were compared according to blood pressure level, smoking status and body mass index.

Results: The dysfunction of endothelial depended vasodilatation had 78,3% patients with COPD (75% - decreased endothelial depended vasodilatation and 25% - pathological vasospasm) and 47,6% patients with COPD (80% - decreased endothelial depended vasodilatation and 20% - pathological vasospasm). Serum level of total cholesterol was higher in COPD patients (5.87 ± 0.3 vs 5.07 ± 0.2 mmol/l, $P<0.05$), and lipoproteins level was increased in COPD group (53.5 ± 2.8 vs 42.5 ± 2.6 mmol/l, $P<0.05$). No significant difference was found between HDL-cholesterol and triglycerides levels in both groups.

Conclusion: In patients with arterial hypertension and COPD more often occurs remodeling of the vascular wall, which may be one of the links in the further development of cardiovascular diseases. Patients with arterial hypertension and BA showed lower serum levels of total cholesterol and lipoproteins compared to hypertensive patients with COPD. Thus, COPD could increase a cardiovascular risk for comorbid hypertensive patients.

P1669**Risk of development and progression of left ventricle hypertrophy depending on arterial wall stiffness in patients with arterial hypertension and chronic heart failure**N Natalia Koziolova¹; M Surovtceva¹; A Chernyavina¹¹Medical Academy, Perm, Russian Federation

Aim: to evaluate relative risk of development and progression of left ventricle hypertrophy (LVH) depending on arterial wall stiffness in patients with arterial hypertension (AH) and ischemic chronic heart failure (CHF) with preserved LV ejection fraction (LV EF).

Methods and materials: 90 patients with CHF and stable angina were examined. 38.2% got a MI in past. Average age was 56.2 ± 6.4 yrs. Male 58.8%, female 41.2%. Duration of angina was 5.9 ± 2.6 yrs, average functional class (FC) 2.27 ± 0.37 . Duration of CHF was 6.2 ± 2.1 , average FC 2.52 ± 0.08 , average LV EF $60.5 \pm 9.3\%$. Duration of AH was 6.7 ± 2.8 yrs. Aim BP was achieved in 83,2%.

LVH was estimated by LVMMI. To estimate arterial wall status volume sphygmography was done with VaSera VS-1000 device. To evaluate collagen matrix condition TIMP-1 was used. Also NT-proBNP level has been evaluated to confirm CHF presence and to evaluate myocardial stress severity. To study interconnection between the parameters Hazard ratio (HR) and Relative risk (RR) (95% confident interval - CI) have been established.

Results: in PWV in aorta > 6.0 m/sec HR of LVMMI elevation increased in 11,33 (95% CI= $1.36-252.22$), RR in 1,54 (95% CI= $1.09-1.69$), ($p=0.018$). In increase of PWVcf > 12.0 m/sec HR was 38,7 (95% CI= $4.07-898.86$), and RR - 20,84 (95% CI= $3.14-428.84$), ($p=0.0006$).

Increase of CAVI1 > 9.0 has accompanied with significant increase in RR of LVH in 18,53 (95% CI=2,69-385,73) and with HR 31,27 (95% CI=3,28-728,08), (p=0,0008). Along with NT-proBNP elevation > 400 pg/mL there was significant increase of LVH estimated in 12,86 (95% CI=3,57-49,13) with HR 4,08 (95% CI=2,08-7,82) (p=0,0005). Also, along with NT-proBNP elevation > 700 pg/mL there was significant increase in risk of arterial wall fibrosis development according to TIMP1 level: in TIMP1 > 138 ng/mL HR consisted of 33,07 (95% CI=5,83-224,9); and RR - 8,64 (95% CI=2,99-32,06), (p=0,0005).

Conclusion: in patients with AH and CAD, complicated with CHF and preserved LV EF, an arterial wall stiffness elevation has accompanied with reliable increase of relative risk in development and progression of LVH and myocardial stress. Also, disorders in collagenolysis were observed. In complex, it testifies that these unfavorable ventricular and vascular interconnections are forming in these patients.

P1670

Remodeling of the left ventricle and the rate of formation of superoxide radical in patients with hypertension, working under the influence of EMR UHF

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Materials and Methods: The study involved 48 men (mean age 37,6 ± 6,4 years) with hypertension (group I). Working period under the influence of EMR UHF composed from 4 to 22 years. The received dose from EMR UHF was from 4320kVt to 31065 kVt for the entire period of work (on average 17151,7 ± 7102,4 kVt). The comparison group included 35 men with hypertension with corresponding sex and age without the influence of harmful factors of production. Patients in both groups received antihypertensive treatment in accordance with the recommendations of the European Society of Cardiology. All patients underwent left ventricular geometry by echocardiography and were daily measured for urine marker of oxidative DNA damage 8-oxodGu by spectrophotometry using the SF-46 unit.

Results: In 30% of patients in group 1 relative wall thickness did not exceed 0.45 infarction, in patients of group 2 - in 27.5% of cases. In 26% of the patients of group 1 revealed a normal left ventricular geometry and speed urinary excretion of 8-oxoG 4,4 ± 2,4 nmol/kg/day, in 41% of the patients - concentric hypertrophy and speed of urinary excretion of 8-oxoG 10,8 ± 2,3nmol/kg/day, in 29% - concentric left ventricular remodeling at the speed of urinary excretion of 8-oxoG 7,9 ± 1,2 nmol/kg/day and only in 4% of patients - eccentric left ventricular hypertrophy with speed of urinary excretion of 8-oxoG 8,5 ± 2,4 nmol/kg/day.

In group 2 normal LV geometry was found in 24% of patients and speed of urinary excretion of 8-oxoG 9,6 ± 1,2 nmol / kg / day, concentric LV hypertrophy - in 37%, the rate of urinary excretion of 8-oxoG 7,8 ± 0,9 nmol / kg / day, concentric LV remodeling - in 35%, the rate of urinary excretion of 8-oxoG 12,1 ± 2,4 nmol/kg/day, eccentric LVH - in 4%, the rate of urinary excretion 8-oxoG 6,1 ± 1,8nmol/kg/day.

Conclusion: It was not found pattern changes in the rate of formation of superoxide radical depending on the type of LV remodeling.

P1671

Clinical Impact of obesity on blood pressure levels in childhood

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The presence of obesity in childhood increases the risk of metabolic syndrome and it is an important cardiovascular risk factor. The aim of our study was to analyse the effects of obesity on blood pressure levels among children with obesity.

Methods: Cross-sectional study of 51 children with obesity. Demographic and anthropometric data were gathered. Blood tests were also performed to check for blood glucose, total cholesterol, and triglycerides. Obesity was defined as BMI value exceeding ≥95th percentile. Blood pressure (BP) was obtained and evaluated according to the National High Blood Pressure Education Program Working Group, subjects whose blood pressure was above the 90th percentile of the standard normal distribution were considered to have high blood pressure.

Results: High blood pressure was identified in 27 (52.9%) children of the study population. The mean systolic blood pressure for hypertensive children was 133.9 ± 5.4 mmHg compared to normotensive children 107.8 ± 10 mmHg. Diastolic blood pressure was 77.4 ± 6.3 mmHg vs. 60.6 ± 7.2 mmHg. They had high blood pressure in 50% of man and 54.8% of girls. Children with high blood pressure were characterized by older age 11.07 ± 6 vs. 9.2 ± 2.2 years, p=0.002; high cholesterol 174.8 ± 25 mg / dl vs. 148.5 ± 26 mg / dl, p=0.018, body mass index (BMI) 95.3 ± 9.4 kg/m² vs. 89.7 ± 9 kg/m², p=0.033 and higher body weight 72.9 ± 14 kg 56.16 ± 12.9kg, p=0.001. In multivariate logistic regression analysis we found the independent

predictors of had high blood pressure: BMI [OR=3.45 (95% CI 1.033 to 11.51), p=0.04]; Low-density lipoprotein cholesterol (LDL) [OR=1.15 (95% CI 1.002 to 1.323), p=0.04] and as protective factors had low cholesterol [OR=0.87 (95% CI 0.779 to 0.982), p=0.024].

Conclusions: In our series, the obesity increases the likelihood of having high blood pressure. The anthropometric parameters such as BMI and lipid profile are especially useful for identifying children with high blood pressure.

P1672

The rigidity of the arteries of patients with arterial hypertension of advanced and senile age depending on pulse arterial pressure

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Aim: To analyze the rates of the rigidity of the arteries of patients with arterial hypertension (AH) of advanced and senile age depending on size of pulse arterial pressure (PAP).

Materials and methods: 26 patients of advanced and senile age were examined, aged from 61 to 83 (mean age is 70,8 ± 6,4 years old) with arterial hypertension of 2-3 degree, 19 of them are with PAP ≥51mmHg (in average 62,8 ± 9,8 mmHg) and 7 are with PAP ≤50 mmHg (in average 45,7 ± 3,6 mmHg). The experience of AH is from 3 to 40 years (in average 20,6 ± 12,1 years). All patients were carried out daily monitoring of arterial pressure (DMAP) with determination of parameters of a rigidity of the central and peripheral arteries with averaging of indicators for 24 hours "BPLab" (Nizhny Novgorod).

Results of the research. Due to daily monitoring of arterial pressure systolic (SAP), diastolic (DAP) and average (AAP) for 24 hours arterial pressure of patients with PAP ≥51 mmHg was for certain higher than of patients with PAP ≤50 mmHg. Thus the time of reflected wave transit time (RWTT) and pulse wave velocity in aorta (PWVao) of patients with high PAP were greater than in the group with PAP ≤50 mmHg for 2,3% and 9,9% respectively that corresponded to the increase of stiffness of the vascular wall. Arterial stiffness index (ASI) and ASI equated to SAP =100 mmHg and heart rate (HR) =60 beats/sec was higher for 36,6% and 48,4% in comparison with similar index in PAP ≤50 mmHg group. Augmentation index (Aix) was positive in both groups. But Aix equated to HR 75 beats/sec in group of patients with PAP ≤50 mmHg was negative while in group with PAP ≥51 mmHg it was positive. Ventricular Contractility Assessment (dP/dt) in brachial artery was for certain higher in PAP ≤50 mmHg group.

Conclusions: Thus, the received results of velocity and density of pulse and reflected waves transit attested to distinction of degree and rigidity of walls of aorta and peripheral vessels of patients of advanced and senile age with AH and different PAP. In this way the more expressed density of reflected pulse wave (according to average Aix) was noticed at patients with PAP ≥51 mmHg that apparently may serve as an additional predicative parameter of an adverse course of isolated systolic AH. Reflected wave transit time, ambulatory arterial stiffness index decreases at PAP ≥51 mmHg

HFpEF – HEART FAILURE WITH PRESERVED EJECTION FRACTION

P1673

Diastolic heart failure: what's new in diagnosis, MEDIA study

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Background: The diastolic heart failure (DHF) amounts the 50% of cases of heart failure. Diagnosis and prognosis of this disease are still uncertain. The diagnosis of DHF is based on signs and symptoms of heart failure, normal or mildly abnormal left ventricular ejection fraction (LVEF) and evidence of left ventricular (LV) diastolic dysfunction (DD) identified by Doppler evidence of increased LV filling pressure. The plasma values of natriuretic peptides (BNP or proBNP) are correlated with symptomatic LVDD.

Object of the study: identify and study patients with DHF diagnosed on the criteria already defined by the European Study Group in order to validate biomarkers and compare them with arterial stiffness parameters.

Methods: enroll patients with signs and symptoms of heart failure (NYHA class> II) that meet the criteria previously established (Eur Heart J. 2007 Oct; 28 (20):2539-50): 1) normal or mildly reduced left ventricular ejection fraction, 2) echocardiographic evidence of diastolic dysfunction (E/E' > 15); a)E/A >0,5 and DT>280 ms b) Ard-Ad > 30 ms; c) LAVI (left atrial volume index)>40 ml/m²; d) LVMI (left ventricular mass index)>122g/m² for women and > 149g/m² for men; e) atrial fibrillation. Determination of NTpro-BNP>220 pg / ml. Finally we use applanation tonometry method to determinate the arterial stiffness by the pulse wave analysis (PWA) and pulse wave velocity (PWV).

Results: We enrolled 52 patients (EF 59.15 ± 6.3). Only 8 patients demonstrated an E/E' >15 at the echocardiogram, 44 patients had E/E' values between 8 and 15 (10,13 ± 2.06). No patients had E/A <0.5 and DT >280 msec. An Ard-Ad >30 ms (60,5 ± 27.5) was present in 36 patients, LAVI >40 ml/m² in 40 patients (61,85 ± 19.15) and a LVMI >122g/m² in 16 female patients (144 ± 22) and LVMI >149 g/m² in 10 male patients (163,3 ± 13.1), 10 patients had atrial fibrillation and 4 patients a rhythm induced by pacemaker. Finally, regarding the biomarkers, we observed values greater than 220 pg/ml of NTpro-BNP in 49 patients (mean 1484,3 pg/ml); in 3 patients the NTpro-BNP values were less than 220 pg/ml but always in the range of pathological values. Up to now, we compare the pulse wave analysis (PWA) with E/E': at higher values of E/E' are the highest values of PWA.

Conclusion: important results have emerged from the validation of the diagnostic criteria for DHF. In particular, Ard-Ad >30 ms and LAVI are demonstrated present in almost patients in patients in sinus rhythm. These are the preliminary data because the study has been recently completed and in a few weeks we'll get the final statistics between different diagnostic methods used.

P1674

Heart failure with preserved and reduced left ventricular ejection fraction- from hospital presentation to outcome

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Purpose: Heart failure with preserved left ventricular ejection fraction (HFpEF) (LVEF) is a matter of growing interest, due to insufficient data about its characteristics and outcomes. The aim of this study was to investigate the differences in hospital presentation and long term survival between acute heart failure (AHF) patients (pts) with HFpEF, and reduced LVEF (HFrEF).

Methods: We included 168 patients (pts) (mean age 72 ± 8.3 years, 60.1% male) hospitalized due to AHF. Routine laboratory measures and physical examination were done at presentation. LVEF was measured by standard two-dimension echocardiography. HFpEF was defined as HF with LVEF > 45%. Based on LVEF, pts were divided in two groups: Group I (HFrEF; 70.2%) and Group II (HFpEF). The outcome of interest was death during one year after hospitalisation.

Results: Mean LVEF was 32.2% in Group I, and 51.9% in Group II ($p < 0.001$). There were no differences between groups with regard to: age, clinical presentation (New York Heart Association- NYHA Class, heart rate, peripheral oedema, rales, hepatomegaly, diastolic arterial tension), presence of comorbidities (arterial hypertension, atrial fibrillation, chronic kidney failure, diabetes mellitus, chronic obstructive pulmonary disease), tobacco use, HF etiology, de-novo AHF rate. Pts with HFpEF had higher systolic tension (146.2 vs. 137.3 mmHg, $p = 0.029$) and lower haemoglobin (116.4 vs. 129 g/l, $p = 0.001$). HFrEF was associated with male gender (83.2 vs. 62.7%, $p = 0.003$), higher end-diastolic diameter (EDD) (62.3 vs. 54.8 mm, $p < 0.001$), N-terminal brain natriuretic prohormone (NT-proBNP) (7442.2 vs. 5212 pg/ml, $p = 0.007$), bilirubin (20.9 vs. 16.3 umol/l, $p = 0.041$), aspartat and alanin transaminase (61.2 vs. 34.7 IU/l, $p = 0.014$; 60.3 vs. 33.1 IU/l, $p = 0.046$), gama-glutamyl transferase (101.5 vs. 59.1 IU/l, $p = 0.003$), alcohol use (86.4 vs. 71%, $p = 0.043$). Other laboratory parameters were similar in both groups. All pts were similarly treated after hospitalization, except for calcium channel blockers, which were more used in Group II (32.4 vs. 15.1%, $p = 0.019$). Forty-one patient died during one year follow up (28.5%) and 24 were lost. LVEF wasn't associated with the one year death event, and pts from both groups had similar outcome risk ($p = 0.137$).

Conclusion: At hospital presentation, patients with HFrEF are usually men with higher NT-proBNP, liver enzymes and EDD, comparing to HFpEF patients who only show higher systolic arterial tension. Despite this presentation differences end echocardiographic measures, long term outcome of HFpEF is as poor as for HFrEF.

P1675

Patterns of heart failure with preserved ejection (HFpEF) fraction in diabetics from southeast asia

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Introduction: Diabetes mellitus increases the risk of heart failure independent of coronary heart disease and hypertension. It is also associated with diabetic cardiomyopathy of which the epidemiology is not well defined. We sought to study the pattern of HFpEF in an asymptomatic diabetic population from Malaysia.

Objectives: To assess prevalence of HFpEF and the predicting factors.

Methods: Subjects were recruited as part of a community study on cardiovascular diseases between the years 2007 to 2011. Demographic details, cardiovascular risk

factors along with echocardiogram were obtained. An exclusion criterion is abnormal left ventricular ejection fraction less than 40%.

Results: A total of 1932 subjects with echocardiogram were analyzed. Mean age was 54.6 ± 11.6 . Majority of the subjects were male 98.3% (1899). Mean systolic ejection fraction (EF) was 64.5% ± 7.0 . Prevalence of HFpEF was 52.8% (1021). Of all the subjects with HFpEF, 29.9% (578) had impaired relaxation, 21.0% (406) pseudonormal and 1.9% (37) restrictive defect. In subjects with HFpEF, 26.1% (266) were diabetic and 9.6% (185) were pre-diabetic (impaired fasting glucose). 60.6% (619) had dyslipidemia of LDL level more than 3.4 mmol/L. 32.9% (336) were hypertensive and 64.0% (653) were obese. Table below summarize the univariate analysis of the cardiovascular risk factors among the subjects with HFpEF. In multivariate analysis hypertension was the only predictor of HFpEF $\beta = -0.65$, $t(505) = 18.6$, $p < 0.001$. OR of hypertensive subjects to get HFpEF is 0.52 (0.39-0.70).

Conclusion: The prevalence of HFpEF in our findings is higher than reported. Diabetes mellitus, hypertension and obesity remained significant risk factors associated with risk of developing HFpEF. After adjusted, hypertension remains a strong predictor for HFpEF.

CV risk factors in diabetics HFpEF

CV risk factors	Diastolic dysfunction (%) N=1021	No diastolic dysfunction (%) N=911	P value	OR	95% CI
Diabetes	26.1	12.1	0.04	0.76	0.58-0.99
Hypertension	32.9	18.6	< 0.001	0.45	0.38-0.57
Dyslipidemia	60.6	59.5	0.37	-	-
Obesity	64.0	57.3	< 0.001	0.66	0.55-0.79

P1676

Beta blockers in heart failure with preserved left ventricle ejection fraction

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Introduction: It is estimated that about 50% of patients over 70 years old with symptoms of heart failure (HF) have a "diastolic heart failure" or HF with preserved left ventricle ejection fraction (HFpEF). Patients with HFpEF have a poor prognosis and even asymptomatic patients with diastolic dysfunction are at increased risk for adverse cardiovascular events. Optimal therapy for left ventricle (LV) diastolic dysfunction is unknown. Beta blockers are widely used in this indication however we do not have data from randomized clinical trials to support their short and long term benefits.

Objective: The aim of our study was to determine the effects of up-titration of beta blockers on diastolic function in patients from CIBIS ELD trial.

Methods: 250 patients from CIBIS ELD trial had HFpEF (LV ejection fraction $\geq 45\%$), however we enrolled in this sub-study only 176 patients (age 73.4 years, 34% male) in whom adequate echocardiographic measurements could be obtained. Prior to randomization participants had to be clinically stable and beta-blocker naive or on $\leq 25\%$ of the guideline-recommended target or equivalent dose. We gradually increased beta blocker daily dose (either bisoprolol or carvedilol) up to maximum tolerated dose during 3 months. Diastolic function was assessed using an A/E ratio obtained from mitral inflow Doppler echocardiography (grade I of diastolic dysfunction defined as an E/A ratio <0.8 m/s; grade II as an E/A ratio 0.8-1.5 m/s; grade III-IV: E/A >1.5 m/s). NT-proBNP - marker of ventricular dysfunction was measured at the beginning and at the end of the study.

Results: Grade of diastolic dysfunction increased significantly during the study (grade I: 60.8% vs. 44.9%; grade II: 38.6% vs. 54%; grade III-IV: 0.6% vs. 1.1%, $p < 0.001$). Accordingly, NT-proBNP increased at the end of study (523.6 vs. 445.5 pg/mL, $p = 0.25$) though insignificantly.

Conclusions: During an up-titration of the beta blocker diastolic function in patients with HFpEF significantly deteriorated. The goals of therapy for HFpEF are to normalize cardiac loading conditions, and optimize the resting heart rate to provide normal separation of early and late diastolic filling which could be achieved by beta blockers. Our results suggest that gradually increasing of the beta blocker dosage in HFpEF patients in line to achieve lusitropic effect has no effects as we could theoretically expect. Increasing number of patients with HFpEF and enduring therapy challenges advocate the need for controlled randomized trials.

P1677

Factors affecting 30-day rehospitalization in heart failure with preserved ejection fraction: a perspective from Indonesian patients

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Purpose: Rehospitalization among Heart Failure (HF) patients is not uncommon, and several factors have been studied as possible causes. Because its characteristic differences with other forms of HF, HF with Preserved Ejection Fraction (HFpEF) needs to have studies on factors affecting its rehospitalization rate. To our knowledge, there have been no such studies in Indonesia before.

Method: 198 rehospitalized HFpEF patients' data were collected from the 2012 HF registry in National Cardiovascular Center Harapan Kita. Patients' data were then grouped into two (≤ 30 days and > 30 days of previous hospitalization). The variable was analyzed in respect to possible factors, including prior/current history of medical condition and medication prior to rehospitalization, using bivariate and multivariate analysis. All data referred to European Society of Cardiology (ESC) Heart Failure registry.

Result: Bivariate analysis showed that prior usage of ARB and diuretics, no prior ACE inhibitor usage, history of myocardial infarction (MI)/angina, chronic kidney dysfunction (CKD), Coronary Artery Bypass Graft (CABG) surgery, and valvular surgery were moderately related with 30-day rehospitalization ($p < 0.25$). After multivariate analysis, only prior usage of ARB ($p = 0.01$ OR 2.681 (CI95% 1.266-5.680)) and MI/angina history ($p = 0.034$ OR 3.000 (CI95% 1.087-8.276)) were independent predictors of earlier rehospitalization.

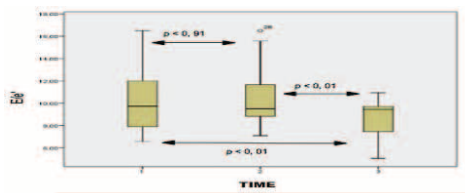
Conclusion: Prior ARB usage and MI/angina history are independent factors for rehospitalization ≤ 30 days from previous ones.

P1678

Acute and sub-acute effects of inspiratory muscle training on left ventricle filling and pulsatile hemodynamics in heart failure with preserved ejection fraction patients?

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Purpose: in patients with heart Failure with Preserved Ejection Fraction (HFpEF) inspiratory muscle weakness and altered pulsatile hemodynamics were already referred as contributing factors to low functional capacity. The study aims to assess the impact of acute and sub-acute effects of inspiratory muscle training on arterial pulsatile hemodynamic indices and on left ventricle (LV) diastolic function in patients with HFpEF. **Methods:** we submitted 17 patients with HFpEF ESC diagnostic criteria to an inspiratory muscle training section at intensity of 80% of maximum inspiratory pressure for 30 minutes. LV diastolic indices derived from echocardiogram with Doppler and arterial pulsatile hemodynamics estimated by oscillometric system were assessed before (basal), immediately after (time 2) and 1h after (time 3) the exercise section. Statistics: to detect differences among the indices in three moments we performed Generalized Estimative Equation (GEE). $P < 0,05$ was considered statistically significant. **Results:** the population was composed predominantly of female (66.7%), mean age $61,3 \pm 7,2$ years and 83.3% presented NYHA II functional class. There were significant changes in echocardiographic indices E/e' basal to time 3 ($10,33 \times 10,38$, $P < 0,01$) and time 2 to time 3 ($10,38 \times 8,73$, $P < 0,01$), as well as in arterial pulse velocity basal to time 3 ($8,3m/s \times 7,6m/s$, $P < 0,01$) and time 2 to time 3 ($8,2m/s \times 7,6m/s$, $P < 0,01$). **Conclusion:** our preliminary data demonstrated that inspiratory muscle training could determine significant acute and sub-acute changes in LV diastolic function and in pulsatile hemodynamic indices.



E/e'index basal, time 2 and time 3

ISCHEMIA/REPERFUSION/PRECONDITIONING/ POSTCONDITIONING

P1679

Acute coronary syndromes without chest pain: a high risk group?

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Introduction: Many patients (pts) with acute coronary syndromes (ACS) have atypical symptoms and don't complain of chest pain. Some studies point to a worse prognosis of these pts because of misdiagnosis and undertreatment. The aim of this study was to compare the prognosis of the patient with ACS that presents without chest pain (WOCP) to the one with typical clinical presentation (WCP).

Methods: We retrospectively analyzed the registries of ACS's included in the Portuguese National Registry of ACS, between October of 2010 and October 2014. We compared pts WCP and WOCP at presentation regarding demographic data, cardiovascular risk factors and previous history, admission data, coronary angiography results, treatment and complications during hospitalization. Then we analyzed the prognostic implications of presentation WOCP when considering the clinical outcome in-hospital mortality (IHM). Pts presenting in cardiac arrest were excluded.

Results: A total of 11058 ACS were considered, 999 (9.0%) WOCP at presentation. The most common type of ACS was without ST-segment elevation (61.8%). Pts WOCP were mostly males (57.2%) and significantly older, more frequently diabetic and hypertensive and with a higher prevalence of previous heart failure (HF), valvular heart disease, previous stroke, peripheral artery disease, renal failure, neoplasia, chronic obstructive lung disease and dementia. The main complain was dyspnea (49.4%) followed by non-cardiovascular symptoms (22.2%) and syncope (21.2%). Time to first medical contact was similar between groups but time from symptoms onset to admission (TSOA) and time from first medical contact to admission were significantly higher in pts WOCP (median 289 vs 221; $p < 0.001$ and 194 vs 110 minutes; $p < 0.001$ respectively). 2-3 vessel disease was more frequent in this group (60.7% vs 49.5%; $p < 0.001$) and they were less likely to undergo reperfusion therapy (41.0% vs 67.4%; $p < 0.001$). During hospitalization pts WOCP had more frequently HF (42.3% vs 14.1%; $p < 0.001$), atrial fibrillation (10.7% vs 4.8%; $p < 0.001$), stroke (2.4% vs 0.7%; $p < 0.001$), major bleeding (3.1% vs 1.4%; $p < 0.001$) and higher IHM (11.2% vs 3.0%; $p < 0.001$). These complications remained significantly higher among the group WOCP despite adjustment for TSOA or type of ACS. In multivariate analysis presentation WOCP was not an independent predictor for in-hospital mortality.

Discussion: In this study pts presenting WOCP had a worse prognosis with more complications during hospitalization including higher IHM. This higher risk didn't seem to be explained by delayed start of treatment or the type of ACS.

P1680

Pre-infarction angina and the prognosis of patients with st-segment elevation myocardial infarction

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Introduction/Goal

Pre-infarction angina (PIA) has been suggested to exert beneficial effects on ST-segment elevation myocardial infarction (STEMI). Proposed mechanisms include ischemic preconditioning with an associated decrease in mortality, acute heart failure (HF), arrhythmias and infarction size. Nevertheless, the results of different studies are conflicting and the cardioprotective effects of PIA are still controversial. The goal of the present study was to evaluate the influence of PIA on the prognosis of STEMI patients (pts).

Methods: We retrospectively analyzed the registries of pts with STEMI, included in the Portuguese National Registry of Acute Coronary Syndromes, between October of 2010 and October 2014. We compared pts previously diagnosed as having angina pectoris to the ones without this diagnosis regarding demographic data, cardiovascular risk factors and previous history, admission data, coronary angiography results, treatment and complications during hospitalization. Then we specifically analyzed the prognostic implications of PIA concerning HF and in-hospital mortality (IHM) through univariate and multivariate analysis.

Results: A total of 4549 STEMI pts were considered, 628 (13.8%) with PIA. They were mostly males (70.4%), significantly older and, excluding smoking status, they had more frequently conventional cardiovascular risk factors as well as more previous HF, myocardial infarction and revascularization procedures and more renal failure. Time to first medical contact was superior in the PIA group (median 150 vs 120 minutes, $p = 0.006$) but there were no differences regarding time from symptom onset to admission (median 354 minutes) or time from first medical contact to admission (median 169 minutes). PIA pts had more frequently 2-3 vessel disease (56.0% vs 42.4%, $p < 0.001$) but were less likely to undergo reperfusion therapy during hospitalization (77.4% vs 82.3%, $p = 0.003$). HF was significantly higher (24.8% vs 18.1%; $p < 0.001$) and there was a trend towards higher IHM in this group (7.3% vs 5.5%; $p = 0.070$). In multivariate analysis PIA arose as an independent protective factor for IHM in the subgroup who didn't underwent coronary angiography (OR 0.18, CI95% 0.04-0.85; $p = 0.031$) but not in the subgroup who had angiography. There was no independent relation regarding HF.

Discussion/Conclusions: In this analysis pts with PIA had a worse prognosis with more HF and IHM, although they also had worse baseline characteristics. In the subgroup of pts that didn't undergo coronary angiography and didn't receive reperfusion in the acute phase of STEMI, PIA was protective.

P1681**Management of multivessel coronary disease detected at the time of primary percutaneous coronary intervention in st-segment elevation myocardial infarction: preliminary analysis**

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Introduction: The management of multivessel coronary disease detected at the time of primary percutaneous coronary intervention (PPCI), in the context of ST-segment elevation myocardial infarction (STEMI), is controversial. Current guidelines state that, in most cases, PPCI should be limited to the culprit lesion. Nevertheless, recent trials have shown benefits in complete revascularization performed at the index event or during hospitalization.

Goal: Compare the prognosis of STEMI patients (pts) who underwent treatment of the culprit lesion only (group A) to the pts completely revascularized during hospitalization (group B).

Methods: Retrospective analysis of all STEMI pts who performed PPCI in our hospital, between January 2013 and November 15th 2014. Inclusion criteria were: infarct artery plus at least one non-infarct related artery (nIRA) with a $\geq 70\%$ diameter stenosis in a vessel ≥ 2 mm. We excluded pts presenting in cardiogenic shock, stent thrombosis, pts referred to cardiac surgery and total chronic occlusions as the only significant nIRA. Considered endpoints were: in-hospital mortality (IHM), acute coronary syndrome (ACS), PCI driven by ischemia (ACS or ischemia test), admission for heart failure (HF), cardiovascular death (CD), composite of major cardiovascular events (MACE) and total mortality (TM).

Results: From a total of 222 PPCI's, 99 were considered. The mean age was 69 ± 13.1 years, 65.7% were men. 71 (71.7%) pts were included in group A and 28 (28.3%) in group B. The groups were similar regarding baseline characteristics, heart or renal failure at admission, total ischemic time, infarct location and number of diseased vessels. There were no statistically significant differences regarding any of the analyzed endpoints: IHM (n=3; 4.2% vs 0), ACS (n=5; 7.0% vs n=1; 3.6%), PCI driven ischemia (n=5; 7.0% vs n=1; 3.6%), admission for HF (n=2; 2.8% vs n=2; 7.1%), CD (n=3; 4.2% vs 0), MACE (n=11; 15.5% vs n=2; 7.1%) and TM (n=4; 5.6% vs 0), groups A and B respectively. Median follow-up time was 10.5 ± 5.7 months for population A and 6.3 ± 4.6 months for B ($p=0.001$). Pts from group A underwent 17 (23.9%) planned PCI's and didn't have any event. There were no significant differences between groups regarding contrast nephropathy, major haemorrhage, stroke and hospitalization length.

Conclusions: The comparison between groups is impaired by the low number of registered endpoints and the discrepancy between follow-up times. Available data suggests that immediate treatment of the culprit lesion only with planned additional PCI's after hospitalization might be a valid option.

P1682**Pathologic Q waves in electrocardiogram: impact on treatment and prognosis in acute coronary syndromes**

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Purposes: The presence of pathologic Q waves in electrocardiogram (Q-EKG) in an Acute Coronary Syndrome (ACS) can provide important information inferring when symptoms began and permitting the anticipation of possible final outcomes. The objective of the study is to evaluate ACS characteristics in patients presenting with or without Q-EKG, as well as therapeutic approach and mortality rate.

Methods: A retrospective study of patients admitted for ACS was performed. The clinical, analytical, angiographic and echocardiographic parameters were evaluated at hospital admission and again at 12 month follow-up. Patients were divided into two groups: group A (GA) without Q-EKG vs group B (GB) with Q-EKG. Statistical analysis was performed with SPSS. Statistical relevance verified when $p < 0.05$.

Results: Total of 1077 patients, 68.7% men, mean age 68 ± 12 years. Q-EKG were observed in 25.1% of patients.

No differences was noted when evaluating gender, age, symptoms, medication or past medical history between the two group. The only exceptions were obesity, more prevalent in GA, and previously diagnosed coronary heart disease, more evident in GB. GB had a longer time interval between symptom development and hospital admission. However, there was no difference in the time between hospital admission and arrival to the catheterization room.

Statistical differences were recorded when accessing diagnosis on hospital admission between the two groups, STEMI 43.8% vs 54.1% and NSTEMI 54.2% vs 44.1%, $p=0.046$. Although no difference was found when evaluating Killip-Kimball classification at admission, during hospitalization there was greater hemodynamic instability observed in the group with Q-EKG, with greater need for inotropic support. No significant differences were found when accessing medication use or invasive therapeutic approaches. No difference in complications rates was observed.

Echocardiographically, there was a higher prevalence of akinesia in GB and a greater

left ventricular ejection fraction (LVEF) in GA. Blood work revealed statistically higher troponin values in GB patients.

Patients with Q-EKG presented higher mortality during hospitalization (6.7% vs 11.9%, $p=0.008$), as well as at 12 month follow-up (3.7% vs 7.0%, $p=0.044$, Kaplan-Meier log-rank 0.032). Multivariate analysis showed that this increase in mortality was dependent on LVEF.

Conclusion: The presence of Q-EKG did not alter the initial therapeutic approach. However, Q-EKG is associated with an increased prevalence of hemodynamic instability and a greater short-term and long-term mortality due to reduced LVEF.

P1683**Predictors and prognosis of contrast-induced acute kidney injury in patients undergoing percutaneous coronary intervention**

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Objective: Contrast-induced acute kidney injury (CI-AKI) is a serious potentially preventable complication of percutaneous coronary interventions (PCI). It remains a challenge as use of PCI is growing, patient population is aging, diabetes and chronic kidney disease are coming more common. The predictors and prognosis of CI-AKI are not well defined. The aim of the study was to evaluate the predictors and prognosis of CI-AKI in patients undergoing PCI.

Methods: 502 patients (346 male, 64 ± 12 years ($M \pm SD$), arterial hypertension 92%, previous myocardial infarction 38%, diabetes mellitus (DM) 22%, known chronic kidney disease 19%, anemia 16%, heart failure 62%, left ventricular ejection fraction $40 \pm 16\%$) who underwent PCI (stable angina pectoris (SAP), n=50; unstable AP/non-ST-segment elevation myocardial infarction (UAP/NSTEMI), n=236; STEMI, n=216) were examined. CI-AKI was defined using 2012 KDIGO Guidelines. Mann-Whitney test and multivariate logistic regression analysis were performed. $P < 0.05$ was considered statistically significant.

Results: 18% of total population, in SAP patients 12%; UAP/NSTEMI, 15%; STEMI, 20%, developed CI-AKI, $P < 0.01$. Patients with versus without CI-AKI in total population were older (68 ± 13 vs 63 ± 12 years, $p < 0.05$), had higher baseline SCr (114 ± 31 vs 92 ± 23 $\mu\text{mol/l}$, $p < 0.05$), white blood cells (WBC) (11.08 ± 2.41 vs $9.62 \pm 3.86 *10^9/\pi$, $p < 0.05$), higher rate of DM (25 vs 15%, $p < 0.05$), anemia (30 vs 15%, $p < 0.05$) and higher rate of therapy with nephrotoxic antibiotics (53 vs 17%, $p < 0.0005$), loop diuretics (28 vs 13%, $p < 0.001$), higher rate of main left coronary artery disease (29 vs 15%, $p < 0.01$), higher contrast media volume/estimated glomerular filtration rate ratio (CV/eGFR) (4.32 ± 2.35 vs 2.47 ± 1.02 , $p < 0.05$). Main independent predictors of CI-AKI were, therapy with nephrotoxic antibiotics (odds ratio (OR) 5.58; 95% confidence interval (CI) 3.43-9.09; $p < 0.0005$), loop diuretics (OR 2.55; 95% CI 1.48-4.39; $p < 0.001$), anemia (OR 2.42; 95% CI 1.43-4.09; $p < 0.05$), main left coronary artery disease (OR 2.29; 95% CI 1.35-3.89; $p < 0.001$), DM (OR 1.82; 95% CI 1.05-3.17; $p < 0.05$). Patients with CI-AKI had higher risk of 30-days mortality (11 vs 4%, $p < 0.05$) and similar rate of 6 months rehospitalizations (63 vs 48%, $p > 0.05$).

Conclusions: CI-AKI was associated with higher rate of comorbidities (DM, anemia), therapy with nephrotoxic drugs and loop diuretics, higher baseline serum creatinine and WBC, main left coronary artery disease. CI-AKI had negative impact on 30-days mortality.

P1684**Do patients with acute coronary syndromes without conventional risk factors have a better prognosis?**

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Introduction: The great majority of patients (pts) with acute coronary syndromes (ACS) have at least 1 conventional cardiovascular risk factor (CCRF). The relationship between each one of these factors and atherosclerosis is well established but less is known about pts without any of these. The aims of this study were to establish the profile of the pt with ACS without conventional cardiovascular risk factors (WCCRF) and compare its prognosis to the pt with at least 1 conventional cardiovascular risk factor (WCCRF).

Methods: We retrospectively analyzed the registries of ACS's included in the Portuguese National Registry of ACS's, between October of 2010 and October 2014. We compared pts WCCRF to pts WCCRF (hypertension, dyslipidemia, diabetes, active smoking or family history of heart disease) regarding demographic data, previous history, admission data, coronary angiography results, treatment and complications during hospitalization. We performed multivariate analysis to evaluate the impact of having at least 1 CCRF on cardiovascular adverse events. We also compared the mortality and readmission for cardiovascular disease at one year follow-up between the two groups.

Results: A total of 10756 ACS's were considered, 332 (3.1%) WCCRF. The pts were mostly males (72.3%) with a mean age of 67 ± 15 years, similar to the ones WCCRF. Previous dementia and neoplasia were more frequent in the group WCCRF (3.8% vs 1.8%; $p=0.011$ and 6.1% vs 4.4%; $p=0.155$ respectively) unlike

cardiovascular diseases, heart failure (HF), renal failure and pulmonary diseases. Pts WCCRF most commonly presented ST-segment elevation myocardial infarction (STEMI) (47.3% vs 40.6%; $p = 0.014$) compared to pts WCCRF who more frequently presented non-STEMI (48.1% vs 44.3%; $p = 0.175$). There were no differences regarding the symptoms being chest pain the main complaint (90.7% average). 2-3 vessel disease was less common in pts WCCRF (33.6% vs 51.1%; $p < 0.001$). The groups were similar regarding total ischemic time, infarct location, percentage of reperfusion therapy and complications during hospitalization, including in-hospital mortality (IHM), HF or re-infarction (rMI). In multivariate analysis having at least 1 CCRF was neither an independent predictor of IHM nor the composite endpoint of IHM, HF or rMI. At one year follow-up, cox regressions for cardiovascular death and hospital readmission showed similar results between groups. Discussion/Conclusions In this analysis the absence of CCRF was not a protective factor as these pts didn't have a better in-hospital or one year follow-up prognosis compared to those WCCRF.

BASIC SCIENCE: MITOCHONDRIA AND METABOLISM

P1686

Impact of diabetes mellitus on myofilaments phosphorylation and calcium sensitivity in aortic stenosis patients

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Background: Diabetes mellitus (DM) is an independent risk factor for progression of aortic valve stenosis (AS) and significantly impacts long-term outcome after valve replacement. Our aim was to clarify myofibrillary changes induced by DM on AS patients.

Methods and Results: Patients with severe isolated AS ($n=20$) and AS plus type-II diabetes patients (AS-DM+, $n=16$) with preserved left ventricular (LV) ejection fraction and no clinical or angiographic signs of coronary artery disease were studied. Doppler echocardiographic data was used to compare in vivo LV function. Biopsies were used to isolate and permeabilize cardiomyocytes allowing to assess active force (Factive), resting force (Fpassive) and calcium sensitivity (pCa50) before and after incubation with PKA as well as to measure phosphorylation of myofibrillary proteins.

Compared to AS patients, AS-DM+ patients presented aggravated diastolic dysfunction, increased myofilaments pCa50 and a lower PKA-induced drop of pCa50 which was correlated with higher baseline levels of PKA-induced phosphorylation of Troponin I on Ser23/24.

Conclusions: We have shown that myofibrillary changes induced by DM in AS patients are related to PKA-mediated hyperphosphorylation status of troponin I. This study highlights the need for earlier therapeutic interventions in order to prevent these myofibrillary alterations that accelerate the progression of diastolic dysfunction in diabetic AS patients.

P1687

Application of label-free autofluorescence lifetime in vivo to measure changes in myocardial fibrosis and metabolism associated with myocardial infarction and heart failure

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We are developing an autofluorescence lifetime (AFL)-based technique as an "optical biopsy" to characterize the signatures associated with histological, morphological, metabolic and functional changes in myocardial disease states. AFL spectroscopy exploits the inherent photo-physical properties of a number of endogenous molecules without the issues associated with use of exogenous compounds. AFL measurements of fluorophores such as NADH and flavins present an opportunity to discern information about myocardial energetics, whilst extra-cellular matrix molecules provide information on structural changes to the heart. AFL measurements are independent of fluorophore concentration and excitation intensity and furthermore can report on changes to microenvironment e.g. protein binding.

We investigated the potential of a single-point fibre-optic based instrument combining time-resolved spectrofluorometry and diffuse reflectance spectroscopy to measure structural and metabolic changes in cardiac tissue in vivo in a rat left anterior descending artery ligation heart failure model 1, 2, 4 and 16 weeks post-infarction. Stable AFL signals were observed across the heart in all controls ($n=17$). At 16 weeks, when the heart failure phenotype is fully established, significant differences in AFL signals between MI-HF ($n=6$) and control ($n=6$) in infarcted left ventricle (LV) anterior wall ($p < 0.0001$) were seen. Here the signature is characterised by a large increase in collagen. More interestingly, both metabolic and fibrotic changes

were detectable using this methodology in remodelled distal viable myocardium: LV posterior wall ($p < 0.01$) and right ventricle (RV) ($p < 0.001$), with changes in flavin lifetime attributable to this altered energetic state and increased fibrosis. At earlier time points 1 week ($n=3$) & 2 weeks ($n=4$) post-infarction, before maturation of the scar and full increase in collagen content, energetic changes were observed in all areas. Diagnostic accuracy to predict tissue disease state (i.e. presence of MI-HF) was 100% in LV anterior wall and >77% in remote remodelled regions at 16 weeks post-infarction. The increase in collagen content predicted by altered AFL signals was highly correlated with quantitative histological measurement ($r = 0.9844$, $p < 0.05$). Overall, our results demonstrate the sensitivity of our instrument to characterise changes in the failing heart in vivo without the use of exogenous labels. Incorporation into coronary catheters or pacing leads could offer rapid additional diagnostic information and monitoring of myocardial physiology in heart failure patients.

P1688

MicroRNA-216a links brain-adipose tissue communication to heart function

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Background: Obesity is a multi-organ disorder associated with a number of comorbidities, including heart disease. Genome-wide association studies identified the chromosomal locus 2p16.1 as a human obesity susceptibility locus, which contains the highly conserved microRNA-216a (miR-216a). Following bioinformatics screens, several serotonin receptor 3'UTR regions were identified as potential targets of miR-216a. Serotonin, also known as 5-hydroxytryptamine (5-HT), is a monoamine neurotransmitter known to be involved in controlling body weight homeostasis.

HYPOTHESIS: We hypothesize that decreased expression of miR-216a induces serotonin receptor-mediated development of obesity, leading to heart disease.

METHODS & RESULTS: Abdominal subcutaneous white adipose tissue (WAT) from obese patients as well as ob/ob mice, a mouse model for obesity, was analyzed. In both obese humans and mice, miR-216a expression levels were decreased compared to controls. By addressing the functional role of miR-216a, we observed that miR-216a levels were decreased from the first day of the differentiation process in 3T3L1 cells. Oil red O staining revealed that transfection with anti-miR-216a molecules, which inhibits miR-216a expression, leads to formation of hypertrophic mature adipocytes, while treatment with Ketanserin (5-HT receptor 2A/2C antagonist) or SB-699551 (5-HT receptor 5A antagonist) antagonized this anti-miR-216a-mediated effect. In line, adipocyte differentiation is completely inhibited upon a miR-216a mimic treatment. Furthermore, total body miR-216a knock-out (KO) mice showed an increased food consumption, an increased body weight and a higher percentage of WAT mass compared to wild-type (WT) mice. Echocardiographic measurements demonstrated that targeted deletion of miRNA-216a causes left ventricular dilatation, accompanied by a decreased fractional shortening (%FS). Following a high fat diet, miR-216a KO mice displayed an exaggerated form of obesity, shown by increases in body weight, percentage WAT mass, food consumption and decreased cardiac contractile function compared to WT mice. RT-qPCR measurements revealed that expression of the 5-HT receptors HTR1D, HTR2A, HTR4 and HTR5A were increased in both WAT and brain tissue of miR-216a KO mice, suggesting these 5-HT receptors to be downstream targets of miR-216a in vivo.

Conclusion: Our data suggest that miR-216a directs serotonin receptor expression and thereby is able to control body weight homeostasis and heart function. Thus, this miR-216a-serotonin-receptor-pathway poses a molecular link between obesity and heart failure.

P1689

Identification of transcription factors involved in the negative modulation of sST2 induced by metformin in myocardial infarction.

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Purpose: Previous results of our group suggested that metformin (MET), an anti-diabetic drug, could prevent adverse cardiac remodeling by blocking the increase of sST2 induced after myocardial infarction (MI), a decoy receptor that inhibits the anti-remodeling effect of interleukin-33. The mechanism that explains the modulatory effect of MET on sST2 expression is unknown.

Methods: Wistar rats underwent MI by left coronary artery ligation and were sacrificed at 1, 2, 4, 12, or 24 weeks after surgery ($n=7$ per group). Sham-operated animals were also included. Additional rats were treated with MET (250 mg/kg/day, $n=8$) from the day of surgery until sacrifice (4 weeks post-MI). Cardiac cells (H9c2 cell line), pretreated or not with 4 mM MET for 24h, were subjected to biomechanical stress by treatment with 0.08 μ M PMA and 0.4 μ M A23187 for 6h. The expression of

sST2 and two transcription factors related to biomechanical stress, Mef2a and Yin Yang-1 (Yy1), was analyzed by quantitative RT-PCR in the infarcted area of animals and in extracts from cardiac cells. Each value is expressed as fold of control \pm SEM.

Results: Compared with sham group, sST2, Mef2a and Yy1 were increased in infarcted rats, showing similar expression kinetics and positive correlation. The highest increase was shown 1 week post-MI and remained elevated up to 24 weeks. Compared with infarcted rats (MI 4 weeks), MET treatment showed significant decreased levels of sST2 (21.9 ± 8.7 vs. 2.5 ± 0.5 , MI vs. MET), Mef2a (2 ± 0.2 vs. 1.1 ± 0.1) and Yy1 (1.7 ± 0.1 vs. 1.2 ± 0.2). H9c2 cells subjected to biomechanical stress showed increased level of sST2 (3.5 ± 0.8), Mef2a (3.1 ± 0.3) and Yy1 (2.8 ± 0.5) compared to untreated cells. The pretreatment of H9c2 cells with 4mM MET for 24 h prevented the increase of sST2 (1.8 ± 0.8), Mef2a (0.9 ± 0.4) and Yy1 (0.9 ± 0.2) induced by the biomechanical stress.

Conclusions: This study suggests that Mef2a and Yy1 are transcription factors involved in the cardioprotective effect of MET on myocardial infarction and provides knowledge to the development of further therapies.

P1690

High-fat diet does not induce structural changes or oxidative stress in heart of Wistar rats

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Purpose: Obesity and metabolic syndrome are the main factors for cardiovascular events. Our aim was to evaluate the influence of high-fat diet on heart morphological and functional parameters, inflammation, and oxidative stress.

Methods: Adult Wistar rats were fed with standard rat chow (control) (n=18) or high-fat diet (HFD) (n=19) for 21 weeks. The animals were weighed, tested for insulin tolerance (ITT) and oral glucose tolerance (OGTT). The morphological and functional parameters were analyzed by echocardiography. After that, the rats were killed and had the left ventricle (LV) dissected, weighted, and stored (-80°C) for further evaluation of biochemical, molecular, and inflammatory parameters. Data were analyzed by t-test.

Results: The animals fed with HFD presented no difference in body mass when compared with those receiving standard diet. However, HFD caused an insulin resistance, evidenced by an 11% increase in area under the curve (AUC) of OGTT ($p=0.002$) and 20% increase AUC of ITT ($p=0.001$). HFD did not influence ventricular weight, diastolic diameters or ejection fraction, evidenced by echocardiography. Also, there were no disturbances in antioxidant enzymes, catalase and superoxide dismutase, or in the protein oxidative stress marker carbonyl. However, protein sulfhydryl oxidation could be found in heart from HFD fed group when compared with control group (7 nmol/mg prot vs. 4 nmol/mg prot, respectively; $p=0.03$). Diet also did not influence the inflammatory status, assessed by IL-10 and IL-1beta levels.

Conclusion: Despite clear influence on insulin resistance, high-fat diet did not caused any molecular imbalance that could indicate inflammation or damage. In the same way, cardiac architecture and function seemed to be preserved. Taken together, these data suggest that the heart is resistant to the early metabolic alteration caused by HFD. Longer times of diet should be evaluated to unveil the heart susceptibility to the stimuli induced by diet.

P1691

Er stress, autophagy, and inflammation are involved in obesity-induced cardiomyopathy via a metabolically-healthy obese minipig model

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Background: About 10-45% of obese individuals are insulin sensitive and maintain normal plasma lipid profiles, therefore these individuals are defined as metabolically healthy obesity (MHO). Recent evidences show that MHO subjects are prone to induce heart failure, and metabolic dysregulation did not contribute to MHO-induced cardiomyopathy. The underlying mechanism is not fully elucidated. The objective of this study was to explore the molecular mechanism of MHO-induced cardiomyopathy via a minipig model.

Methods and Results: Five-month-old Lanyu minipigs were induced obesity via high-fat diet (HFD) for 6 month-feeding. No significant differences in plasma lipid profile and glucose level were observed between obese and control minipigs. Obese pigs had heavier heart weight and more cardiac fibrosis than the control pigs. These findings demonstrate that a MHO-induced cardiomyopathy animal model was established. Left ventricular samples were obtained for protein analysis. Cardiac protein expression of AMPK, LC3I and LC3II was upregulated in the obese pigs.

Obese pig had a higher ratio of LC3II to LC3I in the heart than the control pig, suggesting that HFD activated autophagy initiation, while caused more autophagosome accumulation in the heart of MHO pigs. HFD increased CHOP and decreased Grp94 expression in the heart of obese pigs, suggesting that unfolded protein response was suppressed, and ER stress-specific apoptosis was induced. Neither TNF-alpha nor IL6 in the heart was different between MHO and control pigs. Similar cardiac TBARS values were detected between two groups.

Conclusion: Long-term HFD induced obesity in Lanyu pigs without any metabolic dysfunctions. ER stress and autophagy were involved in MHO-induced cardiomyopathy. Neither inflammation nor oxidative stress was participated in MHO-induced cardiomyopathy.

P1692

Modulation of NO levels by melatonin and omega-3 fatty acids in the isoproterenol injured normotensive and hypertensive rats

This work was supported by grants: SAIA, VEGA 2/0046/12 and APVV-0348-12.C Vicenczova¹; K Chaudagar²; T Benova¹; B Szeiffova-Bacova¹; M Barancik¹; N Tribulova¹

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Objectives and Purpose: Nitric oxide (NO) promotes the process of tissue remodeling to combat the injury prone dysfunction in the heart, vessels and other organs. NO is mainly synthesized by eNOS, however, eNOS independent NO production might also be involved in the homeostasis. We aimed to explore whether omega-3 FA and melatonin affect basal NO levels in serum, aorta and heart of isoproterenol-injured normotensive and hypertensive rats.

Methods: There were four groups of male Wistar (W) and SHR (S) rats. Controls; rats injured by isoproterenol (118mg/kg, s.c., 7days); isoproterenol-injured rats treated with melatonin (10mg/kg, p.o. 60days); isoproterenol-injured rats treated with omega-3 FA (Omacor 200mg/kg, p.o., 60days). The heart left ventricle and aorta were dissected from each rat, cut into small pieces and incubated in the K-Henseleit solution. NO was estimated using Griess method.

Key Results: Serum NO levels were lower in hypertensive compared to normotensive rats and isoproterenol suppressed NO in the latter only. Omacor but not melatonin increased serum NO levels in hypertensive isoproterenol-injured rats only. NO levels were higher in aorta of hypertensive versus normotensive rats and isoproterenol did not affect it. Interestingly, melatonin increased while Omacor suppressed NO in aorta of isoproterenol-injured normotensive rats only. NO levels were significantly lower in the heart of hypertensive compared to normotensive rats. Isoproterenol increased NO in normotensive rats only and this was suppressed by Omacor. Surprisingly, neither isoproterenol nor treatments affect NO in hypertensive rat hearts

Conclusion: Data indicate that isoproterenol decrease serum and increase heart NO levels in normotensive but did not affect it in hypertensive rats. Both melatonin and Omacor modulated NO levels in isoproterenol-injured rats by strain and tissue-dependent manner.

P1693

Intake of a standardized crataegus extract prevents DOCA-salt-induced hypertension, and alteration of cardiac, vascular and renal structure and function in rats: role of oxidative stress

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Hypertension is a leading risk factor for the development and progression of chronic heart, vascular and renal diseases. The hypertension-induced end target organ damage is characterized by alterations of the heart, vascular and kidney functions and structure associated with oxidative stress. The present study has examined the possibility that a standardized polyphenol-rich Crataegus extract prevents hypertension-induced end target organ damage in an experimental model of hypertension, the DOCA-salt non-nephrectomized rat. Male Wistar rats were divided into a control group, a Crataegus extract group (100 or 300 mg/kg/day in the diet), a DOCA-salt group (50 mg/kg i.p. per week) and DOCA-salt + Crataegus extract group for 6 weeks. Systolic arterial blood pressure (SBP) and target organ damage (vasculature, heart and kidney) were examined. The DOCA-salt treatment increased systolic blood pressure, and this effect was associated with the induction of pronounced endothelium-dependent contractile responses in second order mesenteric resistance artery rings to acetylcholine. The increased contractile response was prevented by indomethacin (a cyclooxygenase inhibitor) and associated with vascular oxidative stress as assessed using dihydroethidine, a reduced expression of eNOS, and an increased expression of NADPH oxidase subunits (gp91 phox, p47 phox), COX-1 and COX-2. Echocardiography and histological analyses indicated

left ventricular (LV) hypertrophy, fibrosis, and impaired systolic and diastolic cardiac functions associated with oxidative stress in the DOCA-salt group. Renal dysfunction characterized by increased urea and uric acid plasma levels, glomerular and arteriolar hypertrophy, tubulo-interstitial fibrosis associated with oxidative stress was observed in the DOCA-salt group. Chronic intake of the Crataegus extract significantly reduced in a dose-dependent manner systolic blood pressure, target end organ damage in the heart and kidney, and improved the vascular function by preventing oxidative stress and the expression of target molecules. Thus, the Crataegus extract was able to retard the hypertension-induced end organ damage in the heart, kidney and resistance arteries most likely by preventing oxidative stress.

P1694

Metformin prevents adverse cardiac remodeling by modulation of IL-33/ST2 signaling

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Purpose: IL-33 via the cardiac receptor ST2L improves cardiac function after myocardial infarction (MI). The soluble ST2 isoform (sST2) is a decoy receptor that attenuates the cardioprotective effects associated to IL-33/ST2L. We evaluated whether the IL-33/ST2L signaling is involved in the anti-fibrotic effect of metformin (MET), an anti-diabetic drug able to ameliorate cardiac remodeling in several models of heart failure (HF).

Methods: Infarcted Wistar rats were randomly assigned to not receive treatment (MI group, n=12) or to receive MET (250 mg/kg/day, n=21) from the day of surgery and for 4 weeks. A sham group was used as control (n=8). MI size, left ventricular ejection fraction (LVEF) and LV volumes were analyzed by echocardiography at 24 hours and 4 weeks after MI. MI size was also evaluated by histology. The mRNA expression of IL-33, ST2L, sST2 and fibrosis markers were analyzed by RT-PCR in the infarcted area. Each value is expressed as fold of control \pm SEM.

Results: There were not significant differences in the MI size (WMSI 1.73 \pm 0.20 vs. 1.67 \pm 0.13; p=0.108) or LVEF (44.0 \pm 13.7 vs. 40.1 \pm 14.6; p=0.410) at 24 hours after the surgery between the rats with and without MET, respectively. After 4 weeks of treatment, the group of rats treated with MET presented lower MI size evaluated by histology (20.7 \pm 14.9 vs. 40.7 \pm 7.4; p=0.011) and echocardiography (WMSI 1.40 \pm 0.2 vs. 1.66 \pm 0.1; p=0.04) and higher LVEF (49.8 \pm 12.1 vs. 35.1 \pm 8.7; p=0.039). Compared to sham group, MI group showed higher levels of IL-33 (173 \pm 61, p<.001), ST2L (35 \pm 10, p<.001) and sST2 (22 \pm 8.7, p<.001). The treatment with MET reduced the expression level of ST2L (10 \pm 2.3, p=.037) and sST2 (5 \pm 1.3, p=.004) and increased the expression level of the protective cytokine IL-33 (316 \pm 49, p=.037). MI group also showed higher levels of fibrosis markers than the sham group: collagen III (170 \pm 85, p=.014), TIMP-1 (63 \pm 16, p<.001), α -sma (16 \pm 5.1, p=.005) and TGF- β (9 \pm 1.9, p<.001). The treatment with MET significantly reduced the expression level of all fibrosis markers: collagen III (8.1 \pm 2.6, p=.022), TIMP-1 (12 \pm 1.9, p<.001), α -sma (5 \pm 1.1, p=.015) and TGF- β (3.6 \pm 0.7, p=.001). In addition, the expression levels of ST2L, sST2 and IL-33 were correlated with each other, while ST2L and sST2, but not IL-33, were correlated with TIMP-1 and TGF- β (p<.001). The relationship between MET and the IL-33/ST2 system was confirmed in cultured cardiac myocytes.

Conclusions: Our results suggest that the IL-33/ST2L signaling may be an important mechanism involved in the anti-fibrotic effect of MET in the context of post-infarction HF.

P1695

GRK2 inhibition with small peptide improves cardiac function and metabolism during heart failure

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GRK2 is known to participate in the setting of heart failure (HF) through downregulation and desensitization of β -adrenergic receptor. Recently, GRK2 appears also to be involved in cardiac metabolism, which is known to be affected in HF, with altered mitochondrial function and reduced ATP content. Here we tested the therapeutic effects of a small peptide, whose has demonstrated the ability to inhibit GRK2 activity in vitro, on an animal model of HF and evaluated its effects on cardiac biochemical, metabolic and functional alterations observed during HF. For this study, 8 weeks old C57BL/6 mice were used and myocardial infarction (MI) of left ventricle was induced by means of a cryogen probe. Cardiac volume and function was assessed by Echocardiography pre- surgery and at 4, 6, 8 and 10 weeks post MI, followed by terminal hemodynamic evaluation by catheterization with Millar pressure transducer. Finally, mice were sacrificed and heart samples collected for beta binding and cAMP assay, RT-PCR for mitogenesis and Chemoluminescence assay for

ATP production. Also, 6 weeks after MI, mice were implanted with a micro osmotic pump set to deliver 0.24 mg/day of grk2 inhibitor for 2 weeks.

Results: MI induced a significant increase in left ventricle diastolic dimension (LVDD) and reduction of Ejection Fraction (EF) respect to control (LVDD: 4.27 \pm 0.23 vs 3.7 \pm 0.09, EF: 35.9 \pm 0.02 vs 57 \pm 3.4, MI vs control) at 6 week post surgery. At 8 weeks post MI, treated group showed a significant amelioration of cardiac function (EF: 51.7 \pm 4 vs 38.81 \pm 1.68, MI+pump vs MI) and attenuation of cardiac remodeling respect to MI control group (LVDD: 3.96 \pm 0.11 vs 4.9 \pm 0.1, MI+pump vs MI). These results were still effective at 10 week post MI, while terminal hemodynamic evaluation showed a significant amelioration in left ventricle diastolic pressure (LVDP: 1 \pm 2.5 vs 14.3 \pm 1 mmHg in MI treated respect to MI Control group) and contractility after isoproterenol intravenous infusion (Δ to basal: 4544 \pm 320 vs +3197 \pm 205, MI+pump vs MI) indicating an improved emptying and a preserved contractile reserve of left ventricle induced by treatment. Moreover, grk2 inhibitor restored beta adrenergic density in post MI-HF (55 \pm 1.02 vs 40 \pm 1.43 fmol/mg, MI+pump vs MI) and cAMP production (15.9 \pm 0.53 vs 8.59 \pm 0.85 pmol/mg, MI+pump vs MI). Finally, we observed recovered mitogenesis (Cyt B: 1.1 \times 10⁻² vs 0.6 \times 10⁻⁴, MI+pump vs MI) and ATP production (18.5 \times 10³ vs 11 \times 10³, AU, MI+pump vs MI). GRK2 inhibition through a small peptide is an effective therapeutic strategy to correct biochemical, metabolic and functional alterations observed during HF.

BASIC SCIENCE: REGENERATION

P1696

Decreased proliferation kinetics of primary myoblasts from chronic heart failure patients

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Background: Peripheral muscle wasting is a common finding in chronic heart failure (CHF) and is associated with decreased patient survival. The mechanisms that underlie CHF-related muscle wasting are currently not clear.

Purpose: To evaluate the proliferative capacity of primary skeletal muscle myoblasts from CHF patients and healthy donors in culture.

Methods: Satellite cells were isolated from skeletal muscle biopsies (m. vastus lateralis) of 6 CHF patients (20% female; age 61 \pm 4 y; New York Heart Association II-III) and 6 age- and gender- matched healthy subjects, and propagated in vitro to myoblasts. Cell proliferation was evaluated using two different techniques. First, we analyzed the kinetics of clonal growth over a 10-day period by phase contrast microscopy. Secondly, dynamic high-resolution assessments of proliferation were made every 15 minutes for a time period up to 180 hours using the impedance-based xCELLigence technology.

Results: Using microscopy, CHF myoblasts underwent 2-7 mean population doublings (4,00 \pm 1,06) and control myoblasts 2-10 mean population doublings (4,87 \pm 1,17). Cell indices measured by the impedance assay and taken during the logarithmic growth phase at 90 hours were significantly different between groups (p=0.032). In addition, CHF myoblast concentration reached its maximum at 136,53 \pm 5,16h whereas control myoblasts showed a maximum cell index at 104,49 \pm 12,05h.

Conclusion: Our findings suggest that skeletal muscle myoblasts from CHF patients demonstrate a slower growth rate than myoblasts from age- and gender-matched healthy donors. Further research is needed to clarify whether this impaired proliferative capacity of myoblasts in CHF contributes to muscle weakness.

P1697

The impact of atorvastatin treatment on endothelial progenitor cells in patients with ischemic heart failure

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Purpose: Circulating endothelial progenitor cells (EPC) contribute to reendothelialization and repair of damaged endothelium in heart failure (HF). Statins with anti-inflammatory and pleiotropic properties can restore endothelial function in HF. We investigate the effects of different doses of atorvastatin treatment, on mobilization of EPC and endothelial function in patients with ischemic HF of different severity.

Methods: We studied the effect of 4 weeks atorvastatin treatment in 23 subjects with ischemic HF at New York Heart Association (NYHA) functional class II and III. The study was carried out on two separate arms, one with atorvastatin 40mg/d and one with atorvastatin 10mg/d (randomized, double-blind, cross-over design). Endothelial function was evaluated by flow-mediated dilation (FMD) of the brachial artery. Serum levels of tumor necrosis factor alpha (TNF α) were measured by ELISA. The number

of circulating CD34(+)/CD133(+)/KDR(+) EPCs were evaluated by flow cytometry.

Results: From the study population, 15 subjects were categorized as NYHA II and 8 subjects as NYHA III. Compared to baseline, treatment with 40 mg/d of atorvastatin improved FMD ($3.16 \pm 2.98\%$ vs. $6.05 \pm 2.45\%$, $p=0.001$), TNF α levels ($p=0.01$) and circulating EPC [$362 (209-456)$ cells/ml vs. $175 (143-232)$ cells/ml, $p=0.002$]. Similarly, compared to baseline, treatment with atorvastatin 10mg/d also improved FMD ($3.24 \pm 3.12\%$ vs. $4.20 \pm 2.09\%$, $p=0.08$), TNF α ($p=0.01$) and EPC [$201 (151-309)$ cells/ml vs. $169 (115-228)$ cells/ml, $p=0.01$]. The increase in EPC ($p=0.02$) and FMD ($p=0.001$) was greater with the dose of 40mg/d. Moreover, in the 40mg/day atorvastatin treatment group baseline FMD was associated with the increase in EPC numbers ($r=0.48$, $p=0.03$). Importantly, in the 40mg/day atorvastatin treatment group, the increase in EPC was higher in NYHA II subjects compared to NYHA III subjects (217 ± 142 cells/ml vs. 60 ± 150 cells/ml, $p=0.03$).

Conclusions: In ischemic HF subjects, atorvastatin treatment mobilizes EPC and improves endothelial function with a parallel anti-inflammatory effect. This improvement is more pronounced in subjects with better clinical status and better endothelial function.

P1698

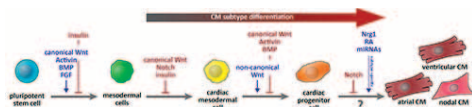
Custom-tailored cardiomyocytes: a directed in vitro differentiation of human pluripotent stem cells into defined cardiomyocyte subtypes

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Cardiomyocytes derived from human induced pluripotent stem cells (iPS cells) are a promising tool for regenerative applications by cardiomyocyte transplantation, for the study of cardiac development and disease modeling as well as for drug discovery and cardiotoxicity screenings. The generation of relatively homogenous populations of subtype-specific cardiomyocytes in large numbers and high purities is crucial for potential clinical applications in cell based therapies as well as for a better understanding of the predominantly cardiac subtype-restricted disease mechanisms and their therapeutic approaches. The goal of our study is to develop a reproducible, efficient and cost-effective method for a directed in vitro differentiation of human iPS cells into a defined cardiomyocyte subtype in feeder-free culture conditions.

Our findings indicate that the ratio of heterogeneous populations of ventricular, atrial and pacemaker-like iPS cell-derived cardiomyocytes can be directed into a more homogeneous cardiac atrial subtype by temporal treatment with distinct small molecules. Taken together, this study will provide an efficient tool of a directed in vitro differentiation of iPS cells into defined functional cardiomyocyte subtypes for a more specific cardiac disease modeling as well as for potential clinical and therapeutic approaches.



Cardiomyocyte subtype differentiation

P1699

Genomic effects of SDF-1 on rat neonatal cardiomyocytes: comparison between commercial SDF-1 and supernatant of mesenchymal stem cells overexpressing SDF-1

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Given the keen interest in using SDF-1 α , alone or in combination with a stem cell therapy, as a stem cell homing factor for treatment of myocardial infarction, it is essential to investigate direct effects of these interventions on cardiomyocytes. We determined modulation of gene expression by SDF-1 α in rat neonatal cardiomyocytes. The purpose of the study was to identify new signaling pathways modulated by SDF-1 α in cardiomyocytes and to compare effects of SDF-1 α administered alone to effects of supernatant of mesenchymal stem cells (MSC) overexpressing SDF-1 α .

Passage 4 MSC isolated from bone marrow of adult rats were transduced with the lentiviral particles SDF-1 α -IRES-GFP-pWXLd or GFP-pWXLd. Neonatal rat cardiomyocytes were culture-expanded then stimulated 1 hour with commercial SDF-1 α (5 μ M) diluted in cardiac culture medium or with cardiac culture medium alone, and with conditioned medium of MSC overexpressing SDF-1 α after lentiviral transduction or with conditioned medium of MSC transduced with GFP-pWXLd. Gene expression profile was analyzed by microarray and confirmed by RTQ-PCR and ELISA. SDF-1 α protein concentration in supernatant of MSC transduced with

SDF-1 α -IRES-GFP-pWXLd was 2.4 ± 0.1 nM. Micro-array analysis revealed that SDF-1 α regulated 1.21% of all transcripts in rat cardiomyocytes. Among the 60 unique annotated common genes that were rapidly modulated in the 2 conditions (commercial SDF-1 α and supernatant of MSC overexpressing SDF-1 α), 34 were upregulated and 26 downregulated. Two new pathways implicated in lipid metabolism (the adipocytokines and PPAR signaling pathways) were downregulated. We confirmed by RTQ-PCR that SDF-1 α upregulated JAK2 and AKT, factors implicated in the anti-apoptotic and pro-survival pathways. We also showed that commercial SDF-1 α downregulated fatty acid binding protein, angiopoietin-related protein 4 precursor and adiponectin gene expression, factors implicated in fatty acid transport and metabolism. Protein expressions of adiponectin and lipoprotein lipase were also downregulated by SDF-1 α . Interestingly, supernatant of MSC transduced with the GFP-pWXLd lentivirus upregulated gene expression of fatty acid binding protein and angiopoietin-related protein 4 precursor while this response was inhibited by SDF-1 α overexpression. In conclusion, SDF-1 α modulates negatively expression of several factors implicated in lipid metabolism. Modulation of cardiomyocytes gene expression by conditioned medium of MSC overexpressing SDF-1 α cannot be deduced from the response to commercial SDF-1 α .

P1700

Assessment of bone marrow-derived progenitor cells in stable chronic heart failure in relation to cytokine profile

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Purpose: Stem cell dysfunction could explain reduced efficacy of autologous stem cell therapy in chronic heart failure (CHF). Hence, we evaluated numbers and function of stem/progenitor cells in CHF patients and explored the relation with inflammatory cytokines.

Methods: Bone marrow (BM) and peripheral blood (PB) was obtained from 18 CHF patients (LVEF $32 \pm 14\%$) and 8 healthy subjects (HS) during surgery. We quantified hematopoietic (HPC; CD45dimCD34+SSC^{low}) and endothelial (EPC; CD45dimCD34+KDR+) progenitor cells in BM and PB and evaluated migration to SDF-1 α /VEGF and granulocyte/macrophage differentiation capacity (GM-CFU) of BM mononuclear cells (MNC). Plasma IFN γ , TNF α and IL-6 were measured in BM and PB.

Results (Table 1). Numbers of HPC and EPC were elevated in PB of CHF patients, EPC related to LVEF ($r = -0.732$; $p = 0.007$), while those in BM were comparable to HS. Passive, but not active migration of BM-MNC was increased in CHF. GM-CFU numbers did not differ, but correlated with LVEF ($r = 0.894$; $p < 0.0001$). All cytokine levels were lower in BM vs. PB ($p < 0.05$). CHF patients had higher BM IL-6, BM TNF α and PB IL-6 levels compared to HS. Increased passive BM-MNC migration correlated with higher IL-6 in BM ($r = 0.680$; $p = 0.003$) and PB ($r = 0.735$; $p = 0.001$), increased circulating HPC numbers with elevated BM TNF α ($r = 0.561$; $p = 0.019$).

Conclusion: In contrast to the anticipated deficiency of BM progenitor cells, BM in CHF was not depleted from HPC/EPC and there was an active recruitment into the circulation, which was strongly related to increased levels of inflammatory cytokines in CHF. Moreover, BM-MNC showed a preserved migratory and GM-CFU differentiation capacity.

P1701

Three-dimensionally engineered fibrin patch comprising human umbilical cord blood-derived mesenchymal stem cells induces a post-infarction functional recovery in mice

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Table 61027.

	BM of CHF	BM of CHF	BM of CHF value BM	PB of CHF	PB of HS	p-value PB
HPC (/E6 CD45)	12803 (9507-16346)	15179 (12126-20636)	0.320	1367 (988-2180)	684 (603-787)	0.020
EPC (/E6 CD45)	204 (79-350)	303 (151-550)	0.417	69 (30-261)	34 (20-44)	0.057
Passive Migration (%)	5.9 (4.2-15.4)	3.2 (1.8-3.7)	0.003	N.A.	N.A.	N.A.
Active Migration (%)	27.6 (21.9-31.1)	24.8 (20.9-32.6)	0.972	N.A.	N.A.	N.A.
GM-CFU	44 (36-72)	76 (50-92)	0.157	N.A.	N.A.	N.A.
IFNy (pg/ml)	3.58 (0.83-6.87)	1.07 (0.20-3.20)	0.081	4.48 (2.38-8.14)	4.34 (2.44-4.66)	0.393
TNF α (pg/ml)	1.93 (1.49-2.54)	1.29 (1.05-1.63)	0.013	2.21 (1.26-3.18)	1.74 (1.32-2)	0.067
IL-6 (pg/ml)	1.13 (0.52-2.14)	0.18 (0.05-0.48)	0.003	1.26 (0.69-2.72)	0.37 (0.11-0.51)	0.002

Results are expressed as median (IQR); p-values for comparison between CHF and HS, respectively in BM and PB.

Purpose: Considerable research effort has been dedicated to restoring myocardial cell slippage and limiting ventricular remodeling after myocardial infarction (MI). We examined the capacity of a three-dimensionally (3-D) engineered fibrin-based patch filled with human umbilical cord blood (UCB)-derived mesenchymal stem cells (MSCs) to induce recovery of cardiac function following MI.

Methods and results. CBMSCs modified to co-express luciferase and fluorescent protein reporters were mixed with fibrin and applied as a 3-D adhesive construct (fibrin-cell patch) over the infarcted myocardium in mice (MI-UCBMSCs). Non-invasive bioluminescence imaging demonstrated early proliferation and vascular differentiation of UCBMSCs within the construct in the post-infarcted animals implanted with the fibrin-cell patches (MI-UCBMSCs).

The implanted cells also participated in the formation of new, functional microvasculature that connected the fibrin-cell patch to both the subjacent myocardial tissue and the host circulatory system. Treatment of infarcted hearts with the patch comprising cells also resulted in functional improvement relative to post-infarction values of left ventricular ejection fraction, reaching contractility parameters similar to those of sham-treated animals. In contrast, animals treated with fibrin alone (MI-Fibrin) exhibited worsening values, similar to those of untreated control-MI animals.

Conclusions: A 3-D engineered fibrin patch comprising UCBMSCs transplanted locally over an infarcted myocardium wound promotes a general recovery of lost cardiac functions.

P1702

Intravenous adipose-derived stem cell therapy one day after acute myocardial infarction results in fast recovery of cardiac function in rats

This study was funded by a grant from the Dutch Technology Foundation STW (project 10507) and an unrestricted grant from ViroPharma Inc. R Reindert Emmens¹; M Varma¹; L Woudstra¹; BA Naaijken¹; E Meinster¹; A Van Dijk¹; M Van Ham²; JWM Niessen¹; LJM Juffermans³; PAJ Krijnen¹

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Purpose: In rats, we examined the therapeutic efficacy of intravenous (IV) adipose-derived stem cell (ASC) administration 1 day after acute myocardial infarction (AMI). Administration at this timepoint may be beneficial compared to 7 days (commonly used timepoint for ASC administration), as the infarct core actively expands between both timepoints. However, the inflammatory status of the infarct area 1 day post-AMI makes stem cell retention and survival difficult. Therefore, to enhance ASC infiltration and retention, a novel technique was used, where ASCs are coupled to microbubbles (referred to as StemBells) and guided into the infarct area using ultrasound.

Methods: AMI was induced through a 40 min coronary artery ligation in 31 male Wistar rats, resulting in an anterior wall infarction. The rats were divided in four groups, and received an IV injection of 1 million StemBells 1 day post-AMI (StB1, n=8), 7 days post-AMI (StB7, n=9) or both 1 and 7 days post-AMI (StB1+7, n=7). The fourth group did not receive StemBells (control, n=7). Cardiac function was measured by echocardiography 7 days and 42 days post-AMI. The rats were terminated at day 42, after which the hearts were examined (immuno)histochemically for infarct size and macrophage infiltration.

Results: In all three StemBell groups, a significant reduction in infarct size was observed compared to the control group. In addition, in all three StemBell groups, a macrophage population with a higher percentage of the ED2+ anti-inflammatory macrophage subset was also observed compared to control rats. Infarct size and macrophage populations did not differ between the StemBell groups. At 7 days post-AMI, the StB1 and StB1+7 groups had a significantly higher (left ventricular) fractional shortening and anterior wall contraction compared to the control and StB7 groups. At day 42 all three StemBell groups showed an increase in fractional shortening and anterior wall contraction compared to control rats, and again did not differ significantly between each other.

Conclusions: We observed that at day 42, IV administration of StemBells at day 1, day 7 or both resulted in an equal restoration of infarct size and cardiac function. However, administration at day 1 resulted in a faster restoration of cardiac function, which would be beneficial for patients recovering from AMI.

P1703

Improvement of rat left ventricle function and vascularization after application of cell sheets from VEGF165-expressing adipose-derived stromal cells

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Aim: Cell sheet (CS) technology is a rapidly developing approach, which allows transplantation of large cell grafts to the site of injury without disruption on cellular matrix. Moreover, CS transplantation allows to cover injured tissue to ensure its survival and - possibly - influence remodeling, which is of crucial importance for heart.

Here, we developed CS from adipose-derived stromal cells (ADSC), which represent a feasible cell type with profound regenerative capacity, and examined the effects of CS transplantation on the restoration of infarcted heart.

Methods and Results: CSs were formed in a 12-well uncoated plate overnight from 1.2 mln. of primary rat ADSC, which were modified by baculovirus to induce overexpression of VEGF165. Baculoviral modification was carried out in a rapid (6 h) manner to ensure cell survival and overall feasibility of the procedure and resulted in significant (up to 300 ng/10⁶ cells) production of human VEGF165 by rat ADSC. Modification was conducted to increase ADSC engraftment and therapeutic potential, which relies on their paracrine activity. Control cells were transduced by baculovirus with eGFP (resulting in up to 85% efficacy by FACS) or remained unmodified (mock medium treatment for 6 hours).

MI in rats was induced by descending coronary artery ligation and CS from VEGF-ADSC, GFP-ADSC or control ADSC (n=4-5/group) was applied to ischemic region with fibrin glue to ensure CS position and adhesion. Fibrin glue without CS was used as a negative control.

Ultrasound echocardiography conducted at Days 0 and 14 showed significant change of ejection fraction in ADSC and GFP-ADSC group compared to negative control, which was supported by histology findings, which showed increased capillary density and reduction of MI size and collagen deposition. Most profound beneficial effect was observed in VEGF-ADSC group at day 14. CS also remained intact at the site of application and were found at both - gross evaluation and in histology section (at H&E and labeled cells assay) and was significantly vascularized by capillary (CD31+) and arteriolar (a-SMA+) vessels indicating cell engraftment and survival.

Conclusion: Thus, we can conclude, that baculoviral modification of ADSC is a feasible and effective method to generate VEGF-expressing CS, which have regenerative potential in MI and heart failure due to their pro-angiogenic capacity and ability to alleviate reduction of LV function.

P1704

Efficacy of epicardial delivery of cardiac stem based cell sheets after myocardial infarction

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Aims: For the last decade, cell therapy has emerged as one of the most promising therapies for patients suffering from post-MI heart failure. Several studies employing the direct injection of different types of cells have been already clinically performed. However, a massive loss of transplanted cells due to physical strain, poor cell survival in inflammatory and hypoxic environment or cell wash-out and difficulty to control the location of the grafted cells remain problems to be solved. In contrast to direct cell injection novel cell transplantation methodology based on cell sheets transplantation has been proposed to recover damaged heart function. We here investigated the integration and survival of scaffold-free cardiac stem cells-based sheets and their potential for myocardial regeneration.

Methods: After coronary artery ligation in rats, syngeneic c-kit+Lin-cardiac stem cells (CSC) marked with vital fluorescent dye (Cell Tracker CM-DIL) were grafted by epicardial placement of CSC sheets generated using temperature-responsive dishes. Cell sheets neovascularization and integration to underlying myocardium, transplanted CSC proliferation and differentiation were assessed by immunofluorescence analysis of myocardial frozen sections, obtained 14 days after transplantation.

Results: Immunofluorescence analysis of CSC sheets before transplantation has shown that CSC in sheets interact with each other via connexin 43, produce extracellular matrix proteins, proliferate and express of the cardiac transcription factor Gata 4. Histological analyses of heart frozen sections revealed that on day 14 the CSC sheet grafts had produced thick tissues, with a high-cell density, and promoted vascularization. Proliferation and migration to underlying myocardium of marked (Cell Tracker CM-DIL) cells from sheets were observed. Part of transplanted CSC showed signs of differentiation to cardiomyocytes and endothelial cells.

Conclusion: Transplantation of cardiac stem cells in cell sheets resulted in CSC survival, proliferation, migration and differentiation, and was associated with neovascularization and structural integration of cell sheets in myocardium. These data strongly support the potential of CSC sheet transplantation for the treatment of damaged heart.

P1705

Exosome secreted miR-27a-3p and miR543 are critical modulator of PDI activity in cardiac stem cells during hypoxia

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Background: Protein disulfide isomerase (PDI) is an enzyme involved in the unfolded protein response necessary to prevent protein misfolding during stress. The objective of this work was to investigate the role that the exosomes secreted during hypoxia may have in modulating PDI function in cardiac stem cell (CSCs).

Methods: Surgical specimens were collected from myocardium of 21 patients undergoing CABG and CSCs were isolated and characterized. The modulation of PDI in CSCs and its redox state were evaluated during hypoxia (1% O₂) and analyzed at 12, 24, 48 and 96 hours. Moreover, exosomes from normoxic and hypoxic CSC conditioned medium were isolated and the RNA was extracted in order to evaluate the modulation of a panel of 174 microRNA (miR).

Results: No differences were found in PDI expression comparing CSC cultured in normoxia vs hypoxia. Importantly, we found that hypoxia leads to an increase of the oxidative form (active) of PDI in CSCs, which induces an efficient folding of the substrate proteins, decreasing cellular apoptosis and senescence during hypoxia: when PDI was silenced with the use of specific siRNA a 4-fold increase in the rate of apoptosis was observed in CSCs ($p < 0.005$).

Moreover, we found that this effect is mediated by CSCs exosomal secreted miR-27a-3p and miR-543: the downregulation of these miRs during hypoxia led to an increased expression of the target protein ERO1L in CSCs that in turns oxidizes PDI, which directly catalyzes the formation of disulfide bonds, protecting the folding of proteins involved in CSCs survival and differentiation such as IGF-1 and IGF-2.

Conclusion: Our results indicate that exosomal secreted miR-27a-3p and miR-543 are critical modulator of PDI activity in CSCs during hypoxia. Importantly, this autocrine/paracrine mechanism is fundamental for the survival and preservation of the stem cell pool during stress and induces the transition from the replicative state to lineage specification of CSCs during hypoxia.

P1706

Protein disulfide isomerase is a fundamental regulating factor of cardiac stem cell survival during hypoxia

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Background: The human heart is characterized by the presence of cardiac stem cell (CSC) stored in niches and widespread within the myocardium. Stem cell niches are exposed to low oxygen tension and this metabolic adaptation offers a selective advantage to CSC compared to terminally differentiated cells, such as myocytes,

during hypoxia. However, the molecular mechanisms are poorly understood. Protein disulfide isomerase (PDI), is a member of the unfolded protein response, which is activated to prevent the protein misfolding during stress, as occurs during ischemia. The objective of this work was to determine whether PDI is present and functional in CSC and in myocytes.

Methods: Surgical specimens were collected from the atrial and ventricular myocardium of 21 patients and hCSCs and myocytes were isolated. This cohort of patients included 10 women and 11 men affected by ischemic cardiomyopathy.

Results: The PDI was very low expressed in the myocytes and interestingly, by qRT-PCR, a 2000-fold difference was found in PDI expression comparing CSC and myocytes. Subsequently, the effects of hypoxia (1% O₂) were studied in hCSCs and analyzed at 12, 24, 48 and 96 hours. With respect to differentiated cells, CSC showed consistently higher expression of PDI both at RNA and at protein level. Moreover, hypoxia led to upregulation of HIF1 α transcripts in a time dependent manner both in myocytes and CSC. This results were coupled with an increase of the transcripts for the stemness associated genes Oct4, Nanog and IGF-1R in CSCs. However no differences were found in PDI expression comparing CSC cultured in normoxia vs hypoxia. Subsequently, the red-ox state of PDI cysteines was evaluated in normoxia and hypoxia: the two catalytic sites of PDI exist at equilibrium between both the oxidized and reduced form. We found that hypoxia, even not changing the total protein expression of PDI, leads to an increase of the oxidative form (active) in CSCs, which could lead to efficient folding of the substrate proteins potentiating cellular protection. Apoptosis assay was performed in hCSCs cultured in hypoxia for 48h: when PDI was silenced with the use of specific siRNA a 4-fold increase in the rate of apoptosis was observed.

Moreover, a high correlation was found between the expression of PDI in the CSC and the left ventricular remodeling evaluated 5 months after revascularization ($p < 0.05$; R² 0.41).

Conclusions: Our data indicate PDI is a key regulator of CSC response to hypoxia and favors the conservation of their undifferentiated phenotype and most importantly their potential activation after injury.

P1707

Assessment of myocardial blood supply and metabolism after autologous bone marrow mononuclear cells intracoronary injection in patients with inoperable coronary artery disease

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Purpose: Little is known about mechanisms of stem cell therapy.

Methods: Autologous bone marrow mononuclear cells were injected during coronary procedures in 22 patients with coronary disease without percutaneous revascularization. Valuation of myocardial blood supply and metabolism performed by single-photon emission computed tomography (SPECT) and positron emission tomography (PET), as well as nitroglycerine consumption, exercise test and 6-min walk test were determined.

Results: Improvement of functional class of angina pectoris was detected in 90% of patients after 6-9 months of follow up. The duration of clinical improvement and duration of improvement of myocardial blood supply measured by SPECT lasted for 3-4 years. Repeated procedures of autologous bone marrow mononuclear cells injections in 5 patients led to repetitive improvement of myocardial blood supply.

Conclusions: 1. Autologous bone marrow mononuclear cells intracoronary injections improve myocardial blood supply and metabolism in majority of patients with inoperable coronary artery disease for 3-4 years. 2. Repeated procedures lead to repetitive improvement of myocardial blood supply.

P1708

Optimised differentiation and 3D cell culture conditions modulate function and fate of human pluripotent stem cell-derived endothelial cells

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Background: Endothelial derivatives of human pluripotent stem cells may offer potential regenerative treatments in ischemic cardiovascular diseases. Here we studied the suitable differentiation conditions toward arterial and venous endothelial subpopulations and fate of these cells during 3D culturing and in vivo engraftment.

Methods and Results: Human embryonic stem cells (hESC) were differentiated via embryoid body (EB) or monolayer method in normoxigenic and hypoxic conditions. CD31-positive endothelial cells (EC) were sorted by FACS and compared with human induced pluripotent stem cell derived endothelial cells (hiPSC-EC). Both hESC-EC and hiPSC-EC showed endothelial characteristics: cobblestone pattern, ac-LDL uptake, tube formation in vitro and CD45 negativity. Proteome

profiling revealed high abundance of angiogenesis-related proteins in cell lysates and in supernatant. As assessed by qPCR, angiopoietin2 mRNA levels increased in hESC-EC when differentiated via EB method (EB in normoxia 353.17 ± 86.29 ; EB in hypoxia 323.89 ± 86.63 , monolayer 27.20 ± 9.92 vs. hESC, $p < 0.001$). High expression of arterial (EphrinB2, Notch1-2) and venous (EphB4) endothelial markers was shown, suggesting the presence of mixed endothelial population in culture. However, no significant differences were found in ratio of arterial and venous subpopulations in the different developmental protocols. For engineering 3D vascular constructs decellularised human aortic slices (300µm) were repopulated with hESC-EC and hiPSC-EC. As shown by vital dyes, hESC-EC and hiPSC-EC remained viable on engineered matrices in vitro and upon subcutaneous engraftment into athymic nude rats in vivo. We found an increase in mRNA levels of all arterial and venous marker genes after in vivo conditioning of cells. Engineered bioscaffold activated the antithrombotic effects of the cells (secreted levels of chemokine Rantes (pg/ml): hESC-EC 229.60 ± 37.95 , hESC-EC on bioscaffold 83.66 ± 52.06 ; hiPSC-EC 234.93 ± 22.84 , hiPSC-EC on bioscaffold 127.96 ± 63.65 , $p < 0.01$, $n=6$). **Conclusions:** Differentiation conditions influenced arterial and venous endothelial fate. 3D culturing increased antithrombotic function. Levels of endothelial marker genes increase in vivo, suggesting further maturing. Angiogenic potential of pluripotent stem cell derived endothelial cells promises vascular tissue engineering.

P1709

Epigenetic balance of aberrant rasal1 promoter methylation and hydroxymethylation regulates cardiac fibrosis

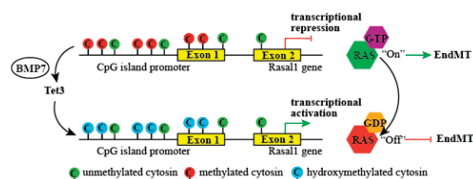
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Background- Methylation of CpG island promoters is a prototypical epigenetic mechanism to stably control gene expression. The aim of this study was to elucidate the contribution of aberrant promoter DNA methylation in pathological endothelial to mesenchymal transition (EndMT) and subsequent cardiac fibrosis.

Methods and Results- In human coronary endothelial cells TGFβ1 causes aberrant methylation of RASAL1 promoter, decreased Rasal1 expression and EndMT. In endstage failing versus nonfailing human myocardium, increased fibrosis was associated with significantly increased RASAL1 promoter methylation, decreased RASAL1 expression, increased Ras-GTP activity and EndMT marker activation. In mice with pressure overload due to ascending aortic constriction, Bone Morphogenic Protein 7 (BMP7) significantly reduced RASAL1 promoter methylation, increased RASAL1 expression, decreased EndMT markers and ameliorated cardiac fibrosis. The Ten eleven translocation (TET) family enzyme TET3, which demethylates RASAL1 promoter was decreased in fibrotic mouse hearts and in human coronary endothelial cells upon EndMT-induction with TGFβ1, and was restored in both systems with BMP7. Knockdown of TET3 in human coronary endothelial cells abolished the BMP7 effects. In addition, ChIP assay revealed specific binding of TET3 to the RASAL1 promoter and BMP-SMAD binding motifs were identified in the TET3 promoter.

Conclusions- Our study provides proof-in-principle evidence that transcriptional suppression of RASAL1 through aberrant promoter methylation contributes to EndMT and ultimately to progression of cardiac fibrosis. Such aberrant methylation can be reversed through Tet3-mediated hydroxymethylation, which can be specifically induced by BMP7. This may reflect a new treatment strategy to stop cardiac fibrosis.



P1710

Pharmacological reprogramming of cardiac cells by small molecules: identification of a potent TBX5 gene expression enhancer

DFGGrant BE 2025/8-2, Werner Otto Stiftung 2010SY Sari Yohana Panjaitan¹; MP Zafriou²; C Noack²; JP Von Kries³; E Specker⁴; E Klussman⁵; T Eschenhagen¹; A Hansen¹; MW Bergmann¹

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Background and Purpose: Previously, we found inhibition of β-catenin transcription activity to be necessary and sufficient for cardiomyocyte differentiation in the adult heart similar to cardiac embryonic development. Transcription factors driven by β-catenin inhibition include TBX5 also found to be central for reprogramming of fibroblasts towards a cardiomyocyte cell fate. Here we describe the identification and characterization of a small molecule potentially enhancing TBX5 gene expression in human induced pluripotent stem cells (hiPS) as a first step towards pharmacological reprogramming.

Methods: A 1000 bp TBX5/luciferase promoter construct was stably transfected into a HEK293T cell line to screen for small molecules as TBX5 gene activators. Retinoic acid (RA; 10µM) served as positive control. A large automated screening has identified 352 small molecules linked to TBX5 from a public library of 22,500 molecules, which were further validated manually. Identified molecules were then subjected to a well established in vitro cardiac differentiation model based on hiPS. Cardiac differentiation of hiPS is started by generation of embryoid bodies from undifferentiated hiPS. Mesodermal differentiation took place by addition growth factors such as Activin A. Cardiomyocytes induction is triggered by Wnt-inhibitor supplemented into cells media. Contracting cardiomyocytes are observed from day 15- day 20. Following addition of small molecules, expression of TBX5 and other cardiac markers such as TBX1, alpha-MHC, HAND1/2, ISLET-1 and NKX2.5 as well as beating cell clusters was investigated.

Results: Out of 352 small molecules, eight small molecules stimulated the TBX5 promoter more potently than the positive control RA. Small molecule "A15", previously not linked to any cell differentiation or heart pathophysiology, showed 2.47-fold reporter gene activation. Real-time PCR showed that hiPS endogenous TBX5 expression started at day4 and increased up to day 14. Adding "A15" in hiPS at concentrations between (0.01 µM) to (10 µM) on day4 have increased TBX5 and TBX1 gene expression by 4- and 90-fold, respectively. Beating cell clusters have decreased with higher "A15" concentration suggesting a toxic effect. At 0.1 µM, "A15" was as potent as the positive control regarding alpha-MHC expression and beating cell clusters.

Conclusion: The data demonstrated "A15" to be a potent activator of TBX5 gene expression. Activation of TBX5 alone appears not to be sufficient to drive hiPS differentiation towards a cardiomyocyte cell fate.

P1711

Overexpression of the muscle specific chaperone Melusin delays heart failure and mortality in a mouse model of Emery Dreyfus cardiomyopathy

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Purpose: Familial cardiomyopathies are caused by genetic mutations that induce accumulation of misfolded proteins with consequent cardiomyocyte death and maladaptive cardiac remodelling. Molecular chaperones are a family of proteins devoted to prevent accumulation of misfolded proteins by promoting either their refolding or degradation via the ubiquitin-proteasome or the autophagosome systems and can, thus, represent a potential mean to counteract familial cardiomyopathies.

Methods: Melusin is a muscle specific chaperone protein whose overexpression effectively prevents maladaptive cardiac remodeling and heart failure both in pressure overload and myocardial infarct mouse models. In this study we use in vivo gene delivery with cardiotropic adeno associated virus 9 vector to induce increased melusin expression in the heart of mice carrying H222P Lamin A mutation mimicking human Emery-Dreifuss familial cardiomyopathy. Mutant male mice develop spontaneous dilated cardiomyopathy from 5 months of age and die within 10-12 months of age.

Results: Homozygous mutant mice were injected with AAV9-Melusin (i.v. injection of 1012 viral particles/mouse) either at 1 month of age before development of the cardiomyopathy or at 5 months when cardiomyopathy was already present to test for both preventive and therapeutic activity. Cardiac function was monitored by echocardiography in the months following AAV injection. While untreated mice progressively developed left ventricle dilation and reduced contractility (FS%), mice injected with AAV9-Melusin retained physiological level of contractility and were protected toward LV dilation. Ten months after the treatment, 40% of mutant mice died, while 100% of melusin-treated mice were alive. A second group of mutant male mice was injected with AAV9-melusin at 5 months of age when the cardiomyopathy was already detectable. Interestingly melusin prevented the deterioration of contractility in the following 6 months and significantly reduced mortality.

Conclusions These data indicate that melusin chaperone overexpression can effectively delay the onset of Emery-Dreifuss cardiomyopathy as well as arrest the progression of the already established pathology.

P1712

Physiologically trained cardiac adipose tissue derived progenitor cells within fibrin scaffolds restore post-infarction scars

RD12/0042/0047; RD12/0019/0029; 122232; SAF2008-05144-C02-01 and SAF2011-30067-C02-01; Fundació Privada Daniel Bravo Andreu; NMP3-SL-2009-229239A Aida Lucia-Valledeperas¹; C Soler-Botija¹; C Galvez-Monton¹; C Prat-Vidal¹; S Roura¹; I Perea-Gil¹; J Rosell-Ferrer²; R Bragos²; A Bayes-Genis³

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Purpose: Cardiac tissue engineering aims to develop biostructures capable of re-establishing physiological organization and function of the infarcted myocardium. Cardiac cells are subjected to mechanical and electrical forces, which regulate gene expression and cellular function. Therefore, in vitro electromechanical stimuli could benefit further integration of therapeutic cells into the myocardium. Our goals were: 1) study the viability of a tissue engineered construct with cardiac adipose tissue-derived progenitor cells (cardiacATDPCs); and 2) examine the effect of electromechanically stimulated cardiacATDPCs within a myocardial infarction (MI) model in mice.

Methods: CardiacATDPCs were electromechanically stimulated, harvested and labelled to generate the 3D fibrin construct. The electromechanical stimulation protocol was designed to mimic the physiological heart environment: 2ms pulses of 50mV/cm at 1Hz and 10% stretching during 7days. Cell viability was evaluated through a Life&Dead assay. The cellular construct was implanted in the murine heart and animals were sacrificed at 3weeks post-implantation. 40 animals were randomly distributed: without cells (control MI, fibrin MI) and with stimulated or non-stimulated cells (treated MI and sham). Echocardiography, gene and protein analysis were also carried out.

Results: In vitro electromechanical stimulation on cardiacATDPCs showed increased expression of cardiac transcription factors, structural genes and calcium handling related genes. After 3 weeks of in vitro culture in the fibrin construct, cells exhibited high viability and remained labeled. Cell treatment resulted in functional improvement of left ventricular ejection fraction (LVEF) relative to post-infarction values; indeed, stimulated cardiacATDPCs produced a 4.7% average increment compared to non-stimulated cells, as revealed by echocardiography. On the contrary, control MI and fibrin MI presented a decrement in LVEF (4.1% and 3.0% reduction, respectively). Finally, histology showed cell proliferation and main cardiac markers expression of implanted cardiacATDPCs, but also scarce migration to the mouse myocardium.

Conclusions: The electromechanical stimulation protocol designed enhances cardiac properties of therapeutic cells at genetic and protein level. Furthermore, the construct used in our study confers a suitable environment for cell viability, proliferation, cardiac maturation and migration to infarcted myocardium. All together, electromechanical stimulation of therapeutic cells previous implantation could be a valuable tool for cardiac regeneration approaches.

Results: Klotho mRNA and FGFR were detectable in non-ischemic cardiomyopathy and in healthy hearts by RT-PCR and immunohistochemistry. Expression of both Klotho mRNA and FGFR1 mRNA was significantly upregulated in cardiac biopsies derived from patients suffering from non-ischemic cardiomyopathy as compared to healthy controls by quantitative RT-PCR (2.65 ± 0.70 vs. 1.32 ± 0.43 ; $p = 0.002$, and 1.65 ± 0.43 vs. 1.08 ± 0.21 ; $p = 0.01$, respectively). Immunohistochemically, double staining revealed colocalization of Klotho and FGFR in diseased cardiomyocytes.

Summary and Conclusion: We show that Klotho and FGFR are concomitantly and highly expressed in non-ischemic cardiomyopathy. Whether adverse cardiac effects of FGF23 are mediated by its coreceptor Klotho and / or cardiac expressed Klotho and its soluble ligand exerts independent effects in heart failure has to be addressed in future studies.

P1714

The H19 long non-coding RNA is linked to pathological cardiac hypertrophy

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Objective: It has been shown in the past that small regulatory RNAs like microRNAs are key players in the development of cardiac diseases. Recent reports have started to reveal the importance of long non-coding RNAs (lncRNAs) in heart development and suggest a potential role in human disease, notably cardiovascular maladies. The regulation of the H19 gene has been well described as a paradigm of genomic imprinting and further implicated in human genetic disorders and cancer. After birth, H19 is predominantly expressed in muscle tissue where it promotes differentiation and regeneration. The lncRNA's biological function in the heart remains largely unclear. Thus, we elucidate the role and function of H19 in cardiac hypertrophy.

Methods and Results: In adult mice, H19 is globally repressed in several tissues, but is abundantly expressed in the skeletal and cardiac muscle. Furthermore, this transcript can be detected in all cardiac cell types, including cardiomyocytes. Cardiac hypertrophy induced by pressure overload or by angiotensin II infusion lead to a significant reduction of H19 expression in mouse hearts. To mimic this situation in vitro, we modulated the lncRNA levels in cardiac cell lines as well as primary cardiomyocytes. Silencing of H19 by esiRNAs induced a hypertrophic response including an increase in cardiomyocyte cell size and an alteration of the cardiac expression pattern. Since the sequence and genomic organization of H19 is well conserved between mice and humans, we assessed its role in diseased human hearts. In accordance with our findings in the mouse model, hypertensive heart tissue from aortic stenosis patients demonstrated a strong downregulation of H19, suggesting a preserved role in cardiac disease.

Conclusion: In this report we identified the lncRNA H19 as an important player in cardiac hypertrophy. A decrease in H19 expression in pressure-overloaded murine hearts and in hypertrophied human hearts might be related to an increase in cardiomyocyte cell size. Consequently H19 is a prospective therapeutic target to influence the genesis of heart failure.

BASIC SCIENCE: HYPERTROPHY SIGNALING

P1713

Klotho and FGF receptor are concomitantly expressed in human individuals with heart failure

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Introduction: In clinical studies elevated levels of FGF23 have been linked with the advent and progression of heart failure. Klotho acts as essential coreceptor for FGF23 whereby tissue-specific expression of Klotho determines target organs of FGF23. Moreover, Klotho is an antiaging protein and actively involved in the prevention of arteriosclerosis. Previous data in mice suggest that FGF23 exerts its effects on LV hypertrophy independently of Klotho due to not detectable expression of the Klotho receptor. Since no information is available on Klotho expression in human individuals with heart failure we aimed to investigate the cardiac expression of Klotho and FGF receptor in patients with heart failure.

Methods: Endomyocardial biopsies from patients with non-ischemic cardiomyopathy (n=6) and patients 3-4 weeks after successful heart transplantation (n=6) were analyzed for the expression of Klotho and FGF receptor. The latter were considered healthy controls after exclusion of graft rejection. Total RNA was isolated and reverse transcribed using QuantiTect RT kit. Exon spanning primers for human Klotho were designed. Using SYBR green (Applied Biosystems, USA) quantitative gene expression was calculated using the comparative $\Delta\Delta Ct$ -method with RPL32 as a reference gene. Immunohistochemistry was performed utilizing monoclonal mouse and rabbit antibodies against FGFR and Klotho protein, respectively (Abcam, USA)

P1715

Effect of emap II to cardiohemodynamics in hypertension

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Endothelial monocyte-activating polypeptide-II (EMAP II) is a cytokine that has strong effects on endothelial cells, such as inhibition of cell proliferation, migration and vascularization and induction of apoptosis, stimulates monocyte migration. EMAP-II is widely investigated as an antitumor agent. It is known that increased indicators of non-specific inflammation (C-reactive protein, interleukin-1, 6, 18) may be associated with the development of cardiovascular diseases, including hypertension, but the literature data about the connection EMAP-II with hypertension have been identified. The aim of work was investigate effect of EMAP II on heart function of spontaneously hypertensive rats (SHR) and control group. The researches were conducted on six-month Wistar and SHR male rats. The functional cardiohemodynamic indicators registered via Pressure-Volume System. The recombinant EMAP II ($10 \mu\text{g}$) was administered intravenously. It was shown that after EMAP II ES pressure in Wistar rats was increased in 26,4%. ES- and ED pressure of SHR didn't change. In SHR after EMAP II stroke volume increased by 18,2%, cardiac output - by 22%. In Wistar rats after EMAP II stroke volume decreased by 17,5%, cardiac output - by 32,2%. The end-diastolic myocardial stiffness reduced in 4,7 times in SHR after EMAP II, arterial stiffness decreased by 23,2, but in Wistar rats arterial stiffness increased by 22,7%. In hypertension, the positive effect of EMAP II was noted in the reduction of arterial stiffness, end-systolic- and maximum myocardial stiffness, increase indices of heart pump function, improvement of left ventricular relaxation. Thus, exogenous EMAP-II can have a positive effect on cardiohemodynamics in hypertension.

P1716

Long non-coding RNA Chast promotes cardiomyocyte hypertrophy

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Purpose: Long non-coding RNAs (lncRNAs) are a new class of regulators that recently have been implicated to play an important role in the pathophysiology of the heart. However, the underlying mechanisms remain largely unknown. To address this issue, we aimed to identify lncRNAs involved in the development of cardiac hypertrophy as well as their biological function.

Methods and Results: Global lncRNA expression profiling revealed that several lncRNA transcripts are deregulated during pressure overload induced cardiac hypertrophy. Among these transcripts, we identified the so far unknown lncRNA Chast (cardiac hypertrophy associated transcript) that was strongly upregulated in hypertrophic mouse hearts after transverse aortic constriction. Cell fractionation experiments indicated that Chast was specifically elevated in cardiomyocytes. Chast was further induced in cardiac tissue of calcineurin transgenic mice, suggesting that this transcript acts downstream of the pro-hypertrophic NFAT pathway. Overexpression of Chast *in vitro* was sufficient to induce cardiomyocyte hypertrophy, while GapmeR-mediated silencing attenuated phenylephrine and isoproterenol induced cardiomyocyte growth as well as expression of cardiac stress marker ANP. Structure-sequence alignments to the human system indicated four central conserved patches. Examining the expression in hypertrophic human heart tissue from aortic stenosis patients and healthy controls, one transcript revealed a strong upregulation in diseased hearts.

Conclusion: Based on genome-wide lncRNA profiling we identified a novel lncRNA that seems to promote cardiomyocyte hypertrophy and highlight a general role of lncRNAs in heart diseases.

P1717

Incomplete reverse remodeling in mice after surgical removal of chronic pressure-overload

Fundação para a Ciência e a Tecnologia (PTDC/BIM-MEC/0998/2012)/P G Rodrigues¹; D Miranda-Silva¹; M J Mendes¹; C Ferreira¹; A F Leite-Moreira¹; I Falcao-Pires¹

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Incomplete myocardial reverse remodeling (MRR) is a major determinant for heart failure patient worse outcome. We aim to establish and characterize an animal model that mimics the structural and functional changes in MRR after chronic pressure-overload (PO) relief.

PO was established in 7-weeks-old C57BL/6 mice by ascending aortic constriction. Seven weeks later, an echocardiographic evaluation was performed to assess cardiac function. Subsequently, a surgical debanding procedure (DEB) was performed in half of the banding (BA) and the control group (SHAM), resulting in 2 additional groups: BA DEB and SH DEB. Cardiac function in these 2 groups was re-evaluated by echocardiography 2 weeks later. Tissue was collected for the quantification of interstitial fibrosis and cardiomyocyte cross-sectional area using Red Sirius and hematoxylin-eosin staining, respectively.

Comparing to SHAM, PO induced left ventricular (LV) hypertrophy as confirmed by increased values of BA versus SHAM of: LV weight/tibia length: 37.59 ± 3.10 vs 26.78 ± 1.10 mg/cm, $p=0.018$; LV interventricular septum and LV posterior wall thickness in diastole and systole (IVSd/BMI): 0.88 ± 0.03 vs 0.76 ± 0.03 mm/cm², $p=0.007$; IVSs/BMI: 1.14 ± 0.03 vs 0.94 ± 0.05 mm/cm², $p<0.001$; PWD/BMI: 1.09 ± 0.04 vs 0.86 ± 0.03 mm/cm², $p<0.001$; PWS/BMI: 1.40 ± 0.04 vs 1.11 ± 0.05 mm/cm², $p<0.001$) and in LV cardiomyocytes cross-sectional area (530.00 ± 18.48 vs 467.50 ± 15.85 μm², $p=0.04$). Moreover PO raised interstitial fibrosis (4.30 ± 1.44 vs $0.51 \pm 0.15\%$, $p=0.03$). Regarding diastolic function, BA animals presented an increasing in the ratio E/E' comparing to SHAM (E/E': 17.24 ± 1.17 vs 14.17 ± 0.90 , $p=0.04$).

In BA DEB PO relief led to regression of hypertrophy to values similar to SH DEB: LV/TL - 28.88 ± 2.17 vs 25.22 ± 1.75 mg/cm; IVSd/BMI - 0.80 ± 0.03 vs 0.78 ± 0.03 mm/cm², IVSs/BMI - 1.07 ± 0.06 vs 1.06 ± 0.05 mm/cm²; PWD/BMI - 0.93 ± 0.04 vs 0.88 ± 0.03 mm/cm²; PWS/BMI - 1.16 ± 0.06 vs 1.13 ± 0.07 mm/cm². Regarding diastole, also E/E' was normalized (13.46 ± 0.64 vs 14.37 ± 0.87). Interestingly, the LV diameter of BA DEB animals was significantly higher comparing to SH DEB animals (LVd: 0.93 ± 0.03 vs 0.88 ± 0.04 mm/cm²).

The relief of LV PO normalized LV hypertrophy and diastolic function but was unable to prevent LV dilation. Further studies to clarify the mechanisms behind LV dilation in this model are needed. We have shown that this mice model

of reversible banding might represent an interesting model to better understand the pathways associated not only to incomplete MRR, but also to LV dilation.

P1718

Statin therapy initiated pre- instead of post-high cholesterol diet is more beneficial in attenuating hypercholesterolemia-induced cardiovascular cell apoptosis

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Hypercholesterolemia is a common health problem that significantly increases risk of cardiovascular disease in part through the activation of apoptotic pathways. We evaluated the impact of dietary and statin therapy modification (measures known to favorably influence hypercholesterolemia outcome) on the incidence of cardiovascular apoptosis and modulators of the apoptotic response, the S100 proteins B, A1, and A6 and their receptor, the receptor for advanced glycation end-products (RAGE). Male New Zealand white rabbits (16 weeks old) were fed either a normal diet for 8 weeks, a high cholesterol diet (HCD) (containing 2% cholesterol) for 8 weeks, simvastatin (SIM) (3 mg/kg/day) for 8 weeks, HCD for 8 weeks and SIM for an additional 8 weeks, or SIM for 8 weeks and HCD for an additional 8 weeks. HCD compared to a normal diet increased plasma and cardiovascular (cardiac and aortic) tissue cholesterol, triglycerides and LDL levels that were attenuated to a greater extent in the SIM+HCD compared to the HCD+SIM. HCD induced cardiovascular cell (cardiac myocyte and aortic smooth muscle cell) apoptosis as defined by increases in terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) positive nuclei (1.75-fold), caspase-3 activity (1.3-fold), BAX/BCL2 mRNA ratio (3-fold), compared to control. Cardiovascular cell apoptosis was progressively more attenuated in SIM+HCD compared to HCD+SIM. HCD induced the pro-apoptotic S100B 8-fold, RAGE 5-fold and decreased anti-apoptotic S100A6 by 65 per cent. SIM+HCD attenuated the expression of S100B and RAGE (3-4 fold) and increased S100A6 (3-fold) to a greater extent than HCD+SIM. S100A1 was not affected by HCD or SIM therapy. Thus, we conclude that statin therapy, initiated prior to rather than after the development of hypercholesterolemia is more beneficial in attenuating hypercholesterolemia-induced cardiovascular cell apoptosis by a mechanism that may involve the up-regulation of anti-apoptotic S100A6 and down-regulation of pro-apoptotic S100B.

P1719

Growth hormone administration influence on soleus muscle of heart failure rats

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Skeletal muscle atrophy is usually observed in heart failure. Growth hormone (GH) increases muscle mass in several clinical settings.

Objective: To evaluate growth hormone (GH) administration effects on satellite cells activation and expression of trophism-related proteins in soleus muscle of rats with aortic stenosis-induced heart failure.

Methods: Male Wistar rats were subjected to thoracotomy for ascending aortic stenosis (AS) induction. After developing tachypnea, rats were assigned into three groups (n=8): Sham, AS and AS treated with GH (AS-GH, 2 mg/kg/day for 14 days). Echocardiogram was performed before and after treatment. Muscle trophism was evaluated by histologic analysis. Protein expression was analyzed by Western-blot and satellite cells activation by immunofluorescence. Statistical analysis: Anova and Tukey or Kruskal-Wallis and Student-Newman-Keuls.

Results: Before treatment, cardiac variables did not differ between AS and AS-GH groups. GH administration preserved body weight (Sham 492 ± 32 ; AS 420 ± 32 ; AS-GH 486 ± 69 g; $p<0.05$ AS vs Sham and AS-GH). Left ventricular posterior wall thickness and right ventricle weight/body weight ratio were higher in AS and AS-GH than Sham ($p<0.05$). Soleus cross-sectional area was smaller in both AS groups than Sham (Sham 3.56 ± 45 ; AS 2.88 ± 42 ; AS-GH 2.87 ± 59 μm²; $p=0.016$). IGF-1 expression was higher in AS-GH (Sham 1.00 ± 0.25 ; AS 0.96 ± 0.46 ; AS-GH 1.67 ± 0.45 arbitrary units; $p=0.004$). p-PI3K/GAPDH (Sham 0.94 (0.74-1.28); AS 3.99 (3.01-5.46); AS-GH 3.71 (1.97-9.62) arbitrary units; $p=0.004$) was higher in AS and AS-GH than Sham and total PI3K (Sham 0.98 (0.63-1.32); AS 1.26 (1.00-2.51); AS-GH 2.51 (2.07-6.05) arbitrary units; $p=0.037$) was higher in AS-GH than Sham. MyoD, MRF4, myogenin, myostatin, follistatin, akt, atrogin-1, MuRF-1 and Pax-7 protein levels did not differ between groups. Satellite cells activation was increased in both AS groups than Sham.

Conclusion: Growth hormone administration increases IGF-1 and PI3K intracellular signaling in the soleus muscle of heart failure rats.

P1720

The neuro-cardiac interaction defines an extracellular microdomain required for neurotrophic signaling

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Purpose: Cardiac activity is tuned by sympathetic ganglia neurons (SGNs), whose survival depends on neurotrophins released in low amounts by the myocardium. Cardiac innervation is altered in heart failure, and its dysfunction is linked to arrhythmias. This study aims to i) determine whether specific cellular structures are present at the SGN-cardiomyocyte (CM) contact site, ii) investigate the role of SGN/CM contact in NGF-mediated signaling.

Methods and Results: Electron microscopy and immunofluorescence on mouse heart slices and rat SGN/CM co-cultures showed close association between SGNs and CMs, neurotransmitter vesicle accumulation, increased membrane protein density and enrichment of the NGF receptor (TrkA) at the contact site. These data support that specialized and locally organized signaling domains exist (neuro-cardiac junction, NCJ).

We tested the functional role of the NCJ in NGF-mediated pro-survival signaling. NGF expression by CMs was assessed by western blot analysis and its silencing in co-cultures caused a 66% decrease of neuronal density, suggesting that SGNs depend on NGF released by CMs. NGF binding to its receptor triggered TrkA retrograde transport to neuronal soma, that was monitored using fluorescently labeled TrkA-RFP. Retrograde receptor movements were faster in processes contacting CMs than other cardiac cells, further supporting that NGF signaling is activated by CMs. SGNs cultured on NGF-silenced CMs showed 20% decrease in the NCJ area when compared to those on wild type CMs of the same culture. Moreover, NGF uptake was observed only in processes contacting NGF-overexpressing CMs, supporting that the NCJ is central to neurotrophin-mediated signaling. Consistently, cultured SGNs in contact with CMs survived NGF withdrawal, whereas neurons alone treated with CM-conditioned medium did not survive because of the very low NGF concentration (0.13pM).

An anti-NGF antibody and a TrkA inhibitor (k252a) were used to antagonize receptor activation by NGF. Only the small membrane permeable k252a reduced SGN density, suggesting that the NCJ is an isolated microdomain. K252a was used to estimate NGF concentration at the contact site, which resulted 0.14nM, about 1000-fold higher than that in CM-conditioned medium, supporting that the NCJ allows amplification of intercellular NGF signaling.

Conclusions: Taken together, our results suggest that NGF-dependent pro-survival signaling to the neurons requires the direct interaction with myocytes, facilitating TrkA activation thanks to the development of an isolated microdomain characterized by high NGF concentration.

P1721

Loss of aquaporin-1 attenuates Ang II-mediated myocardial hypertrophy and fibrosis: role of aquaporin-1 inhibitory S-nitrosylation ?

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Changes in interstitial and cellular water content are key components of tissue edema that accompanies pathological myocardial remodeling. Aquaporins are a family of transmembrane water channels known to mediate rapid water movements following osmotic gradients. We previously identified AQP1 as a major isoform expressed in endothelial and muscle cells both in the peripheral vasculature and cardiac muscle. We now further characterized its cell-specific expression, sub-cellular localization and function in myocardial remodeling in response to neurohormonal stress.

AQP1 was clearly identified in peripheral membranes of capillary endothelial and cardiac muscle cells and is detected in peripheral membrane caveolae. Nitric oxide synthase (e.g. eNOS) is also a known caveolar resident in cardiac myocytes and inhibits cardiac hypertrophy, suggesting a potential functional interaction between the 2 proteins. To test this, we first used *Xenopus* oocytes injected with AQP1 cRNA to measure AQP1-dependent membrane permeability. These oocytes expressed AQP1 at the membrane and exhibited osmotic swelling that was classically inhibited by HgCl₂. Exposure of AQP1-expressing oocytes to NO donors or co-expression of eNOS significantly attenuated water permeability and was restored upon acute exposure to a reducing agent (DTT), suggesting an inhibitory S-nitrosylation. Indeed, we detected an EPR signal compatible with protein nitrosylation on purified AQP1 with spin-trapping. Mutation of Cys189 in the pore region of AQP1 to Serine abrogated the inhibitory effect of NO, suggesting this as the target residue for S-nitrosylation. Therefore, NO produced by eNOS inhibits AQP1-dependent water transport. To test the functional importance of AQP1 inhibition on cardiac remodeling, we used mice with genetic deletion of AQP1 (vs WT) treated with minipump

infusion of angiotensin II for 14 days. Blood pressure was measured in all mice by implanted telemetry. Ang II resulted in similar increase in BP in both genotypes. WT mice developed cardiac myocyte hypertrophy and fibrosis, which were significantly attenuated in AQP1 KO (myocyte area in WT: 702±/-23 μm² vs AQP1 KO: 462±/-13μm²; p < 0.01; n=12 mice for each genotype).

We conclude that invalidation of AQP1 critically attenuates the development of myocardial hypertrophy and fibrosis in response to chronic angiotensin II infusion. Inhibition of AQP1 by S-nitrosylation on Cys189 may participate to the anti-hypertrophic effect of cardiac eNOS. Similar inhibition could be exploited therapeutically to attenuate stress-induced cardiac edema and subsequent remodeling.

BASIC SCIENCE: NEUROENDOCRINE ACTIVATION AND RECEPTOR PHARMACOLOGY

P1722

Eplerenone via MicroRNA-208a inhibits THRAP1 to regulate hypertrophy in heart failure of rats

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ABSTRACT

Background: The role of eplerenone has been more investigated compared to the rein-angiotensin-aldosterone system in heart failure.

Methods: SD rats (N=40) were randomly divided into 4 groups after modeling of TAC with 12 weeks (n=10 in each group): control group (group A), eplerenone group (group B), ACEI group (group C) and combined treatment group (group D, also called combined group). The rats of group A,B,C,D were given 0.9% normal saline 2 ml / day, eplerenone 5.1 mg / kg · day, captopril 3.86 mg / kg · day + Metoprolol 5.1 mg / kg · day, eplerenone 5.1 mg / kg · day + captopril 3.86 mg / kg · day + Metoprolol 5.1 mg / kg · day with gavage, respectively. BNP, EF and LVDs, LVDd were measured to assess the function of eplerenone in heart failure, as well as miRNA-208a and THRAP1 were evaluated to appraise the role of eplerenone on cardiac remodeling.

Results: EF increased in eplerenone group than control group (71 ± 0.54 vs 69.66 ± 2.33, P < 0.05), while BNP decreased in placebo group compared with eplerenone group (29.07 ± 2.38 vs 23.43 ± 0.48, P < 0.05). Treatment with eplerenone from the beginning of the heart failure with TAC model increased EF and decreased BNP significantly as measured in relation to control group at 8 weeks. There was no significant change in serum potassium between eplerenone group and ACEI group (5.96 ± 0.86 vs 5.71 ± 0.39, P > 0.05), but eplerenone group evaluate the serum potassium relative to control group (5.96 ± 0.86 vs 5.17 ± 0.12, P < 0.05). In eplerenone group, miRNA-208a significantly decreased correlation to control group by QT-PCR (1.67 ± 0.75 vs 4.00 ± 0.20, P < 0.05). The level of THRAP1 in eplerenone group was higher than control group (0.32 ± 0.02 vs 0.20 ± 0.03, P < 0.001). MiRNA-208a had an effect on THRAP1 in heart failure. The level of THRAP1 in-group treated by anti-miRNA-208a increased compared with blank and negative group by QT-PCR (2.267 ± 0.140 vs 1 ± 0.003, P < 0.001; 2.267 ± 0.140 vs 1.028 ± 0.017, P < 0.001 respectively) and by Western blot with fold of change (0.6 vs 0.3, P < 0.001; 0.6 vs 0.26, P < 0.001 respectively). There was significantly pathological changes in heart failure with treatment with eplerenone.

Conclusion: This study demonstrated that eplerenone treatment not only improved the function of heart failure but also reverse the cardiac hypertrophy. Eplerenone was an effective drug in treating heart failure through miRNA-208a-THRAP1 pathway. However, we need pay more attention to the level of serum potassium.

P1723

Mechanisms of action and comparative efficacy of the novel vasodilator apelin

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Purpose: Apelin (AP) is a novel endogenous peptide and the ligand for the G protein-coupled APJ receptor. Both are widely expressed throughout the cardiovascular system. AP has vasodilator, aquaretic and inotropic properties and antagonises angiotensin II. We investigated the mechanism of action and comparative efficacy of AP (pyr1-apelin-13) in rabbit mesenteric arteries (MAs).

Methods: 3mm segments of MA were obtained from 13 male New Zealand White rabbits and were isolated and mounted on a 4-channel myograph. Following standard assessment of viability and endothelial integrity, MAs were precontracted

with 10-5M norepinephrine. Cumulative concentration-response curves were then constructed with AP (1x10-8M - 3x10-5M) in the presence and absence of the nitric oxide synthase inhibitor L-NAME (10-4M); and also in arteries with mechanically denuded endothelium. We also compared the vasodilator efficacy of AP to that of acetylcholine (Ach), bradykinin (BK) and B-type natriuretic peptide (BNP).

Results: AP produced concentration-dependent vasodilatation in rabbit MAs. The maximum relaxation with 3x10-5M AP (46[SEM 9.2]%) was significantly reduced by both L-NAME pre-treatment (15.5[SEM 5.7]%; $p=0.014$), and by endothelial denudation (10.0 [SEM 6.0] %, $p=0.018$). At maximum concentrations, AP produced greater vasodilatation than BNP (15.8[SEM 3.8]%; $p=0.001$) but less than Ach (85.4[SEM 2.5]%; $p=0.002$). There was no significant difference between the maximal responses to AP and BK (43.0[SEM 8.9]%, $p=0.83$) (See figure).

Conclusion: AP has a moderate vasodilator effect in small arteries which is NO and endothelium dependent. Apelin may have therapeutic potential in hypertension and heart failure.

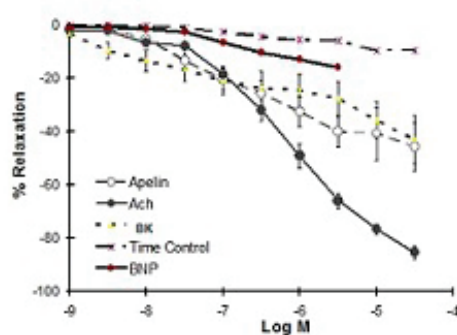


Fig 1

P1724

Hetero dimerisation between serotonergic 5-HT4 and muscarinic M2 receptors in patient with heart failure

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Autoantibodies against serotonergic receptor involved in Neonatal LUPUS (NEL), as well as increased 5-HT4 receptor expression in congestive heart failure have prompted us to look for the presence of pharmacological active anti-5HT4 receptor autoantibodies (AAB) in sera of patients with heart failure. Sera from 333 patients and 150 controls were screened against second extra cellular loop (SEC) of 5-HT4 and M2 muscarinic receptor, using indirect and inhibition ELISA. The ability of AABs to bind native receptor was explored in fluocytometry. AABs' pharmacological activity was explored using chronotropy on neonatal rat cardiomyocytes. Five different truncated peptides from SEC of 5-HT4 were used for epitope mapping. The specificity of the AABs for 5-HT4 and M2 receptors were verified pharmacologically with ML10375 and atropine specific 5-HT4 antagonist and M2 agonist. We found 21 and 19% of sera positive for 5-HT4 and M2 receptors respectively with 90% of exact identity for both receptors, all with negative chronotropic effect. Peptides derived from SEL of both receptors cross-inhibit sera interactions with 5-HT4 and M2 receptors. Atropin eluted M2 receptor in its heterodimerised form with 5-HT4 receptor. AABs interacted with 5-HT4 receptor which in turn activate M2 receptor downstream signaling. These results defines a subset of heart failure patients with cross reacting pharmacological active AABs against SEC of 5-HT4 and M2 receptors, which could underline the pathophysiology of their disease.

P1725

Neoinnervation and neovascularization in decellularized pericardial implants after myocardial infarction in swine

SAF2011-30067-C02-01 & 2012-33526, RIC (RD12/0042/0027 & RD12/0042/0047), TerCel (RD12/0019/0019 & RD12/0019/0029), and SCC2014. C Carol Galvez-Monton¹; MT Fernandez-Figueras²; M Marti³; C Soler-Botija¹; S Roura¹; I Perea-Gil¹; C Prat-Vidal¹; A Lucía-Valdeperas¹; A Raya²; A Bayes-Genis²

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Purpose: Engineered bioimplants for cardiac repair require functional vascularization and innervation to ensure integration with the surrounding myocardium. The aim of this work was to study nerve sprouting and neovascularization in an acellular pericardial-derived scaffold used as a myocardial bioimplant.

Methods: seventeen swine were submitted to a myocardial infarction followed by implantation of a decellularized human pericardial-derived scaffold. After 30 days, animals were sacrificed and hearts were excised and analysed with hematoxylin/eosin, and Masson's and Gallego's modified trichrome staining. Immunohistochemistry was carried out to detect nerve fibers within the cardiac bioimplant using β III tubulin and S100 labelling. Isolectin B4, smooth muscle actin (SMA), CD31, Von Willebrand factor (vWF), cardiac troponin I, and elastin antibodies were used to study scaffold vascularization. Transmission electron microscopy was performed to confirm the presence of vascular and nervous ultrastructures.

Results: H/E and Masson's and Gallego's modified trichrome staining provided a histological description of the pericardial-derived scaffold. Newly formed nerve fibres composed of several amyelinated axons as the afferent nerve endings of the heart were identified by immunohistochemistry. These nerve fibres were positive for S100 protein and β III tubulin. Additionally, neovessel formation occurred spontaneously as small and large Isolectin B4-positive blood vessels within the scaffold. They were also positive CD31 and vWF. Furthermore, TEM images helped to discern, within the scaffold, nerve structures composed of several amyelinated axons, and vascular structures with erythrocytes within the lumen, confirming functional conduits with blood flow.

Conclusions: In summary, this study demonstrates for the first time the neof ormation of vessels and nerves in cell-free cardiac scaffolds applied over infarcted tissue. Thus, the search for an optimal scaffold that preserves the natural tunnels needed for vascular vessels and nerves and with the porosity to nest cells may be crucial to ensure a functional and successful engineered bioimplant.

BASIC SCIENCE: CANCER AND COMORBIDITIES

P1726

Role of mineralocorticoid receptor in the regulation of skeletal muscle differentiation and function

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Purpose: It is known that macroautophagy plays a pivotal role in cell differentiation and function. We recently showed that MR antagonism reduced autophagy rate and induced browning of adipose tissue. Interestingly, a critical role of autophagy has been recently shown also in skeletal muscle development and it is known that MR antagonism is able to improve insulin-stimulated glucose transport in rat skeletal muscle. Therefore we investigated a possible involvement of MR in regulating skeletal muscle differentiation and function in vitro and in vivo.

Methods: We investigated the involvement of MR in regulating macroautophagy in murine skeletal muscle cells (C2C12) and we started to characterize the impact of adipose MR activation on skeletal muscle metabolic profile and development in a novel adipose-specific MR Knockout (MRKO) mouse model.

Results: We first characterised the ontogenesis of MR in a murine myoblast cell line (C2C12) by RT-PCR analysis in order to evaluate the expression of MR during myotube differentiation in vitro. We observed a 2,5 fold-increase in basal MR mRNA expression in skeletal myoblasts compared with myotubes after 72h of differentiation. To evaluate the effects of MR activity on C2C12 cells we treated C2C12 myoblasts and myotubes with aldosterone (Aldo, 10-8 mol/L) for 24h and observed a marked increase in LC3 mRNA expression suggesting an increased autophagic rate. This effect was reverted by treatment with MR antagonist spironolactone (Spiro, 10-5 mol/L). However, protein levels of LC3 were not affected by any treatment, suggesting that longer treatments could be necessary to reveal an effect. Moreover we observed that Aldo significantly reduced in Heavy Chain Myosin (MHC) mRNA levels, suggesting that MR activity represses muscle cell differentiation. Such effect was also MR dependent, given that Spiro was able to revert such effect.

We also analyzed skeletal muscle insulin sensitivity in vivo in MRKO mice evaluating soleus muscle insulin receptor substrate-1, tyrosine phosphorylated IRS-1, GLUT4 levels mRNA expression and Akt phosphorylation. Interestingly, we observed improved soleus muscle insulin signalling parameters and systemic insulin sensitivity in MRKO mice compared to controls. Further studies are necessary to explore the effect of MR activation on skeletal muscle development in vivo.

Conclusions: These data reveal a potential role of MR in modulating skeletal muscle differentiation, autophagic rate and insulin sensitivity, which suggest a potential application of MR antagonists to improve skeletal muscle function.

P1727

Febuxostat reduces cancer cachexia-induced cardiomyopathy

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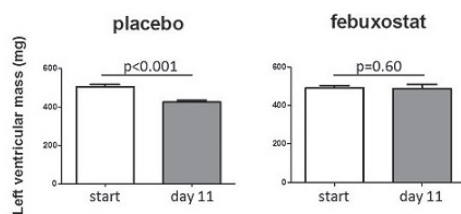
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Background: We have previously shown that the activity of the xanthine oxidase is induced in cancer cachexia and that its inhibition by the second generation xanthine oxidase inhibitor febuxostat improves survival and reduces wasting in the Yoshida hepatoma cancer cachexia model. Here we characterize the effects of febuxostat on cardiac function in the same model.

Methods: The Yoshida AH-130 hepatoma cancer cachexia rats were treated with febuxostat at 5 mg/kg or placebo per gavage daily. Cardiac function was analysed by M- and B-mode echocardiography on day 11.

Results: Left ventricular mass was similar at the beginning of the study among 2 groups (506 ± 10 mg in placebo vs 490 ± 13 mg in febuxostat, $p=0.57$) and decreased significantly on day 11 in placebo group (425 ± 11 mg, $p < 0.001$) but not febuxostat group (487 ± 23 mg, $p=0.60$). The difference between before and after treatment was -81 ± 10 mg in placebo and -3 ± 28 mg in febuxostat group ($p < 0.01$). Whereas changes in left ventricular fraction shortening (-10.3 ± 1.3 % vs -9.7 ± 1.7 %, $p=0.79$) and dimension in diastole (-1.1 ± 0.1 mm vs -0.8 ± 0.3 mm, $p=0.20$) were comparable among 2 groups, changes in stroke volume (-76 ± 6 μ l in placebo vs -53 ± 15 μ l in febuxostat, $p=0.09$) and cardiac output (-401 ± 25 ml/min in placebo vs -287 ± 69 ml/min in febuxostat, $p=0.06$) tended to be mitigated in febuxostat group, suggesting the attenuated cardiac involvement of cancer cachexia.

Conclusion: Inhibition of xanthine oxidase by febuxostat had beneficial effects on cardiac mass and function in a rat model of severe cancer cachexia. This effect may contribute to better outcome of animals treated by febuxostat.



P1728

Possible reappraisal of the angina pectoris drug trimetazidine in the treatment of skeletal muscle atrophy

Ricerca finalizzata RF-2010-2318508F Molinari¹; L. Gatta¹; S. Gorini¹; L. Vitiello¹; G. Rosano¹; E. Elisabetta Ferraro¹

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Purpose: Trimetazidine (TMZ) is a modulator of cell metabolism. TMZ is used to treat angina pectoris since it enhances the efficiency of myocardium metabolism. Its ability to optimize energy production in cardiac muscle cells led us to investigate the effect of TMZ also on skeletal muscle cells, in particular during myogenic differentiation and during muscle regeneration. We have recently found that TMZ has a protective effect against atrophy in vitro this supporting a possible reappraisal of TMZ in the treatment of cachexia. Among several features, cachexia is also associated with loss of regenerative potential, which we analysed upon TMZ treatment.

Methods: We incubated immortalised C2C12, satellite myoblasts and mesangioblasts with TMZ during differentiation. We also administered TMZ to mice during regeneration following muscle injury by cardiotoxin.

Results: Our data showed that TMZ significantly stimulates glucose and glycogen consumption in C2C12 myotubes. TMZ also transcriptionally down-regulates PDK. Notably, we also found that the administration of TMZ potentiates myogenic differentiation in both C2C12 and satellite cells. In fact, TMZ up-regulates MyoD, Myogenin, MyHC and Desmin and increases myoblast fusion in differentiating cells. Finally, we found that TMZ does not induce apoptosis in our cell lines as demonstrated by absence of Caspase-3 and PARP cleavage and that TMZ has no effect on cell proliferation, as assessed by BrdU staining and cell cycle analysis by propidium iodide. In order to study the effectiveness of TMZ on muscle regeneration in vivo, we administered TMZ to mice following focal injury on tibialis anterior (TA) skeletal muscle. TA analysis after the injury showed that TMZ increases the expression of MyoD, Myogenin, neonatal myosin heavy chain (neoMyHC) and Desmin used as markers of satellite cell activation and differentiation into nascent regenerating myofibers.

Conclusions: Our finding strongly suggest that TMZ stimulates myoblast differentiation and muscle regeneration following injury; this makes this drug appealing for its possible use in the treatment of several skeletal muscle pathologies.

P1729

Trimetazidine counteracts stress-induced atrophy in C2C12 myotubes and improves muscle function in mice bearing the C26 tumor and in aged mice

Ricerca finalizzata RF-2010-2318508E Elisabetta Ferraro¹; F. Pin²; L. Pontecorvo¹; AM. Giammaroli³; W. Malorni³; P. Costelli²; G. Rosano¹

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Purpose: The metabolic modulator Trimetazidine (TMZ) blocks fatty acid β -oxidation and shifts ATP production towards glucose oxidation, resulting in improved cell energy metabolism. TMZ is commonly used to treat angina pectoris and has been found to enhance both the efficiency of myocardium metabolism and patient exercise capacity. For this reason, TMZ effects on skeletal muscle cells were investigated in the present study.

Methods: In this study, the potential protective effect of TMZ against atrophy-inducing stimuli was analyzed. C2C12 myotube cultures were exposed to serum deprivation or to the proinflammatory cytokine TNF α . Moreover, in order to study the effectiveness of TMZ also in vivo, the drug was administered to mice bearing the C26 colon-carcinoma, a well-characterized model of cancer cachexia and to 22 months old mice as model of sarcopenia.

Results: The results show that TMZ significantly prevents myotube reduction in size caused by both treatments. In addition TMZ also markedly increases MyHC expression. Such an effect is associated with: a) increased levels of phosphorylated S6-kinase, suggestive of enhanced protein synthesis, and b) activation of the PI3K-AKT-mTORC2 pathway, and reduction of muscle-specific ubiquitin ligase mRNA levels, likely inhibiting proteasome-dependent degradation. Finally, TMZ also induces autophagy in untreated myotubes. Treatment of tumor hosts with TMZ does not modify food intake, body weight and muscle mass. By contrast, muscle fiber cross-sectional area and voluntary muscle grip strength are improved by TMZ.

Conclusions: On the whole, these results suggest that TMZ positively interferes with skeletal muscle cell response to stress both in vitro and in vivo, supporting a possible reappraisal of TMZ in the treatment of conditions characterized by muscle atrophy, among which cancer cachexia and sarcopenia.

Moderated Poster Session 7 – Multidisciplinary team: innovation in care and management

Tuesday 26 May 2015 10:00–11:00

Location: Poster Area

1744

Changes of end-tidal pressure of carbon dioxide in patients with chronic heart failure and chronic obstructive pulmonary disease during six minute walk test

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Background: Exercise tests are used to determine exercise tolerance in patients with chronic heart failure (CHF) and in patients with chronic obstructive pulmonary disease (COPD). Breathlessness is one of the most common reason patients who stopped during 6-minute walk test (6MWT). Dyspnea is combined with changes of pulmonary ventilation and gas exchange of CO₂. Significance of end-tidal CO₂ (PETCO₂) is a constant, which shows the activity of respiratory system.

Methods: We studied 45 patients with CHF in New York Heart Association (NYHA), age 58 ± 6,24 years (18 patients (40%) in NYHA class II, 22 patients (48.9%) in NYHA class III, 5 patients (11.1%) in NYHA class IV). Also we studied 30 patients with COPD II-III, age 60 ± 7,48 years (1st group - 14 patients (46.7%) with COPD II, 2nd group - 16 patients (53.3%) with COPD III). Standard 6MWT was performed. Dyspnea was evaluated on a scale of Borg, MRS and VAS. We recorded capnogram before, during, after the 6MWT and in the recovery period.

Results: Significance of PETCO₂ in 18 patients with CHF in NYHA class II was 38,4 ± 2,34 mm Hg, in 22 patients in NYHA class III was 34,5 ± 2,62 mm Hg, in 5 patients in NYHA class IV was 32,6 ± 1,84 mm Hg. Significance of PETCO₂ in 1st group patients with COPD was 36,4 ± 2,53 mm Hg, in 2nd group patients was 34,2 ± 1,62 mm Hg. All patients performed 6MWT. The 6MWT distance in patients with CHF in NYHA class II was 390 ± 20,56 m, in NYHA class III was 284 ± 17,24 m, in NYHA class IV was 140 ± 3,5 m. The 6MWT distance in 1st group patients with COPD was 450 ± 35,48 m, in 2nd group was 384 ± 35,42 m. There is reduction PETCO₂ in all patients with CHF during the 6MWT. PETCO₂ in patients with CHF in NYHA class II was 33,34 ± 2,51 mm Hg, in NYHA class III was 31,75 ± 2,89 mm Hg, in NYHA class IV was 28,8 ± 1,32 mm Hg. 33 patients (73.3%, p = 0,034) reported dyspnea as the main reason for a stop during the 6MWT. There is increase PETCO₂ in all patients with COPD during the 6MWT. After the 6MWT the significance of PETCO₂ in 1st group was 43,21 ± 2,81 mm Hg, in 2nd group was 45,05 ± 3,26 mm Hg. All patients reported dyspnea as the main reason for a stop during the execution 6MWT. When we analyzed the trend of PETCO₂ we found that these patients showed signs of periodic breathing.

Conclusion: Thus, capnography increases the diagnostic value of the 6MWT, helps to make interpretation of dyspnea in patients with CHF and COPD better.

1745

25 years after the fall of the wall - still substantial regional differences in hospitalization for heart failure between eastern and western Germany

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Background: Heart failure (HF) is a major cause of hospitalization in subjects aged over 65 in the western world. Morbidity and mortality remain high, and the prevalence of HF is still increasing, reflecting demographic changes, detrimental lifestyle habits, and medical progress. We analyzed temporal trends in HF hospitalization and in-hospital (i-h) death in Germany between 2000 and 2013 with a focus on regional differences.

Methods: The analyses are based on the German Federal Health Monitoring System, an annual census of inpatient characteristics in all German hospitals provided by the Federal Statistical Office. Data collection is statutory, and uniform criteria for diagnosis were applied throughout the period of examination.

Results: The number of HF related hospitalizations in Germany increased continuously from 239,694 in 2000 to 396,165 cases in 2013 (+ 65%). The New Länder (NL) showed a more pronounced increase (79%) compared to the Old Länder (OL; 57%). Between 2000 and 2012, HF expanded its share in total hospitalization from 1.40 to 2.03%, which represents a relative growth of 45%. As a result, HF today represents the leading cause of disease-related hospitalization in Germany. The relative growth in NL was 61% (from 1.50 to 2.43% of all hospitalizations) and more pronounced than in OL (42%; from 1.38 to 1.98%).

Consistently, in an age-standardized chart, the number of admissions for HF per 100,000 population was higher in NL (393) than in OL (313); in subjects aged ≥65, the resp. numbers were 2,212 (NL) vs. 1,815 per 100,000 population (OL).

Despite a continuous reduction in mean length of stay (from 14.3 to 10.7 days; -25%), the absolute number of hospital days due to HF rose by 21%. In 2012, HF accounted for 4.13 million hospital days making it the second leading cause of days spent in the hospital, causal for 3% of total occupant days. The number of hospital days due to HF increased by 31% in NL vs. 18% in OL.

The absolute number of i-h deaths attributable to HF was constantly high at 35,000 per year. In 2012, i-h mortality rate in HF patients was 9.2% (NL: 9.4%, OL: 9.2%). HF was by far the leading cause of i-h death responsible for 8.8% of total i-h mortality, with a persistently and substantially higher share in NL compared to OL (2012: 10.2% vs. 8.5%).

Conclusion: HF has become the leading cause of disease-related hospital admission and i-h death in Germany. Key morbidity and mortality indicators are more pronounced in NL compared to OL. The increasing burden of HF underscores an urgent need for improved diagnostic, therapeutic, and preventive strategies.

1746

Light-to-moderate alcohol consumption and heart failure incidence: the HUNT study

Swedish Research Council Grant and KID grant, Karolinska Institutet
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Purpose: To analyze the association between light-to-moderate alcohol intake and risk of heart failure (HF).

Methods: We studied individuals free of HF involved in the second Nord-Trøndelag Study conducted in 1995-97 in Norway. A total of 60 665 study participants provided information on alcohol consumption. Data on sociodemographic factors, cardiovascular risk factors and common chronic disorders were assessed by questionnaires and/or by a clinical examination. The cohort was followed for an average of 11.2 ± 3.0 years for a first HF via hospital records and the National Cause of Death Registry.

Results: Mean alcohol consumption was 2.95 ± 4.5 grams/day and 1 588 HF cases

occurred during follow-up. The amount of alcohol consumption was inversely and linearly associated with incident HF, multi-adjusted hazard ratio (HR) and 95% confidence intervals (CI) for a one drink increment: 0.78, 0.66-0.99, but the lower risk of HF in moderate drinkers was eliminated among those who reported problem drinking. Excluding former drinkers and controlling for common chronic diseases had minimal effect on this estimate. Consuming alcohol more than 5 times/month was associated with the lowest HF risk, multi-adjusted HR controlled for the amount of alcohol: 0.83, 95% CI: 0.68-1.03 relative to less frequent consumption than once a month. We found no evidence for a differential effect according to beverage type, nor that the competing risks of death from other causes modified the association. Among potential mediators, high-density lipoprotein cholesterol appeared to account for 20% of the association, but accounting for myocardial infarction during follow-up did not alter these findings.

Conclusion: Frequent light-to-moderate alcohol consumption without problem drinking was associated with a linearly decreasing risk of HF in this population characterized by a low average alcohol intake.

1747

Clinical characteristics of hospitalized and ambulatory patients with heart failure- results from ESC heart failure long-term registry- egyptian cohort

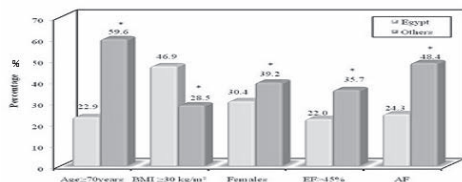
This Survey was funded by the ESC. Each participating national cardiology society was given a grant of €10 000 to help with the organizational needs of M M Hassanein¹; M Abdelhamid²; BS Ibrahim³; A Elshazly⁴; MW Aboleineen⁵; H Sobhy⁶; G Nasr⁷; F Elmisseiry⁸; A Abdelmoniem⁹; M Ashmawy¹⁰
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Aims: To describe the clinical characteristics of patients hospitalized with acute heart failure (HHF) and ambulatory patients with chronic heart failure (CHF) in Egypt and compare them with heart failure (HF) patients from other countries in the ESC-HF long-term registry.

Methods and Results: The ESC-HF Long-Term Registry is a prospective, multi-centre, observational study of patients presenting to cardiology centres in member countries of the ESC. From April 2011 to February 2014, a total of 2145 patients with HF were recruited from 20 centres all over Egypt. Of these patients, 1475 (68.8%) were hospitalized with acute HF, while 670 (31.2%) had chronic HF. Less than one third (32.1%) of all patients were females. HHF patients (median age of 61 years [IQR,53-69]) were older than CHF patients (median age of 57 years [IQR,46-64]); $p < 0.0001$. They had more diabetes mellitus (45.4% vs. 31.8%; $p < 0.0001$). Left ventricular ejection fraction $>45\%$ was present in 22% of HHF vs. 25.6% of CHF ($p = 0.17$). Atrial fibrillation (AF) existed in about a quarter of all patients (24.5%). Ischaemic heart disease was the main cause of HF in Egyptian patients. All-cause in-hospital mortality was 5%.

Egyptian patients presented at a much earlier age than in other European countries in the registry. They had more diabetes mellitus. AF prevalence was remarkably lower. Other co-morbidities (renal dysfunction, stroke and peripheral arterial disease) occurred less frequently.

Conclusion: Patients in the Egyptian cohort exhibited distinct features from heart failure patients in other countries in the ESC-HF Long-Term registry.



Comparison between hospitalized heart fa

1748

Continuous monitoring with an implantable loop recorder improves outpatient heart failure care

unrestricted research grant medtronic inc.

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Introduction: Heart failure (HF) patients have an increased risk of future adverse events. Little is known about the incidence of (sub)clinical arrhythmia's in sta-

ble ambulatory HF patients. Timely detection of relevant events could improve patient management. Implantable loop recorders (ILR) allow for continuous intensive monitoring of HF patients in an ambulatory setting, however no studies are available whether an ILR can impact HF care. We investigated whether ILR diagnostic data could change HF patient management in 3 large community hospitals.

Methods: Eligible patients were in stable ambulatory condition (NYHA II or III), had systolic or diastolic HF with EF $>35\%$, a virtual CHADS2 score ≥ 2 , no device indication, no anticoagulant use and no previous AF documentation. After ILR insertion (Medtronic Reveal XT), patients were put on home-monitoring and seen every 3 months up to one year at the outward clinic by their cardiologist. Relevant pre-specified ILR data (pauses ≥ 3 sec, patient registered pauses, AF or SVT >6 min, NSVT ≥ 3 beats, 2nd or 3rd degree AV block) were shared with their cardiologist. Subsequent therapeutic decisions were documented.

Results: Between July 2011 and May 2013, 30 patients were implanted with an ILR. At baseline, patients were age of 72 ± 9 and in NYHA II (25) or III (5). 24 patients had systolic HF and 66% had an HF history of >6 months. Mean EF was 44.5 ± 7.8 , 83% were on beta blockers and 90% on ACE-inhibitors. The ILR had excellent sensing throughout the study (R wave amplitude 0.54 ± 0.19 mV). During FU 4 ILR were removed. Mean time to a pre-specified event was 5.8 ± 3.4 months. In 15 patients (50%) pre-specified events were detected: 5 pauses ≥ 3 sec, 2 NSVT, 7 AF >6 min, 1 SVT >160 bpm). Based on the ILR data the following therapeutic changes were executed: 1 pacemaker implant; 7 initiations of (N) OAC, and 6 adjustments beta-blocker dose. Of the pre-specified ILR events detected in the study, none were detected by the routine outward clinic visits.

Conclusion: Ambulatory HF patients have a high incidence of subclinical but relevant arrhythmias. Intensive continuous monitoring with an ILR significantly changed patients management in 47% of patients.

1749

Deactivation of an implantable cardioverter defibrillator at the end-of-life; how do healthcare professionals decide?

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Purpose: Although cornerstone in the treatment of life-threatening arrhythmias, the therapeutic benefit of an Implantable Cardioverter Defibrillator (ICD) during the final stages of any illness remains uncertain. International guidelines recommend that professionals discuss deactivation, but clinical practice lags behind. We aimed to identify factors impacting on professional judgement regarding ICD deactivation.

Methods: Methodological Phases

1. Systematic narrative review of empirical studies (published 2008 - 2014) on patients' perceptions of deactivation ($n = 19$)

2. Retrospective case note review of patients ($n = 55$) with an ICD or biventricular ICD who died September 2012 to September 2013 at a regional implantation centre.

3. Qualitative data through semi-structured interviews with patients ($n = 9$) and carers ($n = 9$) as well as focus groups with professionals ($n = 7$).

Data from these sources were combined to identify factors which were then incorporated into a European online professional factorial survey.

Results: Nine factors were identified (refer *) within Phases 1-3. Preferences for the discussion and deactivation were diverse in Phases 1&3 with some patients' expressing reluctance to discuss deactivation through-out their illness, where others valued information and early discussion*. Contrary to guidelines, most patients in Phases 2&3 were not informed about deactivation possibilities pre-implantation. Samples in Phases 1&2 were predominantly male (gender*) and patients with more than 1 chronic illness (co-morbidity*). Ethical and legal considerations dominated Canadian and American literature focusing on treatment intent* and the varied role of next of kin (social support*). Data from Phases 1&3 emphasized facing the future and the impact of advanced age*, yet despite deteriorating heart failure symptoms* and increased hospital admissions*, patients in Phase 3 remained optimistic about life expectancy with many anticipating surviving for more than 10 years. A shock* from the ICD prompted many patients to consider deactivation in Phases 1&3, however counter-intuitively 83% of patients within Phase 2 who experienced a shock had an active ICD at death, while 88.2% who had their ICD deactivated never had a shock ($p = 0.003$).

Conclusions: These data evidence generation of 9 implicit factors that we postulate affect decision-making about deactivation at end-of-life. They have been used to develop an anonymous electronic survey for professionals involved in ICD management. Data collection is ongoing and results will be presented in 2016.

1750

Thirst in patients with heart failure

Lindhés Advokatbyrå Stiftelseförvaltning; Klebergs Stiftelse.

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Purpose: Thirst can be aggravated in patients with heart failure (HF), and treatment of HF can be a cause of increased thirst. The aim of this study was to describe the change in thirst intensity in patients with HF before and after optimization of HF treatment and to explore factors related to high thirst intensity after the optimization of HF treatment.

Methods: Sixty-nine patients with HF (mean age 73 ± 7 years, 83% men, 46% NYHA III-IV) who were referred for optimization of HF treatment at nurse-led HF clinics participated in a prospective observational study. Data were collected before treatment optimization and at the time of discharge from the HF clinic. Thirst intensity was measured with a visual analogue scale (0-100 mm) and thirst distress with the Thirst Distress Scale for HF (score 9-45). Additional clinical and demographic data were collected through questionnaires, medical charts, and blood samples. High thirst intensity was defined as thirst intensity >20 mm on the visual analogue scale. Logistic regression analysis was used to identify factors independently associated with high thirst intensity.

Results: At baseline, median (25th and 75th percentiles) thirst intensity was 14 mm (6-36). Thirst intensity increased in 64% of patients and decreased in 36% of patients at the time of discharge. Compared with patients with low thirst intensity, patients with high thirst intensity had more frequent diuretic doses ≥40 mg per day (P < 0.05), higher thirst distress (score 21 [14-25] vs. 12 [10-18]; P = 0.001), NYHA class III/IV (49% vs. 21%; P = 0.02), higher plasma urea (9 [7-11] mmol/L vs. 7 [5-8] mmol/L; P = 0.002), and higher NT-proBNP (2300 [787-4310] ng/L vs. 1260 [349-2860] ng/L; P = 0.03). They were more often prescribed fluid restriction (64% vs. 21%; P < 0.001). Plasma urea (odds ratio [OR] 1.43; 95% confidence interval [CI] 1.04-1.97) and fluid restriction (OR 9.28; 95% CI 1.88-45.84) were independently associated with high thirst intensity in patients with HF.

Conclusions: In total, 64% of patients increased and 36% decreased in thirst intensity after a period of treatment optimization in a HF clinic. Patients with high thirst intensity may fluctuate more in fluid volume balance and neurohormonal activities as reflected by the higher concentration of plasma urea. Fluid restriction is strongly associated with thirst intensity, and health professionals should carefully consider the necessity of fluid restriction.

1751

Cognitive-behavioral psychological intervention for self-modulation of heart rate variability to psychological stress in heart failure patients

Consejo Nacional de Ciencia y Tecnología (CONACyT) [Studentship 262555]
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Background: Psychological stress can reduce Heart Rate Variability (HRV) and predict cardiovascular events and mortality in Heart Failure (HF) patients. Multidisciplinary programs reduce mortality and hospitalizations. The therapeutic approach should include pharmacological, surgical treatment, changes in lifestyle and emotional management.

Objective: To investigate the effect of a brief cognitive-behavioral psychological intervention in the modulation of HRV on psychological stress in chronic stable HF outpatients adults

Methods: An experimental design with pretest-posttest control group was used, in a twelve weeks of follow-up. Heart failure patients (n = 53) randomly assigned to Control Group (CG, usual medical treatment, n = 27, mean age 61.07 ± 15.96,

55.6% men) or Experimental Group (EG, usual medical treatment and psychological intervention, n = 26, mean age 58.42 ± 16.42, 65.4% female), were included. One psychophysiological assessment was conducted to measure changes in HRV to psychological stress, using a computerized biofeedback equipment. The psychological intervention program included psycho-education, diaphragmatic breathing, progressive muscle relaxation and training in problem solving, in four sessions of 90 minutes each, deferred weekly.

Results: To estimate the effect of the intervention was conducted an analysis of variance for repeated measures. The GC showed no statistically significant changes, while EG significantly increased HRV in its high frequency band (F = 0.92 [8,352], p < 0.05), i.e. their ability to produce parasympathetic activity. In parallel, decreased sympathetic activity in low frequency bands (F = 1.61 [8,352], p < 0.05) and very low frequency (F = 0.92 [8,352], p < 0.05). The changes were consistent during the follow-up.

Conclusions: Psychological intervention induced the patient's self-regulate ability, reducing vulnerability to psychological stress and increasing relaxability, and improved the prognosis and welfare.

1752

Utility of post-discharge support: 72 hour follow up phone call for heart failure patients

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Purpose: The hospital guidelines at discharge in Heart Failure (HF) patients include a 72h follow up phone call and an appointment within the next 8-10 days at their GP's clinics. The purpose of the study is to evaluate the utility of the phone call in detecting patients' care needs and early signs of decompensation.

Method: The phone call is carried out by a pool of nurses in a call centre working 24/7. This call centre has the ability to arrange and modify appointments with GP's and/or community nurses according to the results obtained in that phone call. These appointments can be scheduled at patient's homes, avoiding the need to travel depending on the patient situation. The 72h follow up phone call allows nurses to registrar the results in the patient's notes (electronic health record), information which can be accessed and shared by GP's and also Dr's in the hospital setting. These nurses know the medication the patient is on.

This 72h phone call consists on a number of questions which depending on the answer given will determine different alarms which will ask for different actions, as per protocol.

- No alarm: Advice regarding, diet, exercise, weight and indications to take the medications prescribed correctly. Nurses also remind the patient of their next scheduled appointment to see their GPs.
- Yellow alarm: New appointment with the Nurses in the community to see the patient in their homes in the next 24-48h.
- Orange alarm: Nurses arrange an appointment with their GPs to see the patient in their homes in the next 24-48h.
- Red alarm: Nurses will contact emergency services.

Results: We have performed 350 phone calls since June 2013. We present the results of 160 consecutive calls. Average age 77 years of age and 44% were women. 23% no alarms. 40% generated an appointment with their nurses in community (yellow alarm) as aspects of adherence to treatment and self caring habits needed reinforcing. 27% required an early appointment with their GP due to medication side effects or weight gain. 9% required emergency services due to dyspnoea at rest or temperature. Problems related to adherence to treatment were the ones that generated most alarms.

Conclusions: The 72h follow up phone call helps us in the continuity of care and enhances the integration of the professionals dealing with heart failure patients.

This 72h follow up phone call guideline allows us to detect early warning signs of decompensation in HF and signs of the no compliance of their treatment and as a result, schedule early appointments with their Dr's or activate emergency services upon severity of symptoms.

Clinical Case Corner 6 – Conventional and novel diagnostic and therapeutic approaches

Tuesday 26 May 2015 10:00–11:00

Location: Poster Area

1753

Heart rate reduction with ivabradin in a case with non-ischemic heart failure and LBBB who is candidate for CRT

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Introduction and case report description: Elevated resting heart rate (HR) is associated with worse clinical outcomes and the reduction of raised resting HR in patients with heart failure (HF) has been proven to reduce mortality or rehospitalization. Here, we reported a case of idiopathic dilated cardiomyopathy (DCM) with LBBB and refractory to optimal HF therapy who was candidate for cardiac resynchronization therapy (CRT), in which HR reduction with ivabradine has been observed to improve clinical status and reverse LBBB.

Description of the problem: A 59-year-old female with idiopathic DCM, in sinus rhythm, LVEF 16%, dilated LV, LBBB, angiographically proven normal coronary arteries presented with NYHA III symptoms. She was on optimal HF therapy including angiotensin converting enzyme inhibitor, beta blocker, diuretics, mineralocorticoid receptor antagonist and digoxin. She has also had an indication for CRT based on the evidence of QRS duration (>150 msec). Echocardiography revealed abnormal septal wall motion with a septum-posterior wall systolic delay (≥ 187 msec). Her resting heart rate was >80 bpm.

Questions or problems: What should be done for her symptomatic clinical status before CRT?

Answers and discussion: According to the ESC HF guidelines recommendation, ivabradine treatment was added on her evidence-based standard HF therapy. After adding ivabradine 5 mg bid, 2 weeks later, resting heart rate reduced from 80 bpm to 68 bpm. Ivabradine dose was increased to 7.5 mg twice daily and 1 week later, ECG revealed sinus rhythm with a heart rate of 55 bpm and LBBB. After one month of ivabradine treatment and achieving considerable reduction in heart rate, NYHA functional class improved from III to I, ECG showed sinus rhythm, narrow QRS, no LBBB with a resting heart rate of 53 bpm and echocardiography demonstrated normal septal wall motion with a better synchrony in LV contraction with an LVEF 22%. Patient removed from the CRT list. HR reduction with ivabradine treatment in addition to standard of care including ACE inhibitor or ARB, beta blocker and MRA in SHIFT Trial has been shown to improve not only cardiovascular mortality or rehospitalization but also improve quality of life, LVEF and NYHA functional class. Conduction in the left bundle branch can be compromised by both structural and functional factors, including rate-related bundle branch block. If LBBB is caused by functional reasons and rate related, HR lowering may reverse BBB.

Conclusions and implications for clinical practice: In HF patients with LBBB, optimal standard medical therapy and elevated resting HR, HR reduction with ivabradin treatment improves LVEF, NYHA functional capacity and may also reverse LBBB, which is considered to be probably due to frequency dependent bundle branch block.

1754

First clinical use of serelaxin (recombinant human relaxin-2) for treatment of acute decompensated heart failure

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Acute decompensated heart failure (ADHF) is a life-threatening condition with high in-hospital and post-discharge mortality, particularly in patients with persistent or recurrent end-organ dysfunction during the first days after hospitalization having worse short- and long-term prognosis.

We present a case of the first clinical use of a novel drug Serelaxin in a patient with dilated cardiomyopathy, severe mitral insufficiency, pulmonary hypertension and left bundle branch block (LBBB) presenting with ADHF and target-organ damage.

The patient was 64 years old, female, with orthopnea (following progressive dyspnea for the last 4.5 months), marked peripheral edema, severe fatigue. Her pre-admission daily medications were bisoprolol, ivabradine, perindopril, torasemide and spironolactone. She presented in sinus rhythm with HR of 103 bpm, PQ - 160 msec, QRS - 180 msec (complete LBBB). Arterial blood pressure was 135/75 mm Hg, respiration rate - 23 per minute and capillary SaO₂ - 91%.

On chest X-ray: cardiac enlargement and bilateral pulmonary congestion. On echocardiography: LV dilatation (EDV - 247 ml, ESV - 196 ml), systolic dysfunction (EF - 21%), restrictive transmitral flow pattern, grade 3 mitral and tricuspid regurgitation with estimated pulmonary artery systolic pressure of 60 mm Hg, no pericardial effusion. Blood tests: elevated liver transaminases (AST - 68 IU, ALT - 72 IU), urea (10.8 mmol/l), creatinine (132 mmol/l), TnI (0.058 ng/l), NT-proBNP (2870 pg/ml).

The treatment was initiated with intravenous furosemide (80 mg bolus) followed by continuous infusion of nitroglycerine and furosemide. Emergency coronary angiography showed chronic total occlusion of right coronary artery (RCA) and no other abnormalities.

Several options for patient's management were: 1) to continue with furosemide and nitroglycerine infusion; 2) PCI of occluded RCA; 3) intra-aortic balloon pump insertion; 4) i/v inotropes; 5) ICD or CRT/D implantation. The continuous intravenous therapy and monitoring were chosen and the patient was clinically improving with less dyspnea, increased urine output and weight loss. However, the blood biochemistry showed progressive worsening within first 2 days of admission: AST - 77 IU, ALT - 79 IU, urea - 12.4 mmol/l, creatinine - 157 mmol/l, TnI - 0.066 ng/l, NT-proBNP - 3100 pg/ml.

Next choices for patient's management included: 1) to continue with furosemide and nitroglycerine infusion; 2) to switch to serelaxin infusion; 3) dialysis; 4) surgical mitral valve repair; 5) ICD or CRT/D implantation. The option of serelaxin treatment was chosen and infusion of the drug at a standard dose of 30 mcg/kg/day for 48 hours was started under strict clinical, hemodynamic and biochemical control. No adverse or side effects were observed, except for an expected initial blood pressure decrease to 110/70 mm Hg followed by stabilization at 120/75 mm Hg.

After 48 hours of serelaxin infusion patient's condition was stable, blood tests were markedly improved (AST - 42 IU, ALT - 45 IU, urea - 8.7 mmol/l, creatinine - 119 mmol/l, TnI - 0.037 ng/l, NT-proBNP - 1800 pg/ml). Due to severely depressed LVEF, complete LBBB and echocardiographic signs of LV dyssynchrony, the CRT/D device was implanted, AV delay of 110 msec and LV-RV delay of 0 msec were programmed based on maximal stroke volume by echo-Doppler calculations. Patient was discharged on day 7 after admission with reduced mitral regurgitation severity (grade 2) and pulmonary artery pressure (47 mm Hg), near-normal blood biochemistry values, increased EF of 33%.

This case illustrates marked positive effect of serelaxin (used for the first time beyond clinical trials) in ADHF patient with multiple organ damage providing successful recovery and discharge.

1755

Pulmonary embolism and type A free-floating thrombus in the right heart with an unexpected outcome - a case report

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Introduction:

Detection of right heart thrombi on transthoracic echocardiography in the context of pulmonary thromboembolism is uncommon (4-18%), and it appears to substantially increase the risk of mortality beyond the presence of pulmonary thromboemboli alone. Three patterns of right heart thrombi have been described. Type A thrombi are morphologically serpiginous, highly mobile and associated with deep vein thrombosis and pulmonary embolism. It is hypothesized that these clots embolize from large veins and are captured in-transit within the right heart. This type of thrombus

is associated with a very high mortality rate that exceeds 60% in untreated patients. Case report:

A 79 year old woman presented to the ER following an episode of syncope. She had undergone a total hysterectomy 2 weeks before, and had complaints of worsening dyspnea in the previous days. She was hypotensive (85/49mmHg) on arrival and quickly recovered haemodynamic stability after fluid therapy was initiated.

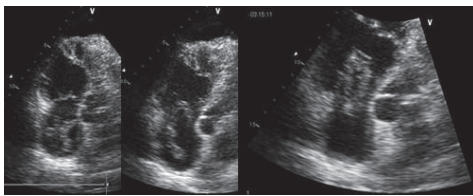
Urgent computed tomography angiography revealed bilateral pulmonary embolism and dilatation of the right ventricle and suggested the presence of a thrombus on the right atrium. Transthoracic echocardiography demonstrated a big worm-like thrombus floating in the right atrium, protruding into the right ventricle in diastole. Severe dilatation of the right heart chambers (right ventricle: 41mm) and moderate pulmonary hypertension (pulmonary artery systolic pressure: 58mmHg) were also documented.

Considering the recent surgery and clinical stability, conservative treatment was decided, with immediate anticoagulation with unfractionated heparin and haemodynamic monitoring in the cardiac ICU. Significant clinical improvement was observed on the following days and echocardiographic follow-up (4 days later) revealed complete thrombus dissolution, partial recovery of right ventricle function with free-wall hypokinesia and mild tricuspid regurgitation with no signs of pulmonary hypertension. Transthoracic echocardiography assessment 9 days after admission was unremarkable, with normal right ventricle function. The patient was discharged from the hospital on anticoagulation with warfarin.

Conclusion:

Although it is widely recognized as an ominous finding, the existing literature does not offer a clear consensus for management of pulmonary embolism with co-existing mobile intra-cardiac thrombus, but most recommend immediate treatment with fibrinolysis and/or embolectomy followed by effective anticoagulation with heparin.

In this case, a favorable course was observed despite a conservative approach with treatment with UFH alone.



Type A thrombus protruding to the RV

1756

Right ventricle heart failure pretending liver cirrhosis in a 65-year-old female with a severe primary tricuspid regurgitation

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A primary tricuspid regurgitation among elderly is a rare heart dysfunction leading to a right ventricle failure with many symptoms that are mainly present in patients with gastrointestinal and liver disorders. Therefore cardiologic diagnostics that allow the proper diagnosis and treatment are performed usually late when a patient already develops symptoms of left ventricle heart failure. In the presented case report a 65-year-old woman first underwent cholecystectomy and then liver cirrhosis was suspected based on the computer tomography of the abdomen, a slowly growing ascites, increasing fatigue, a pain in the upper right abdomen and elevated liver enzymes (ALT, AST) as well as alkaline phosphatase (ALP) and gamma-glutamylotranspeptidase (GGTP) in laboratory tests. Additionally an endoscopy of the gastrointestinal tract revealed a portal gastropathy and colopathy. No peripheral oedema was observed. The heart failure was suspected when an increasing dyspnoea and atrial fibrillation appeared. Echocardiography revealed a severe tricuspid regurgitation with vena contracta of 16mm without symptoms of pulmonary hypertension (right ventricle systolic pressure of about 25-30mmHg) as well as the vena cava inferior (VCI) diameter of 25mm without respiratory change and a reverse flow in hepatic veins. The systolic function of both ventricles was preserved and there was no significant dysfunction of the left heart valves that would allow classification of the tricuspid regurgitation as secondary. The NT-pro-BNP level was 1649pg/ml. After one-week-long pharmacological treatment with bisoprolol, digoxin, trandalapril, furosemide and spironolactone the dyspnoea and the ascites significantly decreased and the liver enzymes as well as ALP and GGTP normalised. Warfarin was initiated as the thrombo-prophylaxis in atrial fibrillation. No further invasive diagnostics of liver cirrhosis was needed and the congestive hepatopathy was diagnosed. The patient was presented to cardiosurgery specialists and is currently being qualified for the further treatment. Ischemic hepatitis, congestive hepatopathy and cardiac cirrhosis may occur as a result of heart or circulatory

system failure. Recently, mainly due to advances in treatment of heart diseases but simultaneously due to growing heart failure development rate, the prevalence of cardio-hepatic disorders in adults is increasing. Rarely some hepatic symptoms are the first manifestation of a severe heart disease as described in the case. The reverse attitude is frequently observed: patients with cirrhosis and portal hypertension are searched for cardiac complications as the presence of cardiomyopathy in cirrhotic patients has been described since 1960s and is well documented. This case report proves the necessity to diagnose patients with hepatic symptoms and portal hypertension for cardiac diseases that can be responsible for hepatic disorders instead of being their consequence.

1757

Low-dose oral pimobendan emancipates patients with severe ischemic pump failure from intravenous catecholamine infusion for cardiogenic shock

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Background: Although it has been reported that calcium-sensitizing agents, pimobendan increases mortality of patients with chronic heart failure, inotropic therapy should be regarded as temporary supportive management of low output states and hypotension complicating acute myocardial infarction. We present two cases of acute myocardial infarction with cardiogenic shock that were successfully treated with low-dose oral pimobendan. Case 1 is a 57-year old male presented with decompensated heart failure. Coronary angiography showed three-vessel disease and he needed coronary artery bypass grafting (CABG). However, catecholamine could not be reduced because of hypotension and recurrent congestive heart failure. Thus we administered pimobendan of 1.25mg daily per oral. Then hypotension improved and intravenous catecholamine could be discontinued. CABG was successfully done and he walked home. Case 2 is a 55-year old male transferred to our hospital of ST-segment elevation myocardial infarction with cardiogenic shock. Left anterior descending artery occlusion was successfully treated by primary percutaneous coronary intervention (PCI) for with intra-aortic balloon pumping (IABP) support. Treatment of bifurcation lesion of 90% stenosis in left main to left circumflex artery (LCx) was planned after stabilization of hemodynamics. However, his hypotension continued and catecholamine could not be reduced. Then we administered pimobendan of 1.25mg daily per oral. Then his blood pressure was increasing and IABP and intravenous catecholamine could be discontinued. Then PCI to LCX was successfully done. Summary: Low-dose oral pimobendan can be used as an alternative therapy of cardiogenic shock for patients with catecholamine dependent severe ischemic heart failure, even if it can be considered only for short-term therapy.

1758

Recurrent pulmonary edema with preserved LV systolic function and severe MR unmasked by stress TEE

MH Majidi Halabi¹; SD Saleem Dabbach¹; IR Inna Rosenfeld¹; TL Tatyana Levinas¹

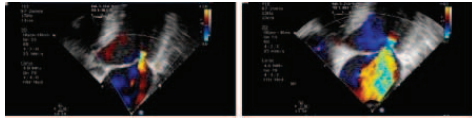
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Introduction: The most common causes of acute heart failure (AHF) are systolic or diastolic Left Ventricular (LV) dysfunction, or valvular heart disease. Identification of the pathophysiologic mechanism implicated in AHF is essential to target treatment and prevent further events. Echocardiography is the first imaging modality in evaluating these patients and in most cases it provides accurate noninvasive evaluation of the ventricular function and valvular abnormalities.

Case presentation: A 66-year-old man was admitted to our cardiac department due to acute pulmonary edema, in the previous two months he had experienced three similar episodes of AHF without any definite diagnosis. His medical history included hypertension, diabetes mellitus and mild chronic renal failure. His medications included aspirin, calcium channel blocker and insulin. On admission physical examination revealed symptoms of pulmonary edema with elevated blood pressure (160/90mmHg). His ECG showed normal sinus rhythm without acute ischemic changes. The patient was successfully treated by noninvasive ventilation and diuretics, his blood pressure was controlled by ACE-I and CCB. On resting echocardiogram (TTE) there was preserved LV systolic function (EF 60%), mild MR and the SPAP was 35 mm Hg. Cardiac catheterization revealed normal coronary arteries. During his stay in the ICCU we noticed that he developed severe dyspnea even at non-significant blood pressure elevations. Taking all this into account, we decided to complete our investigation by Transesophageal Echocardiography (TEE). On regular TEE we identified the previous valvular findings, but the mitral valve looked markedly abnormal, which led us to think that the mild MR might be under-evaluated. At this stage we decided to challenge the patient with an infusion of catecholamine in order to increase the blood pressure and the afterload. Few minutes after starting an infusion of noradrenaline the blood pressure was raised and the MR became severe.

Discussion: we presented a patient with recurrent pulmonary edema without recognizable precipitating factor and only after catecholamine challenge during the TEE we were able to appreciate the severe MR as a cause for this patient's

condition. The patient was referred for valvular surgery with successful result. This combined technique that we described- "stress TEE"- to confirm severity of MR may add to the diagnosis in selected patients and thus prescribing the appropriate treatment according to the findings.



MR at rest and stress TEE

1759

A long-term regular exercise training allows to maintain fitness in a man with ischaemic cardiomyopathy

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Impaired exercise capacity constitutes one of the fundamental symptoms of heart failure (HF). Exercise intolerance and numerous hospitalizations result in bedrest/sedentary lifestyle and avoiding of physical activity and it enhances symptoms of HF and deteriorate quality of life.

Case report description: A 60-year-old man with ischaemic cardiomyopathy with functional mitral valve regurgitation. Past history: CABG in 2001, MI in 2001,2005, NSTEMI March 2009, PCI: SVG 2002, LAD 2005, CX 2007. Implantation of ICD in primary prevention of SCD 2007. April 2009 coronary angiography - all the SVGs occluded, ECHO: EF 25%, LVEDD 76mm, MR +++, ERO 0,25 E/A 1,5 ; E/E' 16. Patient underwent a 12-weeks supervised training program - 3x/week based on Nordic Walking exercises [NW] with gradually increasing loading. On a follow-up visit 3 months after the end of the training , we observed a decrease in the physical fitness level. The patient was motivated to start their own activities - daily marches with sticks. A training program was adjusted to the patient's need: include intensity (70% peak VO2 / 75 - 85% peak HR), frequency (3-5/week), and duration (60-75min). Until now, the patient trains NW 5/week, covering the distance between 4-6 km. Training quality has been self-controlled using training tester. He is under constant control of the HF clinic. He has periodic assessment of the level of physical fitness and the modifications of the training program witch depending on the clinical status, well-being and weather conditions. 2011 year: PCI Cx + DES, ECHO: EF 25%, LVEDD 78mm, MR +++/++++;ERO 0,45cm2; E/A 3,64; E/E' 23 2012; year: PCI RCA+ DES, ADHF, ECHO: EF 25%, LVEDD 75mm, MR +++;ERO 0,3 cm2;E/A 2,96; E/E' 20 2013; year - without hospitalization , ECHO: EF 25%, LVEDD 81mm, MR +++;ERO 0,6 cm2; E/A 3,05; E/E' 14,1 December-2014; year, MitraClip, ECHO: , ECHO: EF 20%, LVEDD 75mm, MR++/ +++; ERO 0,1 cm2; E/A 1,75; E/E' 19,6

Conclusion: Systematic, NW training method can increase and maintain good physical fitness level, quality of life and clinical outcomes in the patient with ischaemic cardiomyopathy despite not optimal revascularization and increase in mitral regurgitant jet.

1760

Refractory cardiogenic shock after acute myocardial infarction

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¹Institute of Emergency for Cardiovascular Diseases "Prof. Dr. C. C. Iliescu", Bucharest, Romania

Introduction: Cardiogenic shock complicating acute myocardial infarction represents a challenge for intensive care units, having very high mortality. Very often, cardiogenic shock associates multiple organ dysfunction syndrome (MODS) that requires complex medical and technological therapies. Case presentation: A 47 year old female patient, smoker, was admitted 2,5 hours after an acute anterior ST segment elevation myocardial infarction (STEMI), Topol I class. The patient presented with cardiogenic shock and ventricular arrhythmias. At admission, left ventricular ejection fraction (LVEF) was severely depressed, 25%. At the cath lab, after insertion of intra-aortic balloon pump (IABP), emergency coronarography revealed thrombotic occlusion of the left anterior descendant (LAD) coronary artery. Thromboaspiration was performed, but with distal embolization of the LAD and TIMI flow 1-2. Afterwards she was transferred in the intensive care unit (ICU). ECG performed 90 minutes after the coronary procedure, showed less than 50% ST segment resolution. Clinical signs of cardiogenic shock persisted and Swan-Ganz catheter was implanted. Invasive measures showed: cardiac index 1,6l/min/mp, cardiac power output 0,4W, pulmonary capillary wedge pressure 24mmHg. The patient received iv inotropes (dobutamine), which in the absence of favourable hemodynamic response was progressively escalated. Follow up echocardiography showed the development of bilateral pleuresia (multiple times drained) and signs of high left and right ventricular filling pressures. As of day 4 she presented persistent hyponatremia and anuria, for which continuous vena-venous ultrafiltration (CVVUF) was initiated. Hepatic cytolysis was accentuated after an initial trend towards normal values. The following 2 days, systemic vascular resistances began to decrease, leucocytosis and C reactive protein increased and vasopressor therapy (norepinephrine) was required. Systemic inflammatory response syndrome (SIRS) progressed, but no evidence for a septic aetiology was documented (negative procalcitonin and negative microbiological cultures). In one of the CVVUF sessions, an extracorporeal cytokine filter was used and this resulted in resolution of inflammatory response and rapid weaning from the high inotropic and vasopressor doses. Renal and hepatic function recovered. Weaning from IABP was possible after 21 days, with hemodynamic stability (including pulmonary artery parameters), but low dose dobutamine was maintained as the patient was awaiting transplantation. Discussion: Although the patient was timely reperused and received the recommended therapies, the difficult in-hospital course may be consequently to no-reflow phenomena and the associated SIRS. The deleterious effects of SIRS on hemodynamics were efficiently counteracted when a cytokine filter was used during CVVUF.

Conclusion: Despite the use of medical and interventional therapies (GpIIb/IIIa inhibitors, thromboaspiration, statin, IABP), no-reflow syndrome may prevent the recovery of cardiac function. Because cardiogenic shock often associates MODS, maintaining pharmacological and mechanical circulatory support may not be sufficient. Other complex novel therapies should be added to address systemic inflammation and organ dysfunction.

Physical fitness and QoL- 6 y. follow-up

Variables	Before NW training	End of NW training	3 months after finish of NW training	Systematic training without counselling	Before MitraClip	3 months after MitraClip			
	VI 2009	IX 2009	II 2010	VI 2010	I 2011	XII 2011	XI 2012	XI 2014	II 2015
6MWT [m]	520	575	533	552	575	520	550	540	562
Up and go [s]	6,4	4,9	5,8	4,9	4,6	4,6	4,9	5,3	5,0
Chair stand [numbers]	10	17	13	17	19	14	15	16	18
Arm curl [numbers]	15	22	23	20	19	16	16	17	19
Peak VO2 [ml/kg/min]	13,3	16,0	17,1	18,9	18,1	---	16,6	---	---
Slope VE/VCO2	47,6	40,8	41,3	45,0	41,4	----	48,1	----	----
Ex-time [min]	6,25	8,5	9,4	11,3	12,18	----	10,9	---	----

1761

The cause of severe pulmonary hypertension: differential diagnosis in case of acute heart failureIlrina Alitoit¹; J Celutkiene¹¹University Hospital Santariskiu Klinikos, Cardiovascular medicine, Vilnius, Lithuania

Introduction and case description: The differential diagnosis of the cause of pulmonary hypertension (PH) is often challenging, especially in patients with heart failure with preserved ejection fraction (HFpEF), requiring many diagnostic tests. A 76 years female was admitted to hospital with severe dyspnea at rest. Medical history, use of diuretics, development of pulmonary hypertension, history of hospitalisations and changes of biomarkers are presented in the table.

Description of the problem: Echocardiography: preserved left ventricular ejection fraction. Dilated right sides of the heart with pressure overload, pulmonary hypertension with sPAP of 70 mmHg. Right ventricle failure. The cause of progressive PH was questioned.

Questions, problems and differential diagnosis: Neither evidence of acute or chronic pulmonary embolism in previous computed tomography and pulmonary ventilation perfusion scans was shown, nor pulmonary or systemic diseases were found. Polisomnography did not show sleep apnea.

Answers and discussion: Right heart catheterisation confirmed severe postcapillary pulmonary hypertension (PAP 72/31/44 mmHg, PCWP 28/22/23 mmHg, PVR 2,7 Wood). Goals of further treatment shifted to stimulation of the diuresis with peroral and intravenous medications with specified target for fluid balance, ACE inhibitor instead of ARB, selective beta-blocker (bisoprolol) instead of calcium channel blocker, oxygen therapy. Patient was discharged with NYHA functional class III on the 28th day of hospitalisation. No readmissions occurred during the last 10 months continuing in-hospital treatment.

Conclusions and implications for clinical practice: The diagnosis of HFpEF is not always straightforward, and studies have found that it is indeed a major cause of unexplained dyspnea (1). Recognition of HFpEF can be confounded by multiple co-morbid conditions that can impair exercise capacity and mimic the signs and symptoms of heart failure, thereby limiting a clinician's ability to make early diagnoses and initiate therapeutic interventions (2). Importantly, HFpEF patients with PH have reduced survival and increased hospitalisation compared to those without PH (3-5).

Years	Diagnoses	BNP level (ng/l)	sPAP (mmHg)	Diuretics	Hospitalisations
1980; 1997	Arterial Hypertension; Atrial Fibrillation			Indapamide 1,5 mg per day	
2000; 2001	Obesity; Diabetes Mellitus			Hydrochlorothiaside 12,5 mg per day	
2005	Heart Failure		46	Indapamide 1,5 mg per day; Torasemide 10 mg every second day	Twice (pacemaker and dyspnea)
2008		2775	62	Spironolactone 50 mg per day; Torasemide 20 mg every second day	Dyspnea
2010	Gout	526	57	Did not change	Diabetes Mellitus
2011		112	55 (Oxygen Therapy)	Spironolactone 50 mg per day; Torasemide 50 mg per day	Dyspnea
2012		202	65	Did not change	Dyspnea
2013		174	55	Did not change	Diabetes mellitus
2014	HFpEF; Pulmonary Hypertension	243	72 (Right Heart Catheterisation)	Spironolactone 25 mg per day; Torasemide 200 mg per day; Indapamide 1,5 mg per day; Furosemide 60 mg per day	Dyspnea; AV node modification
2015		112	54	Did not change	

Medical history, use of diuretics, development of pulmonary hypertension, history of hospitalisations and changes of biomarkers

Poster Session 4

Tuesday 26 May 2015 08:30–12:30

Location: Poster Area

ACUTE HEART FAILURE

P1768

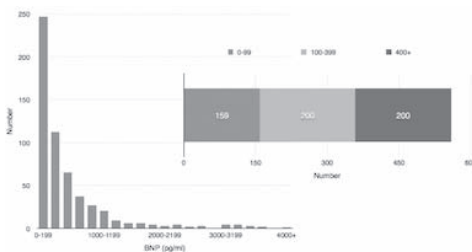
Distribution of BNP when available in a general NHS hospital does not differ from reported use elsewhereCJ Christopher John Cassidy¹; A Seed¹¹Blackpool Victoria Hospital, Lancashire Cardiac Centre, Blackpool, United Kingdom

Purpose: Acute diagnosis of heart failure by non-specialists is suboptimal and has been shown to be aided by the use of natriuretic peptides. Despite effectiveness data in many health settings uptake by NHS hospitals has been limited. Concerns regarding cost and inappropriate requesting persist. In out hospital BNP has been available to all acute admissions since late 2013 and we report the distribution seen when it has been established into practice.

Methods: All BNP tests on hospitalised patients from 1st October to 31st December 2014 were reviewed. The result and location of the patient when requested were determined.

Results: 559 BNP tests were carried out in the three month period. 159 (28%) were <100 pg/ml, the level established as optimally excluding heart failure in acute presentation. This is less than reported in some other populations. 200 (36%) were >400 pg/ml which we considered significantly elevated. The distribution is shown on the histogram. Tests were performed in the ED, medical admission ward, and elsewhere respectively: 192 (34%), 159 (28%), and 208 (37%) times.

Conclusions: When available for acute admissions in a general NHS hospital a similar distribution of BNP result is seen as reported elsewhere. If anything the number of negative tests is less than may be expected for a difficult to diagnose condition with a test with a strong negative predictive value. Over a third of tests were performed after a patient had moved from the initial assessment areas and so efforts are needed to ensure early use of biomarkers when available. Our data at the end of a year of BNP availability suggests that concerns about overuse are unsupported.



P1769

Syncope in patients presenting to the ER with acute PE: a forgotten symptomD Dinis Valbom Mesquita¹; A Carvalho¹; C Nobre¹; C Sousa¹; L Santos¹; T Ponte¹; A Pona¹; M Almeida¹; F Campante¹; J Tavares¹¹Hospital N.S. Rosario, Barreiro, Portugal

Purpose: Most patients presenting to the emergency room (ER) with pulmonary embolism (PE) complain of dyspnea. Low output states in PE due to the adverse hemodynamic consequences of a dilated right ventricle(RV) on

ventricular-ventricular interaction coupled with obstructed central pulmonary arteries may result in syncope.

Methods: In a retrospective study conducted in a district general hospital, in a time span of 36 months, we assessed the number of patients who presented with syncope as their primary symptom, their multidetector CT pulmonary angiography (MDCTPA) findings and outcomes at 30 days.

Results: Thirty seven patients with PE, with a mean age of 59 years, 14 males (37,84%), presented with cardiopulmonary arrest (8,11%), dyspnea (48,65%), syncope (24,32%), angina (5,4%), fatigue (8,11%) or dizziness (5,4%). All patients other than the three in cardiopulmonary arrest were normotensive. Of the nine patients who presented with syncope, seven (24,3%) had central PE and all had a dilated RV on MDCTPA. Eight out of nine of these patients (89%) had an ECG showing the classical sign of PE (S1Q3T3, or a variant form - S1Q3 or Q3T3) or other signs of right heart chamber strain. All the patients were in sinus rhythm (4 cases of tachycardia and none of bradycardia) and showed no AV conduction abnormalities. The all-cause mortality and PE-related mortality at 30 days was zero and no patient had a bleeding complication. The group who presented with syncope was younger (mean age of 50 years) compared to the general cohort (mean age of 59 years).

Conclusions: Syncope as a clinical presentation of PE should not be overlooked and may occur in upto 24% of patients. MDCT often shows findings suggestive of adverse clinical outcome.

P1770

Differential pattern of matrix remodeling during and post acute decompensated heart failure episodes: comparison between patients with reduced and preserved left ventricular systolic function

CNPq; CAPES; FIPE-HCPA

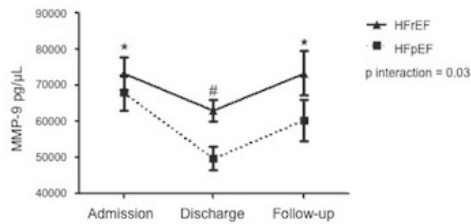
N Nadine Clausell¹; D Silvello¹; L Orlandin¹; A Garbin¹; MR Mendoza¹; ME Andrades¹; LEP Rohde¹; A Biolo¹¹Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil

Purpose: Metalloproteinase (MMP)-9 is a well known agent involved in matrix metabolism, acting on different collagen types. We assessed whether extracellular matrix cardiac remodeling differed in acutely decompensated heart failure (ADHF) patients with reduced ejection fraction (HFrEF) compared to patients with preserved ejection fraction (HFpEF).

Methods: A prospective cohort study was performed with patients admitted with ADHF in an university hospital, presenting with HFrEF (EF<50%) or HFpEF (EF≥50%). Blood samples were collected on three distinct moments: hospital admission, discharge and at two months follow-up after discharge. Serum levels of MMP-9 were measured by ELISA in duplicates. Data were analysed using a general linear model.

Results: A total of 100 patients were included in the study: 61 with HFrEF (mean EF 28±8%) and 39 with HFpEF (mean EF 63±8%). More females (59 vs.33%) and older patients (68±11 vs. 61±12 years) were noted in the HFpEF group. As expected, BNP levels were higher (p=0.008) and cardiac chambers were echocardiographically larger (p<0.001) in patients with HFrEF. Levels of MMP-9 were higher at all time-points in patients with HFrEF compared to HFpEF (p=0.03), in both groups levels reduced at discharge but increased at follow-up. Figure.

Conclusions: We showed that extracellular remodeling appeared to be more actively disarranged in ADHF patients with HFrEF compared to patients with HFpEF at all time-points although in both groups active remodeling was attenuated at discharge compared to baseline values. However, reactivation of the process was noted 60 days after discharge. This latter finding may indicate that HF-associated cardiac remodeling is a dynamic process requiring constant monitoring and tailoring therapies in order to avoid/limit disease progression.



Figure

P1771

Prevalence of intraventricular gradient and cardiogenic shock in patients with stress cardiomyopathy

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Although Takotsubo Cardiomyopathy (TCM) is not a frequent disease, case reports are increasing in last years. It usually debuts with an episode of chest pain and transient ventricular dysfunction. Because its common spontaneous recovery, TCM is usually considered a benign condition, however, sometimes it can complicate with significant instability and Cardiogenic Shock (CS).

In this study we present a retrospective review of 12 patients admitted to our hospital with the diagnosis of TCM during the last 5 years. Different prognostic factors have been analysed emphasizing on those related with the development of CS.

All patients were women with a medium age of 70 years old. Only one patient had previous history of cardiovascular disease. The main trigger was surgical stress. Four patients developed CS, two of them with intraventricular gradient secondary to marked basal segment hyperkinesis. The two patient who developed intraventricular gradient evolved to CS. There was no case of exitus during admission nor during the follow up. Recovery of left ventricular ejection fraction was similar in all patients (with and without intraventricular gradient) and no case of recurrence was found during the follow up.

Especially we present the case of a patient with CS who developed intraventricular gradient (Addend graphic). This case illustrates how proper treatment of intraventricular gradient can improve hemodynamics of these patients.

As the presence of intraventricular gradient requires a unique and different therapeutic approach (to avoid inotropes and as far as possible to associate beta-blockers) this complication should always be ruled out in patients admitted with TCM, especially in those who develop hemodynamic instability.

Addend Graphic (Variation in Intraventricular Gradient, Mitral Insufficiency and Apical Contractility, in a patient diagnosed of Takotsubo Cardiomyopathy complicated with Cardiogenic Shock): Variation in Intraventricular gradient (Blue), Mitral insufficiency (Orange) and Apical contraction (Yellow), in a patient diagnosed of Takotsubo Cardiomyopathy complicated with Cardiogenic Shock. Data are shown at admission (Admission), after esmolol infusion (After 1) and after betablockers, diuretics and Intra-Aortic Balloon Pump (After 2).

P1772

QRS duration and QTc interval can be predictors of reversed left ventricular systolic dysfunction in nonischemic dilated cardiomyopathy

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Purpose: Recent studies have shown that 12-lead electrocardiogram(ECG) parameters such as QRS duration and PR interval are associated with clinical outcome in patients with heart failure. However, their significance in the reversed left ventricular systolic dysfunction(RLVSD) is not defined well. In this study, we assessed whether ECG parameters are associated with RLVSD in non ischemic dilated cardiomyopathy(NIDCM) to identify their role in predicting RLVSD.

Method: We reviewed data of 28 RLVSD patients with NIDCM from the heart failure database of our institute. Among them, ECG and echocardiographic data were available for 26 patients. The control group consists of 30 NIDCM patients who showed no ejection fraction(EF) improvement(EF increase <5%). This population was matched for age, sex and EF. RLVSD was defined as absolute increase in Left ventricular EF more than 15%.

Result: The RLVSD group included 22 men (86.4%) with a mean age of 49 ± 14.5.

Among the RLVSD patients, the causes of heart failure were tachycardia induced cardiomyopathy (n = 12, 46.2%), alcohol induced cardiomyopathy (n = 6, 23%), hypertensive cardiomyopathy (n = 4, 15.4%) and idiopathic (n = 4, 15.4%). The prevalence of atrial fibrillation was significantly more frequent in the RLVSD than in the non-RLVSD group (38.5% vs. 13.3%, respectively; p = 0.03). QRS duration (95.8 ± 8.9 vs. 115.2 ± 20.48, respectively p < 0.001) and QTc interval (435.2 ± 28.5 vs. 465.2 ± 27.5, respectively; p < 0.001) were significantly longer in the non-RLVSD compared to the RLVSD. In the multiple regression analysis, QRS duration more than 110 ms (OR 23.91, 95% CI 2.09 to 273.70, p = 0.011) and QTc interval more than 440 ms (OR 5.92, 95% CI 1.32 to 26.57, p = 0.02) were independent risk factors of non-RLVSD.

Conclusion: QRS duration and QTc interval were associated with reversibility of left ventricular systolic dysfunction. This result suggests that QRS duration and QTc interval may have value in the predicting for RLVSD in the patients with NIDCM.

Table 1

Variables	OR(95% CI)	p
Atrial fibrillation	0.208(0.036-1.191)	0.078
QRS >110 ms	23.91(2.09-273.7)	0.011
QTc >440 ms	5.92(1.32-26.57)	0.02

Multivariate factors of non-RLVSD

P1773

Cardiorenal syndrome is not associated with left ventricular systolic function, but NT-proBNP level: an analysis of the Korean heart failure (KorHF) registry

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Purpose: Cardiorenal syndrome (CRS) is a well-known prognostic marker in heart failure (HF) patients, and neurohumoral activation plays an important role in its development. Patients with HF with preserved ejection fraction (HFpEF) and those with reduced EF (HFrEF) have different degree of neurohumoral activation, for whose assessment N-terminal pro-brain natriuretic peptide (NT-proBNP) is a useful marker. We evaluated the association between renal function and plasma NT-proBNP level according to the types of HF in acute heart failure (AHF) patients.

Methods: Among 3,200 consecutive AHF patients enrolled in the Korean Heart Failure (KorHF) Registry, data on glomerular filtration rate (GFR), ejection fraction (EF), and NT-proBNP levels were available in 1,948 patients. Chronic kidney disease (CKD) was defined as GFR < 60 mL/min/1.73m² and HFpEF as an LVEF ≥ 40%.

Results: Overall, 1,081(55.5%) patients had HFpEF and 867 (44.5%) HFrEF. HFrEF patients had higher NT-proBNP level (median: 5,644 pg/mL [interquartile range: 2,446-11,650] vs. median 3,312 pg/mL [IQR: 1,930-8,126], p < 0.001), but GFR did not differ between both groups (GFR 60.6 ± 32.7 mL/min/1.73m² vs. 62.6 ± 43.1 mL/min/1.73m², p = 0.274). GFR did not correlate with ejection fraction (p = 0.458), but significantly with NT-proBNP level (r = -0.336, p < 0.001).

51% of the study population had CKD. Although HFrEF patients had higher NT-proBNP level, the prevalence of CKD did not differ between HFpEF and HFrEF (52.3% vs. 50.3%, P = 0.371). When stratifying the patients according to the NT-proBNP level, CKD is more frequent in patients with NT-proBNP > median than those with NT-proBNP < median (66% vs. 37%, P < 0.001).

Patients with CKD had higher 12-month mortality than those without CKD in all (16.4% vs. 8.4%, log-rank P < 0.001), in HFpEF (15.8% vs. 7.3%, log-rank P < 0.001), and HFrEF patients (16.9% vs. 9.2%, log rank P < 0.001).

Conclusions: Cardiorenal syndrome is independent of left ventricular systolic function, but dependent on NT-proBNP level. CKD is a strong risk factor for worse clinical outcome irrespective of the HF type.

P1774

Statin effects on clinical outcome in patients with acute myocardial infarction with severe systolic dysfunction

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Purpose: The CORONA and the GISSI-HF trials failed to elucidate a beneficial effect of statin treatment in systolic heart failure. But there are lacking data demonstrating statin effects on acute myocardial infarction (AMI) patient with severe LV systolic dysfunction.

Methods: Between 2008 and 2011, 12,557 patients were enrolled in KorMI registry, and 495 patients who had severe left ventricular dysfunction (EF \leq 40%) with AMI were analyzed. They were divided into 2 groups; treated with statin group (n=337) and treated without statin group (n=158). To overcome the differences of baseline characteristics and discharge medication between 2 groups, we performed propensity score matched analysis. And 1-year incidence of major adverse cardiovascular event (MACE) and all-cause mortality were analyzed.

Results: In original cohorts, 1-year composites of MACE (all-cause mortality, MI and any revascularization) was similar between 2 groups (1-year MACE-free survival rate (SR) of treated with statin group: 87.1%; 1-year MACE-free SR of treated without statin group: 86.2%; $p=0.78$). Likewise, 1-year all-cause mortality was not statically different between 2 groups (1-year SR of treated with statin group: 93.8%; 1-year SR of treated without statin group: 90.8%, $p=0.42$). Propensity-score matching yielded 158 pairs, and in that cohorts, we could elicited comparable results in terms of MACE (1-year MACE-free SR of treated with statin group: 87.2%; 1-year MACE-free survival rate of treated without statin group: 86.2%, $p=0.85$) and mortality (1-year SR of treated with statin group: 94.0%; 1-year SR of treated without statin group: 90.8%, $p=0.51$). And Cox-regression analysis showed that statin therapy was not an independent predictor for MACE (Hazard ratio (HR) 1.06, 95% CI 0.56-2.03, $p=0.85$) or all-cause mortality (HR 1.34, 95% CI 0.56-3.17, $p=0.42$).

Conclusions: Statin did not reduce the MACE or number of deaths from any cause in AMI patients with severe LV systolic dysfunction.

P1775

Post-traumatic cardiomyopathy resulting in refractory severe heart failure rescued by emergency extra-corporeal life support

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Background: The sequel of severe poly-trauma may include myocardial dysfunction followed by acute heart failure and death. The Post-traumatic Cardiomyopathy is a variant of stress cardiomyopathy, characterised by a contractile abnormality with extensive left ventricular circumferential dyskinesia or kinesis with, sometimes, a hyperkinetic apex.

We report our experience with refractory cardiogenic shock and/or cardiac arrest, triggered by post-traumatic cardiomyopathy, treated with emergent extracorporeal life support.

Methods: From June 2008 to December 2014 we treated 6 adult poly-trauma patients (5 men, 1 woman, mean age: 25.3+/-14.2 years, mean ISS score 55.3+/-16.1) with veno-arterial (V-A) extracorporeal life support for refractory to conventional treatment cardiopulmonary failure/ cardiac arrest due to post-traumatic cardiomyopathy.

Results: Post-traumatic myocardial dysfunction appeared 13.8+/-12.2 hours after intensive care unit recovery and rapidly evolved to refractory cardiopulmonary failure and Cardiac Arrest (within 4.4+/-2.6 hours of the onset). At ECLS initiation median pH was 7.10+/-0.16 (6.91-7.25), median lactate was 6.9+/-3.1 (4-10) mmol/L and median vasoactive-Inotropic Score was 194.3+/-52.7 μ g/kg/min. Tissue Perfusion improved significantly within 4 h on ECLS. Cardiac function improved gradually but consistently (initial median ejection fraction was 13.6% +/- 5.2%, the median global longitudinal strain test -7.4+/-4.7 and at complete recovery (after 59.1 and 73.2 hours) was 63.56% +/- 8.2% and -18.43+/-2.5 respectively).

Conclusions: In poly-trauma patients, refractory post-traumatic cardiomyopathy predominates in the young and is often associated with severe head injury. Rapid heparin-free ECLS can improve therapy and outcome in the most severe.

Left Ventricular Global Strain

		Before-ECLS (1)	Before-ECLS explant (2)	At discharge	P value (1 vs 2)
GLOBAL	Radial Strain	20.72 \pm 8.7	34.27 \pm 17.51	40.71 \pm 16.82	0.013
	Circumferential Strain	-6.84 \pm 3.4	-11.91 \pm 2.52	-13.43 \pm 3.25	0.003
	Longitudinal Strain	-7.4 \pm 4.7	-17.6 \pm 3.1	-18.43 \pm 2.4	

P1776

Morbidity and mortality in a group of patients with heart failure followed by a combined model between hospital and general district medicine

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Introduction: Heart Failure (HF) confirms itself a considerable problem because of the amount of its morbidity and mortality. During the last decades the concept of a multidisciplinary approach as the right way to guarantee an appropriate outpatient care has been developed in order to reduce the hospitalization rate and the mortality of patients (pts) with HF. Aim of the study: estimate the 6 month morbidity and the mortality of pts discharged with the diagnosis of HF NYHA II-III class and followed by an early and combined management between hospital and general district medicine.

Methods: we evaluated 116 pts (59 M e 57 F; mean age 82.1 \pm 8 years old) included in the HF protocol for 6 months and then submitted under a clinical, laboratory and instrumental evaluation. Pts referred to the combined group have been visited by trained territorial nurses and physicians through a week-to-week schedule with the activation of an alarm center in case of worsening. So we analyzed the frequency of hospital readmissions 15 days-off and 60 days-off and we also estimated their 6 months-off mortality in comparison with an outpatients population uniform by features and discharged from Bologna AUSL Hospitals then followed by a traditional plan.

Results: 15 days and 60 days after discharge hospital readmissions in the combined management group were respectively 0% e 4.3% against 3.9% e 8.1% in the traditional group. 6 months-off mortality in the combined management group was 6%, definitely under the regional average.

Conclusions: Combined management care through a collaboration between hospital specialized physicians, family doctors and nurses on general district medicine allows the reduction of morbidity and mortality of patients with HF. Pts become the target of the medical support net by a continuous and coordinated support at home as in the hospital with a related global improvement of prognosis

P1777

Gender differences in presentation, management, and outcomes of patients hospitalized for heart failure (HF) in India

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Objective: To evaluate the gender differences in presentation, management, and outcomes of patients hospitalized with heart failure (HF) in India.

Methods: Trivandrum Heart Failure Registry (THFR) enrolled consecutive patients who were admitted in 13 urban and 5 rural hospitals with a diagnosis of HF from January-December 2013. Clinical characteristics at presentation, treatment, in-hospital outcomes and the 90-day mortality data were collected. "Optimal" medical treatment was defined as the combination of beta blockers, angiotensin converting enzyme inhibitors or angiotensin receptor blockers, and aldosterone receptor blockers in patients with left ventricular systolic dysfunction (LVSD).

Results: 1205 cases (834 men, 69%) were enrolled into the registry. Mean (SD) age was 63 (14.5) years in women and 60.5 (13.2) years in men. The most common etiology was coronary heart disease (CHD) (72%). Heart failure with preserved ejection fraction (EF>45%) constituted 33% and 23% of the population in women and men, respectively. The median duration of hospital stay was 6 days (IQR = 4-9 days) in both men and women. In-hospital mortality rate was 10% (95% CI: 7-13) in women and 8% (6-10) in men. Optimal treatment was given to 23% and 25% of the patients with LVSD during hospital discharge in men and women, respectively. The 90-day all-cause mortality rates were 2.6 (95% CI: 2-3) and 2.4 (95% CI: 2-2.8) deaths per 1000 person-days of follow-up in women and men, respectively.

Conclusion: Patients hospitalized with heart failure in the THFR (First Heart Failure Registry from India) are more likely to be men. The presentation, management and outcomes are not significantly different in men and women. Optimal treatment was given to a small fraction of the total eligible patients.

P1778

Usefulness of non-invasive monitoring of the lung impedance in chronic heart failure patients in out hospital clinic

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Background: Prevention of hospitalizations for decompensation in Chronic Heart Failure (CHF) patients is an unresolved issue. The accuracy of existing devices in predicting deterioration is only 38-76%.

Aim We evaluated the ability of the new a non-invasive method for lung impedance monitoring to predict decompensation in CHF patients.

Methods: Monitoring CHF patients was accomplished by a device which measures "net" lung impedance (LI) instead of traditionally used transthoracic impedance. A

decreasing LI reflects accumulation of lung fluid. Changes in the clinical status and LI were recorded at each monthly outpatient visit. Normal Baseline Lung Impedance (BLI) was calculated according special algorithm for each patient. LI changes are represented as percent from baseline according equation: $DLIR = (LI/BLI - 1) \times 100\%$. Results 250 CHF patients (68 ± 11 years-old, male- 80%, LVEF- 28 ± 7%) at NYHA II/III/IV (107/100/43) were recruited after index hospitalization for acute heart failure (AHF) and followed in an outpatient clinic for 36 ± 22 months. Initial NT-proBNP level was 3594 ± 5114 pg/ml. During the follow-up period 63 patients (25.2%) died due to cardiovascular deaths. 187 patients were hospitalized 548 times for AHF. 528 hospitalizations for other causes were recorded.

DLIR = (LI/BLI-1)*100% decreased progressively before hospitalization. Values of DLIR = (LI/BLI-1)*100% at 1 month, 3 weeks, 2 weeks, 1 weeks, 3 days prior to and at the day of hospitalization decreased by 23.1 ± 10; 25.4 ± 11; 28.0 ± 13.4; 33.9 ± 12.8; 34.9 ± 10.8 and 37.4 ± 10.7% (p < 0.001) from BLI. At the time of hospitalization for a non AHF cause, DLIR diminished only by 13.8 ± 6.1% (p < 0.001). Importantly, in all cases of AHF hospitalizations DLIR decreased by more than 24% from baseline while in 88% of non-AHF hospitalizations, DLIR decreased by less than 20%.

Conclusions: Noninvasive “net” LI monitoring is a very sensitive to predict hospitalization for exacerbation of CHF. DLIR decrease by more than 24% from normal baseline represents a high risk zone for re-hospitalization for AHF with 100% sensitivity and 90% specificity. Changes and intensification of therapy is mandatory when LI decreases by more than 24%.

P1779

Rapid improvement of symptoms, filling pressures and pulmonary congestion estimated by combined echo and lung ultrasound protocol during first 12 hours of AHF treatment

National grant 3500 euros

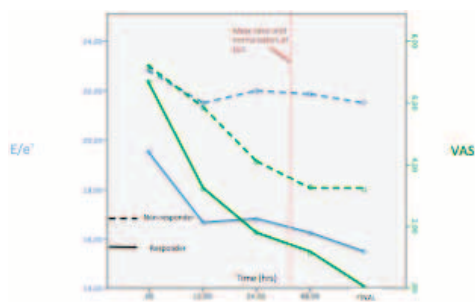
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Introduction: Rapid decline of left side filling pressures (LSFP) during early course of acute heart failure (AHF) treatment could result in rapid improvement of symptoms and pulmonary congestion.

Objectives: To examine the timecourse of response to treatment in pulmonary congestive AHF patients using a thoracic FAST ultrasound protocol including echo derived left side filling pressures (medial E/e') combined with lung ultrasound (LUS), and simultaneous symptom assessment.

Methods: We included 53 adult dyspneic patients with a positive thoracic FAST protocol for AHF who were followed up with FAST and VAS scores simultaneously. The FAST protocol was positive if E/e' was >15 and LUS presented bilateral B-lines (BL) or pleural fluid (PF) (right sided or bilaterally). Patients were classified as “responders” if they became asymptomatic at rest and capable of walking >20 meters. LUS was considered normal when absent of PF and bilateral BL.



Correlation of E/e' and VAS

Results: 27/53 (51%) of the FAST - positive patients were responders. They had a rapid change in mean E/e' and dyspnea VAS scores during the first 12 hours, with a mean E/e' change rate of 5,16 U/24 hrs (SD 6,9) and VAS change rate of 7 U/24hrs (SD 6,07), compared with a mean E/e' change rate of 0,39 U/24hrs (SD 1,15) (p = 0,004) and a mean VAS change rate of 0,80 U/24hrs (SD 0,83) (p < 0,001) during the rest of hospitalization. The mean time until normalization of LUS among responders was 43 hours. Among non-responders, the VAS score changed slowly and linearly (7,19 (SD 2,40) - 3,19 (SD 3,26)), and E/e' very little at all (22,82 (SD 4,48) - 21,52 (SD 6,99)) during hospital stay.

Conclusions: Both symptoms and echo derived LSFP improve rapidly among responsive AHF patients. These changes foresee decongestion as measured by normalization of LUS.

P1780

Hyperglycemia prognostic indicator in acute heart failure syndrome

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Purpose: Several biological prognostic indicators were analyzed in the acute heart failure syndrome (SICA) such as: hemoglobin, serum sodium, troponin levels ... Initial hyperglycemia appears among these prognostic indicators. The objective of this work was to investigate the prognostic impact of the initial hyperglycemia on mortality among patients with SICA admitted to the emergency department.

Methods: We conducted a single- center, prospective, observational study. Inclusion of patients with SICA. Standardization of treatment according to clinical scenario (CS). Hyperglycemia was defined as:

- Diabetic known patient or unknown but with HbA1C ≥ 6.5%: hyperglycemia if glucose level ≥ 11mmol /L.

- No diabetes with HbA1C < 6.5%: hyperglycemia if glucose level ≥ 7mmol /L.

Results: One hundred fifty one patients were included. Mean age = 66 ± 11 years [22-93]. Sex ratio = 1.2. Clinical history N (%): Hypertension 123 (81.5), known diabetes 99 (65). The distribution by clinical scenario N (%): CS1: 102 (67.5), CS2: 11 (7.3), CS4: 37 (24.4), and CS5: 1 (0.7). Twenty three patients had an HbA1C test which allowed to track 8 unrecognized diabetes (HbA1C ≥ 6.5%). Average blood glucose concentration at admission was 14.7 ± 8.2 mmol/L [3.3 - 44]. The initial hyperglycemia was noted in 102 patients (67. 5%): 78 diabetic, 24 without diabetes. Mortality at one month was 7.9% (12 patients), at 3 months 11.3% (17 patients). The table summarizes the prognostic study in both groups.

Conclusion: Elevated blood glucose concentrations at presentation are associated with three months mortality in acute heart failure syndrome admitted in emergency department.

Prognostic study			
	Hyperglycemia + N = 101	Hyperglycemia - N = 49	p
In hospital mortality n (%)	2 (2)	0	0,25
1 month mortality n (%)	10 (9)	2 (4)	0,21
3 months mortality n (%)	15 (14)	2 (4)	0,043

P1781

Predictors of rehospitalization in patients with heart failure: moroccan profile

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Background: Acute decompensated heart failure is the most common cause of cardiovascular hospitalization.

The aim is to examine the rate and predictors of hospital readmission in patients discharged after an episode of heart failure.

Methods: We conducted a prospective observational study at the therapeutic unit of heart failure (UTIC) where 904 patients were admitted for chronic heart failure between June 2014 and December 2014. One hundred patients were readmitted for an acute decompensated heart failure.

Results: 100 patients were included (11% with a male predominance (70 H, 30 F), the average age was 68.3 years. The main comorbidity was diabetes (40%). The principal subjacent heart disease was ischemic heart disease in 74 (74%), valvular heart disease in 18 cases (18%) hypertensive heart disease (4%) and dilated cardiomyopathy in 4 cases (4%). The left ventricular ejection fraction average was 36.84%. Acute right heart failure was predominant in 58 patients (58%). Independent factors of acute decompensated heart failure were a diet gap in 28 cases (28%), an interruption of maintenance treatment in 20 cases (20%), urinary tract infection in 16 cases (16%), a heart rhythm disorder in 12 cases (12%), myocardial ischemia in

10 cases (10%), hypertensive push in 6 cases (6%), anemia in 4 cases (4%) and a lung infection in 4 cases (4%).

Conclusion: Heart Failure rehospitalization within 6 months' follow-up occurred in 11% of our cohort. The highest rates of readmission were noted in those with a diet gap and patients who discontinued maintenance therapy. Education and improvement of living conditions are the main objectives to address this public health problem.

P1782

Co-morbidities and age differences in patients hospitalized for acute decompensated chronic heart failure - does it really matter?

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Purpose: To analyse co-morbidities in two age groups of patients, hospitalized with acute decompensated chronic heart failure (ADCHF).

Methods: We performed single-centre retrospective study of patients consecutively hospitalized for ADCHF. The study was approved by the institution's Ethics Committee. The retrospective analysis included 1534 patients older than 18 years, enrolled in a Department of Cardiovascular Diseases, from June 2006 to June 2012. Only patients discharged alive were included in further analysis. The patients were divided in two groups according to their age (1340 < 85 and 194 ≥ 85 years old). We have considered the following comorbidities: arterial hypertension (AH), diabetes mellitus (DM), peripheral arterial disease (PAD), cerebrovascular disease (CVD), ischemic heart disease (IHD) and anaemia. The difference between two groups according to their co-morbidities and possible impact of co-morbidities on the length of hospitalization was analyzed. In all tests P value of <0,05 was considered statistically significant.

Results: The mean patients age in both groups was 74.7 ± 10.1 years, in those < 85 was 72.8 ± 9.3 years and in ≥ 85 was 88.0 ± 2.7 years (P < 0.001). There were 917 (68.4%) patients with AH < 85 years versus 152 (78.3%) ≥ 85 years (P = 0.005). Likewise, 535 (39.9%) patients < 85 years had DM versus 60 (30.9%) ≥ 85 years (P = 0.016). In patients < 85 years there were 75 (5.6%) with PAD versus 4 (2.1%) ≥ 85 years (P = 0.037). In patients < 85 years 315 (23.5%) had one, 410 (30.6%) had two, 334 (24.9%) had three, 140 (10.4%) had four and 29 (2.2%) had five co-morbidities, while in patients ≥ 85 years, 39 (20.1%) had one, 71 (36.6%) had two, 64 (33.0%) had three and 11 (5.7%) had four co-morbidities. (P = 0.003). The length of hospital stay was 10.8 ± 6.1 days for patients < 85 years and 10.2 ± 9.1 for those ≥ 85 years old, (P = 0.293).

Conclusion: There was statistically significant difference according to AH, DM and PAD between the analyzed groups, but there was no statistical difference between groups according to CVD, IHD and anaemia. The difference, considering the number of co-morbidities between age groups, was found to be statistically significant. Data from the literature show that co-morbidities could extend the length of hospitalization in patients with heart failure. However, in the analyzed groups of patients co-morbidities did not affect the length of stay (P > 0.005).

P1784

Cardio-hepatic syndrome and its influence on acute decompensated heart failure patients in a single tertiary cardiology center

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Purpose: cardio-hepatic syndrome (CHS) is a newly emerging definition for acute liver injury in acutely decompensated heart failure (ADHF) patients (pts); it may be associated with cardio-renal syndrome (CRS); recent data have demonstrated the implication of CHS in HF management and prognosis; the aim of the study was to evaluate the presence of CHS in ADHF patients in a tertiary cardiology center; main predictors of CHS occurrence and the influence of CHS during in-hospital management of ADHF patients.

Methods: we prospectively analyzes clinical and laboratory records on 365 consecutive ADHF patients from 2012 to September 2014; liver function tests were used for the screening of CRS (a ratio of ALT/LDH <1.5 was considered a cardiogenic

injury), a MELD score evaluation was performed on a daily basis; ADHF patients were stratified into three levels: I (CHS absent), II (CHS present), III (CHS & CRS present); a composite endpoint (use of intravenous inotropes, diuretic resistance, a prolonged in-hospital treatment > a week, cardiac death) was defined a complicated clinical course; a Cox proportional hazards model was used to define the relation of CRS presence to the complicated in-hospital clinical course.

Results: CHS was present in 237 (64.9%) pts; between CHS and non CHS patients there were no significant differences in age (67.4 ± 0.3 vs 62.3 ± 0.7, p > .05), sex (males) (57.3% vs 53%, p > .05), diabetes (32.4% vs 29.2%, p > .05); but there were significant differences in MELD score (39.4 ± 7.7 vs 16.2 ± 8.5, p < .0001); re-hospitalizations for AHF 4 (2 to 6) vs 2 (0 to 3), p < .05; cardiac index < 1.5 l/min/m² (61.5% vs 17.6%, p < .0001); PASP (53 ± 18 vs 38 ± 12 mmHg, p < .001); use of inotropes (61.1% vs 19.7%, p < .0001); Charlson Comorbidity index (CCI) ≥ 4 (67.4% vs 46.2%, p < .001); diuretic resistance (26.8% vs 8.6%, p < .0001). main predictors of CHS occurrence in Cox regression were: low cardiac index; high PASP; re-hospitalization for AHF; diuretic resistance; HR (95%CI) of level II to I of ADHF patients was 1.86 (1.24 - 2.67, p = .0025) and level III to I was 3.69 (2.14 - 6.87, p < .0001).

Conclusions: cardio-hepatic syndrome seems to be a clinically important member of the constellation of end-organ involvements in ADHF patients, which presence offers significant clinical and prognostic implications in our daily cardiology practice; identifying patients more susceptible to CHS would help to reduce clinical complications in HF management and thus lower costs of treatment imposed by a prolonged hospitalization; further studies are needed to help clinicians in CHS treatment guidelines.

CHRONIC HEART FAILURE

P1785

Survival analysis of adult patients with congenital heart disease and heart failure

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Purpose: Adult patients with congenital heart disease (ACHD) are commonly faced with various complications due to residual defects, interventions and disease course. The most frequent are heart failure (HF), arrhythmias, pulmonary hypertension, and infective endocarditis which contribute to significant increase in morbidity and mortality of these patients. The aim of this study is survival analysis and identification of mortality predictors in ACHD patients and HF.

Methods: We retrospectively reviewed 173 adult patients with CHD (40% males and 60% females), followed-up for 36 months since their admission at the Department for congenital heart disease in adults of the Clinical center of Serbia, due to complications such as heart failure, arrhythmias, infective endocarditis, pulmonary hypertension, or until death as end-point. They were classified into 3 groups according to CHD complexity (simple, moderate and severe). NYHA functional class at admission, medical history data, physical and echocardiography findings were analyzed variables. Kaplan-Meier techniques were used to assess all-cause mortality. Log-rank testing was used to identify association between heart failure and major events, and multivariate Cox proportional-hazards regression model was used to identify predictors of the worst outcome.

Results: According to CHD type, 45% pts had simple, 28% moderate, and 27% severe CHD complexity. Heart failure was diagnosed in 28% (n = 48) patients. Overall mortality rate was 8.1% (n = 14), and mortality rate among those with heart failure was 22% (n = 11) of patients. Mean survival time in our group of patients with congenital heart disease was 33.8 months, SE 0.635, 95% CI 32.6 to 35.0. Log rank test showed that the survival time is higher in group of patients without HF. Median survival time in group of patients without HF was 35.6 months, SE 0.32, 95% CI 35.0 to 36.2 and in group with HF was 29.0 months, SE 2.0, 95% CI 25.0 to 33.1; p < 0.001. In a multivariate Cox proportional-hazards regression model, NYHA functional class was highlighted as significant predictor of the worst outcome in ACHD patients with heart failure (hazard ratio [HR] = 6.1, 95% CI 1.5 to 25.4, p = 0.013), among others analyzed variables. Higher NYHA class is associate with higher risk of mortality.

Conclusions: Survival analysis showed that adult patients with congenital heart disease and heart failure have higher mortality risk. NYHA functional class is an independent predictor of mortality rate in these patients.

P1786

The influence of frailty syndrome using the tilburg frailty indicator (tfi) on the assessment of illness acceptance in elderly patients with chronic heart failureI Izabella Uchmanowicz¹¹Health Science Faculty Wroclaw Medical University, Wroclaw, Poland

Background: Chronic heart failure is a serious medical condition. Recently, there has been an increasing interest in frailty syndrome and acceptance of illness among patients with cardiovascular conditions. Demonstrating the influence of frailty syndrome on illness acceptance could prevent the adverse effects of frailty syndrome and improve the quality of care.

Purpose of the study: To assess the influence of frailty syndrome on the illness acceptance in patients with chronic heart failure.

Material and methods: Data was collected between March and October 2014. The study included 110 chronic heart failure patients hospitalized in the Cardiology Ward. Frailty syndrome was assessed using the Tilburg Frailty Indicator (TFI) questionnaire, and acceptance of illness was assessed using the Acceptance of Illness Scale (AIS).

Results: The study included 110 chronic heart failure patients (mean age 66.01, SD±11.40), of whom 53.64% were men and 46.36% were women. The analysis showed that patients with higher illness acceptance levels had lower frailty scores in all components of the TFI: physical, psychological and social.

Conclusions: A higher illness acceptance level contributes to better scores in all TFI scale domains. A correlation was shown between acceptance of illness and the physical, psychological and social components of the TFI. Moreover, older age, more frequent hospitalizations and longer time from diagnosis are predictors for worse TFI scores. Better education is a predictor for better TFI scores in the social domain.

P1787

Controlled study of the central hemodynamic changes front a single inspiratory exercise session using different loads in heart failureL Marchese¹; S Chermont¹; D Warol²; LB Oliveira³; M Quintao¹; ET Mesquita¹¹Federal Fluminense University, Niteroi, Brazil; ²Serra dos Orgaos University Center, Teresopolis, Brazil; ³Heart Failure Clinic (CLIC) Serra dos Orgaos University Center, Teresopolis, Brazil

Background: Decreased muscle strength in heart failure with reduced ejection fraction (HFREF) has been observed in 30-50% of patients and has clinical impact on the perception of dyspnea and on hospitalization and death. The inspiratory muscle training (IMT) improves respiratory muscle strength, functional capacity and quality of life in HFREF and has been progressively incorporated into clinical practice. There are few studies on acute changes in central hemodynamic response (CHR) for IMT.

Purpose: To evaluate the CHR front a single inspiratory exercise session using different loads in heart failure.

Methods: The study investigated the changes in variables of flow, strength and contractility. Cross-protocol, randomized, crossover, placebo-controlled, blind, in patients with left ventricular ejection fraction (LV) <45% (Simpson), functional class II and III. Twenty patients, 13 men, mean age: 65±11 years, BMI: 26±4.4 kg/m², MIP: -101±43 cmH₂O, completed a single session of exercise inspiratory of 3 cycles of 15 minutes with washout 1 hour. Involving loads of 30% (C30) 60% (C60) and placebo (P) using a linear load resistor (Powerbreathe Light). Noninvasive hemodynamic study was performed by cardiothoracic bioimpedance. Statistical analysis: Student's test, Pearson correlation and ANOVA two-way, considering significant p≤0.05.

Results: At the end of 15 minutes C60 showed a higher value in the perceived exertion scale (Borg) (0.3±0.9 vs 1.1±1.9 mmHg, p=0.01) and dyspnea (0.2±0.7 vs 0.8±1.5 mmHg, p=0.02). There was a significant increase in heart rate (HR) with the C30 (64±15 vs 69±15 bpm; p=0.005) and C60 (67±14 vs 73±14 bpm, p=0.002), and there was no change on the P. In stroke volume (SV) there was a significant decrease with the C30 (73±26 vs 64±20 ml, p=0.004), not varying P and C60. The cardiac output (CO) (4.6±1.5 vs 5.3±1.7 l/min; p=-0.001) and cardiac index (CI) (2.5±0.8 vs 2.8±0.7 l/min/m²; p=0.02) showed a significant increase only with the C60. There was a moderate correlation between CO and inspiratory muscle strength (r=-0.45; p=0.04). In addition to significant increase in systolic blood pressure (SBP), mean arterial pressure (MAP), pulse pressure (PP) and LV work (LCW), with the C60 (p<0.05).

Conclusion: The results of this study indicate that a single session with the load of 60% promotes elevation in CO, CI, HR, SBP, MAP, LCW and PP in relation to the load of 30%. However it is associated with a higher degree of dyspnea and fatigue after 15 minutes.

P1788

Importance of beta-blocker therapy optimization in elderly patients with left ventricular systolic dysfunctionA Angelica Maria Romero Daza¹; M Cortes Garcia¹; JA Franco¹; JA Palfy¹; E De La Cruz¹; P Avila¹; ML Martin¹; S Briongos¹; I Hernandez¹; JA Farre¹¹Foundation Jimenez Diaz, Cardiology, Madrid, Spain

The elderly population with left ventricle systolic dysfunction (LVSD) has been under-represented in clinical trials of beta-blockers (BB) and maybe this is the reason why these drugs are less used in this population. The objective of this study is to evaluate the importance of the optimization of the medical treatment with beta-blockers in elderly population with left ventricle systolic dysfunction.

We included all patients ≥ 75 years old, with LVEF ≤ 35%, studied in our center between January 2008 and April 2012. In each patient was collected information about treatment with BB and the dose reached. With this data we created a variable that determined the percent dose of BB (BB%) compared to the target level established in clinical guidelines (50 mg / d for carvedilol and 10 mg / d for bisoprolol). To analyze the effect of BB% mortality and cardiovascular events. The variable%BB was categorized into 3 groups (not BB, doses <50% and ≥ 50% doses).

Results: 556 patients were included. The mean age was 81.9 years, mean LVEF was 28%. 143 patients (25.7%) did not take BB, 268 (48.2%) took low doses BB and 145 (26.1%) achieved high doses. During follow 223 patients died (40.2%), 92 in the untreated group, 97 in the low dose and 34 at the high dose. We found an HR estimated of mortality (for each 10% increase over the target dose) of 0.84 (95% CI 0.79-0.90), p<0.001. Finally, another Cox model for major events, showed a HR of 0.93 (95% CI 0.89-0.97) per every 10% increase in the BB dose, P=0.001.

Conclusion: Elderly population with LVSD clearly benefits from optimization BB treatment. In this study we estimate that for every 10% increase in BB dose to the target dose (ie, per 5 mg / d of carvedilol or every 1 mg / d of bisoprolol) the probability of death is reduced by 10 to 21% and the probability of death or hospitalization for heart failure or ventricular arrhythmia between 3 and 11%.

Baseline characteristics of patients

	No BB (143)	BB low dose (268)	BB High dose (145)	Total (556)	P
EF (%)(SD)	27,5 (6,9)	28,1 (6)	28,9 (6,1)	28 (6,3)	0,057
Age (y) (SD)	83,3 (5,4)	81,7 (4,7)	80,9 (4,4)	81,8 (4,9)	<0,001
Sex (Women) (%)	37,8	31,7	33,1	33,6	0,41
COPD (%)	37,8	16,8	15,9	21,9	<0,001
FC III-IV (%)	63	60,9	61,9	61,7	0,74

P1789

Full yogic breathing in complex treatment of patients with chronic heart failureMT Vatutin¹; AM Shevelyok¹; GV Kravchenko¹¹Donetsk National Medical University, Department of Internal Medicine #1, Donetsk, Ukraine

Purpose: to evaluate the effectiveness of full yogic breathing in addition to the standard medical care of patients with chronic heart failure (CHF).

Materials and methods: The study included 65 patients (mean age 65.2±5.7 years) hospitalized due to acute decompensated systolic CHF. All patients were divided into groups: Control Group (CG) (n=33) received only standard therapy of CHF, Intervention Group (IG) (n=32) were additionally taught the full yogic breathing. CHF functional class (FC) (NYHA), 6-minute walk test (6MWT) distance (with the evaluation of dyspnea severity by the Borg scale) and arterial oxygen saturation (SpO₂) were estimated in all patients on admission to the department and at discharge. Length of hospital stay was assessed in all participants.

Results and discussion: At baseline, there were no statistically significant differences in clinical characteristics of the patients and studied parameters between the groups (p>0.05). At discharge both groups showed significant increase in 6MWT distance (from 152.8±24.1 m to 206.7±15.2 m in the CG, p=0.001 and from 149.1±21.2 m to 247.3±24.1 m in the IG, p<0.001) and SpO₂ (from 93 (82; 95)% to 95 (83; 97)% in the CG, p=0.008, from 93 (86; 95)% to 98 (95; 98)% in the IG, p<0.001), reduction of dyspnea severity by the Borg scale (from 8.2±0.4 to

5,1 ± 0,2 points in the CG, $p=0,005$ and from 8,0 ± 0,6 to 3,3 ± 0,4 points in the IG, $p < 0,001$). All of the changes were more pronounced in the IG compared to the CG (all $p < 0,05$). Decrease in CHF FC was observed in 84,7% of patients of the IG and in 65,8% of the CG ($\chi^2=8,91$, $p=0,012$). Average length of hospital stay was less in the IG (16,3 ± 2,4 days vs. 19,9 ± 2,8 days in the CG, $p < 0,001$).

Conclusions: Application of full yogic breathing in addition to standard therapy of the patients hospitalized due to decompensated CHF is associated with significant improvement in exercise capacity and arterial oxygen saturation, decrease in dyspnea severity and CHF FC, and reduced length of hospital stay.

P1790

Inspiratory muscle training improves quality of life, perceived exertion and blood flow to the intercostal muscles in patients with chronic heart failure

Brazilian agencies: CNPq, CAPES, FINEP, FAPERJ
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Purpose: to evaluate the influence of inspiratory muscle training (IMT) on quality of life, perceived exertion and blood flow intercostal muscles in patients with chronic heart failure (CHF) and inspiratory muscle weakness.

Methods: 24 patients (10 women; age 61 ± 14 years, mean ± SD) with clinical stable heart failure (left ventricular ejection fraction 36 ± 6%) and respiratory weakness were randomly assigned either to the IMT group (n = 7; 5 women) or control (no training; n = 7; 5 women). Respiratory muscle performance was evaluated by a respiratory muscle fatigue protocol (1-min increases in inspiratory resistance up to fatigue). Quality of life (QoL) was assessed using the Minnesota Living With Heart Failure Questionnaire pre and post IMT. Also measured: perceived exertion (0-10 scale), beat-by-beat blood pressure, heart rate, cardiac output, capillary lactate concentration, minute volume, respiratory rate, arterial saturation, end-tidal CO₂ pressure, muscle microvascular blood volume and oxygenation (near infrared spectroscopy) recorded at the left 7th intercostal space and oxygen uptake (V̇O₂) was obtained through a gas analyzer. End-tidal pCO₂ was kept stable by controlling ventilation and respiratory pattern. Rearrangement of Fick equation was used to estimate muscle blood flow non-invasively [Q_{cap}=VO₂/Diff(a-v)O₂; where Q_{cap}: capillary blood flow; Diff(a-v)O₂: arterio-venous difference estimated by microvascular deoxyhemoglobin]. Data was analyzed by a two-factor ANOVA, followed by the LSD post-hoc test.

Results: IMT increased peak inspiratory pressure by 77% (pre: 60 ± 13 vs. post: 106 ± 15 cmH₂O, $P < 0.05$). QoL scores improved after IMT (IMT: 38 ± 6 before and 16 ± 5 after; Control: 37 ± 11 before and 39 ± 11 after ($P < 0.001$)). This improvement was attributed to a change in physical dimension of the score that changed from 6 ± 3 to 3 ± 5. Patients submitted to IMT showed a greater blood flow increase during respiratory fatigue (Q_{cap}: pre = 29 ± 7% vs. post = 57 ± 13%; $P < 0.05$), an effect that was not observed in the control group (Q_{cap}: pre = 29 ± 5% vs. post = 22 ± 6%, $P > 0.05$). Intercostal muscle deoxyhemoglobin concentration increased less post IMT (IMT: pre = 53 ± 8% vs. post = 27 ± 3%, $P < 0.05$; control: pre = 51 ± 9% vs. post = 52 ± 15%, $P > 0.05$).

Conclusion: This randomized and controlled trial shows that a short-term, home-based program of IMT results in marked improvement in inspiratory muscle strength and endurance and increase intercostal blood flow along with improvement in quality of life in CHF patients with inspiratory muscle weakness.

P1791

Memory-entailed clock drawing test score was an independent risk factor of readmission in outpatients with heart failure

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Purpose: Self-monitoring in outpatients with heart failure plays a crucial role in the management of their disease. Patients with cognitive impairment often require hospitalization because of insufficient self-care and management. Memory-entailed clock drawing test (Me-CDT) is a 3-minute cognitive screening tool including using a pre-drawn circle and a clock copying task. Here, this study aimed to clarify the association between cognitive impairment and readmission in outpatients with heart failure.

Methods: Totally, 202 outpatients with heart failure received Me-CDT. Patients scored ≥ 9 were defined as normal, whereas those scored < 8.5 were defined as having suspected cognitive impairment. Patients who were already diagnosed as having cognitive impairment and under treatment and those with visual disorder and/or hearing difficulties were excluded from the study population.

Results: The mean Me-CDT score was 7.0 ± 2.4; 130 patients (64%) were diagnosed as having suspected cognitive impairment. Me-CDT score was significantly correlated with Mini-Mental State Examination score ($r=0.63$, $p < 0.0001$). Age was negatively correlated with scores ($r=-0.44$, $p < 0.0001$). The mean number of admissions was 1.2 ± 1.5 times; 48 patients (24%) were readmissions twice or more times. According to the multivariate analysis, Me-CDT score (odds ratio 1.26; 95% confidence interval, 1.07-1.50; $p=0.006$) was an independent predictor of readmission.

Conclusion: The higher prevalence of cognitive impairment was suggested in outpatients with heart failure. Cognitive impairment was an independent risk factor of readmission in outpatients with heart failure. More aggressive intervention will be required for cognitive impairment.

	Univariate analysis			Multivariate analysis		
	HR	95% CI	P value	HR	95% CI	P value
Age (years)	0.97	0.04-1.12	0.07			
BMI (kg/m ²)	0.99	0.91-1.10	0.94			
Me-CDT	1.30	1.14-1.50	0.0002	1.26	1.07-1.50	0.006
Log BNP	0.36	0.18-0.69	0.003			

P1792

Prognostic value of pulmonary hypertension and right ventricular function in heart failure

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Background: Pulmonary hypertension (PH) and right ventricular (RV) dysfunction have been associated with adverse outcome in patients with chronic heart failure. We sought to determine the prognostic importance of noninvasively assessed pulmonary artery systolic pressure (PASP) in stable ambulatory patients with HF and its interaction with RV function.

Methods: We studied 1613 patients with chronic heart failure at the HF Registry of our university. Systolic pulmonary artery pressure (PASP) and RVF (RV function) were determined by echocardiography, pulmonary hypertension was defined as PASP > 50 mmHg and RV dysfunction defined by (S'VD < 10 cm / s and TAPSE < 16 mm). The primary endpoint was the occurrence of acute heart failure decompensation (AHFD).

Results: PH was present in 178 patients (11%) and RV dysfunction in 117 (7.17%). 23% of patients with RV dysfunction had a PH. (Sex: 32.14% women and 67.86% men, an average age of 64 years, 75% LVEF and 25% preserved LVEF). Compared to patients with normal RVF and without PH who had 1.48% to develop AHFD, patients with both RV dysfunction and PH had a greater risk of AHFD (14.28%), while patients with RV dysfunction and without PH had 11.54% of AHFD occurrence.

Patients with PH and normal RVF had a rate of 6.06%.

Data of PH and RVF allowed us to reclassify the HF patient's risk of developing an AHFD.

Conclusions: PH and RV function provide incremental prognostic information in HF. The combination of PH and RV dysfunction is particularly ominous. Thus, the estimation of PASP may be warranted in the standard assessment of ambulatory HF patients.

P1793

Role of anemia in heart failure patients with chronic kidney disease

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Purpose: The association between heart failure, chronic kidney disease and anemia is a vicious circle called cardio-renal anemic syndrome. Anemia, heart failure and chronic kidney disease are each able to worsen each other.

Methods: We present a retrospective study of 80 patients, diagnosed with heart failure II, III, IV NYHA, chronic kidney disease stage III, IV and iron deficiency anemia. They were selected from Clinical Cardiology and Clinical Nephrology. They were followed for 3 years (January 2012-december 2014): dry weight, left ventricular ejection fraction, NTpro BNP on admission creatinine clearance, number of readmissions / decompensation, level of hemoglobin, level serum iron, red cell indices, treatment with iron of anemia.

Results: Treatment of mild anemia with iron did not affect the decrease in glomerular filtration rate in patients with chronic kidney disease stage IV, with class II, III NYHA heart failure with left ventricular ejection fraction greater than 45% (p < 0.005).

Treatment with iron in patients with mild to moderate anemia, with class III, IV NYHA heart failure with left ventricular ejection fraction greater than 15% and chronic kidney disease stage III, IV, reduced the number of decompensation / hospitalizations. (P < 0.003).

Treatment with iron of mild and moderate anemia, at diabetic patients with NYHA class IV heart failure with left ventricular ejection fraction below 30% and chronic kidney disease stage III, IV did not influence the rate of hospitalizations / decompensation and no decrease in glomerular filtration rate.(p < 0,05).

Patients who died, they were underweight, NYHA class IV heart failure, left ventricular ejection fraction below 15%, chronic kidney disease stage IV, V, NT pro BNP> 30,000 pg / dl on admission, with hemoglobin <8.4 g / dl, whether they were or not treatment with iron.

Conclusions: Cardio-renal anemia syndrome must have multidisciplinary approach, with continuous monitoring of the three diseases and the iron therapy in patients with anemia, heart failure and chronic kidney disease plays an important role, reducing readmissions.

P1794

Effect of the angiotensin receptor neprilysin inhibitor LCZ696 compared with enalapril according to systolic blood pressure in PARADIGM-HF

NOVARTIS Pharmaceuticals

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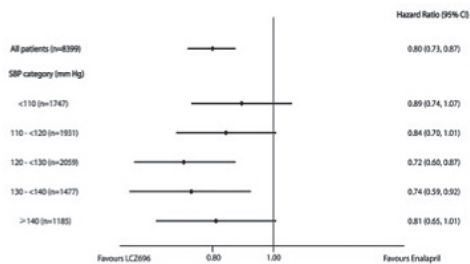
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Background: Low blood pressure (BP) is associated with worse outcomes in heart failure (HF) and may also cause drug intolerance, especially to agents with a hypotensive action. We therefore examined the effect of the angiotensin receptor neprilysin inhibitor (ARNI) LCZ696 compared with enalapril in PARADIGM-HF.

Methods: Patients in NYHA class II-IV, a LVEF ≤40% and a mildly elevated BNP/NT proBNP were enrolled in a run-in period with enalapril 10 mg bid followed by LCZ696 100 mg bid, increasing to 200 mg bid. Patients tolerating both treatments and fulfilling pre-specified safety criteria (systolic BP ≥95 mmHg, eGFR ≥30 ml/min/1.73m² and no decrease >35% from baseline, serum potassium <5.5 mmol/l) were randomized to enalapril 10 mg bid or LCZ696 200 mg bid. We examined the effect of study therapy according to systolic BP (SBP) category at randomization.

Results: SBP at randomization ranged from 90-189 mmHg. Overall LCZ696 reduced the primary endpoint of cardiovascular (CV) death or HF hospitalization (HFH) by 20% (HR 0.80, 95% CI 0.73-0.87; p=0.000004). The effect of LCZ696 according to SBP category at randomization is shown in the figure. The treatment effect was consistent across all categories (SBP×treatment interaction p=0.58). The findings were similar for CV death alone. Of the 10513 patients who entered the enalapril run-in, 146 (1.4%) discontinued the study for hypotension; 164 of 9419 (1.74%) stopped LCZ696 for the same reason. After randomization, 29 of 4212 (0.7%) of enalapril and 36 of 4187(0.9%) LCZ696 treated patients stopped study-drug for hypotension.

Conclusion: In PARADIGM-HF, the benefits of LCZ696 over enalapril were consistent across the SBP-range studied. Hypotension rarely led to drop-out during the run-in period or study drug discontinuation after randomization.



P1795

Results of the TITRATION study: a 12-week, multicenter, randomized, double-blind, safety evaluation of a 3- versus 6-week up-titration regimen of LCZ696 in patients with HFrEF

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Purpose: LCZ696, an angiotensin receptor neprilysin inhibitor, reduced the risk of CV death or HF hospitalization vs. enalapril in the PARADIGM-HF trial. The current study examined two up-titration regimens for LCZ696.

Methods: This randomized, double-blind, study assessed the safety and tolerability of up-titrating LCZ696 from 50mg bid to a target dose of 200mg bid over 3-(Condensed) vs. 6-weeks (Conservative) in patients with HF and reduced ejection fraction (≤35%). An open-label run-in (LCZ696 50 mg bid for 5 days) preceded an 11 week randomization period. The primary endpoints were the proportion of patients experiencing pre-specified adverse events (AEs) and laboratory assessment outcomes. Secondary objectives included the number of patients achieving the LCZ696 200mg bid target dose without any down-titration or dose interruption over 12 weeks (defined as treatment success).

Results: Overall, 498/540 (92%) patients enrolled in the run-in were randomized and 429 (86.1%) completed the study. The results for the primary endpoints are shown in Table 1. Only two cases of angioedema were reported, neither of which involved airway compromise. Excluding those who discontinued for non-AE related reasons (N = 466), treatment success was achieved in 77.8% and 84.3% (p = 0.07) of patients in the Condensed and Conservative regimens, respectively. Among those who received at least one dose of LCZ696 in the run-in period and excluding non-AE related discontinuations (N = 496), 76.2% of patients achieved treatment success. Among those entering the run-in period, 70.3% of patients reached the target dose without any dose interruption or adjustment.

Conclusion: Safety and tolerability were similar regardless of the up-titration regimen. Most patients (≥70%) achieved and maintained the target dose of LCZ696.

P1796

Concordant and discordant left bundle branch block: role in predicting response to cardiac resynchronisation therapy (CRT)?

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Despite the benefits shown for CRT a proportion of patients are non-responders. We review the relationship between left bundle branch block (LBBB) pattern and left ventricular (LV) volumes, to ascertain whether the pattern of electrical dyssynchrony can help optimise CRT response rates.

Patients undergoing guideline-directed CRT between 2011 and 2014 (n = 246) were included. Those upgraded from bradycardia pacing or ICD devices, without baseline or follow up echo data and with atrial flutter or complete heart block were excluded. Standard criteria were used to identify a) LBBB: QRS ≥120msec, rS or QS in V1 or V2, and RSR' in V6 b) discordant LBBB (LBBB-d): +ve or -ve QRS deflection with an opposing T wave, and c) concordant LBBB (LBBB-c): +ve or -ve QRS deflection with same deflection of the T wave. LV volumes were calculated using Simpson's bi-plane method at baseline, 3 months and 6 months post-implant.

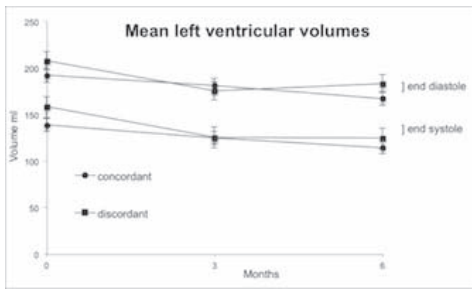
70 patients were included; 58 (83%) male, mean age: 69 ± 10, ejection fraction (EF): 25 ± 12%, and QRS duration: 155 ± 20msec. 23/70 had LBBBc and 47/70 had LBBBd. Each ecg was graded, A: consistently LBBBc/LBBBd, B: consistent in 2 of 3 leads and C: clear morphology in 1 lead with borderline morphology in 2. For grade A LBBB-d- (n = 35), 21 (60%) had a significant improvement in end systolic volume (ESV) and 17 (49%) in end diastolic volume (EDV). For grade A LBBB-c (n = 12) 5 (42%) had significant improvement in ESV and 4 (33%) in EDV. Dependant T tests were performed across the data, with no significant correlations in ESV or EDV with LBBB--c or LBBBd.

The population of guideline compliant LBBB patients undergoing CRT had significant reduction in ESV and EDV on follow up echo, by 7% and 12% respectively. However the pattern of LBBB did not discriminate between echo responders and non-responders.

Table 1. 61071

Regimen	Proportion of patients (%) Hypotension	Renal dysfunction	Hyperkalemia	Angioedema	
Condensed (N = 247)	9.7	7.3	7.7	0.0	
Conservative (N = 251)	8.4 [0.570]	7.6 [0.990]	4.4 [0.114]	0.8 [-]	
[p-value]					
	SBP <95 mmHg	K >5.5 mmol/L	K ≥6.0 mmol/L	Cr >3.0 mg/dL	Cr X2
Condensed (N = 247)	8.9	7.3	1.2	0.4	0.8
Conservative (N = 251)	5.2 [0.102]	4.0 [0.097]	0.4 [0.322]	0.0 [-]	0.4 [0.569]
[p-value]					

AE=adverse event; Cr=serum creatinine; CrX2=doubling of serum creatinine; K=serum potassium.



P1797

Improving medication adherence in patients with chronic heart failure: a feasibility study

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Background: Heart Failure (HF) medication non-adherence increases the risk of mortality and hospitalisation. Given the increasing burden of HF, tackling non-adherence is a priority.

Purpose: To test the feasibility of a pharmacy technician-led service to improve medication adherence and disease markers.

Methods: Primary-care based before and after feasibility study. Non-adherent (<80%) patients with chronic heart failure and ejection fraction <45% were included. No exclusions. Patients were identified via HF multidisciplinary team. Patients were visited by a pharmacy technician at home repeatedly over six months for individualised education, logistic support and cognitive assessment. Technicians liaised with social care teams and mental health services if needed. Tablet counts were undertaken at each visit. Analyses included parametric and non parametric tests as appropriate.

Endpoints: Baseline and discharge angiotensin converting enzyme inhibitor (ACEI), beta-blocker (βB) and loop diuretic adherence (%). Baseline and discharge B-type natriuretic peptide (BNP), New York Heart Association (NYHA) classification and pulse.

Results: 16 patients recruited. 10 male. 11 were from the most socio-economically deprived quintile. 7 had known alcohol addiction. Baseline prescribing: ACEI 14/16, βB 14/16 and loop diuretic 14/16. Patients were visited a mean of 16 times. 1 patient withdrew at three months. Adherence with ACEI, βB and loop diuretic significantly increased (see table). BNP and heart rate trended downwards. There was no significant change in NYHA.

Conclusion: HF medication adherence improved over a six month period through a novel pharmacy technician-led service. A formal randomized controlled pilot study is planned.

Impact on Adherence and Clinical Markers

Parameter	Patients Included	Patients Missing	Before	After	p
Median ACE Adherence (%)	13	1#	46.5	100.0	0.004*
Median βB Adherence (%)	13	1#	64.0	100.0	0.020*
Median Loop Adherence (%)	13	1#	64.0	100.0	0.016*
Median BNP (pg/ml)	15	1#	249	236	0.056
NYHA; 1, 2, 3	15	1#	3,6,6	3,6,6	1.000
Mean Pulse (bpm)	15	1#	76.1	71.2	0.137

* = statistically significant, # = withdrew

P1798

Galectin-3 and histological, molecular and biochemical aspects of myocardial fibrosis in heart failure of hypertensive origin

Ministry of Economy and Competitiveness (Spain) and FP7 of the European Commission

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Aims: The aim of this study was to investigate whether galectin-3 (Gal-3) is associated with myocardial histological and molecular parameters related to fibrosis and with the circulating biomarkers of the extracellular generation of mature fibrin-forming collagen types I (carboxy-terminal propeptide of procollagen type I, PICP) and III (amino-terminal propeptide of procollagen type III, PIIINP) in 2 independent studies of hypertensive patients with chronic heart failure (CHF).

Methods and results: Endomyocardial biopsies and blood samples from 39 CHF patients (invasive study), and blood samples from 220 CHF patients (non-invasive study) were analyzed. Necropsies (n = 7) and blood samples (n = 20) from healthy subjects were used as controls. Invasive study: Myocardial mRNA and protein expression of Gal-3 and collagen types I and III, plasma Gal-3 and serum PICP and PIIINP were all significantly increased in patients compared to controls. Neither myocardial nor plasma Gal-3 were correlated with myocardial collagen and circulating biomarkers. Whereas PICP was correlated with myocardial total (r = 0.819, P < 0.001) and collagen type I (r = 0.744, P < 0.001) deposition, PIIINP was not. Non-invasive study: Both plasma Gal-3 and serum PICP were increased (P < 0.001) in patients compared to controls. No correlation was found between Gal-3 and PICP in CHF patients.

Conclusions: These findings show that although an excess of cardiac and systemic Gal-3 is present in patients with CHF of hypertensive origin, this molecule is not associated with histological, molecular and biochemical parameters related to myocardial fibrosis in these patients.

P1799

Prognostic value of waist circumference in patients with chronic heart failure

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Objective: To examine whether waist circumference (WC) can predict long-term mortality and readmission for heart failure in subjects with chronic heart failure (CHF).

Methods: The study included 179 patients who were followed up for 18 months. Central obesity was defined as WC ≥ 88 cm for women and ≥ 102 cm for men.

Results: There were 91 (54.7%) males and 81 (45.3%) females with a mean age of 64.9 years (range, 24-88). Severe left ventricular systolic dysfunction was present in 38% of patients, 34.6% had moderate systolic dysfunction, 22.3% had mild systolic dysfunction and 5% had chronic heart failure with preserved left ventricular ejection fraction. Central obesity was observed in 24%. Who showed significant changes in the New York Heart Association (NYHA) Class with an indication of hospitalization for 40% of patients with central obesity, versus 19.2% of patients without central obesity (p = 0.004). No mortality was observed in this study.

Conclusion: Waist Circumference is predictive of readmission for heart failure in individuals with chronic heart failure but not for mortality.

P1800

Gender differences exist in the clinical characteristics of Saudi heart failure patients with subsequent stroke

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Background: The prevalence of stroke in developing nations including Saudi Arabia is on the rise, yet there is limited data available as to the clinical presentation of the disease. This retrospective study aims to determine the clinical characteristics of Saudi patients with heart failure (HF) with and without subsequent stroke, and also to find out whether gender differences exist in the presentation of HF patients who had stroke.

Methods: A total of 293 patient (151 males, 142 females) charts from 2002-2008 were reviewed in our Medical City in Saudi Arabia. These charts were from Saudi patients who were diagnosed to heart failure, with and without subsequent stroke. Demographics, HF characteristics, stroke risk factors and metabolic characteristics were noted and analyzed.

Results: There was no difference in HF characteristics and stroke risk factors among HF patients with and without subsequent stroke. In terms of metabolic profile, those who had stroke had significantly higher LDL-cholesterol levels as compared to those without (p-value 0.03). Stratification to gender and adjusting for age and risk factors revealed that a significantly higher LDL- and total cholesterol levels were observed in female stroke patients (p-values 0.02, 0.028, respectively) and a significantly higher BUN levels observed in male stroke patients (p=0.04) as compared to their counterparts who never had stroke.

Conclusion: The gender differences in the metabolic presentation of Saudi HF patients with stroke warrant further clinical investigation. Atherogenic dyslipidemia and renal insufficiency are suggested to be early predictors for stroke should be closely monitored in Saudi HF patients.

P1801

The effects of ramadan fasting on patients with chronic heart failure

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Objective: The effects of Islamic fasting on physiologic functions in normal conditions have been considered in different studies and different topics. This study was to determine the quantitative changes of hemoglobin, lipid profile and renal function during Ramadan fasting in patients with chronic heart failure.

Methods: fifty-three outpatients with chronic heart failure were followed during the month of Ramadan 2014 (1435 H) in our Cardiology departement in 2 stages : one week before the start of Ramadan and then on the last day of Ramadan, by proper blood sampling in suitable time of day.

Results: There were 31 (58.5%) males and 22 (41.5%) females with a mean age of 60 ± 11.06 years. Mild left ventricular systolic dysfunction was observed in 35.8% of patients, 54.7% had moderate systolic dysfunction and 9.4% had severe systolic dysfunction. There were no significant changes in the New York Heart Association (NYHA) Class (P=0.18) nor there were any significant changes in the Canadian Cardiac Society (CCS) class in patients with coronary artery disease (P=0.09). We found non significant decrease in hemoglobin and blood glucose level ; (P=0.76) and (P=0.16) respectively, and non significant increase in creatinine (P=0.07), and non significant changes in TC, TG, HDL-C and LDL-C, at the end of Ramadan.

Conclusion: The effects of fasting during Ramadan on stable patients with cardiac disease are minimal. The conclusions from this study can not be extrapolated to patients with worse functional classes or those who are unstable. It is clear that more work should be carried to discover the significance of Ramadan fasting in patients with heart disease.

P1802

Educative intervention to reduce consumption of sodium in patients with heart failure and their caregivers

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Introduction: Self care in heart failure (HF) patients needing new strategies to relieve symptoms and improve quality of life.

Purpose: To evaluate the effect of an educative intervention to reduce diet sodium consumption on body composition and the patient's and caregiver clinical status.

Methods: In a Randomized clinical trial 53 HF patients from Heart Failure clinic at INCMNSZ were included. They were randomly assigned into 4 groups, 2 intervention (1 with caregiver and 1 without it) and 2 control groups (1 with caregiver and 1 without it). Group 1 (n=10) where patient and caregiver received the intervention that consist in information through didactic resources, classifying food into 3 groups based on sodium content, like traffic light: high sodium (red), medium sodium (yellow) and low sodium (green), also education about the relationship between high sodium intake and symptoms of HF. In Group 2 (n=9) the patient and caregiver received only usual care information. In Group 3 (n=15), only the

patient received the intervention information. In Group 4 (n=19), only the patient received usual care information. Two measurements of body composition with Body-Stat multifrequency equipment were done, at the beginning and after 3 months of follow up.

Results: In Group 1 there was a statistically significant decrease in the impedance index (0.99 ± 0.03 vs. 0.93 ± 0.09 , $p=0.044$) and in diastolic blood pressure (71.40 ± 9.43 to 63.5 ± 10.63 , $p=0.014$) compared to group 4 that did not change (80.84 ± 11.48 to 79.474 ± 12.28). The other groups did not have any significative change.

Conclusions: Implement an educational intervention to reduce sodium consumption including the caregiver has a positive effect in patients with heart failure.

P1803

Living with chronic heart failure: the personal experience of undergoing a change of identity

This research was supported by a PIUNA (Plan de Investigación Universidad de Navarra) grant from the University of Navarra (Spain).

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Background: Chronic heart failure (HF) affects all the essential spheres of a person's life. In the context of that experience, a relevant aspect is the change patients experience on their personal identity.

Purpose: To study the experience of change of identity undergone by patients with HF.

Method: A phenomenological-hermeneutic study was carried out in a specialized cardiology unit; the study was based on 12 patients diagnosed with HF NYHA II-IV. Personal interviews were held with the patients in order to report their experience with HF. This data is part of a more comprehensive study that it is being carried out at the moment.

Results: The change of identity has arisen as an important part of the experience of people living with HF. Patients state that HF has changed them, they are not the same person anymore: "I don't even know myself", "it feels like my skin has been removed and I have been given a different one". They relate this fact among others to: changes on their appearance and changes at cognitive level, mood swings and repercussions on life expectancy, a continuous feeling of sickness, alteration of family and social roles and variations in life style and leisure activities. It has been observed that all these aspects have a negative impact on patients well-being, emphasizing the feelings of sadness, social isolation and self-limiting their own personal development.

Conclusions: This study has shown that patients with HF experience a considerable change in their personal identity, which negatively affects different domains of their life. It is necessary to deepen more in the phenomenon of change of identity and its causes, in order to help people undergo the process of accepting their new identity; thus improving their well-being.

P1804

Chronic heart failure in woman: clinical, biological and echocardiographic features

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Purpose: Chronic heart failure (CHF) is a major cause of morbidity and mortality in the world. Few studies have examined the difference between the two gender and features in african woman.

Methods: We conducted a retrospective study of patients with chronic heart failure followed between 2006- 2012 at our daily hospital. Of the 1613 patients, 603 were women. We studied the prevalence of cardiovascular risk factors, the severity of clinical symptoms and major cardiovascular events (acute coronary syndrom, stroke and acute heart failure). We also collected biological parameters (serum sodium, serum potassium, hemoglobin and creatinine) and echocardiographic criteria with poor prognosis (dilated left ventricular >60mm, ejection fraction <35%, pulmonary hypertension, severe mitral regurgitation). We compared our results with statistical analysis to the men of our population to identify prognostic markers in women with CHF.

Results: Mean age was 68,3 years. Woman is more likely to hypertension (49% vs 33%) and diabetes (39% vs 27%). Smoking is less common in women (with 3.4% vs 48%). Further, metabolic disorder dominates in the male population specially anemia. There is no significant difference in the severity of clinical symptoms. The etiology of CHF is dominated in women by valvulopathy, but man ischemic etiology dominates as in the developed countries. For echocardiographic features, half women has ejection fraction less than 35%. In addition, pulmonary arterial hypertension beyond 40 mmHg was significantly elevated in women. We find a higher

acute cardiac decompensation rate at 9.9% vs. 7.7% ($p=0.01$). Otherwise, the occurrence of major cardiovascular events is lower in women such as myocardial infarction (29% vs 40.3%) and stroke (5.9% vs 19%) $p < 0,001$.

Conclusion: Woman with chronic heart failure is more predisposed to cardiovascular risk factors and acute heart decompensation. Nevertheless, she has fewer major cardiovascular events.

P1805

Analysis of electrocardiographic abnormalities in chronic heart failure: (UTIC) register

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Introduction: The electrocardiogram (ECG) is an important tool in the initial evaluation of patients with congestive heart failure and in the monitoring of these patients. The purpose of this work is to describe the different electrocardiographic abnormalities encountered in patients monitored for chronic heart failure.

Methodes: A retrospective study of major electrocardiographic abnormalities, involving 1622 patients with chronic heart failure, followed between January 2008 and October 2014.

Resultats: The mean age of patients was 68.6 years (± 12 years, ranging from 18 to 104 years), with a sex ratio of 1.67. The main cardiovascular risk factors identified were: hypertension (46.1%), diabetes (38.8%), tobacco (38.6%) and dyslipidemia (14.9%) cases. The etiology of heart failure was in order of frequency: ischemic heart disease (55.6%), DCM (27.5%), hypertensive heart disease (9.8%) and valvulopathy (5.7%). The major electrocardiographic abnormalities were: repolarization disorders (41.9%), the Q wave-necrosis (18.7%) and atrial fibrillation (11.8%). The conduction disorders have been dominated by the left bundle branch block (23.9%), followed by the first atrio-ventricular block (11.02%). The signs of cavitory hypertrophy was noted especially on the left side: left ventricular hypertrophy was observed in 11.4% of cases, while the left atrial hypertrophy was observed in 3.3% of cases. Recorded rhythm disorders had been dominated by the atrial fibrillation (11.8%) followed by the ventricular rhythm disorder (8.8%).

Conclusion: Electrocardiographic abnormalities are common in patients with chronic heart failure and a normal ECG must review the diagnosis. The control of rhythm disorders and prevention of its complications is a major pillar in the management of chronic heart failure.

P1806

Biological variation of the cardiac index in patients with stable chronic heart failure: inert gas rebreathing compared with impedance cardiography

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Aims: In chronic heart failure (CHF), changes in cardiac function define the course of the disease. The cardiac index (CI) is the most adequate indicator of cardiac function. Interpretation of serial CI measurements, however, requires knowledge of the biological variation of CI. Because measurements of CI can be confounded by the clinical situation or the method applied, biological variation might be subject to the same confounders.

Methods and Results: We prospectively included 50 CHF patients who met rigid criteria for clinical stability. CI was measured by both inert gas rebreathing (IGR) and impedance cardiography (ICG) in weekly intervals over three weeks. Each measurement was performed at rest (IGRrest/ICGrest) and during low-exercise 10 Watt pedalling (IGR10W/ICG10W). Intra-class correlation coefficients (ICCs), reference change values (RCVs), and minimal important differences (MIDs) of CI were determined for IGRrest, ICGrest, IGR10W, and ICG10W.

ICG and IGR showed moderate agreement at rest (20% (6-36)) and good agreement at 10W (-4% (-23-16)). Depending on the time interval, measurement modality for CI, and mode, ICC ranged between 0.42 and 0.78, while ICC values for IGR were lower than those for ICG. RCV ranged between 3% and 15%, while MID ranged between 0.2 and 0.5L/min/m². Values for IGR were lower at rest and higher at 10W than those for ICG.

Conclusion: Non-invasive measurements of CI are stable over time. Measurement modalities for CI, however, are not interchangeable. Biological variation is less pronounced when obtained by ICG. The confounding influence of low-level exercise on CI depends on the measurement modality.

P1807

Severe potassium disorders in patients with chronic heart failure admitted to a tertiary hospital: clinical characterization, common causes and prognostic value

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Introduction: Alterations in the homeostasis of serum potassium (K) are common and potentially life threatening. The epidemiology data and prognostic value of these disorders in hospitalized patients (p) with chronic heart failure (CHF) are not well known.

Purposes and Methods: We conducted a retrospective observational study of all adults p with CHF admitted to a large university hospital during year 2013 assessing for the presence of severe K disorders at any time during hospitalization. Cut-offs for hypokalemia were $K \leq 2.5$ mmol/l and for hyperkalemia ≥ 6.5 mmol/l. Epidemiological and biochemical data were collected. We aimed to identify common causes and prognostic value.

Results: Severe K disorder occurred in 602 p (1.6%) of all admissions ($n=37,619$); 81 p associated CHF (0.21%), among this 41 p presented hyperkalemia and 39 hypokalemia. Table 1 shows baseline characteristics of CHF p. Common causes of hyperkalemia were: worsening chronic kidney disease (CKD) (26.8%), acute kidney disease (AKD) (19.5%), stable CKD (17.1%) and use of ≥ 2 renine-angiotensin aldosterone system blockers (17.1%). For hypokalemia were: diuretics (69.2%), gastrointestinal losses (17.9%) and low K diet (10.3%). In-hospital mortality for hypo and hyperkalemia was 11.6% vs 19%, respectively ($p=0.023$). Recurrence of same type K severe disorder at a median follow-up of 198 days (IQR: 13 to 355) was 12.7% for hypokalemia and 14.3% for hyperkalemia ($p=0.38$).

Conclusions: Severe K disorders in p with CHF are associated with high in-hospital mortality and recurrence of the basal K disorder during follow-up.

Baseline characteristics	Hypokalemia (n = 39)	Hyperkalemia (n = 41)	P value
Age, years, median (IQR)	83 (74-88)	77 (66-85)	<0.001
Women, n (%)	27 (69.2%)	18 (43.9%)	0.02
Hypertension, n (%)	32 (82.1%)	37 (90.2%)	0.28
Diabetes Mellitus, n (%)	13 (33.3%)	20 (48.8%)	0.16
Coronary artery disease, n (%)	5 (12.8%)	4 (9.8%)	0.66
Chronic kidney disease, n (%)	13 (33.3%)	26 (63.4%)	0.007
(K), mmol/l, median (IQR)	2.4 (2.2-2.5)	6.9 (6.6-7.2)	<0.001
Creatinine, mg/dl, mediana (IQR)	0.96 (0.62-1.42)	2.4 (1.56-3.38)	<0.001
Ejection fraction <60%, n (%)	12 (32.4%)	13 (37%)	0.68

P1808

Heart rate in heart failure - are we in control? An audit on heart rate control in heart failure patients attending the heart failure units

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Heart rate is an important aspect of heart failure therapy. The ESC heart failure guidelines recommend that heart failure patients in sinus rhythm should have a resting heart rate of < 70 beats per minute (BPM). The Rate Awareness Survey (RAS) Ireland in 2011 showed on average, 32.1% of heart failure patients had resting heart rates of ≥ 70 bpm. We performed an audit of the patients attending our heart failure units to determine how many patients in sinus rhythm had a resting heart rate of ≥ 70 BPM.

In the first phase of the audit, 72 patients were recruited - 36 (50%) had a resting heart rate of ≥ 70 BPM. This was subpar to the national average. There were 2 observations noted during the first phase; (a.) $\frac{3}{4}$ of patients with high resting heart rates were not on target doses of beta blockers; (b.) Heart failure medications were easily stopped by General Practitioners and other doctors when patients attended our hospital services or were hospitalised.

Interventions: (1.) An education session with the heart failure clinical nurse specialists and hospital doctors; (2.) Distribution of patient booklets to promote self-awareness and empowerment.

In the second phase of the audit, 75 patients were recruited - 17 (22.7%) had a resting heart rate of ≥ 70 bpm. This was a 27.3% reduction in the number of patients whose heart rate was not adequately controlled compared to the first phase. This result was statistically significant ($\chi^2 = 11.90$, $p < 0.001$). We also surpassed the national average as set by the RAS by 9.4% (Figure).

There were significant shortcomings with regards to heart rate control in our heart failure patients. Significant improvements were made with the changes that were implemented in this audit. A re-audit would be important to ensure the guidelines are being adhered to.

Percent of Patients with a resting heart rate of ≥ 70 BPM



Figure

P1809

Central apneas and chemoreflex activation influence on pulmonary hypertension in heart failure: role of adrenergic activation

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Background: Pulmonary arterial hypertension (PAH) is an established prognostic factor in patients with heart failure (HF). Beyond a “passive” component due to the increased left ventricular pressure, an “active” component due to pulmonary vascular reactivity may be present. The mechanism behind pulmonary vasoconstriction being not fully understood, we hypothesized that central apneas (Cheyne-Stokes respiration - CSR) through chemoreflex stimulation may contribute to PAH in HF.

Methods: we studied 54 systolic HF patients (left ventricular ejection fraction $< 50\%$), on stable guideline recommended pharmacological treatment, without increased left ventricular pressure (excluding patients with mitral prostheses, and those with grade III either mitral insufficiency or diastolic dysfunction). All patients underwent echocardiographic and neurohormonal assessment, 24-hour cardiorespiratory screening for CSR (patients with obstructive events were excluded) and chemoreflex test for hypoxic (HVR) and hypercapnic (HCVR) ventilatory responses (by rebreathing technique).

Results: Eleven patients (20%) showed significant CSR, as defined by a 24-hour apnea/hypopnea index -AHI- > 15 . HF patients with CSR, compared with patients with normal breathing, presented with higher systolic arterial pulmonary pressure (sPAP: 40.1 ± 7.6 vs 33.1 ± 5.9 mmHg, $p < 0.01$), with no difference in systolic and diastolic function. Furthermore, patients with central apneas also presented with enhanced HVR (median 0.79, interquartile range -IR 0.62-1.27 vs 0.43, IR 0.19-0.69 L/min/%, $p < 0.05$) and HCVR (1.18, IR 1.10-1.31 vs 0.73, IR 0.51-0.95 L/min/mmHg, $p < 0.01$) as well as increased plasma norepinephrine level (559, IR 446-770 vs 367, IR 229-508.5 ng/L, $p < 0.05$). sPAP was indeed correlated with AHI (Spearman's Rho, $R = 0.60$, $p < 0.001$), HCVR ($R = 0.48$, $p < 0.001$), HVR ($R = 0.50$, $p < 0.001$) and norepinephrine ($R = 0.29$, $p < 0.05$). At univariate regression analysis sPAP was associated with AHI, HVR, HCVR, norepinephrine, NT-proBNP. At multivariate analysis only AHI maintained its predictive value ($p = 0.014$).

Conclusions: the severity of CSR occurring either at night- or daytime, likely via recurrent hypoxia and hypercapnia cycles, may determine a chemoreflex-mediated adrenergic activation in patients with systolic HF, and a consequent pulmonary vasoconstriction, responsible of the undesirable increase in pulmonary arterial pressure.

P1810

Relation between anemia and six months outcome in patients with decompensated chronic heart failure (dCHF)

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Purpose: Anemia is frequent in patients with chronic heart failure and might be associated with an increased mortality. The aim of this study was to assess the prognostic value of anemia in patients with decompensated chronic heart failure (dCHF).

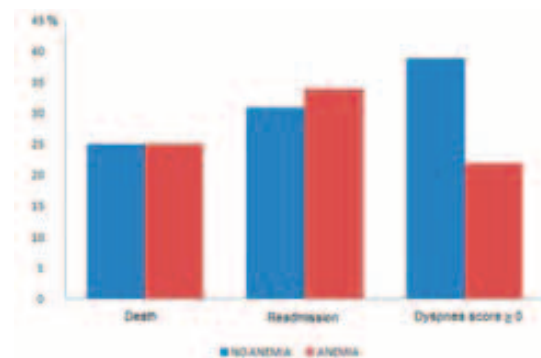
Methods: This is a retrospective cohort study selected 398 patients discharged from emergency department with a primary diagnosis of (dCHF). Two groups were defined according to hemoglobin level at ED admission: anemia group ($n = 193$, $Hb < 12$ g/dl), Non anemia group ($n = 205$, $Hb > 12$ g/dl). For all included patients, we recorded demographic characteristics, mortality, readmission rate and dyspnea score (worse = -1, stable = 0, better = 1) at six month post ED discharge. QL was defined as better or worse clinical status compared to preadmission.

Results: Results are summarized in the table and the figure below.

Conclusions: According to our study, patients with dCHF and anemia had similar mortality and readmission rate. Quality of live seems to be better in the Non anemia patients.

Variables *	Anemia (n = 193)	Non anemia (n = 205)	P
Age (years)	70 (12)	68 (11)	NS
Sex ratio (F/M)	114/80 (1,42)	84/121 (0,69)	$< 0,01$
Systolic blood pressure (mmHg)	155 (38)	146 (31)	$< 0,05$
Hemoglobin (g/dl)	$9,9 \pm 1,3$	$13,6 \pm 1,3$	$< 0,01$
Brain natriuretic peptide (BNP) pg/ml median (IQR)	1920 (1820-2020)	1292 (890-1694)	$< 0,05$
Left ventricular ejection fraction (LVEF) %	42 ± 11	43 ± 12	NS

Patient's characteristics. All the variables were expressed as mean(SD).



Outcomes by presence of anemia.

P1811

Anabolic and metabolic hormones interplay in chronic heart failure

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Purpose: The recognition of a multiple hormonal deficiency syndrome, especially with regard to somatotrope and gonadal axes, is gaining importance as prognostic

indicator. Purpose of this study was to evaluate the interaction among hormones in heart failure.

Methods: We enrolled 235 consecutive patients with CHF. Insulin-like growth factor-1 (IGF-1), total testosterone, dehydroepiandrosterone-sulfate (DHEA-S), glycaemia, insulin, TSH, fT3, fT4 were assayed in the morning in fasting state. Most patients (70%, n=164) underwent a provocative test with GHRH+Arginine to identify subjects with growth hormone deficiency (GHD). Insulin resistance was estimated using the HOMA index. Bivariate analyses were performed between the different hormonal variables. Testosterone levels were only measured in male patients.

Results: Characteristics of the patients in Table 1. 55 CHF patients (33%) showed GHD. GHD was associated with lower HOMA indexes (5.7 ± 1.0 vs. 2.3 ± 0.3 , $p=.023$) and lower circulating DHEA-S compared with CHF (69 ± 10 vs 43 ± 8 , $p=.05$). No significant difference was found with regard to IGF-1 and testosterone levels between GHD vs no-GHD patients ($p=.81$ and $p=.58$, respectively). A significant, direct correlation was found between IGF-1 and fT3 levels ($r=.26$, $p=.006$) and an inverse correlation between total testosterone levels and HOMA index was described ($r=-.25$, $p=.05$) (Fig.). Among hormones, DHEA-S was the only hormone inversely correlating with NT-proBNP ($r=-.30$, $p=.035$).

Conclusion: We herein show a significant interplay among anabolic and metabolic hormones in CHF. Further Registry studies are needed to clarify the prognostic relevance of such abnormalities in CHF.

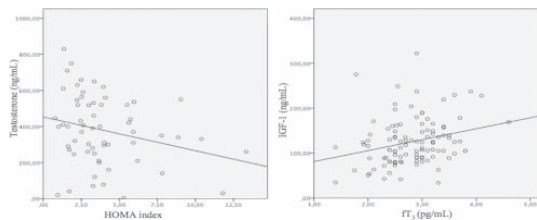


Fig.1

P1812

Prognostic predictors in a population-based cohort study of outpatients across different heart failure phenotypes

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Background: Although heart failure (HF) is a syndrome characterized by important variability in clinical findings and response to treatment, there is paucity of information on the different predictive factors and their prognostic impact across HF phenotypes.

Purpose: To evaluate and compare the predictive power of prognostic factors in a population-based cohort study of outpatients with different HF phenotypes (LVEF \leq 40% - HF_rEF, LVEF 41-49% - HF_bEF, LVEF \geq 50% - HF_pEF).

Methods: From November 2009 to October 2013, we retrospectively considered all consecutive HF outpatients, with available LVEF, enrolled in the Cardiovascular Observatory. Clinical variables of study population were derived from the E-data chart for Outpatient Clinic collected in a regional Data Warehouse.

Results: A total of 2424 patients (57% males; mean age 78 ± 8 ; NYHA 3-4 20%) were considered. Of these, 1457 (60%) had HF_pEF, 358 (15%) HF_bEF, 609 (25%) HF_rEF. At a follow-up of 28 ± 14 months, 502 patient were dead (21%), 168 (28%) among HF_rEF cases, 60 (17%) among HF_bEF and 273 (19%) among HF_pEF. The overall high mean age and frequent non cardiac comorbidities (median number 2) ran similarly across different HF phenotypes. In the overall population, the multivariable model included age (HR 2.41; $p=0.003$), male sex (HR 1.63; $p<0.001$), NYHA class III-IV (HR 1.52; $p=0.009$), systolic blood pressure (SBP) <110 mmHg (HR 2.05; $p<0.001$), hyponatremia (HR 1.68; $p=0.026$), anemia (HR 1.43; $p=0.001$), diabetes mellitus (HR 1.46; $p=0.015$), betablockers (HR 0.76; $p=0.006$), ACEi/ARBs (HR 0.76; $p=0.009$). The multivariate model performed differently across the three HF phenotypes. Among predictors, SBP <110 mmHg (HR 2.45; $p=0.05$) and betablockers (HR 0.67; $p=0.036$) were significant only in HF_rEF, whereas anemia (HR 1.42; $p=0.027$), chronic obstructive pulmonary disease (HR 1.41; $p=0.028$), moderate-to-severe aortic valve disease (HR 1.45; $p=0.048$) and ACEi/ARBs (HR 0.68; $p=0.014$) were significant only in HF_pEF.

Conclusions: In our cohort study of outpatients characterized by advanced age and frequent non cardiac comorbidities, covariates generally included in available HF risk models showed strikingly different predictive power according to HF phenotypes. These data suggest that HF risk models could be effectively applied in real world patients across different HF phenotypes.

P1813

Relation between NT-proBNP and left ventricular end-diastolic pressure in overweight patients with chronic heart failure

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NT-proBNP is frequently used for diagnosing and monitoring patients with chronic heart failure but its utility in overweight and obese patients with chronic heart failure is still unknown. Many recent studies suggested an inverse relation between NT-proBNP levels and body mass index but whether lower NT-proBNP levels are due to changed hemodynamics is unclear.

Purpose: The aim of this study was to investigate the relation between NT-proBNP and LVEDP in overweight patients with chronic heart failure.

Methods: 58 patients with chronic heart failure NYHA Functional class I-III were included in the study. All patients underwent an invasive measurement of LVEDP and echocardiographic assessment of LVEF. Body mass index was determined and biochemical analysis of NT-proBNP was obtained at the start of each case. Overweight was defined as BMI of ≥ 25 kg/m².

Results: Patients were divided into two BMI categories - lean (BMI <25 kg/m²) and overweight and obese (BMI >25 kg/m²). The groups were similar in respect to race, creatinine, history of dyslipidemia and LVEF. Of 58 patients included, 28 (47.5%) were overweight. Median (interquartile ranges) values of NT-proBNP for the lean and overweight groups were 956 ± 342 pg/ml and 551.43 ± 475.26 pg/ml, respectively. LVEDP was higher in the overweight group (18 ± 3 mmHg), compared to the group with BMI <25 kg/m² (12 ± 4 mmHg). The relationship between NT-proBNP and LVEDP was poor (r values <0.1).

Conclusion: NT-proBNP levels are depressed in overweight and obese patients with chronic heart failure despite higher left ventricle end-diastolic pressures. This implements that the secretion of natriuretic peptides is influenced by many determinants and their plasma concentrations should not be considered surrogates for cardiac filling pressures.

P1814

Preliminary results of the study MEETinCY

Cyprus University of Technology's state funded budget 2008e2011 [Startup Fund EX2007 (04)].

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Background: Even though heart failure (HF) management programmes have been improved and proved their efficient, no such programme has been offered until recently in Cyprus. Since 2008 MEETinCY research programme is the first one in Cyprus and it is also a nurse-led management programme for HF patients in Cyprus.

Purpose: To determine the effect of a structured educational intervention and / or telephone follow-up programme for patients with HF.

Methods: The present study is a randomized control trial with various interventions and longitudinal monitoring. As a part of the larger MEETinCY research project, sampling was extracted from the parent sample, which was conducted between April 2014 and June 2014, using the electronic medical records of patients of five government hospitals. Total acute events of HF decompensation including their clinical and demographic characteristics were recorded in 12 and 24 weeks post discharge. Additional information to support the existence or not of decompensation, if needed, was provided by patients and their relatives, through telephone calls. Events were classified as decompensation of pre-existing HF, or decompensation from other causes.

Results: A number of 195 Cypriot HF patients, who received educational intervention and / or telephone follow up calls, were recruited. A reduction of instant risk of HF decompensation at 3 months in 51% [HR: 0,49 (95CI: 0,27-0,88) ($p=0,001$), was found in the group of telephone follow up, compared to control group. There was no difference between groups regarding the occurrence of death [Control n=1 (1,8%) vs Intervention n=2 (2,2%) $p=1$], the total visits to emergency department ($p=0,52$), the total readmissions ($p=0,52$), and the cumulative events (visits & readmissions) ($p=0,79$). No statistically significant difference was found in the mean hospital length of stay [Control $6,17 \pm 8,2$ vs Intervention $6,54 \pm 9,5$ ($p=0,874$)]. Unfortunately, the promising results of the beneficial effect of the intervention in disease-free survival time for the first 3 months after randomization and perspective monitoring, does not appear to be maintained for long.

Conclusions: The present study results showed that advanced nurses in HF who apply structured educational programmes combined with telephone follow up, can enhance the outcome of patients with HF.

P1815

Positive effects of scale in the elderly

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Abstract: The favorable effects of exercise have been widely demonstrated in the patient population over 65. Scopo study: was to evaluate exercise tolerance of a population of elderly people over 65 subject to the need for training induced by the use daily of the scales with respect to a control group who regularly uses the elevator.

Methods: 50 patients aged between 65 and 80 years, 30 males and 20 women, all with a fair degree of functional autonomy, divided into two groups, one with a key requirement: to live in a building at least a third floor in no lift at least 20 years, a condition which required a continuous and progressive exercise lasted over the years (the enrolled subjects reported that they face the stairways on average four times a day, and sometimes burdened with weights vary in size from a few hundred grams to several kg). L'altro group, which normally uses the ascensore. Risultati: from the data obtained, and from our observation shows that the population of elderly people to reach their homes only uses the stairs and on an ongoing basis at least until to a third floor, presents: a better level of training, better chronotropic response to stress and reduced breathlessness during exercise, and then globally presents a better exercise tolerance. The evaluation was performed by use of the 6-minute walking test, the self-assessment scale of VAS for breathlessness, the MRC scale, on the scale of the symptoms reported, on the values of oxygen saturation and frequency cardiaca. Il group that submit daily use ladders tra l'altro presents a better profile carbohydrate, lipid and better pressure profile.

Conclusions: The elderly individuals over 65 who are subjected to daily training of the stairs for lack of elevator and have a better degree of functional autonomy, to exercise tolerance, improved glucose profile / lipemic and better control of the PA, with a lower consumption of drugs. The significant difference in the results between the two groups does not appear to be due solely to physical exercise but also to a different lifestyle that shows in the group without elevator healthier eating habits, a lower propensity to cigarette smoking and increased physical activity and calorie consumption obtained using the most simple as walking, grocery shopping without a car, climbing stairs etc.

ARRHYTHMIAS AND TREATMENT

P1816

Combinations of heart rhythm disorders

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Objective: To analyze and compare the incidence of multiple cardiac arrhythmias (MCA).

Material and Methods: From November 2011 to October 2014 for 1709 patients were undergone interventions. There were 974 (57%) male and 735 (43%) female, respectively. The age of patients ranged from 13 to 80 years (mean age 54 ± 2,08). In most cases, there was a combination of atrial fibrillation (AF) with sick sinus syndrome (SSS). The rest cases (35 patients, 21.7%) had combination of various cardiac arrhythmias and conduction abnormalities. The most frequent combination among other MCA as below: atrial flutter (AFI) in combination with other arrhythmias (23 cases), also with icisional atrial tachycardia (IAT). Frequency characteristic combination of cardiac arrhythmias is given in Table 1 below.

Result: MCA in most cases (51%) was identified in outpatients and in 28% of MCA were diagnosed preoperatively. During the electrophysiological study MCA diagnosed in 21%. In postoperative period in 5 patients the clinical manifestations of other MCA occurred which led to reoperation. In one case there was a complication like complete AV block. Afterwards, all patients were discharged in satisfactory condition on 4-5 days after surgery. All discharged patients after 3, 6 and 12 months were examined with Holter monitoring. During this period, the patients did not complain of sudden attacks of palpitation and according Holter monitoring MCA have not been identified.

Conclusions: Every 10th patient had a combination of arrhythmias. The most frequent combination is combined AF and SSS (126 cases out of 161). In 35's cases mentioned combination of other arrhythmias with different frequency. When multiple arrhythmias are diagnosed it is necessary to determine the tactics of surgical intervention. When proper treatment is selected, in some cases, the patient does not require reoperation.

Combination	number	Combination	number	Combination	number
AFI+IAT	6	AFI+ AV block	2	AVNRT+AP	2
AFI+ atypical AFI	6	AVNRT+ VPB	1	Atrial tachy.+AFI	1
Atypical AFI + IAT	1	AFI+ VPB	1	AVNRT+AFI	6
AP+ SSS	1	Multiple AP	3	VPB+ AV block	1
AFI+SA arrest	1	AVNRT+AV block	2	AFI+SSS	1

P1817

Ablation of ventricular arrhythmias without fluoroscopy

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Introduction: During the last 20 years electrophysiological interventional procedures performed primarily with the use of fluoroscopy. Today, the reduction of fluoroscopy during the catheter ablation procedures is one of the main issues. It is important to understand that the fluoroscopy reduction and the use of navigation system can eliminate the affect of radiation on patients and medical staff.

Objective: To present 13 clinical cases of radiofrequency ablation of ventricular arrhythmias without the use of fluoroscopy.

Material and Methods: From December 2011 to October 2014 were performed 638 interventional procedures on arrhythmias using navigation system CARTO 3. In 162 (25.4%) of them RFA were done on ventricular arrhythmias (VA). Since February 2014 we started RFA on VA without the use of fluoroscopy. Currently there were done 13 (7.97%) catheter ablation procedures without the use of fluoroscopy: 8 patients with ventricular premature beats (VPBs), and 2 patients with ventricular tachycardia (VT) from right ventricle outflow tract (RVOT); 3 patients with VPBs of right ventricle supply tract (RVST). Age ranged from 10 to 62 years. The average age 31 ± 17. 5 men, 8 women, respectively, including three children. Co-morbidity in all cases were not reported. In one case, RFA without fluoroscopy were done on patient with 26-28 weeks of pregnancy. All manipulations controlled by intracardiac echocardiography visualization. Next step was building of right ventricle activation map. According to the results of the activation mapping the earliest areas identified in RVOT (75%), RVST (25%), then successful RFAs were done. The mean time of procedure with usage of fluoroscopy 1,6 ± 0,9 hours, and without usage of fluoroscopy was 1,6 ± 0,7 hours. The average x-ray exposure of 271,264 ± 15,13 mSv.

Results: effective RFA without fluoroscopy in 11 patients with monomorphic VPBs and 2 patients with VT, including a patient with 26-28 weeks of pregnancy. Intraoperative complications were not observed. All patients were discharged 2 days after operation.

Conclusions: Thus, the presented clinical cases demonstrate the possibility of radiofrequency ablation without the use of fluoroscopy. The duration of RFA with fluoroscopy control and without fluoroscopy control is close. However, during RFA without fluoroscopy patients and operating team does not get X-ray exposure. Therefore, awareness of electrophysiologists of 3D mapping and extensive use of intracardiac echocardiography can eliminate the need of fluoroscopy and thus avoid radiation exposure to the patient and medical staff.

P1818

Impact of electrical cardioversion for atrial fibrillation on erythrocytes

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Electrical cardioversion is widely used and effective method to restore sinus rhythm in patients with persistent atrial fibrillation. The impact of electric shock on erythrocytes has not been studied.

The aim of the study was to assess the influence of electric cardioversion on red blood cells.

Twenty five men with lone atrial fibrillation have been included to the study. Patients with persistent atrial fibrillation were treated with oral anticoagulants for 4 weeks before cardioversion. The cardioversion was performed using 50-200J biphasic energy.

Peripheral blood was collected in 3 time points: T0 -during atrial fibrillation and T1 -30 minutes after successful electric cardioversion. Red blood cell system parameters: hemoglobin, hematocrite levels, MCV, MHC, MCHC and RDW were assessed. The level of free hemoglobin before and after cardioversion were also measured (T0 and T1). After 6 hours (T2) parameters of erythrocyte lysis like total and indirect bilirubin level were assessed.

Results: The mean energy used for cardioversion was 170J (+/- 126J). The decrease of erythrocyte count (4,89+/-0,07 vs 4,57+/-0,07; p < 0,0001), decrease of hemoglobin concentration (14,96+/-0,69 to 14,01+/-0,29 g/dL; p < 0,0001),

and decrease of hematocrite (44,09+/-0,69 vs 41,11+/-0,64%; $p < 0,0001$) was observed. Immediately after cardioversion significant increased of free hemoglobin level were observed (15,33+/-2,2 vs 23,3+/-4,02; $p < 0,05$). After 6 hours the increase of indirect bilirubin level from 2,77+/-0,25 to 3,22+/-0,25 $\mu\text{mol/L}$; $p < 0,01$ was also observed.

Conclusion: Electric cardioversion lead to red cell desintegration which could have impact on clinical state of patients.

P1819

Prevention of sudden cardiac death caused by commotio cordis - rugby wiew

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Commotio cordis is a rare mechano-electric arrhythmogenic event, occurring mainly during sports activities, where precordial nonpenetrating blow triggers ventricular fibrillation and could be cause of sudden cardiac death (SCD). However, some authors suggest that this entity may be associated with coronary vasospasm, segmental changes in myocardial contractility or high degree atrioventricular block. This events have been predominantly reported among young male baseball/softball and football players in United States (US) and soccer, cricket and hockey players internationally. Unexpectedly higher frequency among soccer players than expected, seems to contradict the prevailing notion that air-filled projectiles convey less risk than do those with solid cores (e.g., baseball or lacrosse balls).

Data about incidence of commotio cordis as a cause of SCD in athletes varies between 2.9% and 19.9%. US Commotio Cordis Registry reported increasing of aborted SCD rates due to commotio cordis during time, especially among white and competitive athletes. The most important for that improved survival rates (up to 25-30%) are automatic external defibrillator provision during high-risk sports events. Development of chest protectors, safety balls (e.g., baseball) and safer athletic environment in general are important to avoid or reduce this catastrophic injuries. Also, introduction of safe sports regulations and teaching of athletes proper techniques prevent commotio cordis. In comparison with other mentioned sports, this entity is relatively rare in rugby. Authors, explain how sports regulatins can prevent commotio cordis in one rough contact sport.

In comparision with other mentioned sports, commotio cordis is relatively rare in rugby. Authors, using their experience as sports doctors, explain how sports regulations can prevent this entity even in one rough contact sport.

P1820

What about magnesium sulfate in atrial fibrillation with acute heart failure?

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We examine the efficacy of magnesium sulfate infusion, in addition to usual medication, for acute rate reduction in patients with atrial fibrillation and a rapid ventricular response rate, in acute heart failure.

Methods: This was a prospective, placebo-controlled study of intravenous magnesium sulfate in adult patients admitted at the cardiology department with rapid atrial fibrillation responsible of heart failure, or associated with it, magnesium sulfate was given in addition to any therapy that would normally consider appropriate. Patients received either 1.5g of magnesium sulfate over a 30-minute period, followed by 1.5 g over a 2-hour period intravenously, or placebo.

Results: Thirty patients were randomized, 14 to receive magnesium sulfate and 16 to receive placebo. The antiarrhythmic drug most commonly used by treating was digoxin. Magnesium sulfate was more likely than placebo to achieve a pulse rate of less than 100 beats/min (9 [64.28%] of 14 versus 5 [31.25%] of 16, relative risk [RR] 1.79; 95% confidence interval [CI] ; $P < .0001$) and more likely to convert to sinus rhythm (4 [28.57%] of 14 patients versus 2 [12.5%] of 16 patients).

Conclusion: Magnesium sulfate, when used to supplement other standard rate-reduction therapies, enhances rate reduction and conversion to sinus rhythm in patients with rapid atrial fibrillation in acute heart failure

P1821

Takotsubo cardiomyopathy and long QT interval: risk of torsades de pointes

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Prolongation of the QT interval is prevalent among patients with Tako tsubo cardiomyopathy, while torsades de pointes have rarely been reported in these patients.

Objectives: Studying the QT interval in patients with tako tsubo and followed the patient with long QT.

Methods: We have made holters ECG in patients with Tako tsubo syndrome and calculates the corrected QT interval, followed a patient with long QT in search of complication type of rhythm disorder or torsade de pointe. We analyzed risk factors of torsade de pointe in our patients.

Results: The prevalence of long-corrected QT interval was higher among females (25.8% for women vs 4.9% in men). The peak twist occurred in Tako tsubo patients with long QT measured at a predominantly male. Comparing the two patient groups with tako tsubo and long QT with or without torsade de pointes: we don't found a difference in the age, rate of maximum troponin, and ejection fraction.

In total we have 11 patients with torsade de pointes episode, tako tsubo and associated with long QT, torsades had risk factors such as bradycardia, hypokalemia, the recent conversion of atrial fibrillation to sinus rhythm and responsible treatment of QT prolongation.

Conclusion: Men with Tako tsubo associated and long QT interval are at risk for torsades de pointes.

Most patients with torsades de pointes associated with Tako tsubo have risk factors for Torsade de pointes other than systolic dysfunction.

P1822

Study on ventricular arrhythmias in acute myocardial infarction

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Background: Ventricular arrhythmias occur in about 25% of acute myocardial infarctions and are associated with increased in-hospital mortality. The risk of arrhythmic death in survivors of acute myocardial infarction is highest in the first six months after myocardial infarction and remains high for the subsequent two years.

Aim: The aim of this study is to identify predictors of ventricular arrhythmias after acute myocardial infarction.

Methods: Retrospective study of all patients who underwent fibrinolysis for acute myocardial infarction in a National Institute of Cardiovascular Diseases between January 2011- December 2014.

Results: Of the 14600 patients who were treated with fibrinolysis for acute Myocardial infarction, 680 (4.66%) developed sustained ventricular tachycardia (VT) or ventricular fibrillation (VF) before fibrinolysis.

After multivariable adjustment, independent predictors of sustained VT/VF included cardiogenic shock ($P < 0.001$), heart failure ($P < 0.001$), chronic kidney disease ($P = .008$), and presentation within 6 hours of symptom onset ($P = .002$). Patients with sustained VT/VF had greater in-hospital mortality (24% vs 4.66%, $P < .001$). Although successful fibrinolysis was associated with decreased in-hospital mortality in patients with VT/VF

($P < .001$), patients with sustained VT/VF and successful fibrinolysis experienced increased mortality compared with patients without sustained ventricular arrhythmias ($P < .001$).

Conclusion: The arrhythmia commonly appeared initially over the first four days and was preceded by ventricular ectopic beats in 95 percent. Among patients undergoing fibrinolysis for acute Myocardial infarction, sustained VT/VF remains a significant complication associated with an increased risk of in-hospital mortality.

P1823

Patients with compensated relevant heart insufficiency receiving subcutaneous ICD-therapy may be saved from harmful inadequate shock therapies through anatomical selection of implantation site

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Background: Subcutaneous ICD (S-ICD)-implantation in patients in whom out clinical reasons the deployment of a conventional intracardiac lead system is impossible may be vitally threatened by inadequate ICD-shock therapies potentially resulting in left heart failure. However implantation of a S-ICD-can and subcutaneous lead with a wide field of detection may typically lead to inappropriate myopotential detection and S-ICD-therapy. Myopotentials are mediated by proprioceptive sensory nerve receptors (SNR).

Purpose: We searched for number, location and structure of SNR in the adjacent thoracic tissue of the anterior serratus muscle (ASM) in order to identify optimal implantation sites allowing for improvement of postoperative results and to reduce inadequate ICD-therapies.

Methods: Topography and ultrastructure of SNR in the anterior serratus muscle were analyzed in 12 models of adult female NMRI-mice. Three SNR-types were identified using light and electron microscopy: Muscle Spindles (MSP), Lamellated Pacini Corpuscles (PC) and Golgi Tendon Organs (GTO). Their location within the skeletal muscle was determined by 3D- image processing of 3 complete thorax section series.

Results: Within the relevant structure of the anterior serratus muscle (ASM) a total amount of $n=27 \pm 5$ MSP were found per thorax. The vast majority of SNR of the MSP-type were identified either within the area of tendinous origin ($n=11 \pm 4$) or the fibromuscular tissue of muscle insertion ($n=13 \pm 4$) respectively, in all samples only a very small number of MSP were located within the central portions of the ASM ($n=3 \pm 1$). GTO ($n=3 \pm 1$) and rare PC were exclusively found within the fibrous tissue of the tendinous muscle insertions

Conclusion: To avoid SNR irritation near the tendinous zones of origin and insertion of the ASM that are richly supplied with a large number of MSP as well as GTO and PC, special attention should be paid to the implantation of the S-ICD-can within the anterolateral central muscle region close to the landmark of the anterior axillary line. Thus, the risk of secondary heart failure induced by sequential inadequate S-ICD shock therapies resulting from myopotential detection may be reduced in patients with compensated but relevant heart insufficiency by selecting a neuroanatomically guided implantation site.

P1824

Prevalence of first degree heart block and predictors of PR interval duration in heart failure

NIHR

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Background: First degree heart block is an adverse prognostic marker in patients with heart failure (HF), coronary artery disease, sinus node dysfunction, and in the general population. First degree heart block can lead to mitral regurgitation, atrial fibrillation (AF) and higher degrees of block requiring pacemaker implantation. We set to investigate the relationship between HF and PR interval duration.

Methods: We retrospectively analysed patients with HF due to systolic dysfunction [left ventricular ejection fraction (LVEF) <50%] attending a single centre between 1999 and 2014. Of the 2333 patients with HF, 200 (8.6%) were excluded because they had a pacemaker, 553 (23.7%) for AF and 110 (4.7%) because the PR interval was not available. PR interval was adjusted for heart rate (PRc) using a previously validated formula.

Results: 1470 HF patients [LVEF: 32% (26-37); NT-ProBNP: 1294 ng/L (555-3297)] and 1159 non-HF patients [LVEF: 59% (54-64), NT-ProBNP: 86 ng/L (46-140)] were analysed. Compared to those without HF, more HF patients were male (71% vs. 51%, $P < 0.001$), had worse renal function [estimated glomerular filtration rate: 62 vs. 75 ml/min/1.73m², $P < 0.001$] and longer PRc [174 ms (157-196) vs. 163 ms (147-179), $P < 0.001$]. HF patients were more often on a β -blocker, ACE-inhibitor, amiodarone, digoxin or loop diuretic. 318 (21%) of HF patients had first degree heart block (PRc>200ms) vs. 110 (9%) of non-HF patients, $P < 0.001$.

Compared with the lowest PRc tertile, patients with HF in the highest PRc tertile were older, more often male, more likely to have diabetes, had a higher body surface area (BSA), worse renal function and longer QRS ($P < 0.001$ for each). They were more likely to be taking amiodarone or a loop diuretic.

Male sex, increasing QRS duration, age, and BSA, and the presence of diabetes were independent predictors of longer PRc, both in the HF and non-HF groups. In HF patients, NYHA class was positively correlated with longer PRc [166 ms (149-185) for class I vs. 179 ms (157-209) for class IV, $P = 0.017$]. There was no difference in PRc for patients with HF taking β -blockers or not [175 (158-197) vs. 173 (156-194), $P = 0.49$], whilst PRc was longer in HF patients taking digoxin, amiodarone or loop diuretic.

Conclusions: Compared to patients without HF, HF patients have longer PRc and higher prevalence of first degree heart block. Longer QRS, increasing age, male sex, higher BSA and the presence of diabetes are predictors of longer PRc in both groups. NYHA is an independent predictor of longer PRc in the HF group. β -blockers do not significantly affect PR interval duration in HF.

CARDIOMYOPATHY

P1825

Hypertrophic cardiomyopathy: a tunisian experience

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Background: Hypertrophic cardiomyopathy (HCM) is a heterogenous monogenic heart disease studied for more than 50 years and recognized to be an important cause of arrhythmic sudden death, heart failure and atrial fibrillation with embolic stroke.

Our objective is to study the characteristics of this pathology in a Tunisian population.

Methods: We hereby report a retrospective study about 48 Tunisian patients with HCM followed between 1997 and 2013.

Results: The mean age of the patients at diagnosis was 37 ± 16 years and 50% were under 35 years. Patients diagnosed after medical routine examination of familial screening were 19%. Most patients were male (65%); in their third to fifth decade of life, and in New York Heart Association class I or II (70%). The initial tests showed a mean parietal thickness of 23 ± 8 mm and a left ventricular obstruction of 23% of the cases. The prevalence of delayed enhancement was 79%. Eighteen patients (37.5%) had an implantable cardioverter defibrillator. The percentage of appropriate shocks was 39% (11.7% per year) and of inappropriate shocks was 16.6% (5% per year). During a 5-years average follow up, 6 patients had an atrial fibrillation (12.5%), 1 had a stroke (2.1%) and 3 developed heart failure (6.3%). HCM-related death occurred in 3 patients exclusively due to sudden death (6.3%). The mortality rate caused by sudden death was 1.27% per year.

Conclusion: Our study represents one of the first comprehensive attempts to evaluate the clinical impact and management of HCM at a national level.

P1826

Transforming growth factor-beta can predict cardiac adverse events in hypertrophic cardiomyopathy

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Background: Hypertrophic cardiomyopathy (HCMP) is a common genetic heart disease. Transforming growth factor-beta (TGF- β) be a key mechanism in cardiac remodeling in HCMP.

Aim: To investigate the association between TGF- β and clinical outcomes in HCMP.

Method: We compared TGF- β levels of 49 HCMP patients with those of non-HCMP control group. We followed the patients with HCMP for 18 months and divided into two groups as low TGF- β (or <4877 pg/mL) and high TGF- β (>4877 pg/mL). We compared two groups in terms of brain natriuretic peptide (BNP), echocardiographic parameters and clinical outcomes including arrhythmias, intra-cardiac defibrillator (ICD) implantation, hospitalization, New York Heart Association (NYHA) class, acute heart failure and cardiac mortality.

Results: HCMP patients had higher TGF- β levels than control group ($p = 0.005$). In follow-up, high TGF- β group had higher BNP levels, larger left atrial size, thicker interventricular septum, higher NYHA class, more hospitalization and more clinical adverse events including life-threatening ventricular arrhythmias, ICD implantation, acute heart failure and cardiac mortality ($p < 0.001$, $p = 0.01$, $p < 0.001$, $p = 0.002$, $p < 0.001$ and $p = 0.003$, respectively). In receiver operating characteristic analysis, TGF- β >4877 pg/mL can predict adverse events with a specificity of 75% and a sensitivity of 72% ($p = 0.014$). In multivariate regression analysis, TGF- β and BNP were significantly associated with adverse events ($p = 0.032$ and $p = 0.041$, respectively).

Table 1

High TGF- β	Low TGF- β	P	
ICD implantation, n (%)	5 (26)	3 (10)	0.2
NYHA class >1, n (%)	15 (78)	12 (40)	0.003
Acute heart failure, n (%)	5 (26)	4 (13)	0.2
Hospitalization, n (%)	14 (73)	12 (40)	<0.001
Adverse events, n (%)	10 (52)	4 (13)	0.003
Mortality, n (%)	4 (21)	2 (6)	0.1

Table 1. Comparison of HCMP patients with high and low TGF- β

P1827

Influence of genetic study on the risk of sudden death in patients with hypertrophic cardiomyopathy

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Introduction and Objectives: Hypertrophic cardiomyopathy (HCM) is one of the main causes of sudden death in young people. Recent clinical practice guidelines include a risk prediction model for sudden death (HCM Risk-SCD), which facilitates the decision of whether to implant a defibrillator. The aim of our study was to determine the mutations and their relation to the risk scale.

Methods: This is an observational, retrospective cohort study, which includes 83 patients with HCM and genetic testing. Demographic and clinical characteristics were compiled as well as estimated 5-year risk using HCM Risk-SCD and the mutations in the genes encoding sarcomere proteins (a hypertrophic cardiomyopathy panel using "next generation sequencing").

Results: The majority were male (61.4%) and mean age was 49.92 ± 14.43 years. Twenty patients were suffering paroxysmal/permanent atrial fibrillation. The average HCM Risk-SCD was $3.6 \pm 2.85\%$. Sixty-seven (80.72%) of these patients tested positive, and the most frequently affected genes were MYBPC3 (32 patients, 38.61%) and MYH7 (23p, 27.7%). There were no differences in the impact of either sarcomeric protein. Patients with negative genetic study had a lower risk than those with mutations (1.32% vs. 3.05%), but this difference was not statistically significant ($p = 0.09$).

Conclusions: We conclude that the genetic condition of one or other sarcomere protein does not mark prognosis, although in the case of certain high-risk mutations, sudden death risk and treatment need to be individualised.

P1828

Effectiveness of angiotensin-converting enzyme inhibitors perindopril in patients with hypertrophic cardiomyopathy and persistent atrial fibrillation

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Atrial fibrillation (AF) is the most common arrhythmia in patients with hypertrophic cardiomyopathy (HCM) and one of the causes of heart failure (HF) development. There are few data about effectiveness of angiotensin-converting enzyme (ACE) inhibitors in such patients.

Purpose: to assess the effect of ACE inhibitor perindopril in patients with nonobstructive HCM and persistent AF.

Methods: we examined 20 patients with nonobstructive HCM (16 women (80%), average age 57.0 ± 16.5 years, treated with bisoprolol (5.5 ± 1.8 mg). Patients were divided into 2 groups: group I - 5 patients with persistent AF and group II - 15 patients with sinus rhythm. All patients underwent clinical examination, echocardiography with tissue doppler imaging (TDI) and evaluation of the level of brain natriuretic peptide (BNP). After initial examination perindopril (2.8 ± 1.8 mg) was added to the treatment of both groups with repeated examination after 6 months of combined therapy.

Results: There were no significant differences in gender, age, bisoprolol dose between two groups. Patients of group I had higher BNP, higher FC of chronic HF by NYHA, higher of left atrial (LA) size index, lower lateral systolic mitral annulus (MA) s', lower septal systolic MA s', lower posterior systolic MA s', lower anterior systolic MA s', lower lateral tricuspid annulus (TA) s'. After 6 months of combined therapy with perindopril in both groups lateral systolic MA s' (group I - 7.4 ± 0.5 and 8.3 ± 1.0 cm/s, $p = 0.04$; group II - 8.9 ± 1.5 and 10.2 ± 1.6 cm/s, $p = 0.0007$), septal systolic MA s' (group I - 8.0 ± 0.5 and 8.8 ± 1.6 cm/s, $p = 0.04$; group II - 9.4 ± 1.0 and 9.9 ± 1.4 cm/s, $p = 0.046$), lateral TA s' (group I - 12.1 ± 3.2 and 13.3 ± 1.8 cm/s, $p = 0.047$; group II - 14.0 ± 1.9 and 14.8 ± 2.3 cm/c, $p = 0.046$) increased significantly. After 6 months in group I BNP level (from 274.2 ± 136.2 to 157.1 ± 148.9 pg/ml, $p = 0.02$) and FC of chronic HF by NYHA (from 2.0 ± 1.0 to 1.4 ± 0.5 , $p = 0.005$) decreased. After 6 months in group II the same parameters slightly decreased ($p = 0.06$).

Conclusion: therapy with perindopril in patients with hypertrophic cardiomyopathy accompanied by improvement of longitudinal LV systolic function. In patients with persistent AF therapy with perindopril resulted in a decrease of BNP level and FC of chronic HF by NYHA.

P1829

Efficacy of treatment of hypertrophic cardiomyopathy and ability to control of plasma redox-potential

granted by Biotechpharm GE, Ltd and International Centre of Introduction of New Biomedical Technology, Georgia

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Purpose: Hypertrophic cardiomyopathy (HCM) is a common inherited disorder of heart muscle affecting 1 in 500 individuals worldwide. Formation of metabolic vicious circle plays a pivotal role in the progression of cardiac hypertrophy despite an optimal therapy used. Recently it has been shown that exogenous addition of nicotinamide adenine dinucleotide (NAD) was capable of maintaining intracellular levels of NAD and blocking the agonist-induced cardiac hypertrophic response in vitro as well as in vivo. Therefore, we hypothesize that eliminated of this vicious circle and improvement in redox-potential by cardioprotective, NAD-containing drug, Adenocin, with cardiotoxic and antiischemic properties, may lead to additional clinical

benefit in patients with cardiac hypertrophy caused by chronic form of ischemic heart disease (IHD) and accompanied with left ventricle dysfunction.

Methods: 245 patients, mean age was 57 ± 16 years (65% male), caused by IHD and left ventricular ejection fraction ≤ 0.35 were enrolled in the study. All patients were randomized to receive conventional therapy ($n = 123$) or conventional therapy and Adenocin ($n = 122$) in a dose of 181 mg i/v daily during 14 days. Plasma levels of Pro-Brain Natriuretic Peptide (proBNP) by ELISA kit and redox-potential NAD/NADH by Fluoro NADTM: Fluorescent NAD/NADH Detection Kit - Detection of NAD/NADH in tissue extracts/cell samples (Cell Technology, Inc) were determinate.

Results: Adenocin therapy resulted in a significant reduction in heart rate and mean pulmonary artery pressures and a significant increase in stroke volume and left ventricular stroke work. Left ventricular ejection fraction increased 92% in the Adenocin group (from 0.28 to 0.44, $p < 0.0001$ vs. 0.30 to 0.34 in control group). Adenocin-treated patients also reported a significant lessening of heart failure symptoms ($p < 0.05$ vs. control group). The content of ATP in plasma and erythrocytes, ratio of NAD/NADH in plasma, as the important mediators of energy supply system, were significantly improved after treatment with Adenocin. The direct correlation was found between functional class of CHF and NAD/NADH ($r = 0.87$, $p < 0.001$), and negative correlation between the content of pro BNP and redox potential NAD/NADH, $r = -0.71$, $p < 0.001$) have been observed.

Conclusion: Short-term Adenocin therapy improves left systolic function and lessens symptoms of congestive heart failure which is associated with the increasing of plasma redox-potential unlike action of conventional therapy.

P1830

The efficacy of 6- months therapy with carvedilol on cardiac function and inflammatory markers at peripartum cardiomyopathy patients

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The **Aim:** To evaluate the clinical and hemodynamic efficacy of carvedilol, and its impact on inflammatory markers in patients with peripartum cardiomyopathy (PDC).

Methods: The study included 23 patients with PDC, aged 20 to 37 (28.8 ± 1.1) years, with disease duration from 1 to 9 (5.1 ± 0.7) months. All patients underwent ECG, EhoCG, 6-minute walk test (6WT), C-reactive protein in the blood serum before and after therapy.

Results: in the time of study entry, all patients were stabilized against BT, which allowed applying the carvedilol with a starting dose of 3.12 mg 2 times a day with a standard titration step. The application within six months enhanced the LVEF on 24.7% (from 41.6 ± 2.1 to $51.9 \pm 1.9\%$) with a significant decrease in the ESD on 12.4% (c 50.1 ± 0.1 mm to 43.9 ± 0.14 mm, $p < 0.01$) and the EDD on 5.8% (c 64 ± 0.1 to 60.3 ± 0.13 mm; $p < 0.01$), with marked improvement of NYHA class on 50% (from 3.2 ± 0.12 to 1.6 ± 0.1 ; $p = 0.001$), an increase of physical capacity by 6WT on 86% (from 223.2 ± 15.1 to 417 ± 14.9 m; $p = 0.001$). It should be noted that at 13 (56.5%) patients on therapy completely normalized linear dimensions and left ventricular ejection fraction. SBP and DBP were not changed respectively. Decrease of heart rate was 27.5% (from 97.5 ± 3.1 to 70.7 ± 2.2 beats / min; $p < 0.01$). CRP levels in the blood serum during therapy significantly decreased on 56.1% (from 8.2 ± 1.3 to 3.6 ± 0.7 mg / l; $p < 0.01$).

Conclusions: Application of carvedilol at patients with PDC for 6 months in combination with BT improves heart failure signs, significantly increase left ventricular ejection fraction and decrease the concentration of CRP in the serum blood.

P1831

Determinants of Troponin T concentration in chronic stable patients with non ischemic dilated cardiomyopathy

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Background: Cardiac troponin T is a marker of myocardial injury. What are The echocardiographic and clinical predictors of troponin T concentration in non-ischemic dilated cardiomyopathy (DCM).

Methods: Forty patients with stable congestive heart failure (with non ischemic DCM), with New York Heart Association functional class I-II symptoms, and left ventricular ejection fraction $< 40\%$ were included.

Results: The average age of patients was 60 years ± 10 . The sexe ratio was 4/1. Sixty percent of patients were smokers. Half of the population had hypertension. Only thirty percent of them had diabete mellitus which was insulinino-dependant in the majority of cases. The average of ejection fraction of left ventricle (SIMPSON BP) was $35.7\% \pm 9$.

In patients with non ischemic DCM; left atrial volume, male sex, peak systolic mitral annular tissue Doppler velocity (Sm) lateral, peak early mitral inflow velocity (E), E/peak early diastolic mitral annular tissue Doppler velocity (Em) lateral, and global longitudinal strain of the left ventricle (LV-GLS) were included in multivariate model

and LV-GLS was detected to be an independent predictor for troponin T above median ($p=0.02$).

Conclusion: LV-GLS is an independent predictor of troponin T concentrations in patients with non ischemic DCM.

P1832

Increasing incidence of cardiomyopathy among women between the last trimester and the first 6 months post delivery

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Purpose: To determine the pattern of admissions of dilated cardiomyopathy over a 3year period.

Method:- A retrospective study involving 35 patients from January 2011 to January 2014 were examined based on their ages, parity, blood pressures on presentation, Antenatal clinic attendance, place of delivery, ingestion of potash concoction, heating of bed and bathing with hot water, period of occurrence of symptoms, echocardiography and electrocardiography results, co-morbidity, duration of hospital stay, knowledge of family planning, regularity for clinic appointments, compliance with medication and outcome of patient.

Results:-

17 patients \leq 25yrs were pregnant for the first time.

18 patients between the ages of 26 - 40 years had been pregnant before.

5 patients had an un-recordable blood pressure on admission. The other 30 patients had an average of 72mmhg as diastolic blood pressure.

28 patients did not attend antenatal clinic.

30 patients delivered at home.

28 patients ingested potash concoction.

5 patients participated in the heating of the bed.

27 patients engaged in hot water bath.

7 patients developed symptoms in the last trimester of pregnancy, 20 patients developed symptoms within the first 3months of delivery, 8 patients developed symptoms between 3 - 6months after delivery.

14 patients who did echocardiography showed features of contractile dysfunction, dilated left ventricle and impaired left ventricular ejection fraction. The other patients were only able to afford an electrocardiography that showed atrial and / or ventricular hypertrophy typically left sided changes.

7 patients had co-morbidity.

13 patients were admitted and discharged within one week while others were above one week.

None had any knowledge of family planning.

Only one patient was regular for clinic appointments.

20 patients were compliant with medication.

26 patients were successfully managed and discharged.

2 patients were referred to a specialist hospital for further management.

2 patients signed against medical advice.

1 patient absconded.

3 patients were re- admitted for symptoms.

1 patient died.

Conclusion:- Dilated cardiomyopathy is a condition that can be curtailed by discouraging harmful cultural practises, educating women on the importance of antenatal care, opening of more family planning clinics and encouraging patients to come for regular follow up. This can be achieved by publicity through social media and creating awareness in religious houses.

Conflict of interest: Research was initiated by me. I appreciate my colleagues for their advisory roles.

P1833

Meta-analysis on immunoadsorption in dilated cardiomyopathy patients

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Introduction: Cellular and humoral anticardiac immunity are involved in the pathogenesis of DCM. Several anticardiac autoantibodies have been elucidated in DCM patients. Immunoadsorption (IA) may be a promising immunomodulatory regimen in DCM, aiming at elimination of anticardiac autoantibodies.

Methods: Using multiple Pubmed search modes, $n=100$ publications referring to IA in DCM patients were retrieved. Out of these, $n=18$ publications prospective investigations with >8 DCM patients met the inclusion criteria and were analyzed in this systematic evaluation.

Results: The demographic and clinical data of the $n=528$ patients of the 18 included publications were at baseline before IA as follows: age: 51.5 ± 3.1 ; men: $n=431$ (81.6%); history of DCM: 51.4 ± 20.8 months; LVEF: $25.6\pm 4.6\%$; 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. 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 $32.0\pm 6.3\%$ ($p=0.0015$), 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 substantial relative reduction of the 5-year mortality by 41% was reported in one prospective trial in IA treated DCM-patients compared to controls. In one study, IA was accompanied by a significant decrement of immunohistologically quantified intramyocardial infiltrates and HLA expression in DCM patients. In a further study, a significant decrease of indices of oxidative stress was determined in DCM patients.

Conclusions: This meta-analysis on $n=528$ DCM patients under IA summarizes several beneficial effects of immunoadsorption for dilated cardiomyopathy: 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 are certainly prone to known 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".

P1834

Clinical phenotype of dilated cardiomyopathy with lamina gene anomalies

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The objective of this study was to assess genotype-phenotype correlations in patient with dilated cardiomyopathy (DCM) accompanied by conduction disorders and lamina gene anomalies.

Methods: We examined 62 patients with DCM who had the primary manifestation of conduction disturbances (aged 43 ± 12 ; 80,7% male, NYHA $2,9\pm 0,3$; LVEF $25,8\pm 8,2\%$). DNA mutations were detected using single stranded conformational polymorphism method and direct sequencing of the amplified LMNA exons Genetic testing, age, gender, NYHA, 6-MWT, serum BNP and CPK levels, echocardiographic (biventricular: global strains, dimensions, EF) and Holter electrocardiographic data including QTc dispersion, heart rate turbulence (HRT), microvolt T-wave alternans (mTWA) were analyzed.

Results: We detected two lamina gene mutations (novel - c.569G>C 3rd exon and N rs57629361 - already known). Twenty-one (33,9%) patients showed carriage of one or two T-alleles of polymorphic locus rs4641 (C>T) located in exon 10. According to NCBI, this polymorphism does not alter the primary sequence of the protein lamin as it determines synonymous codon for histidine at position 566. A positive correlation was revealed between the polymorphism rs4641 (C>T) and sustained ventricular tachycardia (Spearman $k=0,55$; $p<0,01$), with mTWA ($k=0,64$; $p<0,001$), HRT0 ($k=0,53$; $p=0,01$), CPK levels ($k=0,66$; $p<0,001$) and left ventricular global strain mean (LVGSm) - $k=0,65$; $p=0,001$. By ROC analysis were detected phenotypic predictors of polymorphism LMNA rs4641 C>T: mTWA point cut off 51 mcV ($S=0,77$; 95% CI 0,53-0,99), LVGSm threshold point -5,1% ($S=0,73$; 95% CI 0,46-0,97) and CPK threshold value 132 U/L ($S=0,83$; 95% CI 0,61-0,99). The obtained results support the fact this polymorphism can affect signal transduction processes. Perhaps, the T allele carriage is associated with reduced levels of transcription LMNA gene and potentially it is linked with a "weak" one promoter of this gene.

Conclusion: One-third of the Belarusian patients with DCM and conduction defects are carriers of the T allele at a polymorphic locus rs4641C>T. A significant correlation of clinical phenotype of DCM with carriage of this polymorphism was revealed, which can be used to predict ventricular tachyarrhythmic events.

P1835

Left ventricular dysfunction and heart failure manifestations in patients with Duchenne muscular dystrophy

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Background: Duchenne muscular dystrophy (DMD) is a severe X-linked disease due to loss of dystrophin in skeletal and cardiac muscle. Cardiomyopathy is a leading cause of death. Early use of ACE inhibitors and beta blockers improves the prognosis.

Purpose: The purpose of this study was to evaluate the relation between heart failure manifestations and left ventricular (LV) dysfunction in a group of patients with DMD and to look for early signs of LV impairment.

Material and methods

We evaluated 45 male patients with DMD, genetically verified, aged 6 to 23 years (mean±SD, 11,5±4,3 years). A clinical examination, 12-channel ECG, standard 2D, Doppler and tissue Doppler (TD) echocardiography were performed.

Results: Twenty three patients (51.1%) were disabled, restricted to wheelchair. Five patients (11.1%) suffered from chronic respiratory failure and were on ambulatory noninvasive ventilation. Dyspnea consistent with symptoms of heart failure was found in 2 patients (4.4%). The most common complaint was from palpitations. In 16 (35.6%) of the patients, sinus tachycardia was registered (HR>100 beats per minute), average heart rate 114±11.5 beats per minute. LV systolic dysfunction was found in 11 (24.4%) of the patient, aged 15 years and older. In 24 (53.3%) of the patients there was impairment of the LV diastolic function. The earliest signs of cardiac involvement were reduced early diastolic myocardial velocities at mitral valve annulus, found in 62.2% of the patients, starting at the age of 10.

Conclusion: In boys with Duchenne muscular dystrophy there is a progressive decline in left ventricular systolic function. Heart failure manifestations are not so obvious, mainly because of the restricted physical activity and the accompanying respiratory failure. In our study, the earliest signs of LV impairment were reduced early diastolic myocardial velocities at the mitral valve annulus. This finding may raise the attention for regular screening and early initiation of available treatment for slowing down the progression of LV dysfunction.

P1836

Stress cardiomyopathy - 10 years' experience at a tertiary care hospital

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Background: Stress cardiomyopathy (SC) is an entity recognized since the 1990's. Frequently mimicking the presentation of myocardial infarction (MI), it doesn't seem to be associated to coronary atherothrombosis, although its pathophysiology still isn't fully clear. We present a description of SC cases identified at our hospital in the last 10 years.

Methods: We made a descriptive analysis of retrospectively gathered data on patients (pts) presenting to our hospital and diagnosed with SC, according to the Mayo Clinic diagnostic criteria, between 2005 and 2014.

Results: We identified 58 pts (55 women and 3 men) with a mean age of 64 years (ranging from 33 to 84 years). A precipitating factor was found in 45 cases (78%), an emotional trigger being the most common, present in 31 pts (53%), and physical stress in 14 pts (24%). The most frequent symptom at presentation was chest pain (45 pts, 78%), followed by dyspnea (8 pts, 14%). The electrocardiogram (ECG) on presentation showed in equal proportions (20 pts, 35%) T wave inversion and ST-segment elevation; 6 pts (10%) presented with a normal ECG. All pts had some degree of troponin I elevation, with a mean peak level of 3,05±2,80 ng/mL. Echocardiographic evaluation revealed left ventricular systolic dysfunction in 55 cases (95%), the majority with apical hypokinesia (51 pts, 88%); 5 pts (9%) showed isolated midventricular hypokinesia and 2 pts an "inverted Takotsubo" pattern. In-hospital complications were present in 24 cases (41%). The most common were cardiogenic shock and acute pulmonary oedema, in 6 pts each (10%), 3rd degree atrioventricular block in 4 pts (7%) and left ventricle thrombus, atrial fibrillation and pericardial effusion, in 3 pts each (5%). Other identified complications were acute kidney injury and mitral regurgitation (2 pts each). One patient had in-hospital cardiac arrest, but no deaths were documented. Discharge after hospitalization took a mean of 9±7 days.

In patients with post-discharge follow-up information available (n=38, mean follow-up 28 months) only one death was recorded (non-cardiac) and one patient was admitted for recurrent SC.

Conclusion: Our hospital's 10-year experience, in line with international data, shows SC is frequently associated with severe clinical complications, but has nonetheless a very good short and long-term prognosis. We expect country-wide information, as the current national registry on SC starts being analysed.

P1837

Acute heart failure in takotsubo cardiomyopathy - does race matter?

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Introduction: Takotsubo cardiomyopathy (TCM) or stress-induced cardiomyopathy is a reversible condition most often affecting postmenopausal women after an emotional stressor. The underlying pathophysiological mechanisms are still not completely understood, but several hypotheses have been proposed: microvascular dysfunction, catecholamine cardiotoxicity, and coronary artery spasm. Significant spikes in cases of TCM have been reported worldwide and hospital-related admissions appear to be on the rise. Overall, TCM prevalence is estimated at 1.7 to 2.2% in patients admitted with suspected acute coronary syndrome, and appears to be increasing, especially among Caucasians. The majority of literature has reported TCM among Asian and Caucasian subjects, but rarely among African-Americans. It is still unclear, given the paucity of data, if race and ethnicity influence TCM clinical presentation and outcomes.

Methods: We conducted a retrospective, descriptive study reviewing patients with the discharge diagnosis of TCM from 2003-2013 at our Medical Center, and in another Hospital. Inclusion criteria were as per Modified Mayo Criteria recommendations. A total of 206 TCM patients from different racial and ethnic backgrounds (African Americans, Hispanics, Caucasians, and Asians) were included. Baseline demographic characteristics, past medical history, initial and peak troponin I levels obtained at least 8 hours apart, 12-lead electrocardiogram, left ventricular ejection fraction (LVEF) assessed by 2-D echocardiogram and cardiac catheterization data were collected after study's approval by the hospital's Institutional Review Boards at both sites. TCC patients also had reassessment of LVEF, within 6 months of the index event, to document LVEF recovery.

Results: Mean age was higher in African Americans, who also had longer length of stay. Hispanics had a higher prevalence of both diabetes mellitus and hyperlipidemia. Chest pain upon presentation was more frequent among Hispanics. African Americans had a higher incidence of acute systolic congestive heart failure, lower initial and follow up LVEF, higher incidence of LV thrombus and acute respiratory failure, requiring mechanical ventilation and higher in hospital mortality during index event.

Conclusions: Acute systolic heart failure during index TCM event affects predominantly African Americans. This group also appears to have a more complicated clinical course evidenced by higher frequency of acute respiratory failure and LV thrombus.

P1838

Cardiovascular events in left ventricular non compaction: is 2D strain a good predictor?

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Left ventricular non compaction (LVNC) is a rare cardiomyopathy which is sometimes difficult to diagnose, due to its similarities to other cardiomyopathies and the low correlation among the different morphologic diagnostic criteria with ecocardiography and cardiac MRI. Functional criteria, as it is 2D strain analysis, have proven to be useful in diagnosis. However, its prognostic value of 2D Strain has not been studied. Therefore, the aim of this study is to demonstrate the usefulness of speckle tracking in prediction of cardiovascular events (CVE) in patients with LVNC.

Methods: 26 LVNC patients were included. Diagnosis was established by Chin, Jenni, Jacquier and Petersen criteria. 2D Strain analysis included Longitudinal Strain (Slong), basal/apical rotation and torsion. Patients were prospectively followed from diagnosis to detect CVE.

Results: After a mean FU of 38±13.3 months, 6 CVE were observed: 2 sustained VT, 1 embolic TIA and 3 admissions for HF. Slong value was significantly reduced in patients with events, with an AUC ROC of 0.82 (0.54 to 1, p=0.047. Best cut-off -8,7; S: 75%, E: 95%). Patients with ≥-8.7 Slong values had a lower event-free survival. Among patients admitted for HF, torsion was significantly decreased compared to non-admitted patients (0.7±1.5 vs 4.6±3.3, p=0.02)

Conclusions: Low Slong and torsion values are good CVE predictors in LVNC, and routine measurements could complement classic parameters.

Event predictors in LVNC

	CV event (n=4)	No CV event (n=22)	p
LVEF (%)	26,25±13,7	47,5±13,1	0,007
Atrial fibrillation	25%	9,1%	<0,001
Slong ≥ -8,7%	75%	4,5%	<0,001

Table P1839: Patients' characteristics

	Age	Gender	Symptoms at presentation	NYHA class	Follow up	Cardiac family history	Comorbidities
1	61	Male	Dyspnea + cough + fever	II	18	Yes	Coronary disease, high cholesterol, type 2 diabetes, atrial fibrillation
2	65	Male	Dyspnea + legs edema	II	21	No	-
3	69	Female	Dyspnea	IV	24	No	High blood pressure, type 2 diabetes
4	65	Female	Dyspnea + legs edema	II	3	Yes	High blood pressure, type 2 diabetes, high cholesterol
5	41	Male	Dyspnea	II	18	No	High blood pressure, type 1 diabetes, high cholesterol
6	80	Male	Dyspnea + legs edema + pleural effusion	III	12	No	High blood pressure, high cholesterol
7	55	Female	Dyspnea + legs edema	II	7	Yes	-
8	51	Male	Dyspnea	II	48	Yes	-
9	70	Male	Dyspnea + pulmonary embolism	II	12	No	Atrial fibrillation
10	51	Female	Dyspnea + legs edema	III	96	No	High blood pressure, high cholesterol, atrial fibrillation, pulmonary disease

Patients' characteristics at presentation on the heart failure clinic.

P1839

Left ventricular non compactation: a heart failure clinic experience

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Background: Left ventricular noncompactation (LVNC) is believed to be a distinct type of cardiomyopathy presenting several distinct characteristics. The natural course of this entity is not totally understood. In this study we sought to define the clinical characteristics, complications and survival of patients with LVNC followed at our heart failure (HF) clinic.

Methods: Consecutive series of patients with LVNC treated in our HF clinic, from January 2006 to February 2014. Data on demographics, HF symptoms and cardiac function at the beginning of treatment, the course of LVNC (changes on functional class), side effects and survival were retrieved from clinical files.

Results: Ten patients were included: median age 63 years, 60% males. Nine patients presented with HF symptoms, 7 of them in class II of New York Heart Association. One patient had history of familial dilated cardiomyopathy. All had left ventricular ejection fraction <45%. Nine patients were started on HF medication but only one had optimized HF therapy. One patient was not started on oral hypocoagulation therapy. During follow up, 7 patients had some degree of recovery from HF symptoms. Three patients had hospital admissions related with HF exacerbation. One patient had a cardioembolic stroke. One patient underwent to heart transplant.

Conclusions: This is a small cohort with a short follow up, but patients responded well to HF medication with clinical benefit. Yet, we have to understand more about LVNC and try to manage its complications despite the lack of a specific guideline.

P1840

Does the BNP value at admission correlate with the prognosis of Takotsubo cardiomyopathy? A multicenter portuguese study

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Introduction: Takotsubo cardiomyopathy (TC) is characterized by a transient left ventricular (LV) dysfunction. BNP has been used as a marker of heart failure (HF) and LV dysfunction. It has not been determined if the BNP value at hospital admission correlates with the prognosis of TC.

Aim: To determine if the BNP value at hospital admission is associated with in-hospital and medium term prognosis in patients diagnosed with TC.

Methods: A Portuguese multicenter study involving 11 hospital centers and including all patients diagnosed with TC in the last 10 years. We analyzed the BNP value at hospital admission and determined if it was associated with in-hospital and medium term prognosis.

Results: We included 79 patients with TC with a mean follow up of 39.7 ± 30.7 months. The value of BNP at admission was not associated with the occurrence of atrial fibrillation, ventricular tachycardia, complete AV block, LV thrombus, stroke, or in-hospital death (p = ns). However, it was associated with the development of HF during hospitalization (p < 0.001). The value of BNP at hospital admission was not associated with death, stroke / TIA or recurrence of TC in the follow-up (p = ns).

Conclusion: In this Portuguese multicenter study, a higher BNP value at hospital admission was associated with the development of in hospital HF. The BNP value at admission was not associated with any other prognostic factor.

P1841

Heart failure is the most frequente complication in a portuguese population of left ventricular noncompactation cardiomyopathy a multicentre study

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Introduction: Left ventricular non-compaction cardiomyopathy (LVNC) may lead to left ventricular (LV) systolic dysfunction. Previous studies show that heart failure is one of the main clinical manifestations of LVNC, along with embolic events and arrhythmias. However, natural history of LVNC is not clearly established and current knowledge come from small series.

Aim: To characterize a Portuguese population of patients with LVNC and to determine the prognosis in the medium term follow-up.

Methods: Portuguese multicenter study involving 11 hospital centers and including all patients diagnosed with LVNC. We evaluated the clinical, electrocardiographic, echocardiographic and cardiac MRI data. We evaluated the prognosis in terms of heart failure, embolic events, arrhythmias and death.

Results: We included 72 patients with LVNC, 57% males, with mean age 45 ± 19 years. Symptoms were present in 46% of patients, and dyspnea (38%) and palpitations (28%) were the most common symptoms. Diagnosis was established by echocardiogram in 85% of patients. The average LV ejection fraction was 49 ± 16%. Mitral regurgitation was detected in 15% of cases. Delayed gadolinium enhancement on cardiac MRI was found in 20% patients. Most patients were in sinus rhythm (89%). A history of atrial fibrillation was present on 10% of the patients and non-sustained ventricular tachycardia in 10% of the cases. Family history of LVNC was identified in 8% of cases.

In the medium term follow-up (mean follow up of 4 years), patients with LVNC presented heart failure in 34.7%, arrhythmia in 15.3%, embolic events in 6.9% and death in 2.8% of cases.

Conclusions: In this Portuguese population of patients with LVNC, heart failure was present in one third of the cases and therefore was the most frequent clinical complication in the medium term follow up.

P1842

Predictors of recovery of left ventricular systolic function in the first 15 days after hospital admission in takotsubo cardiomyopathy - a portuguese multicenter study

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Introduction: Takotsubo cardiomyopathy (TC) is characterized by a transient left ventricular (LV) dysfunction. The speed of LV function recovery is variable. There are no studies determining the predictors of the speed of recovery of the LV systolic function in TC.

Aim: To identify the predictors of complete recovery of the LV systolic function in the first 15 days after hospital admission of patients with TC.

Methods: A Portuguese multicenter study involving 11 hospital centers and including all patients diagnosed with TC in the last 10 years. We evaluated demographic, clinical, electrocardiographic and echocardiographic data. We determined the factors that were associated with LV systolic function recovery in the first 15 days after hospital admission. Then we conducted a multivariate analysis to establish the independent predictors of complete recovery of LV systolic function within the 15 days after hospital admission in patients with TC.

Results: We included 142 patients with TC, predominantly women (89.4%). The mean age was 67 ± 12 years. At hospital discharge, 45.1% of patients had complete recovery of LV function and 15 days after hospital admission complete recovery had already occurred in 62.6% of cases. In patients with TC, the following factors were associated with complete recovery of LV systolic function in the first 15 days after hospital admission: absence of angina (97.7% vs 81.9%, p=0.013) and absence of Q waves in the initial ECG (93% vs. 70.8%, p=0.005). In the multivariate analysis, the absence of Q waves in the initial ECG (p=0.024) was identified as an independent predictor of complete recovery of LV systolic function in the first 15 days after hospital admission for TC.

Conclusion: Complete recovery of LV systolic function in patients with TC occurred in almost half of the cases during hospitalization and nearly 2/3 of the cases up to 15 days after hospital admission. This study revealed the absence of Q waves on the admission ECG as an independent predictor of complete recovery of LV systolic function in the first 15 days after hospital admission in patients with TC.

P1843

Prognostic value of the admission ECG for predicting complications in patients with tako-tsubo cardiomyopathy

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Purpose: Tako-tsubo cardiomyopathy (TTC) mimics acute myocardial infarction. A substantial number of patients develop adverse events during the acute course of TTC.

This study assessed the prognostic value of the admission ECG for predicting complications in patients with TTC.

Methods: Over a 9-year period, we observed 76 TTC patients (69f, 7m; 70 ± 12 years). A total of 37 patients (49%) developed one (n=17) or more (n=20) adverse events such as pulmonary oedema (n=14), cardiogenic shock (n=4), ventricular tachycardia (n=7), atrial fibrillation (n=14), right ventricular involvement (n=15), intraventricular pressure gradient (n=8), thrombus and/or stroke (n=6), or death (n=2). Clinical parameters and the admission ECG were compared in patients with and without adverse events.

Results: Patients with adverse events were older (73 ± 12 vs 67 ± 12 years, p=0.05) and more frequently female (52% vs 14%, p=0.05). There was a higher rise in troponin (9.4 ± 9.0 vs 6.1 ± 5.7 times the upper limit of normal, p=0.05) and a lower left ventricular ejection fraction (47 ± 13 vs 55 ± 13%, p=0.007) in patients with adverse events. Angiographic ballooning pattern and left ventricular end-diastolic pressure were not different.

Time from symptom onset to first ECG (7.5 ± 7.2 vs 9.3 ± 9.8 hours, p=ns) was similar in both groups. Patients with adverse events had a higher heart rate on admission (97 ± 23 vs 82 ± 19/min, p=0.003), and there was a trend towards a higher number of leads with ST-segment elevation (4.4 ± 2.3 vs 3.5 ± 2.3 leads, p=0.09) and a greater magnitude of ST-segment elevation (0.64 ± 0.51 vs 0.48 ± 0.36 mV). The number of patients with ST-elevation in V3 (89% vs 74%) and V4 (60% vs 39%, p<0.02) was higher in patients with adverse events. Regarding ST-elevation in the other leads, occurrence of an abnormal Q wave (32% vs 30%), reciprocal ST-segment

depression (27% vs 26%) or T-wave inversion on the admission ECG there was no difference among both groups. Patients with adverse events, however, presented with a longer QTc interval (491 ± 54 vs 460 ± 54 msec, p<0.02).

Conclusion: Almost half of the patients with TTC develop adverse events. Especially elderly females with a high heart rate and a prolonged QTc interval on the admission ECG are at increased risk for developing complications during the acute course of TTC.

CO-MORBIDITIES

P1844

Severity of congestion in patients with chronic heart failure is not correlated to peripheral organ dysfunction

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Introduction: Venous congestion in advanced heart failure (HF) patients is frequently accompanied by dysfunction of several peripheral organs (liver, kidneys), and is associated with unfavorable prognosis. However, there are few data regarding the correlation between the degree of venous congestion and the type and range of hepatic function abnormalities.

Methods: Fifty four patients with advanced HF on optimal medical therapy continuing to have symptoms and signs of congestion despite that the daily furosemide dose was ≥ 250 mg in each patient.

Results: Mean age of patients was 62.7 ± 10.8 years, whereas 65% of them suffered from idiopathic dilated cardiomyopathy. Mean values of New York Heart Association functional class, were 3.5 ± 0.5, of left ventricular ejection fraction 27.5 ± 7.9%, of right atrial pressure (RAP) 16.8 ± 6.8 mmHg of pulmonary capillary wedge pressure (PCWP) 23.6 ± 5.7 mmHg and of cardiac index 1.8 ± 0.6 Lt/min/m².

Serum values of BNP were 1935 ± 1268 pg/ml, serum creatinine 2.9 ± 4.9 mg/dl, bilirubin 1.8 ± 2.1 mg/dl aspartate (AST) 34 ± 27 IU/L, alanine aminotransferase (ALT) 43 ± 122 IU/L, alkaline phosphatase 95 ± 81 IU/L and γ -glutamyl transferase (γ -GT) 122 ± 75 IU/L.

No correlation between RAP, PCWP and liver function enzymes was demonstrated. Patients with severe systematic venous congestion (RAP values up to 30 mmHg) and high values of BNP (up to 3.330 pg/ml) could present with normal values of hepatic enzymes. Contrary, in patients with significant dysfunction of liver biochemistry the values of RAP and PCWP could be within normal range. Indices of cholestasis or liver cell lysis were also irrelevant to the degree of congestion. Interestingly, right ventricular systolic function (sTDI) was demonstrated to correlate with serum creatinine (r=0.517, p=0.049), β NP levels (r=0.584, p=0.046) and the value of direct bilirubin (r=0.754, p=0.031).

Conclusions: The type and range of hepatic biochemistry abnormalities which is noted with congestion seems to be independent of intracardiac filling pressures, possibly indicating a systematic/inflammatory rather than a mechanistic mechanism of their generation.

P1845

Long-time changes in anemia and its correlation with heart failure and renal impairment in patients with chronic systolic heart failure

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Background: Chronic systolic heart failure (HFrEF) is frequently accompanied by co-morbidities, contributing to increased morbidity and mortality. Anemia is a common co-morbidity in patients (pts) with HFrEF and is associated with poor prognosis.

Aim and Methods: Our aim was to define the prevalence of anemia (defined as Hb ≤ 120g/l in female, Hb ≤ 130g/l in male) in pts with HFrEF at the time of diagnosis, and the changes in hemoglobin (Hb) levels during a long-term follow up period (FUP). We also examined its relation with severe HF (defined as LVEF ≤ 35% and NYHA ≥ 3) and severe renal impairment (defined as BUN ≥ 15mmol/l and creat ≥ 150 μ mol/l). Parameters of 495 pts managed at our Heart Failure Outpatient Clinic (mean age: 64.4 ± 31.4y, male: 78.9%, ischaemic: 51.1%, NYHA: 3.0 ± 1.0, LVEF: 29.9 ± 9.2%, Hb: 137.7 ± 18.5g/l, BUN: 9.5 ± 5.5mmol/l, creat: 112.3 ± 53.7 μ mol/l) were evaluated. For statistical analysis we used chi2 test. During the 5-year FUP every pt received optimal medical and device therapy for HFrEF.

Results: At baseline 132 pts (26.6%) had anemia („A“), 363 had not („B“). After a 5-year FUP the proportion (pp) of anemic pts increased to 41.2%. At the end of FUP 90 pts from group „A“ remained anemic („A1“), while normalization of their Hb levels was observed in 31.8% of pts with anemia at baseline („A2“). 114 pts from

group „B“ developed new-onset anemia („B1“), 68.6% (50.3% of whole cohort) had no anemia at all („B2“) during the 5-year FUP. There was no difference between group „A“ and „B“ regarding the pp of severe HF, however the pp of severe renal impairment was significantly higher in group „A“ (12.8 vs. 5.0%; $p=0.0038$). Similarly, there was no significant difference regarding the pp of severe HF between subgroup „A1“ and „A2“, and subgroup „B1“ and „B2“ (52.1% vs. 52.9% and 47.4% vs. 48.1%; NS, respectively), but the pp of pts with severe renal impairment was significantly higher in subgroup „A1“ and „B1“ compared with subgroup „A2“ (38.2% vs. 11.9%; $p=0.0021$), and subgroup „B2“ (22.1% vs. 7.3%; $p=0.0001$).

Summary and Conclusion: In our single centre, real-life cohort 1/3 of HFREF pts presented initially with anemia. During the 5-year FUP the ratio of anemia among HFREF pts increased to 150%. Normalization of Hb was observed in 1/3 of initially anemic HFREF pts after receiving optimal heart failure therapy. 1/3 of pts with no anemia at baseline developed new-onset anemia during FUP. Our results suggest that renal dysfunction plays a more important role in the development of anemia among HFREF pts than the severity of heart failure.

P1846

Galectin-3 in daily routine heart failure care: relationship with co-morbidities

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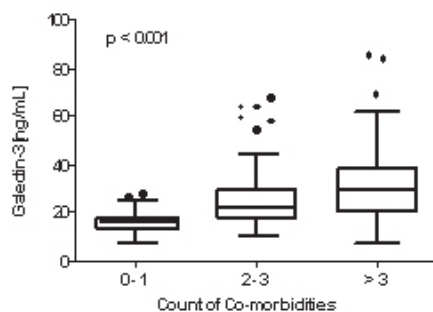
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Purpose: Galectin-3 is a biomarker that may be used in risk stratification of patients with heart failure. Since co-morbidities are important drivers of heart failure outcome, we set out to evaluate if and how galectin-3 would relate to common co-morbidities of heart failure.

Methods: In a tertiary referral Academic Hospital, we routinely measured galectin-3 whenever NT-proBNP was assayed, in 182 consecutive patients who visited the heart failure outpatient clinic using the ARCHITECT platform (Abbott). All patients underwent echocardiography to assess LV function, and several co-morbidities were recorded, such as coronary artery disease, hypertension, diabetes mellitus (DM), renal disease (eGFR < 60 ml/min), chronic obstructive pulmonary disease (COPD), atrial fibrillation (AF), and anemia. Patients were optimally treated according to ESC guidelines. We categorized patients as having either 0-1 (group 1, n=31), 2-3 (group 2, N=68), or 4-6 co-morbid conditions (group 3, N=83).

Results: Mean age was 68 years (± 14), 68% were male, mean weight was 84 kg, mean LVEF was 37% (± 14), and mean blood pressure was 116/71 mm Hg. Patients with increasing number of co-morbidities had increasing galectin-3 levels, irrespective of LVEF: 15.4 ng/mL in group 1, 22.0 ng/mL in group 2, and 28.6 ng/mL in group 3 ($P < 0.001$ for trend; figure). Besides renal dysfunction, hypertension, AF, DM, and anemia were associated with higher galectin-3 levels ($P < 0.05$). Galectin-3 was superior over NT-proBNP when assessing the presence of co-morbidities, even corrected for age, sex and LVEF (OR 2.7 and 1.2; $p=0.01$).

Conclusions: Galectin-3 substantially increases when multiple co-morbidities are present. These data suggest that galectin-3 mirrors the systemic impact of the heart failure syndrome and its associated co-morbidities.



P1847

Impaired pulmonary diffusion capacity does not correlate with central sleep-disordered breathing

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Purpose: Heart failure (HF) is associated with sleep-disordered at a very high prevalence. The details in pathophysiology on this relationship are not well understood. It has recently been suggested, that impaired pulmonary diffusion capacity and hypoxia would correlate with central sleep apnea severity in patients with heart failure.

This study investigated the relationship between HF and DLCO in patients with HF in a larger and more detailed characterized cohort than previously reported.

Methods & Results: 100 patients with HF and all with central sleep apnea (CSA), (mean age 70.7 ± 9.7 years, 95% male, body mass index (BMI) 28.9 ± 5.3 mean left ventricular ejection fraction (LVEF) $33.5 \pm 7.7\%$, 43% New York Heart Association (NYHA) functional class II, 65% NYHA III) were enrolled and underwent multichannel cardiorespiratory polygraphy (PG) and lung function tests. None of the patients was treated with ventilation therapy and all patients were naïve to ventilation therapy. CSA, DLCO and PaO₂ did not correlate with total AHI ($p=0.377$ and $p=0.336$, respectively) in contrast to previously reported data, in our larger cohort. Only BMI remained as an independent predictors of total AHI ($p < 0.05$). Furthermore mean SaO₂, mean O₂ desaturation, CRP and pH were found to be significantly statistically associated with SDB severity ($p < 0.05$). In regard of medication betablocker and digitalis were statistically significantly associated with SDB severity ($p < 0.05$).

Conclusions: In contrast to previously reported data, in patients with HF and CSA, DLCO and PaO₂ were not independently associated with respiratory disturbance during sleep, only BMI remained as an independent predictors of total AHI ($p < 0.05$).

P1848

Simultaneously presented acute myocardial infarction and ischemic stroke ; a dreadful association

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Stroke can complicate the course of patients presenting with acute myocardial infarction (MI). The development of a stroke in the acute phase of MI is rare devastating condition and is associated with a very high risk of death. Comorbidity of heart failure with this condition is extremely fatal. We aim to submit extremely rare condition which was simultaneously presented as acute MI and ischemic stroke in eight patients.

We report eight patients who admitted to our emergency department because of chest pain and various neurologic deficit. They were diagnosed as acute ST elevation MI by ECG and high serum troponin levels. Their cranial brain tomography showed ischemic stroke for all patients. Average age of patients was 58-years-old. All patients had sinus rhythm and their echocardiography showed that all of them had wall motion abnormalities and four of them had left ventricular dysfunction with low EF%, but no thrombus in chambers and no septal defect. Their average renal function was normal. Their cardiovascular risk factors were hypertension, diabetes mellitus, hyperlipidemia, smoking, family history and elevated CRP levels. All patients were treated by thrombolytic therapy in coronary care unit. Two patients died on the second day of hospital treatment because of cardiogenic shock and three patients died within 30 days of admission.

Most of our patients had a lot of cardiovascular risk factors and comorbid heart failure which were both predictors of increased risk of stroke and MI. The individual susceptibility to these risk factors varies greatly but especially heart failure is major predictor of mortality for these patients. There is an atherosclerotic burden with simultaneous acute MI and stroke. Atherosclerotic plaques become vulnerable and lead to atherothrombotic events. Noninvasive tests such as carotid arter duplex scanning, ankle/brachial blood pressure ratios, electron beam-computed tomography and high-sensitivity testing for C-reactive protein may represent a measure of atherosclerosis burden. Identification and quantification of global atherosclerotic burden is a useful tool to identify those patients at high risk of cardiovascular events or cardiovascular death. Simultaneously presented acute MI and stroke is a dreadful association.

P1849

Effect of atrial fibrillation on renal function in heart failure with reduced ejection fraction

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Aim: Atrial fibrillation (AF) and chronic kidney disease are common comorbidities in chronic heart failure with reduced ejection fraction (HFREF). The effect of AF on renal function has been investigated in very few studies in these patients. The aim of this study was to identify the effect of atrial fibrillation on renal dysfunction in patients with chronic stable HFREF.

Methods: Five hundred and fifty six patients (353 males and 203 females, mean age 66 ± 12 years) with HFREF (EF < 0.45) were examined. Etiology of HF was ischemic in 363 patients (65%) and non-ischemic in 193 patients (35%). AF was present in 162 patients (29%) and sinus rhythm in 394 patients (71%). Glomerular filtration rate (GFR) was calculated using the MDRD (Modification of Diet in Renal Disease), CKD-EPI and Cockcroft-Gault formulas.

Results: GFR calculated by CKD-EPI was 51 ± 21 ml/min/1.73 m² in patients with sinus rhythm and 52 ± 21 ml/min/1.73 m² in patients with atrial fibrillation ($p = 0.58$). A GFR < 60 ml/min/1.73 m² was detected according to MDRD, CKD-EPI and Cockcroft-Gault formulas in 89 (56%), 85 (54%) and 82 (52%) patients with atrial fibrillation and in 235 (60%), 221 (57%) and 218 (56%) patients with sinus rhythm respectively (p was not significant for any of them). The patients with AF had larger diameter of the left atrium and higher pulmonary artery systolic pressure, but no difference was detected in uric acid, hemoglobin and hematocrit levels compared to patients with sinus rhythm. The results were similar for study sub-groups: elderly vs. middle-aged, men vs. women and non-ischemic vs. ischemic HF. In logistic regression analysis, none of the clinical and echocardiographic parameters were independently associated with AF, whereas jugular venous distention, right ventricular EF and hemoglobin were independently associated with reduced GFR. **Conclusion:** Presence of atrial fibrillation has no additional deteriorating effect on renal function in patients with HFref.

P1850

Impact of peripheral artery disease on prognosis in heart failure

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Background: The impact of peripheral artery disease (PAD) on heart failure (HF) prognosis still remains unclear.

Methods and Results: Consecutive 388 decompensated HF patients were divided into two groups based on the presence of PAD: HF with PAD (PAD group, $n = 101$, 26.0%) and HF without PAD (non-PAD group, $n = 287$, 74.0%). We compared clinical features, echocardiographic parameters, cardiopulmonary exercise testing results, laboratory findings, as well as cardiac, non-cardiac, and all-cause mortality between two groups. The PAD group, as compared to the non-PAD group, had 1) higher presence of coronary artery disease (40.6% vs. 27.5%, $P = 0.011$) and cerebrovascular disease (34.7% vs. 18.2%, $P = 0.001$), 2) higher circulating levels of tumor necrosis factor- α (1.82 vs. 1.49 pg/ml, $P = 0.023$), high-sensitive C-reactive protein (0.32 vs. 0.19 mg/dl, $P = 0.045$), and high-sensitive troponin T (0.039 vs. 0.021 ng/ml, $P = 0.019$), 3) lower left ventricular ejection fraction (42.4% vs. 48.5%, $P < 0.001$) and higher mitral valve E/E' (17.9 vs. 15.2, $P = 0.021$), and 4) lower peak VO₂ (13.4 vs. 15.9 ml/kg/min, $P = 0.001$) and higher VE/VCO₂ slope (38.8 vs. 33.7, $P < 0.001$). During the follow-up period (mean of 766 days), there were 48 cardiac deaths and 29 non-cardiac deaths (cancer, $n = 8$; respiratory failure and/or pneumonia, $n = 5$; stroke, $n = 4$; infection/sepsis, $n = 4$; renal failure, $n = 2$; aneurysm, $n = 2$; digestive hemorrhage, $n = 2$; and other problems, $n = 2$). In the PAD group, 19 cardiac deaths (18.8%) and 12 non-cardiac deaths (11.9%) occurred. In the non-PAD group, 29 cardiac deaths (10.1%) and 17 non-cardiac deaths (5.9%) occurred. In the Kaplan-Meier analysis, cardiac, non-cardiac, and all-cause mortalities were significantly higher in the PAD group than in the non-PAD group ($P < 0.05$, respectively). In the Cox proportional hazard analyses after adjusting for confounding factors, PAD was an independent predictor of cardiac and all-cause mortality ($P < 0.05$, respectively) in HF patients.

Conclusions: PAD was common and an independent predictor of cardiac and all-cause mortality in HF patients. Thus, screening PAD and its comprehensive management may improve the prognosis of HF patients.

P1851

Renal function and clinical outcomes in chronic heart failure: a moroccan center-based study

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Background: Chronic renal dysfunction frequently coexists with heart failure (HF) and influences outcome. We assessed incidence of clinical outcomes in this population.

Methods: The study population consisted of 1284 patients with CHF. The glomerular filtration rate (GFR) was calculated using the Modification of diet in renal disease (MDRD). We divided patients on 4 groups: group 1 (296 patients, 23%) with normal renal function (GFR > 60 ml/min/1.73 m²), group 2 (859 patients, pts=67%) with moderate renal dysfunction (GFR < 60 and > 30 ml/min/1.73 m²), group 3 (106 patients, pts=8%) with severe renal dysfunction (GFR < 30 and > 15 ml/min/1.73 m²) and group 4 (23 patients, pts=2%) with terminal renal dysfunction (GFR < 15 ml/min/1.73 m²).

Results: Mean GFR in severe renal dysfunction patients was 9.44 ± 3.59 ml/min/1.73 m² (group 4), 24.6 ± 3.59 in group 3, 46.3 ± 7.8 in group 2 and 73.4 ± 15.7 in group 1. Compared to 296 (23%) patients with preserved GFR, they were older, with more co-morbidities and more frequently ischemic etiology of HF. Patients with renal insufficiency had low functional capacity during six minute walking, more left bundle branch block ($p < 0.00001$), more left ventricular hypertrophy ($p = 0.02$), more systolic dysfunction more Increased E/A ($p < 0.00001$). Beta-blockers were used less frequently in those patients ($p < 0.00001$) who

receive high dose of diuretic ($p < 0.00001$), angiotensin enzyme converting inhibitors ($p < 0.00001$) and amiodarone ($p < 0.01$).

Conclusions: Renal dysfunction is more prevalent in patients with heart failure and is prognostic factor in functional capacity, diastolic and systolic dysfunction.

P1852

Do inotropes have different renal protection effects in the setting of acute heart failure?

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Purpose: Cardiorenal syndrome (CRS) is common in acute heart failure (AHF), being associated with poor prognosis. Its pathophysiology combines renal perfusion reduction with increased venous congestion. Levosimendan (Lv) and dobutamine (Db) are inotropes used in AHF treatment. The first, combining a positive inotropic effect with efficient decongestion, might lead to a better renal protection profile. So far, published results have been limited and controversial. Our aim was to evaluate, in patients (P) with AHF, CRS incidence according to the inotrope used (Lv or Db); and determine predictors of CRS in order to identify P that might benefit from the most renoprotective inotrope.

Methods: We studied 206 consecutive P with AHF, admitted to our Intensive Cardiac Care Unit, along 5 years. P ($n = 108$) who required inotropes (74% male, 66 ± 15 years) were divided in two groups: Lv-G (71%) and Db-G (29%). Clinical parameters, therapeutic strategies and in-hospital mortality were evaluated and compared.

Results: P in Lv-G were younger (64 ± 14 vs 73 ± 16 , $p < 0.01$) and more frequent male (81% vs 58%, $p = 0.02$). No differences were found in etiology or past medical history of HF, coronary artery disease or chronic kidney disease.

At admission, Db-G had lower systolic blood pressure (119 ± 32 vs 104 ± 31 mmHg, $p = 0.04$); with no differences in glomerular filtration rate (GFR in ml/min/1.73m²; 61 ± 30 vs 56 ± 28 , $p = 0.42$), cystatin C or NTpro-BNP. Lv-G had lower left ventricle ejection fraction ($27 \pm 9\%$ vs $35 \pm 12\%$, $p < 0.01$).

Concerning therapy, there were no differences in maximum daily dose of furosemide or its form of administration (bolus/infusion). Noradrenaline use (7% vs 28%, $p < 0.01$), renal replacement therapy (1% vs. 10%, $p = 0.04$) and mechanical ventilation (26% vs 48%, $p = 0.02$) were more often in Db-G.

CRS incidence was higher in Db-G (49% vs 77%, $p < 0.01$; minimum GFR: 44 ± 22 vs 31 ± 18 , $p < 0.01$), being GFR not completely recovered at discharge (GFR: 60 ± 27 vs 45 ± 25 , $p < 0.01$).

Db-G had higher in-hospital mortality (9% vs 42%, $p < 0.01$). CRS development (OR 13, $p = 0.02$) and the inotrope used (OR for Db 5, $p = 0.01$) appeared as independent mortality predictors.

In multivariate analysis, cystatin C (OR 14, $p < 0.01$) was a CRS predictor.

Conclusions: Lv seems to have some renal protective effect, being associated with lower incidence of CRS, and full recovery of renal function at discharge. Identification of P at increased risk of renal dysfunction by assessing cystatin C may enable P selection for Lv treatment, probably minimizing the incidence of CRS and its indisputable negative impact on AHF prognosis.

P1853

Risk of development and progression of renal dysfunction in patients with chronic heart failure depending on arterial wall stiffness

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Aim: to evaluate relative risk of renal dysfunction in patients with ischemic chronic heart failure (CHF) depending on arterial wall stiffness. **Methods and materials:** 90 patients with CHF and stable angina were examined. 38.2% got a MI in past. Average age was 56.2 ± 6.4 yrs. Male 58.8%, female 41.2%. Duration of angina was 5.9 ± 2.6 yrs, average functional class (FC) 2.27 ± 0.37 . Duration of CHF was 6.2 ± 2.1 , average FC 2.52 ± 0.08 , average LV EF $60.5 \pm 9.3\%$. To evaluate renal function estimated GFR (MDRD) has been used. Average eGFR was 52.80 ± 6.26 mL/min/1.73m². To estimate arterial wall status volume sphygmography was done with VaSera VS-1000 device (Fucuda, Japan). To evaluate collagen matrix condition TIMP-1 was used. To study interconnection between the parameters Hazard ratio (HR) and Relative risk (RR) (95% confident interval - CI) have been established.

Results: along with CAVI1 elevation >9.0 HR of eGFR decrease lower than $60 \text{ mL/min}/1.73\text{m}^2$ was significant and consisted of 4.05 (95% CI= 1.05 - 16.38), RR was 2.74 (95% CI= 1.04 - 8.18), ($p=0.041$). In PWV in aorta $>6.0 \text{ m/sec}$ HR with renal dysfunction increased significantly up to 6.0 times (95% CI= 1.49 - 26.21), and RR up to 1.71 times (95% CI= 1.14 - 2.27), ($p=0.009$). There were no reliable changes in HR and RR along with increase of PWVcf $>12.0 \text{ m/sec}$ (HR = 2.05 , 95% CI = 0.54 - 7.97 □ RR = 1.71 , 95% CI = 0.63 - 4.94 , $p=0.371$). Along with TIMP-1 elevation $>138 \text{ ng/mL}$ HR in eGFR worsening significantly increased in 5.21 (95% CI= 1.39 - 20.61) as well as RR: 1.75 (95% CI= 1.23 - 2.45), ($p=0.011$).

Conclusions: in ischemic CHF patients arterial wall stiffness increase and its elasticity decrease accompanied with unfavorable disorders in endogenous collagenolysis status were followed with high relative risk of development and progression of renal dysfunction. It demonstrates the presence of unfavorable vascular and renal relationships in these patients.

P1854

Chronic heart failure and cardio-renal anemic syndrome

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Aim: to investigate the effect of cardio-renal anemic syndrome (CRA) on chronic heart failure (CHF) course in patients in primary care setting.

Methods: a cohort of 164 outpatients aged 60-85 yrs with clinically stable CHF II-IV FC NYHA due to ischemic heart disease and/or arterial hypertension were studied. All patients provided written informed consent and had clinical, laboratorial evaluation, ECG, Echo CG measurements, 6 min walking test. Patients were categorized according to the presence of anemia, as defined by the World Health Organization criteria (hemoglobin levels $<13 \text{ g/dl}$ in male and $<12 \text{ g/dl}$ in women).

Results: anemia was found in 32.9%, CRA - in 23.2% outpatients. Anemia was mild degree (Hb $>9 \text{ g/dl}$) and associated with diabetes mellitus 2 type ($p=0.041$, OR 2.2, 95% CI 1.03-4.69), creatinine level ($p=0.012$, OR 2.76, 95% CI 1.25-6.12) and chronic kidney disease ($p<0.001$, OR 5.66, 95% CI 2.51-12.77). During the median of follow-up 1.85 (1.00-4.75) years the mortality rate was the same in the anemic and non-anemic patients (27.8% vs 30%, $p=0.768$). Patients with CRA syndrome appear to have aggravated morbidity and mortality compared to those with no CRA syndrome, $p=0.004$. Age >75 yrs ($p=0.002$, OR 3.58, 95% CI 1.59-7.99), diabetes mellitus ($p=0.018$, OR 2.68, 95% CI 1.19-6.04), past myocardial infarction ($p=0.013$, OR 2.7, 95% CI 1.24-6.04), systolic BP $<110 \text{ mm Hg}$ ($p=0.030$, OR 2.49, 95% CI 1.09-5.71), complete BBBL ($p=0.012$, OR 2.79, 95% CI 1.26-8.22), creatinine level $>130 \text{ mcmol/l}$ ($p=0.004$, OR 3.53, 95% CI 1.51-8.22) were predictors of mortality of patients with CRA syndrome.

Conclusions: these results suggest that CHF elderly patients with CRA syndrome can expect to develop the process of severe chronic heart failure. Age >75 yrs, diabetes mellitus, past myocardial infarction, low systolic blood pressure, complete BBBL, high creatinine level were predictors of mortality of this population. Since CRA syndrome predicts worse outcome, it should be monitored carefully in elderly outpatients.

P1855

Contribution of permanent atrial fibrillation in course and progression of renal dysfunction in patients with chronic heart failure

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Aim: to evaluate the contribution of permanent atrial fibrillation (AF) in course and progression of renal dysfunction in patients with ischemic chronic heart failure (CHF) Methods and materials: 120 patients with ischemic CHF were divided into 2 groups depending on heart rhythm. The 1st group consisted of 60 patients with CHF and sinus rhythm, and the 2nd one included 60 CHF patients with permanent AF. Average age was 61.13 ± 8.42 . Mean CHF functional class (FC) was 2.63 ± 0.46 , and mean FC of stable angina was 2.44 ± 0.39 . To evaluate the functional renal condition estimated glomerular filtration rate (eGFR) was detected by MDRD formula, creatinine clearance (CC) according to Cockcroft-Gault, and serum levels both of creatinine and cystatin C were examined. Groups were equal in age and cardiovascular therapy.

Results: According to NT-proBNP, groups differed reliably in CHF and angina severity. Serum creatinine and CC were significantly higher in patients with permanent AF: 104.92 ± 19.15 and $95.71 \pm 16.68 \text{ } \mu\text{mol/L}$ ($p=0.006$); 99.66 ± 29.30 and $84.38 \pm 24.81 \text{ mL/min}$ ($p=0.003$). CC $<60 \text{ mL/min}$ has been observed in 5.0% in 1st group and in 21.7% in 2nd one ($p=0.037$). EGFR did not differ reliably between the groups. But eGFR $<60 \text{ mL/min}/1.73\text{m}^2$ was 11.7% in 1st group and 36.7% in 2nd one ($p=0.021$). Cystatin C serum level was significantly higher in 2nd group than in 1st one: 1894 ± 681.8 vs $1406.21 \pm 762.71 \text{ ng/mL}$ ($p<0.001$). Correlation analysis showed that eGFR decrease and cystatin C increase are interconnected with

NT-proBNP ($r=-0.51$; $p=0.003$; $r=0.60$; $p<0.001$ respectively). Also, cystatin C level reliably elevated along with diurnal heart rate ($p<0.001$).

Conclusion: in ischemic CHF permanent AF presence provides unfavorable influence on course and progression of renal dysfunction. It is characterized with cystatin C level increase, which is associated with heart rate elevation.

P1856

Characteristics and predictors of renal damage in patients hospitalized for acute heart failure

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Background: Acute heart failure (AHF) represents a significant and growing mortality burden. Treatment of the syndrome is even more difficult in patients with end-organ damage including worsening renal function. Knowing the characteristics of AHF patients at increased risk of renal damage allows their early identification and starting appropriate therapy.

Purpose: To identify the characteristics and prognosis of hospitalized AHF patients with higher risk of concomitant renal damage (CRD) in general population.

Methods: We used the data from SLOVASEZ, nationwide multicenter AHF survey with 860 consecutive patients enrolled in 11 hospitals throughout Slovakia during 3 months. CRD was defined as serum creatinine $\geq 170 \text{ } \mu\text{mol/L}$ at admission. We analysed fifty-six variables in relation to clinical manifestation of AHF in univariate analysis. Significantly associated parameters ($p<0.05$) were subsequently entered into linear regression model for multivariate analysis.

Results: CRD was present in 120 patients (14%). Patients with CRD were more often hospitalized due to worsening of chronic HF (87.7 vs. 76.1%, $p=0.008$) and had higher in-hospital mortality (20.7 vs. 6.8%, $p<0.001$). CRD was also an independent predictor of in-hospital mortality ($p<0.01$). There were eleven significant parameters associated with CRD in univariate analysis. CRD was significantly more common in patients with arterial hypertension (91.7 vs. 81.2%, $p=0.004$), diabetes mellitus (57.9 vs. 39.4%, $p<0.001$), edema (75 vs. 56.9%, $p<0.001$), anemia according to WHO criteria (72.7 vs. 34.1%, $p<0.001$), hyponatremia - serum sodium $<135 \text{ mmol/L}$ (22.3 vs. 12.5%, $p=0.006$) and left ventricular ejection fraction $\geq 40\%$ (69.6 vs. 55.2%, $p=0.03$). Patients with AHF and CRD were more often treated with inotropes (15.7 vs. 5.1%, $p<0.001$), on the other hand less with angiotensin II inhibitors (48.8 vs. 74.2%, $p<0.001$), beta-blockers (45.5 vs. 59.6%, $p=0.004$) and aldosterone antagonists (24.8 vs. 56%, $p<0.001$). Parameters independently associated with CRD were history hypertension ($p<0.05$), as well as finding of anemia ($p<0.001$) and ejection fraction $\geq 40\%$ ($p<0.05$).

Conclusion: AHF patients with CRD have worse prognosis with three-times higher in-hospital mortality despite better left ventricular ejection fraction. They suffer more from comorbidities and get less of the recommended drugs. Frequent monitoring of routine parameters such serum creatinine allows earlier usage of therapeutic strategies with renoprotective potential what can improve prognosis in these high-risk patients.

SURGERY

P1857

Beneficial effects of preoperative administration of levosimendan in patients with left ventricular dysfunction undergoing elective cardiac surgery

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Background and Aims: preoperative left ventricular systolic dysfunction (LVSD) is an independent risk factor for postoperative low cardiac output syndrome (LCOS) development and mortality in cardiac surgery. Levosimendan is a drug with inotropic, vasodilatory and organ-protective properties due to a triple mechanism of action: 1) increases calcium sensitivity of troponin C without increasing calcium release of into the cytosol or modify the levels of intracellular cyclic AMP; 2) activates vascular smooth muscle cells sarcolemmal ATP sensitive K⁺ channels in, and 3) activates cardiomyocyte mitochondrial ATP sensitive K⁺ channels. We study the effects of preoperative levosimendan administration (PLA) in patients with LVSD undergoing elective cardiac surgery on LCOS development and other secondary end-points.

Methods: study of a cohort of patients with LVEF $\leq 45\%$ undergoing elective cardiac surgery from January 2006 to December 2013. Patients who received PLA (infusion of 0.05 to 0.2 mcg / kg / min for 24 hours without loading dose) - (Group I) within 72 hours prior to surgery were compared with those who did not receive it (Group II). Demographic, clinical, hemodynamic, operative characteristics and postoperative outcome were analyzed.

Results: 146 patients, 80% male; mean age 66 ± 9.7 years; LVEF $36 \pm 5\%$; and Euroscore 8.7 ± 8.6 were studied. Group I included 13 and Group II 123 patients.

Among both groups there were no significant differences in age, sex, cardiovascular risk factors, preoperative functional class, LVEF and operative characteristics. Group I patients had a lower incidence of LCOS (7.7 vs 43.6%; $p=0.012$); higher cardiac index (3.2 ± 0.7 vs 2.7 ± 0.8 L/min/m²; $p=0.02$); lower troponin I peak levels of (1.9 ± 1.8 ng/mL vs 10.4 ± 32 ; $p=0.02$); lower creatinine peak levels (0.98 ± 0.4 vs 1.3 ± 0.7 mg/dL; $p=0.03$ and shorter mechanical ventilation (4 [2-7] vs 6 [5-19] h; $p=0.007$). They needed lower maximum dose of dobutamine (1.4 ± 1.9 vs 4.7 ± 5.3 mcg/kg/min; $p=0.016$). De novo atrial fibrillation incidence was similar in both groups (30 vs 32%; $p=NS$). Group I patients had a lower but not significantly postoperative hospital stay (7 [6-10] vs 9 [7-17] days; $P=0.08$). There was no differences in mortality at 30 days (0 vs 7.5%; $P=NS$). After adjusting for preoperative LVEF and NYHA, patients in Group I showed less risk of LCOS development (OR: 0.11; 95% CI [0.01-0.85]; $p=0.005$).

Conclusions: preoperative administration of Levosimendan reduces the incidence of LCOS and exerts beneficial effects on myocardial and renal preservation in high-risk patients with LVSD undergoing elective cardiac surgery.

P1858

Surgical ventricular restoration in cases of ischemic dilated cardiomyopathy: outcome at 13 years in 61 patients

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Objective: Aim of the study was to analyze the long term results (13 years) after left ventricular restoration (SVR) in cases dilated ischemic cardiomyopathy.

Methods: Between March 2003 and September, 2014, 61 patients affected by ischemic dilated cardiomyopathy received a SVR at our unit, along with surgical myocardial revascularization. The STICH trial criteria have been used as indication to SVR. The patients underwent SVR using a typical DOR operation, or, more recently adopting a different surgical technique, with the aim of reshaping the left ventricle also at the dilated equatorial level. A reduction of left ventricular end systolic volume greater than 50% was obtained in the majority of cases.

Results: Total early-in hospital mortality was 3,4%, (0% in the last 31 cases). Reduction of LVED diameter, improvement of EF and NYHA class after surgery and at last follow-up were statistically significant ($p < 0,05$). Residual mitral incompetence, at discharge was absent in 34 patients (59,6%), mild in 2 (3,5%). Late mortality was 44% (25 pts) (mean follow up time: 7,6 yrs), with a cardiac mortality of 20%. Freedom from rehospitalization for heart failure was 87% for the entire group of pts.

Conclusions: Patients affected by ischemic dilative cardiomyopathy, in our experience, have a satisfactory short and intermediate-time outcome after SVR, particularly if accomplished by using a surgical protocol addressing both the volume and the shape of the left ventricle.

P1859

Prognostic value of magnetic resonance imaging for the course of early postoperative period in patients with ischemic cardiomyopathy: choice of a criterion

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Objective: to assess prognostic value of magnetic resonance imaging (MRI) data for the course of the period after cardiac surgery in patients with ischemic cardiomyopathy (ICMP).

Methods: Forty three patients with ICMP were enrolled into the study. Inclusion criteria were as follows: multivessel disease of coronary arteries, end-systolic volume index (ISVI) >60 ml/m², left ventricular ejection fraction (LV EF) $<40\%$. Mean age of the patients was 58.6 ± 6.5 years. All the patients underwent clinical examination and cardiac MRI with contrast enhancement (CE-MRI). End-diastolic volume (EDV), end-systolic volume (ESV), LV EF, area of affected (akinetic) LV myocardium, viable mass of LV myocardium as the mass of LV myocardium not accumulating paramagnetic contrast agent were calculated semi-automatically by the data of CE-MRI. The viable myocardial mass index (lvmm) calculated as "viable myocardial mass of LV/body surface (g/m²)" was offered for the assessment of the outcomes in the early postoperative period. Surgical treatment included reconstruction of the left ventricle, CABG and mitral valve plasty if necessary (the principle of "triple V") in conditions of cardiopulmonary bypass and cardioplegia.

Results: In the postoperative period the patients were divided into 2 groups by their qualitative values. Group 1 (n=31) were the patients with uneventful course of the postoperative period. They did not require additional support of their cardiac function and were discharged from the hospital without complications after the surgery.

Group 2 (n=12) consisted of the patients who demanded intraaortic balloon counterpulsation due to progressing heart failure in the early postoperative period. These patients stayed at the hospital for further prolonged treatment.

Preoperative values of lvmm were significantly higher in Group 1, comprising up to 83.1 ± 21.9 g/m² than in Group 2 where lvmm was 69.52 ± 14.1 g/m² ($\chi^2 = 7.260$; $p < 0.05$). The value of lvmm equal to 70 g/m² was a threshold value dividing the patients into the groups according to ROC analysis.

Conclusions: The value of viable myocardial mass of LV is significant for the prognosis of the early postoperative outcomes in patients with ICMP. In case when preoperative lvmm is less than 70 g/m² progressing heart failure is possible in the early postoperative period.

P1860

One step direct subendocardial implant of autologous stem cells during left ventricular restoration for ischemic heart failure

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Objectives: Aim of the study was to test the benefit of a one step protocol of direct subendocardial implant of autologous stem cells during left ventricular restoration (SVR), in cases of ischemic cardiomyopathy

Methods: Between March, 2007 and March, 2013, 30 patients (PTS) affected by ischemic cardiomyopathy and with homogeneous pre-operative characteristics, received a SVR at our unit. Within this population, 19 pts were randomly assigned to receive cell therapy in association with SVR (group A). In these patients a suspension of 5 to 8cc of mononuclear cells derived from the sternal bone marrow, and processed in a sterile mini-lab, was injected by direct visualization, into the infarcted areas of the myocardium, before the left ventricular reconstruction. Patients were evaluated by accurate Echocardiograms before and during surgery, and at six months and one year follow up. In 10 out of 19 pts a PET-Scan analysis was obtained before operation and at last follow up.

Results: Early mortality was 0% for the entire population. Reduction of LVED diameter, improvement of EF and NYHA class, reduction of infarcted area at PET-SCAN were more significant in the group of patient receiving stem cells therapy ($p < 0,05$). Late mortality at 5 yrs (mean FU time 5,4 years) was similar in the two groups (10,7% versus 14,2%). Freedom from re-hospitalization was 91% in group A, 79% in group B.

Conclusions: Patients affected by ischemic cardiomyopathy seem to have a better short and intermediate outcome after SVR when a protocol of one-step implant of autologous stem cell therapy is associated. A direct vision method of subendocardial implant might be more effective for myocardial regeneration when compared to other systems of stem cells delivery.

P1861

Does reduced preoperative ejection fraction increase nursing scores for patients in postoperative intensive care unit?

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Purpose: The Nursing Activities Score (NAS) and the Nine Equivalent of Nursing Manpower Use Score (NEMS) allow predicting the amount of work in a Cardiac Surgery Intensive Care Unit (CSICU). The aim of the study was to assess nursing workload in CSICU in patients with reduced preoperative ejection fraction (EF).

Methods: The study included 471 consecutive patients with the mean age of 66.12 ± 8.34 years, operated at our Clinic. Coronary, valvular and combined surgery was performed in 185, 156 and 130 patients, respectively. The NAS and NEMS scores were analyzed according to preoperative EF. Patients were divided into 2 groups: group I - EF $\geq 50\%$ and group II - EF $< 50\%$.

Results: Correlation between NAS and NEMS was high ($r = 0.924$; $p < 0.0005$). The mean NAS in group I was 176 (175-206) and in group II it was 178 (176-263). No significant difference was observed between the groups ($p = 0.018$). The mean NEMS in group I was 76 (64-106) and in group II it was 78 (66-113) with significant difference between the groups ($p = 0.009$). Nursing workload was increased in group II according to NAS ($p = 0.004$) and NEMS ($p = 0.029$). Reduced EF was a predictor of increased nursing workload in group II. There was a higher risk of increased nursing workload in group II (NAS, $p = 0.032$ OR = 1.530 (1.037 - 2.258); NEMS, $p = 0.022$ OR = 1.582 (1.067 - 2.346). Reduced preoperative EF increases the risk of higher nursing workload for 54.0% and 58.2%, according to NAS and NEMS respectively.

Conclusion: The NAS and NEMS correlate highly and both confirm increased nursing workload in CSICU in patients with reduced preoperative EF.

P1862**Risk factors associated with early mortality in patients with left ventricular systolic dysfunction undergoing cardiac surgery**

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Aim: To know perioperative factors associated with mortality within the first 30 days after hospital discharge in patients with left ventricular systolic dysfunction (EF≤45%) undergoing cardiac surgery with cardiopulmonary bypass.

Methods: Study of a cohort of patients with LVEF≤45% undergoing cardiac surgery from January 2006 to December 2013. Demographic, clinical, hemodynamic, operative characteristics and 30 days follow-up were analyzed through clinical record and phone call. Low Cardiac Output Syndrome (LCOS) was defined according to guidelines, and preoperative clinical status was defined according to Euroscore.

Results: Of the 194 patients studied, 25 (12.9%) died within the first 30 days after hospital discharge. These patients were older 70 ± 10 vs 65 ± 9.6 (P = 0.019), had high EuroSCORE 33 ± 25 vs 10.3 ± 11.6 (P < 0.001), higher preoperative troponin I 6.8 (1.7 to 39.6) vs 0.7 (0.08 to 2.9) (P = 0.005), poor functional class-NYHA IV- 15 (60%) vs 26 (15.5%) (P < 0.001), preoperative critical status 11 (44%) vs 6 (3.6%) (P < 0.0001), lower preoperative beta-blockade use in ischemic heart disease 14 (36.4%) vs 90 (69.8%) (P = 0.002), combined surgery 7 (28%) vs 21 (12.4%) and another surgery in 4 (16%) vs. 3 (1.8%) P < 0.001, a longer CPB 127 ± 75 vs 95 ± 47 min (P = 0.047), higher dose of dobutamine (DB) 13 (9-24) vs 3.2 (0 to 5.9) and noradrenaline (NA) 1.6 (0.43 to 2.33) vs 0 (0 to 0.37) mcg/kg/min (P < 0.001, both), longer use of DB 23 (6-72) vs 12 (0-44) hours and NA 61 (15-84) vs 0 (0-42) (P < 0.001, both), increased rate of low cardiac output 22 (88%) vs 78 (46%) (P < 0.001), higher levels of postoperative creatinine (Cr) (P < 0.001), need for dialysis techniques 4 (16%) vs 7 (4.1%) (P = 0.017). Higher peak levels of Cr 1.7 (1.2-2.1) vs 1 (0.9-1.5) mg/dL, CK-NAK 952 (540-2111) vs 506 (318-805) IU/L, CK-MB 95 (67-190) vs 41 (29-63) IU/L (P < 0.001), Troponin I 15 (9.1 to 40.5) vs 4.4 (2.4 to 8.1) ng/mL, all of them (P < 0.001), higher frequency of postoperative AMI 8 (36%) vs 1 (0.6%) (P < 0.001) and time of mechanical ventilation 40 (7-93) vs 6 (4-18) hours (P = 0.001).

Age with OR: 1.08 (95% CI 1.01 to 1.15) P = 0.003; the type of surgery P = 0.017; the use of beta-blockade OR: 0.26 (95% CI 0.08 to 0.78) P = 0.013; and the presence of postoperative low cardiac output OR: 5.68 (IC95: 1.44 to 22.4) P = 0.004, were all independently associated with higher mortality.

Conclusions: An older age, a more complex surgery and the presence of postoperative low cardiac output were independently associated with increased mortality at 30 days, while the use of beta-blockade regardless of the disease was associated with lower mortality.

P1863**Relationship between preoperative functional status and postoperative low cardiac output with long-term mortality in patients with left ventricular systolic dysfunction undergoing cardiac surgery**

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Aim: To know perioperative factors associated with long-term mortality in patients with left ventricular systolic dysfunction (EF≤45%) undergoing CPB.

Methods: Study of a cohort of patients with LVEF ≤ 45% undergoing cardiac surgery from January 2006 to December 2013. Demographic, clinical, hemodynamic, operative characteristics and postoperative outcomes were analyzed. Low Cardiac Output Syndrome (LCOS) was defined according to guidelines and preoperative clinical status was defined according to Euroscore.

Results: 194 patients were included. Mean age was 64 ± 10 and 81% were male. Mean Euroscore was 13 ± 16 and LVEF was 36 ± 6%. CABG surgery represented 112 (57.7%) of the procedures, valvular surgery 47 (24.2%), 28 (14.4%) patients had mixed procedure, and 7 (3.6%) other cardiac surgery. 18 (9.3%) patients had a redo-surgery. Preoperative NYHA class were III-IV in 90 (46.4%) patients and 17 (8.8%) of them were in perioperative critical situation (Euroscore...). Overall mortality was 33% (64 patients) and factors associated with poor outcomes were age 69 ± 8 vs 64 ± 10 (P < 0.001); high Euroscore 11.2 (4.5-22.5) vs 6.4 (2.6-12.5), P = 0.002; combined cardiac surgery 12 (19%) vs 16 (12%) and other cardiac surgery 5 (7.8%) vs 2 (1.5%), P = 0.04; high NYHA P = 0.009; critical perioperative status 11 (17%) vs 6 (4.6%), P = 0.004; worsening of renal function with creatinine 1.3 (1-1.7) vs 1 (0.9-1.4), P = 0.002; longer period of mechanical ventilation 8.5 (6-58) vs 6 (4-18), P = 0.003; and a high degree of LCOS 41 (64%) vs 59 (45%), P = 0.014.

Median follow-up was 25 (0.2 to 62) months. Patients who presented LCOS had a lower cumulative survival (Mantel-Cox $\chi^2 = 14$, P < 0.001). Median survival in class IV NYHA patients without LCOS was 45 months vs 12 months in patients with LCOS. Valvular and coronary surgery (P = 0.005), NYHA functional class (P < 0.001) and the interaction between LCOS and NYHA (P = 0.01) were factors associated with higher

long-term mortality in the Cox regression model, after adjusted for age, EuroSCORE, type of surgery, NYHA and LCOS

Conclusions: A complicated postoperative period, specially with the presence of LCOS determines, in patients with left ventricular systolic dysfunction (EF ≤ 45%) and preoperative worse functional class, higher long-term mortality.

P1864**Short- and intermediate outcomes of surgery for tricuspid regurgitation in a tertiary care center**

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Purpose: There is little data available for a regional Tunisian center of cardiology on the outcomes of surgical treatment for severe tricuspid regurgitation (TR). The aim of this study was to analyze clinical and echocardiographic outcomes in a series of patients who received surgical treatment for severe tricuspid regurgitation (TR) and to compare outcomes according to the operative approach to valve repair.

Methods: This is a retrospective study including 81 consecutive patients with severe tricuspid regurgitation undergoing valve surgery between 1996 and 2013.

Results: A total of 43 (53.1%) conventional suture plasty, 32 (39.5%) ring annuloplasties and 3 (3.7%) tricuspid commissurotomy were performed. Perioperative mortality was 1.2%. During clinical follow-up, only nine patients (11.1%) presented iterative heart failure signs. NYHA class III/IV symptoms were reported in 18.7% of patients that underwent ring annuloplasty vs. 20.9% in patients who underwent suture plasty and so there were no statistical significance (p = 0.06). Total mortality after follow-up was 4%. The emergence of new severe tricuspid regurgitation was registered in 19 cases (23.4%). Post-operative severe regurgitation was significantly associated with the technical tricuspid valve repair (p = 0.01) but there was no significant association with the type of regurgitation (functional or organic TR; p = 0.43). No significant differences in perioperative or total mortality were found between the different methods used for repair tricuspid valve (p = 0.33).

Conclusions: Ringless repair was significantly associated with recurrence of severe tricuspid regurgitation.

No significant differences in perioperative or total mortality were found between the different methods used for repair tricuspid valve.

P1865**Mid-term clinical and echocardiographic results of de Vega tricuspid annuloplasty for repair of tricuspid regurgitation in a tertiary care center**

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Purpose: There is an ongoing debate whether the tricuspid valve (TV) should be repaired with a suture annuloplasty or a prosthetic ring.

The aim of this study was to analyze mid-term clinical and echocardiographic results of De Vega tricuspid annuloplasty.

Methods: Forty-three patients underwent a De Vega tricuspid annuloplasty for tricuspid regurgitation (TR) as part of the cardiac surgical procedure. Follow-up information was obtained for 40 patients, with a mean follow-up time of 2 ± 1.2 years. Analysis is based on Doppler echocardiographic evaluation. Survival and development of recurrent TR were evaluated. Risk factors for recurrent TR were identified and analyzed by multivariable ordinal longitudinal methods.

Results: Only 2 deaths had occurred at the time of follow-up. Early predischarge echocardiography quantified TR as 1+ in 15 patients (37.5%), 2+ in 13 patients (32.5%), 3+ in only 1 patient (2.5%) and 4+ in 3 patients (7.5%). The mean TR grade decreased from 3 ± 0.7 preoperatively to 1 ± 1.2 on predischarge echocardiography (P < 0.01). During follow-up, the most recent echocardiogram showed TR was 1+ in 30% of patients, 2+ in 25% of patients, 3+ in 12.5% of patients, and 4+ in 15% of patients, with a small increase in mean TR compared with predischarge echocardiography. Risk factor analysis revealed that higher preoperative regurgitation grade, higher systolic pulmonary arterial pressure (sPAP), and preoperative New York Heart Association (NYHA) grade IV were independent predictors of recurrent TR.

Conclusions: A De Vega suture annuloplasty was effective in eliminating TR and producing right ventricular (RV) reverse remodeling at follow-up, although TR tends to increase with time.

P1866**Current profile of infectious endocarditis: experience of a tunisian center**

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Background: Since the first modern clinical description of infectious endocarditis (IE) by William Osler, the profile of the disease has continuously evolved. It remains a serious disease whose incidence does not seem to decrease.

Objective: The aim of the present study was to update epidemiological, clinical, bacteriological, echographic, therapeutic and outcome characteristics of IE in order to identify changes compared to the 80s in Tunisia in one hand and the industrialized countries on the other.

Methods: This is a retrospective study over a period of 20 years about 50 patients hospitalized for IE in a department of Cardiology.

Results: Our population was predominantly young at diagnosis with a mean age of 43 years and most of them were male (sex ratio: 1.6). IE developed on rheumatic valvular disease in 6% of cases, on cardiac prosthesis in 28% of cases and on pacemaker in one patient. The most frequently origin of contamination was dental (38%). Blood cultures were positive in 30% of cases isolating staphylococcus (12%), streptococcus (10%) and BGN (8%). Ultra-sound examination revealed vegetation in 44 cases, valvular perforation in 3 cases, out of a rope in 6 patients and an annular abscess in 4 cases. Sixty percent of patients underwent surgical treatment with an average delay of 28 days. Vegetectomy was performed in one patient. A holder of pacemaker patient underwent surgical removal of the catheter. Heart failure was the most common cardiac complication (50%). The overall mortality was 24% and fatal heart failure and kidney failure were the two predictive factors of death.

Conclusion: This work is an update about the modification of microbiological profile secondary to the increase of implantation of foreign material and of nosocomial infections. It puts emphasis on the unchanged incidence and prognosis of the disease despite the marked decrease of rheumatic valvular disease in our country.

P1867**The outcomes of heart transplantation in a University: The largest experience of Turkey**

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Purpose: Orthotopic heart transplantation is still the gold standard and definitive therapy for end-stage heart failure. The first heart transplant (HT) was performed in 1968 in Turkey. In this paper we present the data of a single center that has become the leading HT program in our country.

Methods: Between February 1998 and October 2014, 221 patients of whom 193 were adults, underwent heart transplantation with the biatrial cuff technique. Median age was 46 (18-65) and 76% of them were male. The etiology was dilated cardiomyopathy in 46% and ischemic in 26%. Two patients had re-transplantation. Fifty patients (26%) had ventricular assist devices before HT. All patients had a combination of calcineurin inhibitor, steroid, and MMF/azathiopirin for immunosuppression. Myocardial biopsy for the detection of rejection was performed as suggested by ISHLT. Routine coronary angiography was performed for the detection of cardiac allograft vasculopathy.

Results: Median follow-up time was In-hospital mortality was found 20% and main causes were primary graft failure and infection. One-year survival was 73% and risk factors for death at first year were infection and right ventricular failure. Mean donor age was 30.4 years and 78% were male. Eleven patients (5.7%) needed permanent pacemaker due to bradyarrhythmia. Rejection rate was 54% in first year postoperatively. Mean donor age was 29.11 ± 11 and 75% was male.

Conclusion: Since 1998 our center performs heart transplantation. Approximately twenty procedures were performed annually during the last ten years. Our results give hope for the continuing transplantation program in developing country such as Turkey.

P1868**Peak VO2 and physical health predict survival after heart transplantation**

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Purpose: Does physical capacity predict survival in heart transplant (HTx) recipients?

Method: This retrospective study investigated two different HTx populations regarding predictors for long-term survival. Cohort1 includes patients who completed a VO2peak test during their annual follow-up between 1990 and 2003. Cohort2 includes patients who completed a SF-35 v1 questionnaire between 1998 and 2000. Background information and other central variables were collected from our center's HTx-database.

Results: Cohort 1; n = 132, Mean age: 51(12) years, Men: 92%, median time after

HTx: 2(4) years, Mean VO2peak: 19,9(5,3) ml/kg/min, Mean years under observation: 15(6). Cohort2; n = 133, Mean age: 54(11) years, Men: 78%, Median time after HTx: 5(6) years, SF-36 Median Physical Component Sumscore (PCS) 90(30), Mean years under observation: 15(5). Predictive variables were analyzed using cox regression based on p-values < 0.2 from univariate regression and clinical aspects. The two best predictive models (adjusted for gender) were: Cohort 1; Age (p = 0.005), VO2peak (p = 0.016), Ischemic time (p = 0.021). Cohort 2: Age (p < 0.001), years after HTx (p < 0.001), PCS (p = 0.003), Smoking (p = 0.003), and cardiovascular disease (p = 0.079). Other univariate significant predictors that did not reach statistical significance in multivariate regression were: Etiology of HTx, donor age, BMI, ejection fraction, cardiac output, blood pressure, creatinine, Hgb and SF-36 Mental Component Sumscore. Kaplan-Meier analysis showed that groups divided by median VO2peak and PCS had significantly different survival-time (Figure 1A and B).

Conclusion: VO2peak level and self-reported physical health are both strong predictors for survival in HTx recipients.

VO2peak is a crucial measurement, and should be more frequently used after HTx.

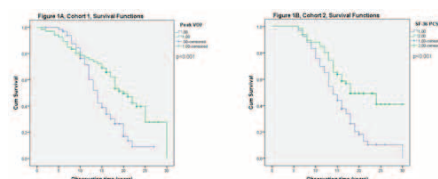


Figure 1A: Peak VO2, and 1B: SF-36 PCS

P1869**Cardiac retransplantation in our university clinic**

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Background: Cardiac retransplantation is one of the only valid option in transplant patients with graft vasculopathy. The experience gained during the last years has made the survival of cardiac retransplantation similar to that obtained with heart transplant. We present our experience in cardiac retransplantation

Methods: Retrospective study of all cardiac retransplantation at our center was made. Data of recipients and donors, surgical aspects and results of diagnostic tests were collected. Survival of transplanted and retransplanted patients was compared. In retransplanted group, survival of the first and second graft was compared and survival according to the indication. Statistical analysis was performed using SPSS V21.

Results: From a total of 279 transplants, 14 retransplants (5%), and two third transplants (0.7%) were studied. The main indication was graft vasculopathy (71.4%). The mean ischemic time was 210 ± 46 minutes. The operative mortality was 14.3% and the latter 35.7%. Median survival for cardiac transplantation was 125 months (144-166 months) and for retransplantation 107 months (74-140 months) not being the difference statistically significant (p = 0.079). There were no statistically significant differences when comparing the survival of the first and second graft in retransplants (median graft first 87 months (38-136) vs 74 months (49-99) in the second; p = 0.851).

Conclusion: Cardiac retransplantation is a valid alternative in selected patients with severe dysfunction of the graft secondary to graft vasculopathy.

P1870**Mortality after 20 years of heart transplantation**

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Purpose: the number of heart transplant (HTx) recipients exceeding 20 years of follow-up is rising. However, little is known about their mortality and causes of death.

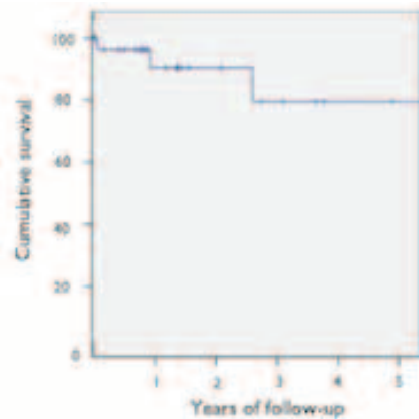
Methods: Clinical records of patients transplanted between 1984 and 1992 were analyzed.

Results: A total of 39 patients who survived >20 years were included (mean age at HTx 35 ± 13.6 years, 84% male) and were compared to the 640 patients in our series who survived from 1 to 20 years. During a median follow-up of 30 months, 6 of the 39 recipients with very long survival died, which implies an overall survival of 84% and an average annual mortality of 6%. (See figure). Only 1 patient was lost to follow-up. When compared with annual mortality rate of HTx recipients with

follow-up between 1 and 20 years (average 3.5%), survival of long-term survivors, the difference was not statistically significant ($p=0.16$).

Of the deaths, 3 were due to infectious complications (pneumonia, septic shock due to peritonitis secondary to colon perforation, and sepsis of unknown origin), 2 were caused by malignancies (lung and tongue cancer), and 1 was due to heart failure associated with allograft vasculopathy.

Conclusions: Mortality 20 years after HTx showed a trend to higher incidence when compared to earlier post HTx period, although the difference did not reach statistical significance in our series. In addition to typical causes of death in the late post-HTx period, such as malignancy and allograft vasculopathy, infection continues to be a major cause of death in these very long-term survivors. Taking into account the very low incidence of acute rejection in this very late post HTx period, substantial reduction in immunosuppression should be considered.



P1871

Beta blockers and ivabradine in heart transplant recipients - is there any impact on survival?

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Purpose: Heart rate (HR) reduction therapy is not routinely recommended in heart transplant (HTx) pts, however it may be prescribed in those with symptoms due to increased HR. Beside beta blockers (BB), ivabradine (Iva) has also been considered in such pts, although without studies comparing outcomes of these therapies. Thus we sought to explore outcomes of pts on BB or Iva therapy as opposed to HTx recipients without HR reduction therapy (non-Rx).

Methods: We retrospectively studied 105 consecutive HTx recipients from our institution between 2001 and 2014 with a minimal 1 mo. survival after HTx. Patients were divided in 2 groups based on therapy lasting ≥ 3 months: BB group (30 pts) and Iva group (11 pts). Outcomes of overall survival, time to vasculopathy and time to graft rejection (requiring treatment) were analyzed for each group and compared to non-Rx pts. Kaplan Meier survival/event curves and χ^2 test were used for analysis.

Results: Median time of BB therapy was 29 months (range 140), and 8 months for Iva therapy (range 18). Although there was a trend towards a better survival, there was no statistically significant benefit of BB versus non-Rx group ($p=0.163$), while this trend was not present in the Iva group (Figure 1). No significant trends were observed for outcomes of time to vasculopathy and time to graft rejection in both studied groups. Furthermore, occurrence of vasculopathy or graft rejection was not significantly different between the BB group and non-Rx pts ($p=0.27$, $p=0.79$), nor between the Iva group and non-Rx pts ($p=0.26$, $p=0.77$).

Conclusion: In this study, we observed a tendency to longer survival in HTx recipients on BB therapy, but no influence of BB therapy on vasculopathy or graft rejection. Conversely, we proved no influence of Iva on the studied outcomes of HTx pts.

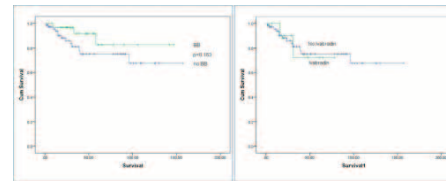


Figure 1

P1872

Impact of invasive treatment in survival of transplanted patients with cardiac allograft vasculopathy

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Background: cardiac allograft vasculopathy (CAV) continues to limit long-term success of cardiac transplantation. It is unclear whether invasive treatment improves survival. We aimed to compare the prognosis of patients with CAV in our institution regarding treatment choice.

Methods: of 202 patients, 58 were diagnosed with CAV. Severity was graded using the International Heart and Lung Transplantation (ISHLT) classification.

Results: patients that developed CAV did not differ in terms of age, sex, classical cardiovascular risk factors, CMV infections or acute rejection episodes. Mean time to diagnosis was 56,63 months ($\pm 37,8$). Higher degree of CAV was related to a decreased survival ($p=0,045$). Of the 58 patients, 17 (29,3%) were treated invasively (15 PCI, 2 retransplant). Survival of patients treated invasively did not differ to patients treated medically, but showed a tendency to a worse survival that was not statistically significant ($p=0,218$) (Figure1).

Conclusion: worsening severity of CAV was related to reduced long-term survival. In our series, invasive treatment of CAV was not associated with an improvement in survival, and in fact showed a tendency towards reducing it.

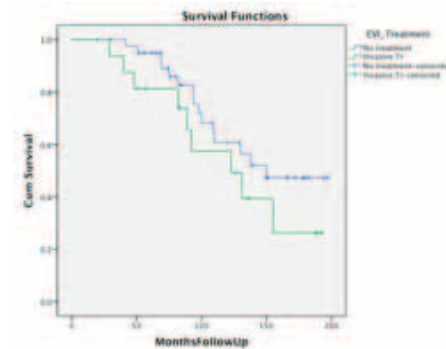


Figure 1

P1873

Gene expression analysis for the predictive diagnosis of heart rejection

Hippocrates

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Purpose: We studied endomyocardial biopsy (EMB) samples of cardiac transplanted patients (CTP) with rejection (ISHLT grade $\geq 2R$) in the first year after heart transplantation (HT), which histopathological data were available. We analyzed genes included in the AlloMap Molecular Expression Test (AlloMap), and other genes involved in heart rejection and immune response, in order to evaluate possible changes in gene expression (GE) levels indicative of a rejection status and therefore correlated with the biopsy results. The purpose of the study is to generate a gene expression molecular test that could be used on PB to predict rejection.

Methods: 26 patient with grade of rejection $\geq 2R$ and 16 with grade of rejection 0R were studied for the retrospective study. Total RNA was purified from paraffin-embedded samples (PES) and reverse transcribed in cDNA that was amplified using real-time PCR assays by relative quantification method ($2^{-\Delta\Delta CT}$). All samples were normalized to the housekeeping gene GAPDH and afterwards, samples with rejection were normalized to samples without rejection (ISHLT grade 0R).

Results: The results of the GE analysis showed that, for the majority of analyzed genes, most of $\geq 2R$ patients had increased GE levels compared to patients without rejection. In particular, among genes considered by AlloMap, ITGA4, PDCD1 SEMA7A, RHOU, PF4, C6orf25 and IL1R2 resulted in agree with AlloMap results (ITGA4, PDCD1 SEMA7A and RHOU resulted upregulated in patients $\geq 2R$ compared with patients 0R and PF4, C6orf25 and IL1R2 downregulated). WDR40A, MARCH8, ITGAM and FLT3 resulted not agree with the results obtained by AlloMap (WDR40A and MARCH8 resulted downregulated in patients 2R compared with patients 0R and ITGAM and FLT3 upregulated). All the other analyzed genes: C3, CCL2, CCL3, CCL5, CCR5, CD28, CD3E, CD4, CD40, CD68, CD8A, CXCL10, CXCL11, FAS, ICAM1, IL2RA, TGFB1, resulted upregulated in patients $\geq 2R$ compared with patients 0R.

Conclusion: GE analysis, as demonstrated by our data, provides useful diagnostic information about the rejection status of patients. This analysis, thus, in certain clinical situations could reduce the need of EMB for the diagnosis of heart rejection, even if GE profile should be evaluated together with additional clinical data. However, we will analyze, prospectively, PB and EMB samples of the same CPT in order to further validate the study and understand if the molecular test developed can be used for predictive diagnosis of heart rejection.

P1874

Quality of life and complications after 20 years of heart transplantation

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Purpose: The number of heart transplant (HTx) recipients exceeding 20 years of follow-up is increasing. However, little is known about their functional status and comorbidities.

Methods: Clinical records of HTx patients between 1984 and 1992 were analyzed.

Results: A total of 39 patients who survived 20 years were included (mean age 33 ± 13.6 , 84% male). During a mean of 30 months 6 recipients died. Most (82%) of the 33 survivors were completely autonomous for daily activities, while 6% were partially dependent and 12% completely dependent. Functional limitations were due to osteomuscular conditions in 50% and vascular and neurologic causes in the rest.

Comorbidities were frequent: Most patients (84%) had chronic kidney disease (CKD); 36% had stage 2 CKD, 48% had stage 3, and 15% stage 4. None has required dialysis. Cardiovascular risk factors were frequent: 94% had hypertension, 87% had hyperlipidemia and 15% had diabetes mellitus.

Infectious complications: 8 patients (20%) had significant bacterial infections, chiefly respiratory and urinary and 10 (26%) had major viral infections (4 due to cytomegalovirus, 1 herpetic encephalitis, 3 cases of chicken pox, 1 hepatitis B infection and 2 hepatitis C infection). In all, 38% of patients had some kind of malignancy, mainly skin tumors (60%), followed by solid-organ neoplasms (tongue, lung and liver), and 1 hematologic cancer.

Cardiac complications: Coronary angiography done every 3 years revealed 35 patients (89%) with some degree of allograft vasculopathy, although most (72%) without significant lesions. Intravascular ultrasound showed Stanford class II lesions in 27%, class III in 11% and class IV in 58%. Only 3 patients required percutaneous revascularization and 2 had systolic dysfunction. Nine patients had significant arrhythmias. One needed ablation for ventricular tachycardia and 8 (20%) a pacemaker for symptomatic bradyarrhythmias.

Regarding immunosuppression, 1 or more of the initial 3 medications had been discontinued in most patients and 76% were receiving 2 drugs. The most common combinations were cyclosporin-steroids (13 patients, 43%), cyclosporin-azathioprine (5 patients, 16%), cyclosporin-mycophenolate mofetil (3 patients, 10%), cyclosporin-everolimus (2 patients, 6%) and everolimus-prednisone (3 patients, 10%).

Conclusions: After more than two decades with the same graft, HTx recipients display frequent complications due to chronic immunosuppression and graft disease. Nevertheless, quality of life of these patients seems satisfactory, as 82% were independent for daily activities.

P1875

The utility of an extended valganciclovir prophylaxis in heart transplant patients. EPICA study

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Purpose: To analyze the efficacy of an extended valganciclovir prophylaxis (1 year) compared to a short valganciclovir prophylaxis (3 months) after heart transplantation (HTx) to prevent CMV infection and its impact over other indirect effects.

Methods: 46 consecutive patients with one-year post-transplant survival were included in the extended valganciclovir prophylaxis and 38 patients with the same survival in the short valganciclovir prophylaxis group. In both groups valganciclovir was given immediately after HTx, at a dose of 900 mg/day unless renal dysfunction (half dose) and independently of the serological relation between donor/receptor. Both groups received a calcineurin inhibitor as immunosuppressant medication, plus mycophenolate mofetil and steroids.

CMV infection was considered when there was an increase in CMV viral load over the reference value (<400 copies). Rejection was considered when the patient needed steroids in bolus or a significant change in the basal immunosuppression. Infection was considered when the patient had to be admitted due to this condition. Coronary allograft vasculopathy (CAV) was defined when the one year IVUS showed a proliferation >1 mm in one point or >0.5 mm in 180° also in a single point.

Results: Table 1.

Direct effects: In the group treated with valganciclovir there was a lower incidence of CMV infection (4.7 vs. 27%; $p = 0.001$).

Indirect effects: Patients in the extended group had fewer rejections (0.77 ± 0.98 vs. 1.29 ± 0.58 ; $p = 0.046$). There was a trend to fewer cases of CAV in the extended group (29.4% vs. 83%, $p = 0.054$).

Conclusion: an extended valganciclovir prophylaxis during one year is associated with fewer rejection rates, fewer CMV infections and a trend to fewer development of CAV.

		Valganciclovir 1 year (n: 47)	Valganciclovir 3 months (n: 38)	p
Before HTx	Age (years)	53±9	21±12	0.90
	Gender (male, %)	85	73	0.19
	Creatinine (mg/dL)	1.05±0.30	1.12±0.37	0.45
	Serology CMV (%)			
	D+/R+	46	31.7	0.405
	D+/R-	15.9	6.3	
After HTx	Creatinine at one year (mg/dL)	1.12±0.37	0.99±0.24	0.09
	Total infections first year	0.55±0.57	0.82±0.77	0.12
	Infección CMV (%)*	4.7	27	0.007
	CAV (%)	59.4	83	0.054
	Number of rejections first year	0.77±0.98	1.29±0.58	0.046

Results

DISEASE MANAGEMENT PROGRAMMES

P1876

Implementation and certification of a heart failure clinical care program in a low middle income country: impact in clinical outcomes after two years

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Purpose: Clinical care programs (CCP) that monitor and optimize care have the potential to improve outcomes, however their real benefits are still controversial. This study aims to evaluate the hypothesis of benefits in clinical outcomes after 2 years of a CCP.

Methods: Prospective study of consecutive patients hospitalized with HF in a Brazilian private cardiovascular center. Two groups were compared based on the time to CCP initiation: the historical group, compounded by patients from the 6 months prior to CCP (group 1) and the intervention group compounded by patients

admitted with diagnosis of HF from July 2012 until June 2014, period when patients and staff were monitored in a daily basis by a case manager nurse and a medical leader which provided educational interventions. The CCP was certified by an international society in October 2012.

Results: In a total of 2,188 patients, the mean age was 69.3 years and 55.8% were male (table). Evidence-based therapies at hospital discharge (ACEI / ARB and beta-blocker in eligible patients) showed no significant change (95.8% pre-CCP and 97.5% post-CCP; $p = 0.12$). The outcomes analyzed in groups 1 and 2, were, respectively: 1) hospital readmissions due to HF within 30 days (13.9% vs 9.1%; $P = 0.008$) 2) length of stay (8.9 days \pm 7.9 vs. 7.9 days \pm 5.6, $P = 0.01$), 3) decompensation of HF by poor adherence (16.8% vs. 10.5%; $P = 0.001$), 4) In-hospital mortality (9% vs 6.9% ; $P = 0.24$).

Conclusions: During the two years of the CCP there was a reduction of one day in the length of stay, and a lower frequency of hospitalizations by poor treatment adherence, and in readmissions in 30 days due to HF.

	Pre-CCP (Historical group)	CCP (Intervention group)
Number of patients	338	1850
Mean age	71 (+- 13.5)	69 (+- 11.2)
Male (%)	55% (CI 95%: 50-60%)	56% (CI 95%: 54-58%)
Mean EF (%)	37% (+- 13.3)	42% (+- 11.1)
Hemodynamic profile C (%)	5.65% (CI95%: 3-8%)	4.2% (CI 95%: 3.4-5.2%)
Ischemic Cardiopathy (%)	48.2% (CI95%: 43 - 53.5%)	58% (CI 95%: 56-60%)
HFpEF (%)	37% (CI95%: 32-42%)	27% (CI 95%: 25-29%)
Cardiorenal Syndrome (%)	35% (CI95%: 30-40%)	33% (CI 95%: 31-35%)
Infection (%)	23%(CI 95%: 19-28%)	22%(CI 95%: 20-24%)

P1877

A multidisciplinary team approach to care transitions for hospitalized heart failure patients reduces hospital readmissions and improves outcomes

Betty Irene Moore Nursing Initiative

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Background: Heart failure (HF) is increasing in prevalence and poses substantial economic burden on healthcare resources in the US and worldwide. A large proportion of costs arise from acute and emergency care. The literature demonstrates that acute hospitalizations for HF exacerbation exact a considerable toll on patients, reducing survival and negatively impacting quality of life.

Purpose: A collaborative, multidisciplinary team approach to create and implement a standardized, evidence-based intervention bundle for HF will reduce 30- and 90-day hospital readmissions and improve patient self-care.

Methods: Our setting is 490 bed tertiary-care medical center with ~450 primary diagnosis HF admissions annually. Using LEAN methodology and under a triad leadership (physician, administrator and nurse), a team comprised of frontline nurses, pharmacists, dietitians, case managers and social workers supported by experts from Quality, Informatics and Analytics formed workgroups. The team assessed current state and designed new interventions based on best practices. These included early identification and risk-assessment of the patient cohort, redesign of patient-friendly education tools and enhanced education for patients/caregivers using teach back, accurate medication reconciliation, follow-up clinic appointments made prior to discharge, and phone follow-up by nurses post discharge. New clinical workflows for physicians, nurses and pharmacists were designed to embed these new processes, and electronic medical record builds facilitated consistency in practice. Our HF Team partnered with community stakeholders (clinics, skilled nursing and home health agencies) and with patients who reviewed interventions and education tools. A team-designed, web-based HF Dashboard, hardwired into the patient electronic medical record and other data sources, provides virtually real-time process and outcome metrics that can be filtered and analyzed in multiple ways. This identifies areas for further improvement and gives feedback on the effectiveness of the interventions.

Results: 30-day readmissions improved from 20% to 11% over 18 months (by 45%) post- implementation of all interventions. 90-day readmissions fell from 31% to 27% (by 13%). Patient responses to survey questions specific to preparedness for self-care improved by 5%.

Conclusions: Multidisciplinary collaboration involving frontline staff, patients and the community results in improved patient transitions from hospital to home. Ready access to metrics including patient feedback permits ongoing refinement of tools and interventions.

P1878

Special features of cardiac rehabilitation programs in patients with systolic dysfunction

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Background and Objectives: despite the benefit of cardiac rehabilitation in patients with systolic heart failure, their referral rate is often insufficient. The particular characteristics of these patients require some degree of individualization in order to achieve the goals. We compared the base-line characteristics of a cohort of patients referred to a cardiac rehabilitation program (CRP), according to their ventricular ejection fraction (EF >35% or ≤35%).

Methods: 921 patients referred to a CRP were studied, EF was determined by an echocardiogram (Simpson method) 1-2 weeks before starting the CRP. 91% of the patients were referred after a recent acute coronary syndrome. Functional capacity was determined in METS with a treadmill exercise test. The patients were classified according to their EF in two groups: patients with EF >35% (n = 749, 81.4%) and patients with EF ≤35% (n = 172, 18.6%). We compared their base-line characteristics in order to determine whether a different kind of intervention was required. Student t-test and Chi-square test were used for continuous and categorical variables respectively.

Results: mean age was 56.9, women were less prevalent in the low EF group (10.5% vs 16.7%, $p = 0.04$). CV risk factors were common in both groups, with a similar distribution. Patients in the low EF group were more likely to have co-morbidities such as chronic obstructive pulmonary disease (7.6% vs 4.2%, $p = 0.02$), renal impairment (6.4% vs 2.7%, $p = 0.01$), atrial fibrillation (6.4% vs 2.8%, $p = 0.05$), or moderate to severe valvulopathies (16% vs 5.3%, $p < 0.001$). As expected, exercise capacity was lower in the low EF group (6,37 \pm 3.0 vs 8,04 \pm 2.4 METS, $p < 0.001$). Patients with low EF were more likely to abandon the program (15,1% vs 10,1%, NS).

Conclusion: patients referred to CRP are mostly coronary disease patients, with a high prevalence of CV risk factors, despite their systolic function. Patients with low EF have more comorbidities and a worse functional status, and therefore require a more individualized intervention.

	EF >35%	EF ≤35%	p
Hypertension	50,1%	51,7%	NS
Diabetes	22,6%	27,6%	NS
Dislipideamia	61,3%	55,2%	NS
Tobacco	53,3%	56,4%	NS

P1879

Hospital admission patterns in the preterminal phase amongst patients with HFREF and HFpEF: experience from a single centre heart failure disease management programme

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Purpose: High risk periods for hospital admission are early after discharge and prior to death (preterminal phase). We examined the hospital admission pattern in patients with heart failure (HF-pEF & HF-rEF) who are managed in a specific disease management programme (DMP), specifically addressing the preterminal phase.

Methods: Patients enrolled in the heart failure DMP at a University Hospital between November 1998 & April 2014 were included in this study. We identified patients who died over this period and examined the all-cause and heart failure admission patterns in the 8 month period prior to death.

Results: 1266 (58.6% male, mean age 72.2yrs) patients were hospitalised for a first heart failure presentation over the study period (410 (32.3%) HFpEF, 856 (67.7%) HFREF). Six hundred and eight patients died following enrolment. Two hundred and eight of these (208/608, 34.2%) were in the HFpEF group and 400 (400/608, 65.8%) in the HFREF group. The all cause admission rates at 6-8, 4-6, 2-4 and 0-2 months before death are shown in table 1. Heart failure readmission accounted for 10% (21/208) of the preterminal admissions (within 2 months of death) in the HFpEF group and for 16.2% (65/400) in the HFREF group.

Conclusions: A peak in hospital admissions occurred in the months prior to death amongst patients enrolled in a heart failure disease management programme. Those

Table 1

Heart failure admission trends in the months prior to death				
Time before death	6 - 8 months	4 - 6 months	2 - 4 months	0 - 2 months
All patients	31/508 (6.1%)	33/540 (6.1%)	56/566 (9.8%)	86/608 (14.2%)
HF-pEF	14/176 (7.9%)	8/187 (4.2%)	18/193 (9.3%)	21/208 (10%)
HF-rEF	17/332 (5.1%)	25/353 (7%)	38/373 (10.1%)	65/400 (16.2%)
Admissions per patient during 8 months before death by admission type Time before death				
Time before death	6 - 8 months (n = 508)	4 - 6 months (n = 540)	2 - 4 months (n = 566)	0 - 2 months (n = 608)
All	86 (16.9%)	87 (16.1%)	155 (27.3%)	274 (45%)
Heart failure	31 (6.1%)	33 (6.1%)	56 (9.8%)	86 (14.2%)
Cardiovascular	0 (0%)	0 (0%)	12 (2.1%)	21 (3.4%)
Non-cardiovascular	55 (10.8%)	54 (10%)	87 (15.3%)	167 (27.4%)

with HFREF have higher rates of preterminal heart failure readmission compared with HFpEF. A significant proportion of preterminal admissions are due to non cardiovascular causes.

P1880

Heart failure management programmes with nurse-based strategies are an important tool to improve outcomes in self-care, quality of life and 6-minute-walk-test in patients with advanced heart fail

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Patients with advanced Heart Failure (HF) have important functional limitations and a poor quality of life. Functional class and quality of life are relevant end-points to improve in HF patients (pts). HF disease-management programmes (HFMP) are recommended in the latest European Guidelines on HF with class I recommendation but it's still not clear which components are more relevant. The purpose of this study was to evaluate the impact of a nurse-based educational intervention on high-risk pts with Chronic HF followed in a HFMP after treatment optimization.

Methods: We included pts admitted to our HF Unit after a HF episode that required hospitalization from March 2011 to December 2014. After discharge and guideline-directed medical therapy optimization, pts and their caregivers were offered a 4-weeks nurse-guided educational intervention (NEI). Pts with no possible self-access to our centre were excluded. Written consent was obtained from every patient. Standardized tests to measure performance in activities of daily living (Barthel Index), cognitive impairment (Pfeiffer's test) and co-morbidity (Charlson Co morbidity Index) were performed. Self-care (The European Heart Failure Self-care Behavior (ESS)), quality of life (Minnesota living with heart failure questionnaire (MQ)) and 6 Minute-Walk-Test (6MWT) were performed and compared pre and 3 months post-NEI. NEI consisted of four weekly consecutive sessions with brochures and audio-visual support that include topics on HF learning (i.e. etiology, decompensation signs and symptoms) and self-care promotion (i.e. healthy eating, ideal weight, benefits of regular exercise).

Results: From 684 patients visited in our HFU during the inclusion period, 225 patients (33%) were included in our NEI. 74% were men, mean age was nearly 70 years (69 ± 10,2). Mean Left Ventricle Ejection Fraction was 31 ± 8%, 91% of pts were on NYHA class II-III and they presented a moderate degree of co-morbidities (mean CCI: 5.27 ± 2.27). 95% were on ECA-inhibitors/ARB, 93% on Betablockers and 35% had cardiac devices implanted. Included pts were mostly independent on daily living (Barthel mean score: 98,5 ± 5,8), without significant cognitive impairment (Pfeiffer's test mean score: 0,94 ± 0,52). 3 months after being included in our HFMP our pts showed a statistically significant improvement in self-care (ESS score from 27 ± 9 to 18 ± 5, p < 0,0001), quality of life (MQ mean score reduction: 12, p < 0,0001) and 6MWT (from 377 ± 72 to 392 ± 59 meters, p = 0,001).

Conclusions: Multidisciplinary approach, including nurse-based strategies in a HFMP improved outcomes in self-care, quality of life and 6MWT of our advanced-HF pts

P1881

Beyond beta-blocker and digoxin: heart rate control in heart failure with reduced ejection fraction patients with normal sinus rhythm

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Purpose: Beta-blocker doses are often suboptimal in heart failure management. Co-morbidities such as significant respiratory diseases and hypotension confounded the uses of optimal beta-blocker doses thus resulting in suboptimal heart rate control in the heart failure patients. Ivabradine, shown to improve outcomes in this population, is an agent which could be utilized more in these groups of patients. We therefore wished to assess the heart rate control in our heart failure disease management programme and assess the beta-blocker usage and suitability of ivabradine use in such population.

Method: The database of 2396 alive heart patients attending Heart Failure Unit in our University Hospital were examined to assess for heart rate, sinus rhythm, left ventricular ejection fraction and heart rate controlling agents used. Primary end points are current heart rate and reasons for non-optimization of heart rate. Secondary end points are type of heart rate controlling agent used.

Result: Total of 566 (396 male, 71.4+/-10.2 years) patients with left ventricular ejection fraction ≤ 35% and New York Heart Association classification ≥ II were included in this study. 374 (66.08%) are in sinus rhythm. 503 (88.87%) were on beta-blocker, 152 (26.86%) on digoxin and 53 (9.36%) on ivabradine. 63 (11.13%) patients were not on beta-blocker. Main reasons for non beta-blocker usage are significant respiratory diseases (28.57%), bradycardia (28.57%), hypotension (20.63%) and intolerant (14.29%). 112 (29.95%) of patients had not achieve target heart rate control of ≤ 70 beats per minute, of which 71 had heart rate of 70-79 beats per minute, 34 between 80-89 beats per minute, 5 between 90-99 beats per minute and 2 above 100 beats per minute. 91 (81.25%) of patients whom had not reach optimum heart rate are deemed suitable for ivabradine.

Conclusion: Our finding reflected that even within a high volume ambulatory heart failure disease management programme, heart rate control is still suboptimal. Beta-blockers contraindications and intolerant are the main reasons for failed up-titration and optimization of heart rate. These patients should benefit from introduction of ivabradine in order to reach optimal heart rate control. In conclusion, there is a need for a heart rate awareness specific follow up within heart failure disease management programme along side the well established ACE-I/ARB and MRA titration followup.

P1882

Multidisciplinary heart failure management program significantly reduces expensive hospital readmissions, length of stay and improves quality of life of high-risk heart failure outpatients

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Advanced heart failure (HF) is associated with substantial morbidity, mortality and frequent hospital readmissions. Repeated hospitalizations represent a high economic burden for Health Systems and have a negative impact in the patients quality of life. Multidisciplinary HF disease-management programmes (HFMP) are recommended for this group of pts in the latest European Guidelines (class I recommendation) but it's still not clear which components are more relevant. The purpose of this study was to determine the impact of a multidisciplinary approach, including nurse-based education, on the number of hospitalizations, hospital length of stay and quality of life of patients with high-risk HF followed-up (FU) at our HF Unit (HFU).

Methods: We included patients admitted to our HFU after a HF episode that required hospitalization from March 2011 to December 2013. After discharge and guideline-directed medical therapy, Pts and their carers were offered a 4-weeks nurse-guided educational intervention (NEI) focused on self-care promotion. Pts with

no possible self-access to our center were excluded. Written consent was obtained from every patient. Standardized tests to measure Self-care (European HF Self-care Behavior (ESS)) and quality of life (Minnesota living with HF questionnaire (MQ)) were performed before and after NEI. Charlson Comorbidity Index (CCI) was registered. HF hospital admissions and the hospital length of stay were registered and compared 1 year before and 1 year after inclusion in our HFMP.

Results: From 606 patients visited in our HF Unit during the inclusion period, 174 (29%) were included in our HFMP. Two patients died before FU (n = 172). 74% were men, mean age was nearly 70 years ($69 \pm 10,2$) mean Left Ventricle Ejection Fraction was $31 \pm 8\%$, 91% of pts were on NYHA class II-III and they presented a mean CCI of $5,27 \pm 2,27$ and a mean HF history of 5 ± 6 years. 95% were on ECA-inhibitors/ARB and 93% on Betablockers and 26% had an Implantable Cardioverter defibrillator. At one year follow-up (FU) our patients showed a statistically significant reduction in the number of HF hospitalizations ($0,74 \pm 0,17$ vs $0,16 \pm 0,6$, $p < 0,001$) and the hospital length of stay ($8,63 \pm 9$ days vs $1,99 \pm 8,4$ days, $p = 0,0001$) in comparison with the previous year. Besides, a significant improvement in self-care (ESS score from 27 ± 9 to 18 ± 5 , $p < 0,0001$) and quality of life (MQ mean score reduction: 12, $p < 0,0001$) was obtained.

Conclusion: In high-risk HF outpatients, specialized multidisciplinary approach with NEI after a HF decompensation, significantly reduced both the number and length of HF rehospitalizations and improved their quality of life.

DRUG THERAPY, OTHER

P1883

Assessment of flow-mediated endothelium-dependent vasodilation in patients with acute decompensated chronic heart failure treated with anticoagulants

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Objective: To evaluate flow-mediated endothelium-dependent vasodilation (FMD) in patients with acute decompensated chronic heart failure (ADCHF) treated with anticoagulants.

Materials and methods: The study included 60 ADCHF patients with sinus rhythm, mean age 69 ± 10 years, 35 women (58%), treated with prophylactic subcutaneous anticoagulants (heparin, enoxaparin or fondaparinux). The control group included 20 patients with compensated CHF (NYHA class I or II), mean age 68 ± 9 years, 11 (55%) women. Brachial artery diameter was measured both at baseline and after anticoagulants had been discontinued, during postocclusion reactive hyperemia (FMD), using a noninvasive echo-Doppler method. Endothelial dysfunction was considered as brachial artery (BA) FMD ratio (artery diameter before/after compression) of less than 10%. The study did not include patients with acute exacerbation of chronic diseases and active cancer.

Results: Ejection fraction in ADCHF group was significantly less than in the control group (40 ± 14 vs $55 \pm 10\%$, respectively, $p = 0,004$). All ADCHF patients had ED, with baseline FMD ratio of $-2,15 \pm 2,86\%$, while in controls it appeared up to $15,40 \pm 1,47\%$ ($p = 0,0001$). After treatment, BA diameter ratio increased in the studied group from $2,15 \pm 2,80\%$ to $14,06 \pm 3,47\%$ ($p = 0,0004$), which was close to the baseline values in the control group ($p = 0,29$). There was significant correlation between enoxaparin treatment ($\beta = 0,34$, $p = 0,019$) and FMD ratio, between fondaparinux treatment and FMD ratio ($\beta = 0,35$, $p = 0,017$).

Conclusion: All ADCHF patients showed a significant deterioration in endothelial function, which after treatment became comparable to the control group. A significant correlation was observed between both fondaparinux and enoxaparin treatment and an increase in BA FMD ratio

Keywords: acute decompensated chronic heart failure, endothelial dysfunction, flow-mediated endothelium-dependent vasodilation, heparin, enoxaparin, fondaparinux

P1884

Relation of optimized treatment with frequency of hospitalization for cardiac decompensation in patients with chronic heart failure

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Background: Heart failure (HF) is a common public health problem. The neurohormonal blockade modifies this natural history; however, it is often suboptimal.

Our objective is to appraise the effectiveness of beta blockers and angiotensin-converting enzyme inhibitor (ACEI) in patients with heart failure and to assess at what percentage we used them to treating HF at target doses.

Methods: We evaluated medication use in a retrospective cohort of 1841 outpatients followed in therapeutic unit of heart failure for heart failure with reduced

ejection fraction. We divided patients on 2 groups: group 1 with cardiac decompensation (n = 497, 27%), group 2 with compensated heart failure (n = 1344, 73%).

Results: The mean age of patients was 65 years with systolic blood pressure = 117.63 in group 1 and 129.4 in group 2, heart rate = 89.3 in group 1, 61.5 bpm in group 2 and sinus rhythm (86.52%).

As for treatment, 47% (235/497) in group 1 received a beta-blocker versus 86.75% (1166/1344) in group 2 ($p = 0,0001$) and 85.51% (425/497) in group 1 received ACEI versus 88.61% (1191/1344) in group 2 ($p = 0,34$).

As for the doses: 6.63% (33/497) in group 1 received an optimal dose of beta-blocker versus 23% (311/1344) in group 2 and 22% (109/497) in group 1 had an optimized dose of ACEI versus 34.44% (463/1344) in group 2 ($p = 0,0001$).

Conclusion: In conclusion, the use of beta blockers and ACEI at target doses is associated with a decreased risk of hospitalization for HF in patients with systolic dysfunction.

P1885

Effect of L-arginine on the clinical and functional parameters at patients with dilated cardiomyopathy

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Aim: To evaluate the effect of the combination of L-arginine aspartate with basic therapy (BT) on the clinical and functional parameters at patients with various types of cardiomyopathies.

Methods: The study included 53 patients (36 women, 16 men; 21 to 54 years old). These were performed: ECG; EchoCG with measurement of systolic pulmonary artery pressure (MPAP). Depending on the type of cardiomyopathy patients were divided into 2 groups: 1g. - 23 patients with isolated right ventricle DCM ($43,4 \pm 8,2$ years old) and 2gr. - 32 pts with DCM, ($42,6 \pm 8,8$ years old). All patients received optimal drug therapy: β -blockers; ACE inhibitors; aldosterone antagonists; antiplatelet agents; if necessary - diuretics, and cardiac glycosides, antiarrhythmics. To optimize the treatment L-arginine as a 4.2% solution intravenously with 100 ml 1 time per day (8-10 days) followed by transfer to an oral solution of 5-10 ml, 3 times daily for 4 weeks was included.

Results: The positive dynamics of intracardiac echocardiography parameters observed in both groups. Thus, in 1 month of treatment, the mean values of RA decreased on 7% (from $48,86 \pm 45,56 \pm 9,43$ mm to 6,43mm) and 3% (from $43,91 \pm 40,72 \pm 5,48$ mm to 6, 22mm), RV- up to 7% (from $49,52 \pm 45,88 \pm 7,43$ mm to 6,82mm) and 6% (from $42,64 \pm 40,09 \pm 5,58$ mm to 4,79mm). Inotropic function of the myocardium characterized by biventricular growth of EF both RV (from $38,84 \pm 8,12\%$ to $41,12 \pm 5,23\%$, $p < 0,055$ and $47,28 \pm 9,31\%$ to $48,14 \pm 7,64$, $p < 0,697$) and LV (from $51,70 \pm 10,11\%$ to $54,86 \pm 8,08\%$, $p < 0,237$ and $30,59 \pm 7,13\%$ to $35,68 \pm 6,46\%$, $p < 0,005$), with the expected decrease in MPAP on 15% (from $38,12 \pm 7,42$ mm Hg to $32,26 \pm 2,21$ mm Hg) and 17% (from $30,54 \pm 10,15$ mm Hg up to $25,12 \pm 7,98$ mm Hg).

Thus, with the improvement of intracardiac parameters in both groups, the combination therapy with L-arginine has contributed to a more pronounced increase in left ventricular ejection fraction and the noticeable decreasing of MPAP.

P1886

Predictors of medication nonadherence differ by racial group among heart failure patients

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Purpose: Heart failure (HF) is a global public health problem and outcomes remain poor especially among racial/ethnic minority populations. We demonstrated previously that medication adherence can improve HF outcomes, but adherence is notoriously poor. The objective of this study was to explore differences in predictors of medication nonadherence by racial/ethnic group (non-White vs. White).

Methods: This was a secondary analysis of data from a prospective cohort comparison study of adults with chronic HF. Participants were enrolled from three out-patient sites in the northeastern US and followed for a 6-month period. Participants had to have documented HF of either reduced or preserved type. Medication adherence was assessed objectively over a 6-month period using the medication-event monitoring system (MEMS). Clinical data were abstracted from the medical record by registered nurses. Demographic data, including race/ethnicity, was self-reported. Valid instruments were used to collect data on depression. Data analysis used adaptive modeling methods to model HF patient medication non-adherence separately for non-White and White participants in order to investigate differences between these two racial/ethnic groups.

Results: Of the 218 participants with medication adherence data (>90% of the enrolled sample), 69 (31.7%) were non-White and 149 (68.3%) were White. For the non-White participants, 31.9% had poor medication adherence compared to 27.5% of the White participants. Among non-Whites, there were 14 individually significant ($p < .05$) risk factors with four of them (live alone, lower serum sodium, worse depression, and fewer activities compensating for forgetfulness) jointly predicting nonadherence. In non-White patients, the numbers of risk factors from the multiple risk factor model ranged from 0 to 4 with 81.2% having at least 1 risk factor. The estimated odds ratio (OR) for medication nonadherence with 0, 1, 2, or 3 risk factors increased 11.2 times with the addition of one more risk factor. Among White participants, there were only 5 significant ($p < .05$) individual risk factors; one of these (older age) explained the individual effects of the other four.

Conclusions: Non-Whites with HF have different and more risk factors than Whites for medication nonadherence. Some of these risk factors are modifiable. Research is needed that focuses on interventions that help non-White patients with HF to overcome these risk factors.

P1887

Prevalence and predictors of medication adherence using a multidimensional adherence model in patients with heart failure: moroccan experience

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Background: The adherence of medical treatment of the chronic heart failure is recognized worldwide as one of the most important issues of the management of this chronic life threatening disease. The demographic and socio-economic particularity of African countries could influence the adherence of the treatment of chronic heart failure in those countries; There is an insufficiency of data on treatment adherence in patients with chronic heart failure.

Purpose: The aims of this study was to assess adherence to medical treatment and explore factors contributing to medication adherence in Moroccan patients with Heart failure by using the World Health Organization's multidimensional adherence model.

Methods: We proceed to a cross-sectional analytic study from September 2014 to January 2015 based on a heart failure population followed in heart failure Unit of Cardiology department of our University Hospital in Morocco, after collecting general demographic characteristics of the study population. The assessment of adherence to the medical regime by questionnaires was based on two different scale: the CARDIA-Questionnaire and the Morisky Medication Adherence Scale (MMAS 4-item version). Information regarding the predictors of medication adherence derived from the multidimensional adherence model.

Results: In this period 147 heart failure patients were included. The level of compliance was respectively 110(74.8%) and 123(83.6%) according to (MMAS 4) and CARDIA-Questionnaire. Concerning the predictors of non-adherence to the medical treatment, factors that were significantly influencing the medical compliance were: depression ($p = 0.034$), low social support ($p = 0.03$) and Patients who did not take medication by themselves ($p = 0.0001$) were less compliant than the rest.

Conclusion: In our knowledge this is the first study in Morocco specifically targeting the prevalence and non-adherence factors of medical treatment in heart failure population; the compliance level to the treatment was similar to the range reported in literature; in addition to low social support and depression, the identification of assistance to take medication as one of non adherence factor suggests the necessity of informing and educating the assisting person as well as the patient it self to expect a better compliance to medical therapy.

P1888

A study on obstacles to commencement or uptitration to target dose of disease modifying therapies in stable patients with heart failure with reduced ejection fraction

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Purpose: Ace Inhibition, Beta-blockade, and Mineralocorticoid Antagonists and Ivabradine are disease modifying therapies (DMTs) that improve outcomes in patients with established HFREF. A significant proportion of patients do not achieve target dose therapy. The reasons for this have not been well studied. Our study attempted to 1) Identify the proportion of patients not achieving target doses for DMTs 2) identify obstacles to commencement or uptitration of DMT encountered in real life patients in a Heart Failure Unit setting.

Methods: Data were collected regarding DMT use for 74 patients attending a dedicated disease management programme. All patients had established HFREF on stable therapy for at least 6 months. Target dose was defined as recommended dose for HF treatment as per ESC. Factors limiting use or preventing uptitration to target dose were prospectively identified by patient account and retrospectively through medical records.

Results: Only 2 (2.7%) of patients achieved target dose in three categories of DMTs. 15(20.3%) patients were titrated to target dose in two categories of DMT while 22(29.7%) patients were titrated to target dose in one category of DMT. Number of patients and reasons for not achieving target dose or not being on each DMT are shown in table 1.

Conclusion: Target dose therapy is difficult to achieve and limited by known side effects of each class of DMT. DMTs lower on the ESC recommended DMT uptitration cascade were less likely to achieve target dose or to be used. This may be explained by a cumulative side effect of DMTs. Compared to target dose, maximum tolerated dose may be a more achievable strategy.

P1889

Transition from randomized trial to real world: ivabradine improves symptoms and quality of life in chronic systolic heart failure patients with different disease severity at baseline

The study was supported by Servier Deutschland GmbH, Munich
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Objectives: The prospective, open-label multicenter INTENSIFY study evaluated the effectiveness, tolerability and effect on quality of life of ivabradine treatment in chronic systolic heart failure (CHF) patients. We performed a subgroup analysis to characterize the effectiveness and safety of ivabradine in addition to standard heart failure medication in patients with different severity of CHF symptoms.

Methods: Heart rate (HR) and heart failure symptoms (NYHA class, decompensation signs) were documented in 1956 ambulatory patients with CHF. BNP was tracked in a subset of patients. Treatment with ivabradine twice daily in flexible doses was initiated for 4 months. Quality of life (QoL) was evaluated at each visit. A descriptive statistical analysis of the results was performed for four subgroups defined by NYHA class at baseline. Treatment response was defined as HR <70 bpm or HR reduction of ≥ 10 bpm at study end.

Results: In total, 1956 patients (intention to treat, mean age 67.2 ± 11.7 years, 56% male) were analyzed. Etiology was ischemic for 62% of the cohort. 78% received beta blockers (e.g. Metoprolol 33%, mean daily dose (mdd) 102.9 mg; Bisoprolol 28%, mdd 6.2 mg; Nebivolol 9%, mdd 5.4 mg; Carvedilol 7%, mdd 27.1 mg). Other concomitant medication consisted e.g. of ACEI/ARB 83%, diuretics 61%, aldosterone antagonists 18%, cardiac glycosides 8%, aspirin 58%, statins 56%. The table shows the effects after 4 months of ivabradine treatment for NYHA subgroups (overall mean dose 12.4 mg/d).

Conclusion: Ivabradine showed to be effective in reducing heart rate and symptoms of CHF in patients with all grades of disease severity at baseline. Furthermore, ivabradine reduced BNP and improved QoL in all NYHA groups, accompanied by high treatment response rates and good tolerability. Symptomatic effectiveness was more pronounced in patients with higher NYHA classes.

P1890

Intravenous iron and prognosis in patients with chronic heart failure: a multicentre study of 2172 patients

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Purpose: Treatment with intravenous (IV) Iron in patients with chronic heart failure and Iron deficiency (ID) has been shown to improve functional capacity, however little is known regarding its impact in survival and long-term safety. We aimed to evaluate the prognostic impact of IV Iron treatment in patients with CHF.

Methods: We evaluated ID in patients with CHF at entry to the heart failure unit of 3 university hospitals. ID was defined as a ferritin < 100 ug/L or a Transferrin Saturation < 20% if ferritin 100 - 299 ug/L. We retrospectively assessed treatment with IV Iron at any point after entry. Survival was evaluated using Kaplan Meier survival curves. We determined if IV Iron was a predictor of survival using multivariate cox regression analysis.

Results: We included 2172 patients, 65% males, 42% diabetics, median age of 72 years, 45% ischemic and median left ventricular ejection fraction (LVEF) of 36%. Median glomerular filtration rate was 53 ml/min, median NT-proBNP of 1484 pg/mL, median haemoglobin of 12.7 g/dL and 37% were in NYHA functional class III-IV. ID was present in 55% and 461 patients (21%) received IV Iron and 6% EPO. Median follow-up was 19 months. Figure 1 shows how IV Iron had a significant favorable impact in survival. IV Iron treatment was an independent predictor of survival with

Table 1 60984:

1	ACEI/ARB 49(66.2%)	BB 54(73.0%)	MRA 68(91.9%)	Ivradadine 63(85.1%)
2	Hypotension or associated symptoms (25)	Target HR achieved (20)	Chronic Kidney disease (11)	A.fib (26)
3	Chronic Kidney disease (9)	Hypotension or associated symptoms (14)	Hypotension (10)	Target Heart Rate Achieved (23)
4	Hyperkalaemia (8)	Fatigue & lethargy (6)	EF Recovered (10)	
5	"General unwell" (4)	Obstructive airways disease (6)	"General unwell" (8)	"General unwell" (5)
6	Incorrect physician assumption target dose achieved (2)	Extreme bradycardia (5)	Hyperkalemia (8)	EF recovered (3)
7	Severe AS (1)	No reason identified (1)	Incorrect physician assumption target dose achieved (7)	No reason identified (6)
		Raynauds disease (1)	No reason identified (13)	

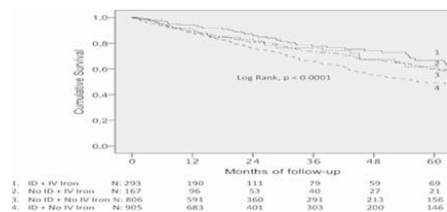
Table 1: Number (top row) and reasons of patients not achieving target dose or not commenced on each DMT.

Table 60740

Δ Baseline - 4 months	NYHA I (n = 184)	NYHA II (n = 981)	NYHA III (n = 715)	NYHA IV (n = 41)
Heart rate	-20 ± 12 bpm	-17 ± 12 bpm	-19 ± 13 bpm	-21 ± 13 bpm
Patients in this NYHA class	+14%	+9%	-22%	-1%
Patients with signs of decompensation	-2%	-9%	-32%	-30%
Patients with BNP >400 pg/ml	-6%	-16%	-37%	-24%
EQ-5D index score (QoL)	+0.10	+0.13	+0.20	+0.24
Patients with treatment response	91%	87%	91%	92%

Percentage changes presented as absolute values

a Hazard Ratio of 0.59 (95% CI: 0.45 - 0.76; $p < 0.0001$) after adjusting for age, haemoglobin, NT-proBNP, Sodium, Diabetes, Hypertension, Iron Deficiency, LVEF, ischemic etiology, GFR, heart rate, blood pressure and EPO treatment.
Conclusions: Patients with CHF who receive IV Iron have better prognosis, especially if ID had been previously documented. Although our data is retrospective, this finding is reassuring regarding the safety of IV Iron in patients with CHF.



BIOMARKERS

P1891

SST2 and galectin provide additional prognostic information when compared to NT-proBNP, proBNP and BNP in ambulatory patient with heart failure

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ST2, an interleukin-1 (IL-1) receptor family member, is a emerging biomarker interesting to assess prognosis in various pathophysiological conditions including acute coronary syndromes, acute heart failure (HF) or patients admitted on hospital for HF.

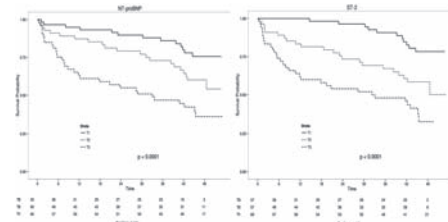
The aim of this work was to investigate the prognosis interest of this marker in ambulatory patients with stable HF.

Patients

180 patients were included in 2008. All the patients gave an informed consent. Clinical characteristics were registered and biomarkers were assessed. Clinical outcomes were registered regularly on clinical follow-up or by phone by a dedicated

physician. Survival curves were built and data presented as means+/-SD when normally distributed.

Results: 180 patients (mean age 72.5y+/-12.5y) were included. Left ventricular ejection fraction was 37.1%+/-14.2%. SST2 and NT-pro-BNP were highly correlated ($p < 0.01$, Figure 1). Both biomarkers were able to discriminate patients survival following the tertile of the patients. Nevertheless the sST2 was able to discriminate more accurately the tertiles (median of survival: 5, 15, 39 months respectively for tertiles 1, 2, 3, $p < 0.01$) versus (median of survival: 10, 20, 36 months respectively for tertiles 1, 2, 3, $p < 0.01$)



P1892

The battle of concepts: absolute discharge levels or relative reduction in NT-proBNP as a target to reduce 6-month mortality after admission for acute decompensated heart failure?

Netherlands Heart Foundation

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Purpose: NT-proBNP is a strong predictor for readmissions and mortality in acute decompensated heart failure (ADHF) patients. Both relative reduction percentages and absolute NT-proBNP levels at discharge have been incorporated in risk models. Which NT-proBNP level (either absolute or relative) should be used as target of treatment in an ADHF population is unknown.

Methods: Our study population was assembled from 7 European ADHF cohorts, which had NT-proBNP measured at admission and discharge. We defined NT-proBNP discharge targets: <1500, <3000, <5000 and <15000 ng/L, and relative reductions from admission to discharge of >30%, >50% and >70%. Population attributable risk fraction (PARF) is the proportion of all-cause mortality in the population within 6 months after discharge that could be reduced if a risk factor (NT-proBNP level above target) was not present. PARF was determined for each target ($\pm 95\%$ CI) and compared with the percentage of patients attaining NT-proBNP target levels. Attainability of targets was investigated by univariate and multivariate logistic regression analysis.

Results: A total number of 1266 patients (median age 74, 60% male) was studied. Six month mortality was observed in 15% of patients and decreased with lower absolute discharge levels and greater percentages reduction in NT-proBNP. For every absolute discharge level of NT-proBNP, a corresponding reduction percentage of NT-proBNP was found that resulted in the same PARF. Highest PARF was observed for <1500 ng/L at discharge or >70% reduction in NT-proBNP but attainability of these targets was low (27% and 22% respectively) Strongest predictor for not reaching these targets was admission NT-proBNP levels. Significant differences in PARF were found between tertiles of admission NT-proBNP for absolute NT-proBNP targets, while there were no significant differences in PARF for relative reduction NT-proBNP targets.

Conclusion: In an ADHF population, absolute or relative reductions as NT-proBNP targets are interchangeable in the effect on PARF. Relative reduction targets show similar PARFs among admission NT-proBNP categories while absolute targets show varying PARFs. A relative reduction target would probably lead to the most consistent mortality reducing effect across the whole spectrum of ADHF patients.

P1893

Combination of neurohormones and clinical signs and symptoms to detect a left ventricular dysfunction

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It is well known, that the prevalence of asymptomatic left ventricular dysfunction is higher than of symptomatic heart failure. It is unknown whether a combination of different biomarkers alone or in addition to clinical parameters could be helpful to detect asymptomatic Stage B heart failure.

Methods: Aim of this study was to develop a system of different biomarkers linked with clinical data to achieve a high discriminatory power between several types of left ventricular dysfunctions: 1. systolic dysfunction (SD), 2. diastolic dysfunction (DD) and 3. No ventricular dysfunction (KG). For this purpose, 1590 patients (DIAST-CHF-study) were analyzed.

We classified the study population into three groups. In addition seven different biomarkers were assessed (NT-proBNP, MR-proANP, hsCRP, CT-proAVP, CT-proET-1, MR-proADM and Pro-collagene III). We choose 3 different models: SD/DD vs. KG, SD vs. KG as well as DD vs. KG.

Results: 136 patients had SD, 428 DD and 1026 patients had a normal ventricular function (KG). E/é medial as the main diastolic function parameter was increased in DD (15,7), and in SD (12,9) and significantly lower in KG (9,3). Additionally, we linked the biomarkers with typical clinical values like Framingham-score, age, sex, atrial fibrillation, diabetes, hypertension, blood pressure, coronary artery disease.

We found that NT-proBNP, MR-proADM and hsCRP were independent of other factors able to detect a left ventricular systolic or diastolic dysfunction.

ROC-curves: KG vs. SD/DD AUC = 0,738, KG vs. SD AUC = 0,840 and KG vs. DD AUC = 0,741.

Conclusion: We developed a combined model of neurohormones and clinical parameters to distinguish between healthy people and patients with a left ventricular dysfunction. Whether such model can improve the diagnosis of left ventricular dysfunction also in clinical practice need to be investigated in future studies.

P1894

Risk evaluation in vascular remodeling in CHF patients depending on N-terminal part of brain natriuretic peptide

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Aim: to evaluate hazard ratio of vascular remodeling development in ischemic CHF depending on NT-proBNP.

Materials and Methods: 90 patients with CHF and stable angina were examined. 38.2% got a MI in past. Average age was 56,2 \pm 6,4 yrs. Male 58.8%, female 41.2%. Duration of angina was 5,9 \pm 2,6 yrs, average functional class (FC) 2,27 \pm 0,37. Duration of CHF was 6,2 \pm 2,1, average FC 2,52 \pm 0,08, average LV EF 60,5 \pm 9,3%. To estimate arterial wall status volume sphygmography was done with VaSera VS-1000 device (Fucuda, Japan). To evaluate collagen matrix condition TIMP-I was used. Also NT-proBNP level has been evaluated to confirm CHF presence. To study interconnection between the parameters Hazard ratio (HR) and Relative risk (RR) (95% confident interval - CI) have been established.

Results: in NT-proBNP >700 pg/mL HR in increase of CAVI1 >90 was 12,55 (95% CI=2,64-68,29), RR 2,65 (95% CI=1,54-3,69), (p=0,001). HR in increase of PWVcf >12 m/sec was 24,75 (95% CI=2,64-590,41), RR 14,57 (95% CI=2,19-311,19), (p=0,002). HR in decrease of PWV in aorta >6 m/sec was 7,5 (95% CI=1,33-55,22), RR was 1,62 (95% CI 1,09-1,93), (p=0,017). In course of elevation NT-proBNP >700 pg/mL there was significant increase of fibrosis in arterial wall extracellular matrix (according to TIMP-1) HR was 33,07 (95% CI=5,83-224,9); RR - 8,64 (95% CI=2,99-32,06), (p=0,0005).

Conclusions: in CAD patients elevation of CHF severity according to NT-proBNP level accompanied with significant increase of relative risk of arterial wall remodeling, which was characterized in elevation of arterial stiffness, decrease of its elasticity, and also in transformation of endogenous collagenolysis.

P1895

Relationship of left ventricular contractile reserve and temporal changes in plasma brain natriuretic peptide levels during exercise stress-echocardiography in patients with dilated cardiomyopathy

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Purpose: To evaluate temporal changes in brain natriuretic peptide (BNP) levels during exercise stress-echocardiography in patients with dilated cardiomyopathy with respect to the left ventricular contractile reserve.

Methods: We studied 55 consecutive patients with dilated cardiomyopathy (mean age 55 \pm 10 years, 49 (89.1%) male). All patients underwent exercise stress-echocardiography on treadmill using modified Bruce protocol. Contractile reserve was assessed by measuring changes in left ventricle ejection fraction (Δ LVEF) at rest and at peak exercise. Levels of BNP were measured at rest, in the first minute and after 20 minutes following termination of stress test. 25 patients had preserved left ventricular contractile reserve, whereas 30 patients had not.

Results: Patients with preserved left ventricular contractile reserve showed continuous rise in BNP levels from baseline to peak exercise and to 20 minutes following exertion (126.52 \pm 179.97 vs. 153.04 \pm 205.14 vs. 165.54 \pm 267.66 ng/L, p < 0.001, respectively). On the other hand, patients without preserved left ventricular contractile reserve showed decline in BNP levels during exercise, but the difference was not statistically significant (350.83 \pm 752.90 vs. 323.63 \pm 601.27 vs. 334.83 \pm 588.79 ng/L, p = 0.10, respectively). Δ BNP was positively correlated with preserved contractile reserve (r = 0.32, p = 0.017), lower WMSI at rest (r = -0.28, p = 0.04), and lower NYHA class (r = -0.32, p = 0.019). However, BNP was not an independent predictor of preserved contractile reserve. Multivariate analysis identified only WMSI at rest (beta -3.365, p = 0.008, 95 CI 0.03 to 0.411) as an independent predictor of left ventricular contractile reserve.

Conclusion: The increase in BNP levels during exercise stress-echocardiography is associated with preserved left ventricular contractile reserve in patients with dilated cardiomyopathy.

P1896

Preventing heart failure using medical intervention guided by NTproBNP

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Purpose: It is well known that NTproBNP is useful in diagnosis of heart failure. This is a pilot study that aims to study the usefulness of NTproBNP in patients without heart failure (but with conditions at risk of developing heart failure) for guiding treatment for preventing heart failure, left ventricular systolic or diastolic dysfunction.

Methods: We included 164 patients who were present at Bagdasar-Arseni Hospital for cardiology consultation during one year, with the following conditions: hypertension, diabetes, ischemic heart disease, valvular disease, arrhythmias.

We excluded patients who are already diagnosed with heart failure, left ventricular systolic or diastolic dysfunction or who had current symptoms of heart failure.

We randomized patients into 2 equal groups: a control group(82 patients) and an intervention group(82 patients). NTproBNP value was determined for all patients.

In the intervention group patients were treated according to the NTproBNP: patients who had NTproBNP <125 pg / dl (36 patients) received standard treatment for their symptoms. patients who had NTproBNP > 125 pg / dl (46 patients) were the ones on which we intervened to prevent heart failure. They were investigated by cardiac ultrasound and other specific tests for each case (blood test, stress test, ECG monitoring/24h). After completing medical balance, each patient received specific treatment.

Patients in the control group received standard treatment for their symptoms regardless of the NTproBNP value.

Results: After one year, the end points were: diagnosis of cardiac failure, left ventricular systolic or diastolic dysfunction, patient death from any cause, the rate of hospitalizations for cardiovascular pathology.

After a year in the control group were 18(21,9%) patients who developed heart failure compared to 10(12,1%) patients in the intervention group. 26(31,7%) patients were diagnosed with left ventricular systolic dysfunction, compared to 26(31,7%) in the intervention group. Also, and rate of admissions for heart disease was higher in the control group 28(34,1%) versus 17(20,7%) in the intervention group.

Conclusions: Patients in the intervention group, in which the value of NTproBNP was used in choosing therapeutic management, have lower rate of incidence of heart failure or cardiovascular events than patients in the control group.

This value NTproBNP in patients without heart failure can detect patients at risk of developing heart failure. And more, medical intervention guided by NTproBNP can prevent or delay of heart failure in these patients.

P1897

Treatment optimization of high risk heart failure patients after acute decompensation by NT-proBNP monitoring

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Purpose: to evaluate the superiority of heart failure (HF) therapy guided by NT-proBNP vs standard treatment of CHF patients (pts) at high risk after acute decompensation (ADHF).

Methods: In the prospective single-center trial, we included 105 hospitalized pts with ADHF III-IV FC NYHA and LV systolic dysfunction due to coronary artery disease, arterial hypertension and dilated cardiomyopathy. After HF symptoms compensation, high risk pts (discharge NT-proBNP >1400 pg/ml) were randomized into group of therapy guided by NT-proBNP (group 1) and standard HF therapy (group 2). Pts in both groups did not differ by the main clinical characteristics. Mean pts age was 63,97 ± 8,7 in group 1 and 63,14 ± 11,8 in group 2, p=0,7. Mean LVEF was 29,4 ± 5,9% in group 1 and 29,6 ± 5,2% in group 2, p=0,4. The goal was to reduce NT-proBNP concentration < 1000 pg/ml, or at least 50% of the initial. At discharge, NT-proBNP concentration was 3651 (2191,5;6613,0)pg/ml in group 1 and 2862,0 (2015,0;4761,50)pg/ml in group 2, p=0,488. The primary end point of the trial was total cardiovascular events for 1-year follow-up period that included cardiovascular (CV) death, hospitalization due to HF, and episodes of HF deterioration needed additional i/v diuretics.

Results: At the end of the study all pts (100%) in groups 1 and 2 have been treated by recommended triple combination of iACE/ARB+BB+MRA, but the mean doses up-titration of iACE/ARB and BB at the 6 months of treatment were higher in NT-proBNP-guided group: 281% and 267% vs 208%, 205% respectively, p<0.05. After 1 year NT-proBNP concentration in group 1 significantly decreased to 1585,5 (976,5; 2612,5)pg/ml (-53.1%), compared with group 2 - 2450,0 (2028,0; 3328,0)pg/ml (-11.1%), p=0.024. At the same period CV mortality rate in group 2 was significantly higher than in 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 in group 1 showed significant improvement in HF clinical and functional status, and quality of life (from 46.1 ± 16.6 to 22.1 ± 4.1, p=0.002), LVEF (from 29,4 ± 5,9% to 38,1 ± 5,6%), LV volumes (ESV from 150,2 ± 57,2ml to 122,6 ± 50,2ml, p<0,01), and SDNN, p<0.05 for all compared with group 2. At the end of the study any differences in the level of blood pressure, serum creatinine, GFR between pts of 1 and 2 were not found.

Conclusion: NT-proBNP-guided therapy was superior to standard therapy in reduction of CV mortality and HF hospitalization, improving quality of life and left ventricular remodeling in high risk patients with systolic HF after ADHF.

P1898

Measurement of dihydroxy-vitamin D and the ratio to PTH strongly predict cardiovascular death in heart failure patients

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Purpose: Vitamin D deficiency and hyperparathyroidism are common in patients with heart failure (HF). A growing body of evidence supports the role of vitamin D

and parathyroid hormone (PTH) in cardiac remodeling. Nevertheless, the prognostic value of the 1,25-dihydroxyvitamin D (1,25(OH)₂D), the most potent biologically active metabolite of vitamin D, remains unclear. We therefore examined the relationship of 1-25OHD levels and cardiovascular (CV) death in chronic HF.

Methods: One hundred seventy chronic HF patients (females n = 36; males n = 134; NYHA II-IV; mean age: 67 years; etiology: ischemic n = 119, dilated cardiomyopathy n = 51; mean EF: 23%) were included. The primary outcome was CV death. Levels of 1,25(OH)₂D were determined at baseline with a fully automated and sensitive immunoassay that uses a specific recombinant fusion protein for the capture of 1,25(OH)₂D (DiaSorin). Levels of 25-hydroxyvitamin D (25OHD), PTH(1-84), B-type natriuretic peptide (BNP), N-terminal proBNP (NT-proBNP) and Galectin-3 (Gal-3) were also measured.

Results: Levels of 25OHD were not significantly different according to NYHA functional classes (p = 0.146). In contrast, serum levels of 1,25(OH)₂D decreased markedly according to HF severity and were 30.9 pg/mL in NYHA class II, 22.0 pg/mL in NYHA class III, and 14.9 pg/mL in NYHA class IV (p < 0.001). Decreased ratios of 1,25(OH)₂D to PTH(1-84) were also significantly related to HF severity. 1,25(OH)₂D and its ratio to PTH(1-84) showed significant negative correlation with BNP, NT-proBNP and Gal-3. Levels of 25OHD were only related to BNP and NT-proBNP. After 8 years of follow-up, 106 patients reached the primary endpoint. Levels of 1,25(OH)₂D and the ratio of 1,25(OH)₂D to PTH(1-84) were strongly predictive of outcome in Cox multiple variable analysis.

Conclusions: 1,25-dihydroxyvitamin D and its ratio to PTH(1-84) are strong independent markers for cardiovascular death in chronic HF and can therefore guide treatment strategy.

P1899

Prognostic value of cystatin c-derived estimated glomerular filtration rate in the patients with acute decompensated heart failure

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Background: Glomerular filtration rate (GFR) is one of the potent prognostic markers in patients with heart failure. Recently, cystatin C-derived GFR has been proposed for more precise estimation for GFR. We aimed to test the prognostic value of cystatin C-derived GFR in patients with heart failure of acute decompensated status in comparison with GFRs from creatinine-only equations.

Methods: This retrospective study included 262 patients with acute decompensated heart failure. Prognostic value of the estimated GFRs, derived from the Chronic Kidney Disease-Epidemiology Collaboration (CKD-EPI) equation containing cystatin C (CKD-EPI-cystatin C equation and CKD-EPI-cystatin C-creatinine equation), were compared with estimated GFR derived from the classic equations containing only serum creatinine levels (Modification of Diet in Renal Disease [MDRD] equation and CKD-EPI-creatinine equation). Prognosis was evaluated with the composite of all-cause mortality and readmission for decompensated heart failure within one year.

Results: Mean age was 65.8 ± 14.9 and 126 (48.1%) were men. Among the patients, 106 (40.5%) were with ischemic etiology. During the follow-up (mean follow-up 264.0 ± 136.1 days), 67 (25.6%) events occurred. Mean estimated GFRs were 67.7 ± 32.2, 64.8 ± 27.4, 54.2 ± 26.2 and 57.2 ± 24.1 [ml min⁻¹ (1.73m²)⁻¹] for MDRD, CKD-EPI-creatinine, CKD-EPI-cystatin C, and CKD-EPI-cystatin C-creatinine equation, respectively. Estimated GFR using CKD-EPI-cystatin C was the best for predicting 1-year outcome in receiver operating characteristic curve analysis (area under curve [AUC] of 0.585, 0.607, 0.669, and 0.652 for GFRs from MDRD, CKD-EPI-creatinine, CKD-EPI-cystatin C, and CKD-EPI-cystatin C-creatinine equation, respectively). AUC of GFR by CKD-EPI-cystatin C equation was significantly greater than that of GFR by MDRD and CKD-EPI-creatinine equation (p = 0.003 and p = 0.016) AUC of GFR by CKD-EPI-cystatin C-creatinine equation was also significantly greater than that of GFR by MDRD and CKD-EPI-creatinine equation (p = 0.001 and p = 0.004) Kaplan -Meier survival curve analysis according to the subgroups of estimated GFR showed that only the two estimated GFRs derived from the equations containing cystatin C significantly differentiated 1-year outcome in patients with acute decompensated heart failure (log rank p of <0.001 and 0.002 for the CKD-EPI-cystatin C, and CKD-EPI-cystatin C-creatinine equation).

Conclusion: Estimated GFRs, which were derived from cystatin C, predicted the prognosis more accurately in patients with acute decompensated heart failure, compared to those from creatinine-only equations.

P1900

The prognostic significance of plasma galectin-3 in patients admitted for acute coronary syndrome

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Purpose of the study was to evaluate the prognostic significance of galectin-3 (Gal-3) level at admittance in patients with acute coronary syndrome (ACS).

Methods: 74 patients (66 (59;74) years old) admitted to the emergency department for ACS were involved in the prospective cohort study. Follow-up period was 12 months. The primary end point (PEP) was the composite of cardiovascular (CV) mortality and rehospitalization (RH) due to worsening of CV symptomatic. Gal-3 was measured by commercially available ELISA kit. Blood sampling was within 24 hours from ACS manifestation. Gal-3 threshold level was accepted as 17.8 ng/mL. In-hospital and post discharge (6 months) risks of death were calculated (GRACE risk models).

Results: The rate of reaching primary end point was 28.4%; CV mortality - 10.8% and RH - 17.6%. Gal-3 threshold was exceeded in 54.1%. Compared with patients with Gal-3 concentration less than 17.8 ng/mL, those with Gal-3 concentrations exceeding this level were significantly more likely to reach the PEP with HR 2.06 (CI 1.57; 2.71). Risk of CV death within 12 month since ACS manifestation was also higher in patients with Gal-3>17.8 ng/mL (HR 3.87 (CI 3.38; 4.43)).

However Gal-3 level in patients who reached PEP was not significantly higher than in those who successfully survived 12 months period (22.15 (17.34; 24.83) vs 17.55 (14.77; 26.54) ng/mL, $p=0.1620$). In this study patients who reached PEP never had Gal-3 concentration lower than 10 ng/mL.

No significant correlations were detected between Gal-3 concentration and calculated risks of in-hospital death and death within 6 months from discharge, as well as between Gal-3 and lifetime without cardiovascular adverse events. Gal-3 inversely correlated with left ventricular ejection fraction ($R=-0.34$, $p<0.05$), acute heart failure Killip class (Kendal $\tau=0.37$, $p<0.05$) and type of diastolic dysfunction (Kendal $\tau=0.49$, $p<0.05$). Gal-3 correlated with self-assessed health status and rehospitalization rate with maximal strength of correlation in women (Kendal $\tau=-0.45$ and 0.50 , $p<0.05$).

Conclusion: Measurement of Gal-3 in the emergency department in patients with acute coronary syndrome can be useful for identifying patients at elevated risk for near-term CV mortality and rehospitalisation.

P1901

Predictors of long-term events in dilated cardiomyopathy

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Introduction: Left ventricular diastolic dysfunction is described as an early change, preceding the systolic dysfunction. Thus, it can be considered that there is an interrelationship between the systolic and diastolic function in patients with heart failure. The marker of heart failure is the elevated LV filling pressure. The determination of echocardiographic parameters and biomarkers associated with elevated LV filling pressures have prognostic value in HF and may be important its joint evaluation in the risk stratification of patients with dilated cardiomyopathy (DCM).

Objectives: identify the echocardiographic parameters of systolic and diastolic function, clinical and analytical parameters, predictors of events at 24 months of follow-up in patients with DCM and determine an event risk score based on these predictors.

Methods: analysis of 127 patients with DCM, initially admitted for acute HF. Clinical, analytical and ecocardiográficos parameters associated with worse prognosis by multivariate analysis were analyzed. The cut-off values were determined by ROC curves. Subsequently given 1 or 2 points (p.) according to the obtained odds ratio ($p<0.05$): $E/E' > 15$ (2 p.), BNP value > 400 ng / ml (2p.), medical history of DM2 (1p.). The prognostic potential was translated by analysis of Kaplan-Meier curves. Statistical significance at $p<0.05$

The endpoint at 24 months (M) was defined by readmission for HF and / or death (R / D).

Results: The average ejection fraction (EJF) was 31.8 ± 10.1 (13 min-max 53). The event rate at 24 months was 33%.

The best prognostic independent predictors were: ratio E/E' ($p=0.01$), BNP value on admission ($p=0.02$) and medical history of type 2 DM ($p=0.03$). The E/e' ratio stood out as an independent predictor of events, with prognostic value superior to others clinical factors above. The ROC curve showed that the ratio E/e' cut-off point for predicting worse prognosis was 15 (AUC=0.772; sensitivity 75%, specificity 81%; $p=0.02$). The Kaplan-Meier curve showed a higher event rate among patients with $E/e' \geq 15$, compared to patients with $E/e' < 15$ (log-rank 23, $p=0.03$).

A score > 2.5 proved to be a predictor of M / D at 24 M (AUC: 0.701, S-71% E-76% $p=0.01$), translated linearly in the survival curves (Kaplan-Meier log rank: $p<0.01$).

Conclusions: The ratio E/e' submitted additional prognostic information independent and proved to be the best predictor of events at 24 months of follow-up. Patients with score > 2.5 p had a poorer prognosis.

P1902

Evaluation of prognostic value of biomarkers ST-2, NT- pro BNP, Galectin-3, Cardiac troponin-I in patients with different functional classes of heart failure according to the course of the disease

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Aim: To compare prognostic value of biomarkers: NT- pro BNP, ST2, Galectin-3, Cardiac troponin-I in patients with chronic heart failure and ischemic and non-ischemic cardiomyopathy.

Methods: NT- pro BNP, ST2, Galectin-3, Cardiac troponin-I blood assessment and hemodynamic of left and right heart were assessed. This study involved pts 18 - 65 years old, with chronic heart failure: I-II functional class (FC) - 70 pts, I-II functional class (FC) - 68 pts. According to the cardiac outcome (CO) within a clinical follow-up period of 6 month all pts were divided into 2 grs: 1) with favorable CO (108), 2) with unfavorable CO (24) (death, cardiac transplantation, emergency hospitalisation).

Results and Conclusions: Concentration of NT-proBNP in blood is connected with the severity of the HF and unfavorable prediction of the disease course in patients with I-II functional classes of the HF.

In patients with III-IV functional classes NT-proBNP blood levels didn't seem to have a prognostic value because in these patients the concentration of NT-proBNP was significantly increased regardless of the outcome of the disease and was close to the values in patients with unfavorable course of the disease in CHF I-II functional classes (tab.1).

The concentration of ST-2, Galectin- 3 was not associated with the severity of HF, but it is closely related to the prognosis of the disease in patients with III-IV functional classes of HF. Thus, in the group with severe HF (III-IV functional classes) the level of this biomarker in patients with cardiac events within 6 months follow-up was 1.6 times higher than in those with a favorable course of the disease (tab.1).

The concentration of Cardiac troponin-I was not associated with the severity of HF and didn't seem a prognostic value in investigation.

Comparison of concentration biomarkers

	FC I-II favorable outcome	FC I-II unfavorable outcome	FC III-IV favorable outcome	FC III-IV unfavorable outcome	P
	1	2	3	4	
NT-proBNP, pg/ml Me (LQ-UQ)	625 (183-2549)	1979 (1109-8059)	2114 (797-2930)	2083 (1017-11112)	P1-2 =0,019 P1-3 =0,002
ST - 2, ng/ml Me (LQ-UQ)	27,3 (19,9-35,3)	25,0 (23,0-30,2)	31,3 (20,4-40,8)	49,1 (29,3-80,8)	P3-4 =0,029 P2-4 =0,04
Galectin - 3, pg/ml Me (LQ-UQ)	11,8 (10,0-13,2)	11,5 (10,9-14,1)	10,6 (9,4-14,6)	16,4 (11,6-20,9)	P3-4 =0,028 P2-4 =0,050

P1903

Neutrophil gelatinase associated lipocalin better predicts early acute kidney injury and outcome respect to bnp and cystatin c in acute heart failure patients

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Purpose: Neutrophil Gelatinase-associated Lipocaline (NGAL) has been described in chronic heart failure (HF) as marker of tubular damage and renal dysfunction, however less data are available in acute HF patients. Because of high rate of acute kidney injury (AKI) development, we aimed to investigate the role of NGAL, in predicting early AKI development; secondly we compared NGAL respect to Cystatin C, B-type Natriuretic Peptide (BNP), renal function and blood urea nitrogen (BUN) for outcome prediction.

Methods: We measured admission serum NGAL, Cystatin C, and BNP, in 231 patients affected to acute HF; all patients were submitted to daily creatinine, estimated glomerular filtration rate (eGFR), measurement to identify in-hospital AKI defined by AKIN criteria. We also measured admission and discharge eGFR, creatinine and BUN to evaluate their prognostic role during a 6-months follow-up period.

Results: 78 patients developed AKI during hospitalization in this subjects, NGAL levels were significantly increased respect to patients without AKI (295 ± 228 vs 129 ± 108 ng/ml $p < 0,001$). A cut-off of 134 ng/ml has been related to AKI with good sensibility and specificity (85% and 80% AUC 0,81 $p < 0,001$). BNP was also mildly increased (1000 ± 906 pg/mL vs 746 ± 580 pg/mL $p = 0,03$) but not Cystatin C. Patients with chronic kidney dysfunction (CKD) demonstrated higher NGAL levels compared to subjects with preserved renal function (258 ± 249 and 120 ± 77 ng/ml $p < 0,001$). The ROC curve analysis demonstrated that increased NGAL values were associated to increased mortality (cut-off: 170 ng/mL; sensibility 60%; specificity 82%; accuracy 71%; AUC:0,77 $p < 0,001$). The same significant correlation was also found for BUN at discharge (cut off: 100 mg/dL; sensibility 65%; specificity 85%; accuracy 71%; AUC 0,77 $p < 0,001$). Multivariable COX regression analysis showed that cutoff 170 ng/ml was related to adverse outcome (HR 1.77 IC 1.24-2.83 $p = 0,01$)

Conclusions: NGAL measurement is a sensible tool to predict AKI during hospitalization. Elevated NGAL levels appear to be related to BUN increase and post discharge outcome. This suggests a prognostic role of tubular damage beyond renal dysfunction.

P1904

High-sensitivity troponin and risk of recurrent hospitalizations after an admission for acute heart failure

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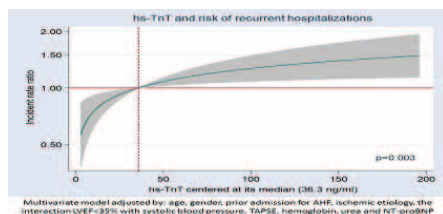
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Introduction: Risk of recurrent hospitalization in patients recently discharged for acute heart failure (AHF) remains prohibitively high. High-sensitivity troponin T (hs-TnT) has emerged as a useful biomarker for predicting death in patients with heart failure; nevertheless, its utility for predicting readmission has not been well established. We aimed to evaluate the association between hs-TnT and risk of recurrent hospitalizations in admitted AHF patients

Methods: We prospectively studied a cohort of 406 patients consecutively discharged for AHF in our cardiology department from January 2011 to March 2014. Patients with a final diagnosis of acute coronary syndrome were excluded (n=21). A multivariable negative binomial regression was used to assess the association between admission hs-TnT with the number of readmissions occurred along the follow-up. A 2-sided p-value < 0.05 was considered to be statistically significant for all analyses. All analyses were performed using Stata 13.1

Results: The mean age of the sample was 73.4 ± 10.9 years, 51.5% were male and 51% exhibited LVEF>50%. Median (IQR) for hs-TnT and NT-proBNP was 36.3 ng/mL (21.4-81.6) and 3785 pg/mL (2000-7783), respectively. At a mean post-discharge follow-up of 1.5 years, 95 deaths (23.4%) and 459 all-cause rehospitalizations in 238 patients (58.6%) were registered. The number of rehospitalizations were distributed as follow: 1=121 (31.3%); 2=61 (16.5%); 3=24 (11.1%); 4=19 (5.8%) and $\geq 5=14$ (3.2%). After a multivariate adjustment, hs-TnT was positive and independently associated with the number of all-cause rehospitalizations (figure below) and evidenced by an IRR (95% CI) of 1.26 (1.08-1.47) $p = 0.003$ for log hs-TnT

Conclusion: In AHF patients, admission hs-TnT was strongly associated to an increased risk of recurrent hospitalizations



NURSING

P1905

Risk factors and sociodemographic variables association analysis with priority nursing diagnosis for heart failure in primary care

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Introduction: Chronic non-communicable diseases (NCDs) bring great impact on mortality rates in the world and in Brazil, being heart failure (HF) a serious and progressive disease. And, for nurses, all the answers are taken into account, clinical

or not, that the individual has towards the disease at his different stages in primary care, so there is the planning of interventions.

Objective: To analyze the association between risk factors and sociodemographic variables with priority nursing diagnosis for heart failure in primary care.

Methods: Cross-sectional study, part of the Study Digitalis, which involved 633 randomized subjects of a database of 137,463 enrolled in the Family Medical Program (FMP), of Niterói municipality/ RJ, aged from 45 years. Data were collected during the nursing consultation, realized from July 2011 to November 2012, in which a single questionnaire was used. Data were organized and analyzed using SPSS program, version 17.0.

Results: The analysis was performed from the association of 25 (twenty-five) priority nursing diagnosis, identified by experts using Delphi Method, with risk factors (smoking, alcohol consumption, obesity, hypertension, diabetes mellitus, arterial disease coronary); sociodemographic variables (gender, age, race and education); and IC stages. Of the 25 diagnoses analyzed, three showed no statistical differences for any of the studied variable: disposal for improved nutrition, low self-esteem and situational fatigue. The remaining 23 diagnoses showed statistically significant differences for a number of variables that ranged 1-7.

Conclusion: The nurse practice reflection in primary care in the chronic disease approach, supported by analysis, proposes to extend the view owing to the use of the nursing diagnosis of an individual for the diagnosis of a community.

P1906

Do our patients have heart rate under control?

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Introduction: Heart failure (HF) is a clinical syndrome of great magnitude due to its high prevalence, morbidity and mortality. Some recent therapeutic innovations have improved the prognosis.

In the year 2010 the SHIFT study revealed the prognostic importance of heart rate (HR) control in patients with chronic HF. Since then, a HR<70 has become a therapeutic goal in clinical practice. In the Guidelines of the European Society of Cardiology (ESC) published in 2012, Ivabradine was a recommended option to decrease HR in patients with chronic HF and reduced ejection fraction (HF-rEF).

Purposes:

- 1) To know if mean HR of the patients in sinus rhythm and HF-rEF visited in the Heart Failure Unit (HFU) is close to ESC recommendations.
- 2) To describe the drugs and the doses used in the HFU to control patient's HR.
- 3) To analyze the reasons for no prescription of beta-blockers (BB).

Method: Descriptive cross-sectional study. Medical records of patients visited in HFU from September 2013 to August 2014 were analyzed.

Inclusion criteria: Patients with sinus rhythm and HF-rEF.

Exclusion criteria: Atrial fibrillation, atrial flutter, pacemaker, titration phase, decompensated chronic HF, LVEF >35%.

Results: 712 medical records were reviewed and 228 of them accomplished the inclusion criteria.

Mean age: 69.7year-old. Males: 73%. Mean LVEF: 30.7%.

Mean HR: 62 b/m.

Conclusions: Eighty-eight% of the patients with HF-rEF followed in our HFU have HR within the ESC Guidelines recommendations. The majority of them (63.6%) reached the target HR with BB, with an average of 37.2% of the maximum recommended dose. The rest of the patients needed ivabradine to control HR, half of them in association with BB. Overall, 16% of the patients of the series were treated only with ivabradine, mainly because of concomitant pulmonary disease.

Results				
Drug	Patients treated (%)	Mean maximal tolerated dose (mg/day)	Target dose (%)	Heart Rate (b/m)
Carvedilol	22.8%	15.2	30.4%	63
Bisoprolol	40.8%	4.4	44.0%	61
Carvedilol + Ivabradine	11.4%	14 + 12	28% + 85.7%	61
Bisoprolol + Ivabradine	9.2%	4.8 + 10	48% + 66.7%	63
Ivabradine	15.8%	13.9	92.6%	63

P1907

Facilitators and barriers: implementation of titrating heart failure drugs by specialized nurses

This project was approved by the Ethics Committee for Clinical Research of Euskadi (CEIC-E).

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Introduction: Up titration drugs in Heart Failure (HF) is associated to the prescription done by the cardiologist. It consists in achieving target dose making gradual increase of the medication dose, taking into account the evolution and clinical and analytical parameters of the patient.

On the other hand, there is large literature that describes the titrating made by the HF specialized nurse with algorithms and support of the cardiologist.

Purpose: In Spain, currently, up- titration of HF drugs by specialized nurses is diverse, being done in some places by nurses, but not in the others. This is the reason why the aim of this study is to know the means that make it easier and barriers among health professionals to implement drug titration by the specialist nurse of patients with HF.

Methods: Design: Qualitative research study that will use grounded theory method. The sample will consist of specialist nurses who attend with HF patients, cardiologists and managers of the health center where nurses work. Theoretical sampling will be used to choose participants.

Inclusion criteria:

1. Specialized nurses who work in Spain in a HF Unit (HFU) or in the community, with up to two years of experience in patients with HF and training in cardiology, HF and drug titration.

2. HFU cardiologists who have participated in the project.

3. Managers of the health center (medical director or nurse director) where nurse works.

4. Specialized nurses who voluntarily agree to participate.

Exclusion criteria:

Cardiology nurses who have no experience or training in HF.

Data collection method will be semi-structured interview. It is estimated the need of about 20 or 25 interviews.

Data analysis: Focus groups will be analyzed based on thematic content, triangulation of results and reporting composed of analytical categories.

P1908

Quality appraisal of international clinical practice guidelines for managing acute heart failure

China Medical Board (no. 04-797)

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Background: Nurses are key healthcare professionals to provide actions to ensure a prompt diagnosis and the safe delivery of care to a patient with acute heart failure during their in-hospital stay. There has been an increase in the development of clinical practice guidelines (CPGs) to improve standards of care in managing heart failure (HF), many of which are disseminated online. However, little is known about the quality and recommendations within clinical practice guidelines for nurses to manage of the acute episode of heart failure or alleviate symptoms during this period.

Objective: The purpose of this study was to undertake a systematic critical appraisal of guidelines, and provide a summary of recommendations for management of acute heart failure.

Methods: The databases of Cochrane Library, PubMed, EMBASE, SinoMed, CNKI, WanFang and the websites of SIGN, NICE, NGC and so on, were retrieved for collecting global guidelines, which were screened according to the inclusion and exclusion criteria. The quality of all guidelines was critically appraised using the Appraisal of Guidelines for Research and Evaluation II instrument. Each guideline was independently reviewed by four reviewers. All relevant recommendations for management of acute heart failure that nurses can undertake were synthesized.

Results: Eight evidence-based guidelines with recommendations concerning acute heart failure were included. Based on the AGREE II, the quality of CPGs varied considerably. The highest average scores on AGREE-II were in scope and purpose (86.46%) and clarity of presentation (86.63%). The lowest average scores were in editorial independence (54.03%) and applicability (41.66%). The overall assessment showed that AHA/ACCF 2013, ESC 2012, NICE 2010, SIGN 2007 editions were the positively recommended, NHFA 2011, CCS 2013, HFSA 2010, China 2014 editions were the recommended guidelines (still need to supplement and improve). Symptoms monitoring, optimized medical management, nonpharmacologic management, and patient education were key recommendations that nurses can undertake reducing symptoms and stabilizing the haemodynamic condition.

Conclusions: Developers of CPGs should improve their reporting of development processes and CPGs' applicability to practice. This critical appraisal can assist Chinese nurses to adapt evidence-based clinical practice guidelines to improve outcomes in managing acute heart failure.

P1909

Improve of the treatment adherence, of the quality of life and the morbidity of the heart failure patients

Fundación Puerta de Hierro

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Objective

Evaluate the effectiveness of a nurse educational intervention in Heart Failure Patients in improving the level of self-care, treatment adherence, quality of life and morbidity.

Method: DESIGN: Randomized controlled clinical test with allocation concealment, in two groups. The CONTROL group received the usual practice. In the INTERVENTION group was applied a educational nurse intervention in 3 sessions of 20 minute, book and DVD with educational content.

Inclusion criteria: patients with heart failure, good cognitive level, literacy, consent and signature.

Variables (Instruments): sociodemographic, clinical, hospital readmissions (Medical History / Interview); quality of life (EQ-5D), self-care (European Scale), treatment adherence (Morisky) dependence (Lawton-Brody), depression (Yasavage).

Results: Groups were comparable at baseline in all variables:

Comparison: Intervention / Control 3 months follow-up. There were no significant differences in any of the studied variables. Comparison: Intervention / Control 6 months follow-up. Differences ($p < 0.05$) between groups with respect to the level observed:

- Self Care 15/18,5.

- Difficulty in walking 24% / 60%

- Recently Seek Emergency 0% / 20%, and recent hospital admissions 0% / 20%.

- At 6 months, the intervention group had better quality of life. No problems EQ-Mobility 62% / 50%. Best Personal Care EQ-76% / 64%. Best EQ-Activities 57% / 50%. Without depression 71% / 64%.

Conclusion: Patients with heart failure who received the nurse educational intervention showed better results in the level of self-care, quality of life and morbidity than those receiving usual practice, after six months of the release from the hospital.

P1910

Prognosis of the co-morbid heart failure and anaemia: a systematic review and meta-analysis

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Anemia is found to be an independent risk factor of morbidity, mortality and hospitalization among patients with heart failure (HF). Over the last decade, the prevalence, as the potential treatment options of anaemia in HF have received increasing clinical interest and epidemiological studies have indicated a wide variation in the prevalence of anaemia in patients with chronic HF.

The goal of the present systematic review and meta-analysis was to investigate the prognosis of comorbid anaemia in patients with HF. The clinical outcomes under investigation were: the mortality rate, the re-hospitalization rate, the length of hospital stay and the association between the co-morbidity of anaemia and the physical functionality of the patients according to NYHA classification.

Electronic search took place in the databases: Pubmed, Cochrane Library and CINAHL. The combination of the words: "heart failure", "anaemia", "readmission" and "NYHA class" was used for the search in order to locate studies in English language that investigated the effect of anaemia in patients with HF outcomes. The overall pooled effect (relative risk, RR) of anaemia as comorbid factor compared with HF patients without anaemia by using a random effects analysis (95% confidence interval (CI) for the outcomes of HF - related mortality rate, re-hospitalization and physical condition.

Twenty-six studies were selected for the meta-analysis. In the overall RR of mortality, re-hospitalization and extended hospitalization was 1.70, 95% CI (1.47-1.98), $p < 0.00001$, for readmission rate 1.57, 95% CI (1.17,2.10), $p = 0.003$ and 1.25, 95% CI (0.59-1.90), $p = 0.0002$ respectively in behalf of heart failure patients without anaemia. Likewise, patients with anaemia tend to have worse functionality according to NYHA classification 1.23, 95% CI (0.99-1.52), $p = 0.06$. A meta-regression analysis conducted in an effort to explain the heterogeneity for the variable mortality. Firstly, to conduct a sensitivity analysis the studies that had

RR >2.5 in the first analysis excluded. Secondly, only the studies that used the definition of anaemia by WHO were included in the sensitivity analysis.

The present meta-analysis gives an outline profile of patients with the co-morbidity HF and anaemia in terms of clinical outcomes. The results point out worse prognosis in HF patients with comorbid anaemia. Nevertheless, the available data did not allow the extraction of a conclusion in which exact Hb levels anaemia becomes a negative predictor of prognosis; thus greater studies are needed focusing on that and giving practical recommendations for clinical practice.

P1911

Caregiving burden of patients with heart failure caregivers

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Purpose: The caregivers who care patients with heart failure encounter many distressing problems in their lives. Therefore, the research was conducted to evaluate the burden of caregivers providing care to patients with heart failure.

Methods: This research was conducted with 110 patients with heart failure diagnosis and patients' relatives who presented to Cardiology Clinic and service of our Medical Center. Before the investigation, written permission was obtained from the relevant institutions and the Ethics Committee of our University, Faculty of Medicine and also the verbal consent was obtained from patients and their relatives. Data was collected a questionnaire including socio-demographic variables that was created with literature and experts' opinion. Additionally, Caregiving Burden Scale (CBS) was used. Minimum 0 and maximum 88 points could be obtained from the scale and the higher scores indicated higher caregiving burden. In the evaluation process, descriptive statistics were used; for comparative data, Kruskal Wallis, Mann Whitney-U, ANOVA and t tests.

Results: It was determined that 40% of the caregiving individuals were in the age group of 33 to 47 years, 52.7% of them were women; 71.8% of them were married; 42.7% of them were primary school graduates; the mean CBS score was 29.84 ± 12.86 , and there was a positive relation between the age of caregivers and the mean CBS score. It was found that CBS scores's mean were higher among the caregivers who provided care for the patients with additional illnesses accompanying heart failure, as well as hypertension and patients who previously hospitalised ($p < 0.05$).

Conclusions: With these results, it is important to support elderly caregivers and who need more care of patients with heart failure by the health care team members. Additionally as a consulted health care team members give advices about the development of coping mechanisms.

P1912

Development and initial evaluation of an internet-based cognitive behaviour therapy program for patients with heart failure and depression. A proof of concept study

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Internet based-Cognitive behavioural therapy (IB-CBT) could be beneficial for heart failure (HF) patients with depression. However no such programs have been developed or been evaluated in HF patients.

Aim: (1) to describe the development of an IB-CBT program adapted to patients with HF and (2) evaluate the feasibility of the IB-CBT program in regard to depression, time-consumption for feedback to participants and patients perceptions of the IB-CBT-program.

Method: A multi-professional team including a cardiac patient was enrolled in the development of the program. Seven HF patients with depression were recruited to the feasibility study. Patient Health Questionnaire-9 (PHQ-9) and Montgomery Åsberg Depression Rating - Self-rating scale (MADRS-S) were used to measure depression. Interviews were performed to capture patients' perceptions of the program.

Results: A nine week program including introduction, psychoeducation, behaviour activation, problem solving and consumption adapted to HF patients, was developed and tested. Participants mean depression score decreased from baseline to the end-of the study (PHQ-9 from 11 to 7; MADRS-S from 20 to 14.5). None of the participants' depression scores was increased. The therapist used approximately a total 3 hours per participant for feedback, i.e. 20 minutes/week. Patients perceived

the IB-CBT program to give them freedom of time disposition and being helpful for learning about their health problems and what they could do about them. Negative perceptions of the IB-CBT program was that some parts required quiet a lot of reading and work, and technical problems with computers and the internet platform.

Conclusion: The nine week IB-CBT program seems to be a feasible and time-efficient tool to treat depression. However the IB-CBT program needs to be evaluated in a larger randomized study.

POPULATION STUDIES / EPIDEMIOLOGY

P1913

Cardiac surgery and sexual dysfunction

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Rational and Objective: Erectile dysfunction (ED) is a condition little studied in patients after cardiocirurgia. Essendo sexual function critical to the morale and welfare of man regardless of race, age, social extraction, from cultural level, although the onset of a temporary erectile disorder, can have truly devastating effects especially on emotional. ED can be easily assessed by specific test. Scopo study evaluating the presence of DE in a population of patients admitted to our UFMetodi: They were then analyzed the data of 600 patients admitted to our department in 6th 7th day after BPCA (70%) or valve replacement (30%). the age was between 40 and 65 years. 75% were smokers, 54% diabetic, 24% dyslipidemia, 54% Hypertensive. All selected patients underwent a re-evaluation program clinical and functional including an electrocardiogram, echocardiogram with color Doppler, vascular color Doppler of TSA / Abdominal Aorta / AV lower limbs, Spirometry, oxygen saturation, arterial blood gases, chest X-ray in AP and LL, blood tests, ECG dynamic sec. Holter 24H. Patients inter alia performed an interview Psychological that in addition to evaluation by the administration of tests like The MMP and MMP II, included an evaluation tests of erectile function of the type IIEF-5. This is a short questionnaire that consists of only 5 questions that analyze the erectile function and the degree of sexual satisfaction with a good degree of sensitivity. Subsequently, patients were reached at home by telephone interview during which resuscitating the test questions on the DE IIEF-5 were obtained and then information on the current sexual performance. Risultati: In a population of patients aged between 40 and 65, the DE was declared by 40% of the patients in our Division of Cardiac Rehabilitation after surgery cardocirurgico (but about 15% declared disorders prior to the event) by both the evaluation of the test IIEF-5 that targeted intervention Psychologist. The analysis obtained subsequent telephone at home, however, confirmed the persistence of the disorder as a percentage of 15-20%, while the remainder had resumed a regular activity the almost sessuale. Conclusioni: The study shows that there is a common disorder of sexual function in this subgroup of patients (undergoing a recent heart surgery), often overlooked and little studied that certainly is closely related with the main cardiovascular risk factors. Frequently this disorder is acute cardiac event and existing intervention cardocirurgico and can be considered as an early marker of atherosclerotic disease multivessel

P1914

The true prevalence of different functional classes of chf in the population of Russia

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Purpose: established the true prevalence of different functional classes NYHA (FC) of chronic heart failure (CHF) in the representative sample in the European part of Russia (EPOCHA).

Methods: 19503 respondents were included in the representative sample from eight subjects Russian Federation and from five regions with a presumptive diagnosis of heart failure patients hospitalized. CHF criteria were: the presence of cardiovascular disease, shortness of breath over the second degree under EPOCHA questionnaire and any degree of fatigue. 931 patients admitted with a presumptive diagnosis of CHF. The diagnosis was confirmed by ECG, chest x-ray, ultrasound of the heart and a 6-minute walk test.

Results: 92.8% of hospitalized patients was confirmed CHF. You can talk about the true prevalence of heart failure in Russia: 7% in a representative sample. Distribution of patients according to NYHA FC was: lack of CHF detected in 7.2% of cases, I FC was diagnosed in 21.1% of patients, II FC installed in 44.0% of cases; III and IV CHF

are diagnosed in 23.3% and 4.4%, respectively. The true prevalence of CHF NYHA FC appeared in Russia: FC I - 22.7%, II FC - 47.4%; FC III - 25.1% and FC IV - 4.7%. Patients NYHA FC I represented among all age groups from 10 to 100 years. In a representative sample of patients in NYHA functional class II found in the age groups from 20 to 100 years, and III and IV CHF NYHA - from 30 years and from 40 years of age or older, respectively. Probably, in the population to form heavier functional class of heart failure requires an average of 10 years. In clinical practice, in 32.2% of cases had been misdiagnosed CHF. In CHF FC I diagnosis is often missing or the contrary exhibited FC II. In the case of diagnosis of NYHA FC III often exhibited FC II. Diagnosis FC IV undercounted in 75% of cases. **Conclusions:** 70% of patients have a low CHF FC in Russia. III and IV NYHA functional class is virtually absent, as there is a high mortality rate of these patients.

P1915

The incidence of heart failure admissions in the cardiology department of a central hospital in Greece

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Introduction: The progressive aging of the population combined with the increase of life expectancy due to the improved therapeutic intervention have led to a gradual increase in the prevalence of heart failure. Consequently, a progressive increase of heart failure admissions has been noticed in Cardiology Departments. In addition, financial crisis has been previously associated with an increase of cardiovascular morbidity and mortality.

Purpose: The purpose of this study was to determine the incidence of admissions due to heart failure in our Cardiology Clinic of a central hospital during the period of Greek financial crisis.

MATERIAL - METHODS

The population of the study consists of patients who went to the cardiac clinic of our General Hospital during the last five years (2009 - 2013). These 5 years coincide with the period of economic crisis in our country.

Results: The results of the study demonstrated at the following Table 1.

Conclusions: In the present study the incidence of heart failure admissions was lower compared to that (one of eight patients) reported in the international bibliography. A possible causative factor for this observation is probably the effective function of the regular outpatients' department of Heart Failure in the certain hospital.

Another observation was made regarding the mean annual duration of hospitalization which was decreased. The explanation of this phenomenon possibly lies in the improvement of the therapeutic interventions and the patients' compliance. Another cause could be the debility of patients without social insurance to afford the economic cost of a long hospitalization. Additionally, a progressive annual increase of the incidence of heart failure admissions ($p < 0.01$) was observed and this was more prominent in women ($p < 0.01$).

TABLE 1

YEAR	TOTAL ADMIS-SIONS	HF ADMIS-SIONS	MEAN HOSPITAL STAY	< 60 YEARS	MEN	WOMEN	NO SOCIAL INSUR-ANCE
2009	654	86	6.2 days	14	59	27	5
2010	712	95	5.8 days	22	60	35	8
2011	739	98	5.4 days	28	62	36	12
2012	780	108	4.8 days	35	66	42	15
2013	840	121	4.0 days	44	72	49	22

P1916

Prevalence of heart failure, risk factors, and hospitalization costs: examining gender effects

This analysis submitted to the Heart Failure Congress, May 23-26, 2015, Seville, Spain was supported by a grant from CDC

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Objective: We examined variations in heart failure (HF) rates, risk factors, and hospitalization costs by gender among HF patients.

Methods: We extracted 2010 data on patients with a primary diagnosis of HF (ICD-9 codes: 402, 404, 428) from the Hospital Discharge Data System (HDDS). The HF sample (n=62,685) included females (49.3%), Whites (57.7%), African

Americans (blacks; 13.2%), Hispanics (24.4%), and Asian/Pacific Islanders (8.7%). The sample average age was 73 years. Age-adjusted prevalence of HF per 100,000 U.S. 2010 population was computed for each gender group per CDC methodology.

Results: Four trends emerged: (1) the overall age-adjusted rate for HF was 262.8 per 100,000; rate was higher for males than females (304.4 vs. 217.8 per 100K); (2) HF among younger males (aged <54) was nearly 2 times higher compared to females; (3) Hypertension (HTN), diabetes mellitus (DM), Coronary heart disease (CHD), Atrial Fibrillation (AFib), and Chronic kidney disease (CKD) emerged as primary risk factors for HF across both gender groups. Additionally, while COPD characterized male HF patients, depression/anxiety was more prevalent among HF females; (4) Hospitalization costs for HF only and total cost for the entire year were significantly higher among males compared to females. Higher costs among males largely reflected their greater number of co-morbidities and hospital re-admissions.

Conclusion: The burden of HF is higher among males, particularly younger males. Additional research is needed to determine whether aggressive primary preventive programs aimed at lowering hypertension, diabetes, and other co-morbidities at the community level might reduce subsequent hospitalization for HF in the younger vulnerable populations.

P1917

Incidence of hyperkalemia in patients with newly diagnosed heart failure: a large observational study in the UK

Research grant from Bayer Pharma

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Purpose: This study aimed to estimate the incidence and risk factors for hyperkalemia in a large population-based cohort of patients with newly diagnosed heart failure in a general practice setting. We also evaluated the impact on incidence rates when using different definitions for hyperkalemia.

Methods: A retrospective cohort study was performed in a UK primary care database (The Health Improvement Network). Patients with newly diagnosed heart failure, aged 1-89 years between January 2000 and December 2005 (N=19,194), were identified and followed after the initial diagnosis until the first occurrence of hyperkalemia or end of follow-up period (December 2011). Different serum potassium (K+) thresholds were evaluated as possible definitions for hyperkalemia, and incidence rates (IRs) calculated.

Results: The highest IR (7.9 per 100 person-years) was found with the least restrictive definition (serum K+ more than the upper bound of general practice's normal range), whereas the lowest rates (0.9 and 1.4 per 100 person-years) were observed with restrictive definitions (serum K+ ≥ 6 mmol/L and $\geq 20\%$ above the upper bound of normal range, respectively). Based on the results of these sensitivity analyses and the existence of considerable differences in the upper bound of serum K+ normal range between practices contributing to THIN (range: 4.4 to 5.7 mmol/L), we considered the most appropriate definition as serum K+ $\geq 10\%$ above the upper bound of normal practice range. Overall, 2,176 individuals with a hyperkalemia episode were identified with this definition, IR: 2.90 per 100 person-years (95% confidence interval: 2.78-3.02) over a mean follow-up of 3.9 years. Using Cox regression, old age, diabetes (HR: 1.87, 95%CI: 1.70-2.07), and severe renal impairment (eGFR <30 ml/min) (HR: 2.96, 95% CI: 2.44-3.60 compared to patients with normal renal function (eGFR ≥ 60 ml/min)) were identified as independent predictors for hyperkalemia after incident heart failure. Also, an episode of hyperkalemia prior to heart failure diagnosis carried a greater risk of a new episode of hyperkalemia (HR: 2.90, 95% CI: 2.50-3.35).

Conclusions: Variations in hyperkalemia definition resulted in substantial differences between IRs, thus caution is needed when comparing published estimates. Studies involving different referral laboratories, such as in primary care settings, might consider using a proportional increase above the upper bound of normal range instead of a fixed K+ value. Since hyperkalemia is a frequent event in this population, patients at high risk should be closely monitored.

P1918

Acute heart failure management: current situation and opportunities for improvement based on the best available evidence

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Introduction: Acute Heart Failure (AHF) accounts for 101,000 hospital admissions per year, being the 2nd most frequent DRGs in patients over 75. The British National Institute for Clinical Excellence (NICE) has recently reviewed its management based on current evidence in CG187.

Objectives: Understand current management of AHF at a secondary hospital with a referral population of 210,000 and identify possible differences between various

departments involved (Cardiology, Geriatric Medicine and Internal Medicine), based on efficiency performance and quality metrics. Benchmark current versus required situation in view of available evidence.

Methods: All 600 discharge reports of patients admitted in 2013 with a CIE9 428 main diagnosis were reviewed. Costs per patient were analyzed using analytical accounting. We studied in-hospital stay, readmissions, echocardiogram performance and mortality. We also applied an age-related risks and APR-DRG adjustment model according to disease severity and likelihood of death according to expected mortality. Organizational and coordination aspects between medical services and levels of care were also analyzed.

Results: Table 1 shows results by service according to different metrics. Solid coordination structures between services and liaison with Primary Care are lacked.

Conclusions: 1. Costs are constant across services with a longer median stay in Internal Medicine.

2. Readmissions rate tends to be greater in Geriatric Medicine.

3. Echocardiogram performance is adequate in Cardiology and far below required in Internal and Geriatric Medicine Departments.

4. Healthcare organization is fragmented and requires greater co-ordination between medical services and healthcare levels.

Table 1

	CARDIOLOGY	GERIATRIC MED	INTERNAL MED	P
Discharges (%)	121(22)	221(43)	185(35)	
Costs (€)	2698	2499	2936	ns
In-hospital stay(days)	6,1	7,5	9,8	<0,001
Readmissions (%)	6	15,1	9,8	0,07
Echocardiogram (%)	97	14	53	<0,001
Mortality (%)	5,8	6,2	4,5	ns

P1919

Prevalence and prognostic relevance of cardiac involvement in ANCA-associated vasculitis: eosinophilic granulomatosis with polyangiitis (Churg-Strauss) and granulomatosis with polyangiitis (wegeners)

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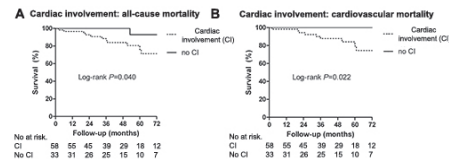
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Purpose: To investigate the prevalence and prognostic relevance of cardiac involvement in a large population of Churg-Strauss syndrome (CSS) and Wegener's granulomatosis (WG) patients.

Methods: Prospective cohort study of fifty EGPA and forty-one GPA patients in sustained remission without previous in-depth cardiac screening. Cardiac screening included clinical evaluation, ECG, 24-h Holter, echocardiography and cardiac MRI. Coronary angiography and endomyocardial biopsy (EMB) were performed upon indication. Fifty age- and sex-matched control subjects were randomly selected from a population study. Long-term was assessed using all-cause and cardiovascular mortality.

Results: ECG and echocardiography demonstrated cardiac involvement in 54% EGPA and 34% GPA patients as compared to 8% controls (both P < 0.002). Adding CMR as diagnostic modality increased prevalence of cardiac involvement to 66% in EGPA and 61% in GPA patients. CMR detected cardiac involvement in all ANCA-associated vasculitis (AAV) patients demonstrating ECG and/or echocardiographic involvement. In 52% EGPA and 44% GPA patients without symptoms and with normal ECG, cardiac involvement was present. After a mean follow-up of 53 ± 18 months, EGPA patients (not GPA) showed increased mortality (Log-rank P = 0.049). Presence of cardiac involvement in AAV-patients demonstrated an increased all-cause and cardiovascular mortality (Figure 1).

Conclusion: Cardiac involvement in EGPA and GPA patients with sustained remission is high, even if symptoms are absent and ECG is normal. Moreover, cardiac involvement is a strong predictor of mortality. Therefore, risk stratification using cardiac magnetic imaging is recommended in all AAV-patients, irrespective of symptoms or ECG abnormalities.



Survival curves for AAV-patients

P1920

Nonagenarians presenting to the diagnostic heart failure clinic

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Background: The prevalence of heart failure (HF) and the complexities of management increase with advancing age. We characterised the patients aged 90-99 years presenting to the diagnostic HF clinic in Sheffield.

Methods: We interrogated the diagnostic heart failure clinic database serving a city with 551,800 inhabitants and a growing elderly population. The size of the 90+ years age group has increased by 26% since 2001 to 4,300. Patients with suspected HF and a natriuretic peptide (NTproBNP) greater than 400pg/ml receive an echocardiogram and a clinical assessment by a heart failure cardiologist. We collected data from patients seen between March 2012 and September 2014. We classified the patients by their heart failure diagnoses, co-morbidities, symptom burden and whether or not their attendance in clinic led to a change in their management.

Results: 1,785 patients in total were seen in the diagnostic heart failure, of whom 160 patients (9%) were nonagenarians. Sixteen patients (10%) were excluded as they had no evidence of heart failure. The male to female ratio was 1:1.38. The diagnoses were heart failure due to left ventricular systolic dysfunction (HF-LVSD) (44%), heart failure with preserved ejection fraction (HFPEF) (38%), pulmonary hypertension (12%), valve disease (5%) and heart failure due to right ventricular systolic dysfunction (HF-RVSD) in one patient (<1%). The co-morbidities included chronic kidney disease stage III-IV (68%), systemic hypertension (67%), atrial fibrillation (38%), cerebrovascular disease (21%), diabetes mellitus (15%), visual impairment (26%), cognitive impairment (12%), hearing impairment (11%) and chronic obstructive pulmonary disease (10%). The average number of co-morbidities was four. The majority of patients had only mild symptoms (New York Heart Association Class II) (62%). The management of 132 patients (92.4%) was changed, most commonly by altering their medication following their attendance at the clinic. Further follow up was offered to 14% of these patients at the HF nurses'-led clinic and 9% of the patients were followed up at the cardiologist's-led clinic.

Conclusion: HF-LVSD, and not HFPEF, is the most common HF diagnosis amongst nonagenarians with raised NTproBNP presenting to the diagnostic heart failure clinic. Beyond making the diagnosis, attending the clinic by these nonagenarians resulted in management changes in at least nine out of every ten patients.

PSYCHOSOCIAL / ETHICAL CONCEPTS / EDUCATION

P1921

Socio-economic position and pharmacological treatment for cardiometabolic risk factors before an acute coronary syndrome

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Purpose: Inequalities in health are highly recognized in the agenda for research and intervention in public health. Our aim was to study the associations between socio-economic factors and pharmacological treatment for cardiovascular risk factors in a cohort of Portuguese adults before an acute coronary syndrome.

Methods: We included 791 patients consecutively admitted for acute coronary syndrome in 2 Portuguese hospitals, covering urban and rural areas, between August 2013 and November 2014. The data was self-reported, collected by trained interviewers during hospitalization. The socioeconomic factors included the educational level, working condition, income and perceived social class. The confounding effect of sex, age and self-reported history of previous myocardial infarction was controlled using unconditional logistic regression.

Results: The mean age was 64.0 ± 13.1 years and 583 (73.7%) patients were men. 65% of patients reported having dyslipidemia (44.5% of whom were treated), 64% hypertension (73.1% of whom treated) and 33% diabetes (66.3% of whom treated). Among patients with risk factors, the higher the education the lower the probability

of being treated pharmacologically (diabetes: adjusted OR 0.28; 95% CI 0.13-0.61, $p=0.001$ for higher education compared to less than elementary school). Housewives and permanently invalid people were more likely to be medicated, independently of sex, age and previous MI (OR 2.94; 95% CI 1.1-7.91, $p=0.033$; OR 3.41; 95% CI 1.87-6.21, $p<0.001$; respectively). Retired people with diabetes were also more likely to be medicated than those actively working (OR 2.41; 95% CI 1.37-4.2, $p=0.002$). Income had no effect on the probability of being treated for any of the risk factors. There was a weak and non-significant trend for higher self-perceived social class to be inversely associated with pharmacological treatment for risk factors (OR 0.51 95% CI 0.14-1.93, $p=0.323$).

Conclusion: Patients with lower education, housewives and permanently invalids were more likely to be medicated for cardiovascular risk factors. We cannot exclude that less likely pharmacological treatment in the higher education group is partly explained by a higher awareness of risk factors in phases in which pharmacological treatment was not yet prescribed. Our findings suggest the need to focus particularly on people actively working in primary prevention, since that group seems rather unprotected against cardiovascular risk factors.

P1922

Targeting device acceptance in patients with an ICD: the role of insomnia, PTSD and patients' support preferences

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Purpose: Psychological factors significantly impact patients' adjustment to living with an implantable cardioverter defibrillator (ICD). Post traumatic stress disorder (PTSD) is an established co-morbidity in this cohort, and patients with an ICD are particularly vulnerable to insomnia as the risk of shock from their device is increased at night. 'Device acceptance' refers to the psychological accommodation and understanding of the device and its benefits. The present study investigated (a) how device acceptance is impacted by sleep disturbance and PTSD in patients with an ICD, and (b) what preferences ICD patients have for support in managing these psychosocial difficulties.

Methods: A cross-sectional study was conducted examining symptoms of insomnia, PTSD and device acceptance in a cohort of 256 patients living with an ICD (82% male; mean age 67.78 years, SD = 12.18). The majority of patients had ischaemic heart disease with an EF $\leq 35\%$, and this was the most common pathology leading to ICD implantation. The Sleep Condition Indicator (SCI) and PTSD Checklist (PCL-C) were used to measure sleep quality and symptoms of posttraumatic stress respectively. Further measures included the FPAS and a study-specific measure of patients preferences for informational / psychosocial support.

Results: 13.2% (34/256) of ICD patients screened as having possible insomnia disorder (ID), and both sleep quality ($p<0.05$) and presence of ID ($p<0.001$) were associated with poorer device acceptance. Similarly, 12.89% (33/256) of ICD patients screened as having a possible diagnosis of PTSD, with both symptoms of post-traumatic stress ($p<0.001$) and PTSD cut-off score ($p<0.001$) associated with poorer device acceptance. Regarding support preferences, an ICD informational booklet was reported by patients (42.2%) as the most acceptable form of informational/psychological support, followed by the cardiac nurse specialist (37.1%) and family physician (27.5%). There were no gender differences in ICD patients' support preferences, but older patients (≥ 60 years) were less likely to endorse either digital health resources [web-based ICD information ($p<0.001$); smartphone ICD App ($p<0.001$); online ICD self-help programme ($p<0.002$)] or a cardiac psychologist ($p<0.009$) as acceptable forms of support.

Conclusion: Both sleep disturbance and posttraumatic stress adversely impact the adjustment of cardiac patients living with an ICD. Accordingly, programmes of care should include access to psychological treatments for insomnia and PTSD. Bibliotherapy is a preferred mode of support for patients with an ICD.

P1923

Particular aspects of communication between doctors, patients and family members in heart failure in an eastern european country

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Purpose: Heart failure (HF) is a chronic condition with multiple complications (including psychological) and high mortality. Patient-centered communication and shared

decision-making provide a better control of chronic conditions and higher level of patient satisfaction about healthcare, thus it is preferred by patients. Doctors frequently use a biomedical communication, predominantly in Eastern European countries, this is way our study analyzes the ways doctors and patients with HF communicate in Romania.

Methods: 46 patients with HF aged over 18 were included in our study after signing an informed consent form. Patients and their families were asked to complete a semistructured questionnaire on doctor-patient communication and shared decision-making. The study design was approved by an Ethics Committee. Statistical analysis was performed using SPSS v16.

Results: All patients wanted to know their diagnosis, regardless of gender, age, background, marital status and education (Fisher test, $p>0.05$) or age (Mann-Whitney test, $p>0.05$). All patients wanted to know detailed informations on their condition, treatment and prognosis, which were provided by the doctors, with patience and empathy for 91.3% of them. However, only 44.4% of patients considered the informations provided by the doctors allowed them to have a complete (100%) understanding of their condition. When asked to elaborate on their condition and severity, 44% failed to do so. They were mostly seniors, from rural areas and less educated. Most patients (75%) believe family should be allowed to know their diagnosis only with their approval, unlike 66.7% of family members. 80% of patients responded family was the most important provider of emotional (love etc) and instrumental (financial, activities of daily life etc) support. In daily practice, family members often ask doctors to „filter” information reaching the patient (arguing it would avert patients becoming scared and discouraged), which would break the law regarding patients rights in Romania. On the other hand, 30% of patients would want to have access to their medical records because they consider information is being hidden or withheld from them - this feature could be considered something specific to patients in our cultural area.

Conclusions: Communicating the diagnosis and medical information to patients with HF needs to be customized and adapted to patient's specific features and preferences. Family members can represent a valuable and significant resource in shared decision-making provided there is no breaking the law regarding patients rights.

P1924

Perception of difficulties in the treatment of heart failure and hypertension for doctors and patients in Russia

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Purpose: The cost of drugs is becoming a barrier to effective treatment of chronic heart failure in Russia.

Methods: 300 patients with CHF and hypertension aged 20 to 89 years interviewed: we used the author's profile, projective technique "incomplete sentences" (a variant technique Sachs-Sydney). For doctors (140 physicians and cardiologists from different cities of the Russian Federation) used the method of evaluation professionally significant situations in the work of the doctor, and the author's questionnaire aimed at analyzing situations doctors interact with patients. The results obtained were processed using content analysis procedures.

Results: To a direct question patients showed the average (35%) and conditionally high (30%) level of satisfaction with the quality of patient care. However, the projective technique "incomplete sentences" showed that the overwhelming majority of respondents with chronic heart failure and hypertension experience negative emotions towards oneself as a patient. Patients experience at the doctor as a "guinea pig" (20%) or "not welcome", "begging" (52%). In men, these feelings appear significantly more often than women ($r\leq 0.02$). Women perceive themselves more "helpless child in pain" than men ($r\leq 0.04$). Women waiting for a doctor's care and attention and speak about the lack of time to receive more often than men ($r\leq 0.001$). Patients do not worry about the cost of treatment (only the fifth level of the frequency). According to doctors, the main difficulties in the treatment are the "unwillingness of the patient to be treated" (65.3%) and "high price of the drug" (64.7%). In appointing the original drugs in the first place for the doctor is worth the price of the drug (79.6%). 25.7% of doctors are experiencing inner experiences. Only 15% of doctors primarily prescribe original drugs. The doctor thinks that the cost of drugs creates additional difficulties for the patient's treatment. The patients often do not trust the doctor, because they think that the doctor will prescribe a cheap and ineffective medicine. **Conclusion:** The cost of treatment significantly affects the effectiveness of the treatment that becomes a barrier between doctor and patient with chronic heart failure and hypertension.

P1925

Depression in chronic heart failure: a common problem

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Purpose: Depression in patients with chronic heart failure (CHF) is associated with increased risk of morbidity, mortality and rehospitalisation. This cross sectional survey assesses the prevalence of depression among male and female hospitalised CHF patients to determine whether routine screening on admission is beneficial and identify ways to improve management.

Methods: A prospective, cross sectional survey in 28 bed cardiology ward was carried out for 30 consecutive days. A standard proforma was used to record patient demographics, diagnosis and Hospital Anxiety and Depression Score (HADS).

Results: In total, 26 patients with CHF were admitted with CHF over a 30 day period of whom 65% (n=17) were male and 35% (n=9) were female. 4 patients had to be excluded as they were unable to fill in the HADS severe cognitive impairment. Out of 22 patients, 23% (n=5) had normal HADS, 13% (n=3) had mild depression, 23% (n=5) moderate and 41% (n=9) severe depression. A higher proportion of female patients compared to male patients were clinically depressed (86% vs 73%) and showed more severe depressive symptoms.

Conclusion: Depression is common and under recognised among inpatients with CHF. Females are more likely to be affected and with more severe symptoms. Routine screening on admission and appropriate referral to a clinical psychologist may be beneficial.

P1926

Can in hospital cardiovascular rehabilitation program make a difference in the expression of anxiety and depression in patients with systolic dysfunction of left ventricle

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Purpose: Previously, it was found that the development of mental disorders in cardiovascular patients is associated with increased mortality. Because of that we need to detect them and take measures to eliminate them. Also previously was shown that smoking cessation and increasing physical activity could had impact on reducing the risk of anxiety and depression.

Methods: study population consisted of 888 patients who had myocardial infarction /MI/ or bypass surgery. They rehabilitated in our in-hospital cardio rehabilitation (CR) unit from september 2013 to may 2014. There started rehabilitation 2-12 weeks after MI or bypass surgery. The duration of in hospital CV program was 3 weeks. The following data were collected: age, sex, left ventricular EF measured by echocardiography and are they smokers. The presence of anxiety and depression was determined using the Hospital Anxiety and Depression scale (HADS).

Results: There were 104 /11,7%/ patients with EF less than 40%. There were 28,1% patients after myocardial infarction and 65,6% patients after bypass cardiac surgery. All of them were man. Mean age was 63,9+/-10,8 years. At admission there were 20 /19,23%/ patients with anxiety and after 3 weeks of CV rehabilitation program 10 /9,6%/ patients had anxiety. At admission there were 11/10,57%/ patients with depression and after 3 weeks of CV rehabilitation program 5 /4,8%/ patients had depression. For other analyzed variables /arterial hypertension, hiperlipoproteinaemia, diabetes mellitus/ there were no significant difference among groups but there were significant differences in patients in smoking (t=4,43; p=0,030)- smoking was more often present in patients with anxiety. There were statistical difference in expression of anxiety and depression at the beginning and at the end of CV rehabilitation program in patients with systolic dysfunction of left ventricle (X² 0,027, df 1; (0,05)=3,84).

Conclusion: In our study we found that in hospital CV program had influence on reducing frequency of anxiety and depression among cardiovascular patients with systolic dysfunction of left ventricle. Because of its significance on the outcome education of patients to stop smoking is important during CV rehabilitation program as well as maintaining their physical activity after discharge as an element of control of anxiety and depression.

PROGNOSIS

P1927

Clinical features and predicting in closing ductal in preterm infants with low birth weight

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The ductus arteriosus closes spontaneously after birth in most infants born at term. However, in premature ductal closure is variable. The aim of our study was to analyze the clinical characteristics and predictors of closure of Patent Ductus Arteriosus (PDA) in preterm with low birth weight.

Methods: Between January- 2011 and November-2012 were included 81 preterm infants with low birth weight and ≤ 32 weeks gestation. Hemodynamically significant DAP was defined when there was a short left-to-right through the DAP.

Results: Of 29 DAP detected, the closure occurred in 19 (65.5%). Of the confirmed closure in 10 (52.6%) did not require treatment, 6 (31.6%) received medical treatment and 3 (15.8%) required surgical treatment closure. The average time to close was 21.8 ± 20 days. Were characterized by to need less vasoactive drugs than those without closed (18.8% vs. 77.8%, $p=0.004$), lower metabolic acidosis (11.8% vs. 77.8%, $p=0.001$), oliguria (11.8% vs. 66.7%, $p=0.004$), lower differential pressure increased (26.7% vs. 75%, $p=0.075$) and higher auscultation of breath 94.7% vs. 30%, $p=0.001$. There were not significant differences in the chamber dilation 35.3% vs. 57.1% $p=0.324$, or flow pattern 31.3% vs. 33.3% $p=0.926$ and ductal size 0.6 ± 1.95 vs. 1.5 ± 0.4 , $p=0.107$. We also found not differences regarding treatment with antenatal corticosteroids (63.2% vs. 70%, $p=0.713$). Was characterized by the presence at increased of apneas 100% vs. 70% $p=0.013$, and treated with caffeine (100% vs. 44.4%, $p<0.001$).

Ductal closure was higher for preterm with higher birth weight, 1178 ± 354 vs. 915 ± 307 , $p=0.057$. There was not mortality in preterm infants with closed ductus. In the analysis of predictors, we found that the absence of metabolic acidosis [OR 0.04 (95% CI 0.004 to 0.329), $p=0.038$] and have previously murmur on auscultation [OR 24 (95% CI 1.25 to 460), $p=0.035$] were the only predictors of ductal closure.

Conclusions: In our series, PDA closure occurred spontaneously in the middle of preterm infants, is related to birth weight and these factors were the absence of metabolic acidosis and previous cardiac murmur

P1928

Relevance of missing ejection fraction registries on primary health care records to assess the prognosis of heart failure patients and associated characteristics

IDiAP Jordi Gol

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Purpose: Our study is aimed at analyzing differences in the prognosis of patients registered as a Heart Failure (HF) in primary healthcare records, depending on reduced Ejection Fraction (HFREF), preserved Ejection Fraction (HFPEF) or missing Ejection Fraction (HF-mEF), and, if possible, to ascertain the causes contributing to these differences.

Methods: Retrospective cohort study based on clinical information including all patients living in the city of Spain between January 2007 and December 2012, who had the diagnostic of HF (International Classification Diseases: 1.50) registered in their primary healthcare medical records on December, 31th.

The prognosis of patients was determined by the hospital admission as a consequence of a cardiovascular event (heart failure, myocardial infarction or unstable angina) or the mortality occurred during the period of the study.

Regression models were performed to analyze the differences in the prognosis of patients depending on the Ejection Fraction (EF) and the existence of previous hospital admission as a consequence of HF.

Results: a total of 8736 HF patients were included. Median follow up was 16,3 months. Women represented 55,9% of patients and mean age was 78.0 (SD 10.2) years. EF was available only in the 89.1% of patients.

HF m-EF were older, obese, took loop diuretics, were more socio economic disadvantaged, needed more home care, and were more dependent of daily living activities.

HF patients with missing EF had an odds ratio for hospitalization or death of 1.9 (95%CI 1.51-2.42), and HFREF had an odds ratio of 1.4 (95% CI 1.02-1.93) respect to those having a HFPEF, respectively.

Patients previously admitted to a hospital from HF had an odds ratio for hospitalization or death during the follow up of 1.87 (95% CI 1.74-2.02).

The prognosis found in the group of patients who had been previously hospitalized as consequence of HF and were HF-mEF was (OR 3.89 (95%CI 2.31-6.27) respect to those having a normal EF and not previous hospitalization.

Conclusions: HF- mEF patients who were hospitalized previously to the diagnosis had the worse prognosis. These patients were more frequently attended at home, which implies a different kind of care

P1929

Can nightly heart rate variability predict one year mortality in patients with acute myocardial infarction

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Introduction: The predictive value of heart rate variability (HRV) could be independent of other factors established for post infarction risk stratification, such as depressed left ventricular ejection fraction, increased ventricular ectopic activity, and presence of late potentials.

Objectives: The aim of the study is to estimate if nightly HRV can predict one year mortality in patients with acute myocardial infarction (AMI).

Methods: We observed 100 patients with AMI; mean age 56.99 ± 11.03 , M/F was 80/20. Anterior localization of AMI had 44 patients and inferior AMI had 56. Time domain HRV analysis was obtained from 8 to 13 days after AMI, by mean of a 24-hour Holter monitoring, and the parameters calculated were: standard deviation of all NN intervals (SDNN), standard deviation of 6-hours NN intervals daily (SDNNd) and nightly (SDNNn); and 24-hour RRmax-RRmin. We also observed the clinical, laboratory and echocardiography variables.

Results: During follow-up period of one year 11 patients died, 10 of them died because of cardiac reason and one died because of stroke. There was significant lower value of 24-h SDNN 60.55 ± 12.84 ms in dead vs. 98.38 ± 28.21 ms in survivors ($p < 0.01$), mean nightly SDNNn was 62.27 ± 18.30 ms in dead and 101.16 ± 43.37 ms in survivors ($p < 0.01$). 24-hour RRmax-RRmin was 472.51 ms in dead vs. 604.56 ms in survivors ($p < 0.01$). Multivariate Cox analysis showed that 24-h SDNN is a significant, independent predictor for mortality in post-MI patients, but not nightly SDNN. Also the independent predictors for mortality are an impaired left ventricular function and a ventricular ectopic activity (number of VPCs > 10/hour).

Conclusion: Nightly HRV can not predict mortality in patients with AMI, only 24-hour SDNN as an autonomic measure is an independent predictor for mortality in post-MI patients.

P1930

A factorial binary score for prognosis of acute decompensated heart failure

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Purpose: Clinical data shows that patients admitted for decompensated heart failure have multiple comorbidities. We tried to find the association between comorbidities and find a risk score for probability of death during hospitalization for acute decompensated heart failure (ADCHF).

Methods: Baseline characteristics and outcome at discharge were evaluated for 138 patients, with in-hospital mortality rate 21%. We calculated for all comorbidities, baseline and discharge clinical and investigational data.

For the evaluation of the risk of worsening we propose the next formula: $S = \sum OR_i \times FRI_i$, where OR_i represent the Odds Ratio for each risk factor and FRI_i is a binary factor, indicating for each patient the absence or the presence of that factor in the patient.

Results: In the poor outcome patients we found as risk factors: male gender ($OR = 2.54$), history of COPD ($OR = 1.31$), impaired renal function at admittance ($OR = 1.40$) or presence of pulmonary edema at admittance ($OR = 2.64$). The most important risk factor was low ejection fraction ($OR = 4.44$). The etiology of heart failure was not a prognostic factor for survival during hospitalization.

The sensibility of the score was 0.727, comparable value with another risk scores. The specificity was also good, the value is 0.708. The accuracy of the method was 0.712.

Conclusion: The proposed score could be an easy tool to appreciate the prognosis for worsening outcome in the group of the patients admitted for a decompensated heart failure. The heart failure therapeutic approach may be influenced in the future by the results of the present research.

P1931

Bundle branch block - illuminating but ominous sign in acute heart failure

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Introduction and Purpose: Risk stratification in acute decompensated heart failure (HF) is poorly defined. The aim of the present study was to assess the impact of bundle branch block (BBB), either left (LBBB) or right (RBBB) on 1-year mortality in patients presenting with acute HF.

Results: We included in our study 201 consecutive patients admitted to ICU due to acute decompensated HF (28.4% with LBBB and 10.9% with RBBB). We did not find significant difference in age between groups without BBB, with LBBB and RBBB (71.6/71.7/70.4 years) nor in gender (males: 59.8%/61.4%/63.6%).

BNP was higher in patients with LBBB than in those without BBB (2074.6 vs. 1326.4, $F = 7.5$, $p < 0.001$) and RBBB (1468.5, $p > 0.05$). Majority of patients without BBB were in NYHA class III (59%) as those with RBBB (59.1%), while majority of patients with LBBB were in NYHA class IV (42.1%). There was significant difference in LVEF between patients with LBBB and those without BBB (30.4% vs. 39.9%, $p < 0.001$)

as with RBBB (30.4% vs. 41.3%, $p < 0.001$). In majority of patients without BBB the cause of HF was acute coronary syndrome (32.8%), in patients with LBBB it was dilated cardiomyopathy (42.1%) and in patients with RBBB it was arterial hypertension (40.9%). Heart failure with preserved ejection fraction was significantly more frequent patients without BBB and those with RBBB (41% and 45.55%) than in those with LBBB (12.3%, $\chi^2 = 16.03$, $p < 0.001$). Patients with RBBB had insignificantly higher incidence of chronic obstructive pulmonary disease (36.4%) compared to those with LBBB (22.8%) and those without BBB (22.1%). Maximal systolic pressure in right ventricle was higher in those with LBBB compared to those without BBB (51.4 vs. 44.8 mmHg) but not significantly higher compared to patients with RBBB (45.7 mmHg).

Patients with LBBB had significantly lower heart rate (88.6/min) than those without BBB (101.8/min) but not significantly lower than those with RBBB (98.3/min).

Patients with LBBB had significantly higher mortality rate during 1 year than those without BBB and with RBBB (64.9%/33.6%/36.4%) and during initial hospitalization (19.3%/6.6%/4.5%). During the last six months of follow up patients with RBBB had the highest mortality rate (27.3%) compared to those with LBBB (26.3%) and without BBB (15.6%).

Conclusions: Patients with BBB had poor short and long term prognosis in acute HF. LBBB indicates structural changes in the left ventricle while RBBB may result from right ventricular pressure/volume overload. Electrocardiography as a routine, safe and inexpensive method could help to stratify risk in acute HF.

P1932

Blood pressure on admission in heart failure - prognosis at short- medium term

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Purpose: Blood pressure (BP) reflects a patient's hemodynamic status and the presence of hypotension on admission proved to be a risk factor for morbidity and mortality in cardiovascular diseases and particularly in heart failure (HF).

Aims: evaluate the relationship between the BP (systolic, SBP and diastolic blood pressure-DBP) with demographic, clinical and echocardiographic findings in a population with HF and determine its prognostic impact at an endpoint, defined by death or readmission for acute HF.

Methods: We studied 600 patients. The PA was assessed at admission. Patients were divided into 2 groups (G): GA ($n = 217$) - SBP < 120 mmHg and DBP < 80 mmHg and GB ($n = 383$) - SBP > 120 mmHg and / or DBP > 80 mmHg. We made a second analysis according to the value of the admission BNP (< 400 pg / ml and > 400 pg / ml). Follow-up was performed at 3, 6 and 12 months.

Statistical analysis with SPSS. Statistical significance at $p < 0.05$.

Results: There are no statistically significant differences in age. On admission GA presents lower hemoglobin levels, estimated glomerular filtration rate (MDRD) and lower sodium levels ($p = 0.02$, $p = 0.003$ and $p = 0.002$, respectively) and higher values of urea and BNP on admission ($p < 0.001$). At echocardiography, the blood pressure was inversely related to left ventricular diastolic diameter (LVDD), left atrial (LA) diameter and pulmonary artery pressure (SPAP) ($p < 0.001$) but was directly related with ejection fraction ($p < 0.001$). No significant differences in the ratio E/e' ($p = 0.35$) between the two groups.

The GA had higher rates of mortality and / or re-admission (30,5% vs 21,5%; $p = 0.027$; OR: 1,68 CI-95%[1,11-2,55]).

After the analysis according to the value of BNP on admission it was found that the BNP level in GA did not show statistically significant correlation with the rate of death or readmission at 3, 6 and 12 months. however, in GB, BNP level's > 400 pg / ml were correlated statistically with higher mortality rate at 3, 6 and 12 months ($p = 0.022$, $p = 0.010$ and $p = 0.026$ respectively).

Conclusions: Low BP on admission was predictive of poor prognosis at the short term. In the presence of SBP > 120 mmHg and / or DBP > 80 mmHg, elevated BNP levels at admission were associated with worse prognosis at the short-medium term.

P1933

Who are the patients that improved cardiac function in acute heart failure with reduced left ventricular systolic function?

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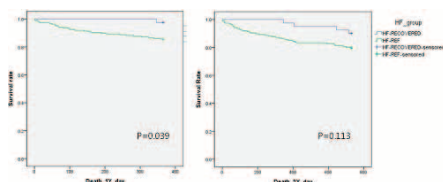
Purpose: We thought that patients with HF who recovered LV function (HF-recovered) have different characteristics. We sought to characterize the HF-Recovered population and their prognosis.

Method: We enrolled 227 patients with AHF with reduced EF who were residents of our Island from 2005 to 2013. They were divided into two groups; HF-recovered

(F/U EF $\geq 50\%$ but initial EF was $<50\%$, $N=40$, 17.6%). and HF with reduced EF (HFREF, initial and F/U EF were both $<50\%$, $n=187$, 82.4%). Clinical characteristics and laboratory findings were reviewed from medical records. They were followed at least 2yrs. Clinical end-points were death or readmission due to congestive HF (CHF).

Results: HF-recovered group were younger (63.6 ± 15.57 vs. 73.4 ± 13.57 , $p < 0.001$), and they had lower peak CKMB (5.6 ± 4.64 vs. 19.79 ± 66.58 , $p = 0.038$), troponin-T (0.05 ± 0.13 vs. 0.78 ± 0.06 , $p = 0.008$) and proBNP level (5091.6 ± 4876.5 vs. 8486.1 ± 8884.9 , $p = 0.002$). In HF-Recovered group, most common etiology of HF was dilated cardiomyopathy ($N=13$, 32.5%). On the other hand, that was ischemic heart disease in HFREF group ($N=89$, 47.6%) HF-recovered patients also had a lower prevalence of coronary artery disease requiring revascularization and consequently fewer with an ischemic origin than HF-REF. 1-year survival rate of HF-recovered group was higher than that of HFREF (98% vs. 85%, $p=0.039$) but 2-year survival rate was not different (90% vs. 79%, $p=0.113$).

Conclusion: In the patients of AHF with reduced EF, small portion of patients had recovery of LV function. Their etiology of HF were non-ischemic. Their short-term prognosis were better than those of HFREF patients, but mid-term prognosis were similar.



P1934

Reasons why patients suffering from chronic heart failure at very high risk for death survive

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Background: An accurate prognostic stratification is essential for optimizing the clinical management and treatment decision-making of patients with chronic heart failure (HF). Among the best available models, we used the Cardiac and Comorbidity Conditions HF (3C-HF) Score, to predict all-cause mortality in patients with CHF.

Methods: we selected and characterized the subgroup of patients at very high risk with the worst mid-term prognosis belonging to the highest decile of 3C-HF score with the aim to assess predictors of survival in subjects with an expected probability of 1-year mortality near to 45%.

Methods and Results: We recruited 1777 consecutive chronic HF patients at 3 Italian Cardiology Units. Median age was 76 ± 10 years, 43% were female, 32% had preserved ejection fraction. Subjects belonging to the highest decile of 3C-HF score were 246 (13.8% of total population). During a median follow-up of 21 [12-40] months, 110 of these patients (45%) survived and 136 (55%) died. The variables that contributed to survival prediction emerged by Cox regression multivariate analysis were the lower degree of renal dysfunction and higher body mass index (fig 1).

Conclusions: The prognostic stratification of chronic HF patients allows in daily practice to select patients at different risk for death and identify prognosticators of survival in outliers at very high risk of death. The reasons why these patients outlive the matching part of subjects who expectedly die are related to the maintenance of a satisfactory renal function and body mass index.

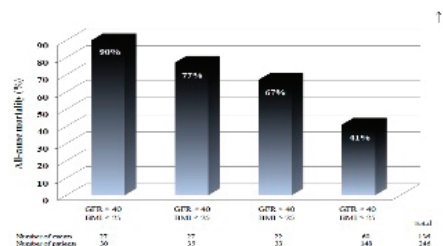


Fig 1

P1935

Survival and factors predicting mortality after transcatheter aortic valve implantation in patients with severe aortic stenosis with the corevalve prosthesis

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Background: Transcatheter aortic valve implantation (TAVI) has become the standard of care extreme surgical risk patients with symptomatic severe aortic stenosis and an alternative to open surgery in those deemed high risk. It is widely known the short and mid-term outcomes, however, is limited about long-term outcomes. The purpose of the present study was to analyze the survival and the factors predicting mortality after TAVI with the CoreValve prosthesis.

Methods: From April 2008 to December 2014, the CoreValve prosthesis was implanted in 441 patients with symptomatic severe aortic stenosis with deemed high risk.

Results: The mean age was 79.2 ± 6.8 years. The logistic EuroSCORE and STS score were $17.6 \pm 11.9\%$ and $7.4 \pm 5\%$, respectively. The implantation success rate was 98.7%. In-hospital mortality was 3.9%, and the combined endpoint of death, vascular complications, myocardial infarction or stroke had a rate of 13.9%. The late mortality (beyond 30 days) was 14.5%. Survival at 1, 2, 3, 4 y 5 years were 86.3%, 79.7%, 74.3% and 67.5% respectively, after a mean follow-up of 26 ± 17 months. The NYHA functional class improved from 3.3 ± 0.5 to 1.77 ± 0.7 after a mean follow-up of 30.5 ± 20 months. The predictors of cumulative mortality were: Charlson index [HR 1.2 (95% CI 1.06-1.36), $p=0.002$], acute Kidney injury [HR 1.93 (95% CI 1.06-3.52), $p=0.003$], Stroke [HR 4.03 (95% CI 1.57-10.2), $p=0.004$] and vascular complications after TAVI [HR 9.26 (95% CI 3.56-24), $p=0.001$] and protective factors were a higher Karnofsky index [HR 0.979 (95% CI 0.965-0.992) $p=0.002$].

Conclusions: Survival during follow-up depends on the associated comorbidities and the complications of procedure

P1936

Development and validation of a risk scoring model to predict net adverse cardiovascular outcomes after CABG in patients with heart failure: rationale and design of the POP-HF study

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The patients with coronary artery bypass surgery (CABS) have physiological changes in coronary artery structure. In these patients, presentation of heart failure (HF) has different influence of new coronary events expression, than in patients without CABS. The prognosis of patients after coronary artery CABS has been noted in many studies, but there were no comprehensive HF risk model to predict net adverse cardiovascular events (NACE) after CABS. The primary hypothesis of the POP-HF study (PostOperative Prognosis-HeartFailure study) is that an accurate risk prediction may be achieved by using clinical, angiographic, and procedural variables available 30-day after intervention.

The present single-center, longitudinal, cohort study will include 2465 consecutive patients with HF, undergoing CABS. The primary end-points of the trial (NACE) include major adverse cardiovascular events (MACE). A logistic regression model will be developed to predict 30-day, 1-year, 5-year, 10-year, 15-year and 20-year NACE after CABS. A risk score derived from study set data will be validated using validation set data.

Until April 1, 1988, 2224 patients have been enrolled. Thirty-day follow-up is available in 2168 patients, 1-year in 1981 patients, 5-year in 1617 patients, 10-year in 1389 patients, 15-year in 1108 patients and 20-year in 1004 patients.

Conclusions: The POP-HF study is designed to develop an accurate risk scoring system, using variables available 30-day after CABS, to predict long-term adverse outcomes in patients with heart failure.

P1937

Availability of prognostic markers for heart failure with preserved ejection fraction in argentina: a cross-sectional study

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Purpose: Predictive risk models for heart failure with preserved ejection fraction (HF-PEF) are crucial for guiding clinical management and targeting populations for clinical trials. However, access to prognostic markers is sometimes restricted due to high costs. This survey has been designed to document the level of access to prognostic markers for HF-PEF in hospitals in Argentina.

Methods: A survey instrument with 13 multiple-choice questions was developed and validated to assess the availability of prognostic markers for HF-PEF. In a cross-sectional observational study, an interviewer-administered survey was applied to one Cardiology resident from each of the 66 hospitals attending a national conference in Argentina in November 2014. Respondents were selected by probability sampling. The primary outcome was the prevalence of access restrictions to prognostic markers for HF-PEF. The associations between access restrictions and the hospital's region and environment were also studied.

Results: Cardiology residents from 57 hospitals completed the survey. 68.4% reported at least one access restriction to prognostic markers for HF-PEF. Among those with access restrictions, 51.3% reported that natriuretic peptide determinations were unavailable, and 46.2% had restrictions to troponin determinations due to costs. No hospitals reported restrictions concerning echocardiographic testing. The association between access restrictions and region was statistically significant (26.3% versus 42.1%; $p = .006$), whereas the association with environment was not (29.8% versus 38.6%; $p = .463$).

Conclusions: Two thirds of the surveyed hospitals in Argentina have access restrictions to prognostic markers for HF-PEF, mainly troponin and natriuretic peptide determinations. Echocardiographic testing may be a preferable, more readily available approach towards establishing prognosis in patients with HF-PEF.

P1938

In chronic heart failure patients T(-786)C polymorphism of endothelial nitric oxide synthase is associated with increased risk of heart failure hospitalisation

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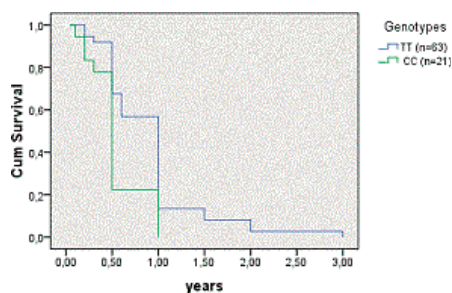
Background: Previous studies demonstrated the link between low endothelium-dependent vasodilatory response and high mortality risk in chronic heart failure (CHF). But it's still lack of data whether endothelial nitric oxide synthase (eNOS) gene polymorphism is associated with survival in CHF patients (pts) or not.

Aim: To evaluate long-term prognosis in systolic CHF in relation to eNOS T(-786)C gene polymorphism.

Methods: 145 stable ischemic CHF pts with left ventricular (LV) systolic dysfunction (LV ejection fraction $\leq 45\%$). Smokers, pts with diabetes and those on carvedilol or nebivolol (nitric oxide bioavailability modulators) were excluded. 5 years prognosis (heart failure hospitalisation data only and both death/heart failure hospitalisation data) was evaluated by Kaplan-Meier method.

Results: The frequency of T(-786)C genotypes was: TT - 43,5% (n=63), TC - 42,0% (n=61), CC - 14,5% (n=21). The pts with CC genotype demonstrated significantly higher heart failure hospitalisation rate at 5 years follow-up as compared with TT homozygote group (log-rank=8,761, $p=0,003$), (Fig.). Simultaneously, combined outcome had no significant differences between TT and CC groups (log-rank=1,271, $p=0,260$). There were no significant differences in above-mentioned heart failure hospitalisation rate and combined outcome between TT and TC groups.

Conclusion: In stable ischemic systolic CHF CC T(-786)C eNOS genotype is associated with increased risk of heart failure hospitalisation along 5 years follow-up.



Kaplan-Meier curves

P1939

Improved long-term survival in overweight heart failure patients is unrelated to age or ventricular function

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Obesity influences heart failure development but may also effect survival from this condition. It is unclear if the improved survival from increased weight persists long-term or is influenced by age and ventricular function.

Purpose

We performed a longitudinal study (14 years) in 329 patients with chronic heart failure to ascertain if increased weight influenced survival long-term and what factors influenced these differences.

Methods: Patients included had been enrolled in our heart failure programme over the last 14 years. Patient demographics, disease type, functional capacity, ventricular size and function and drug therapies were measured.

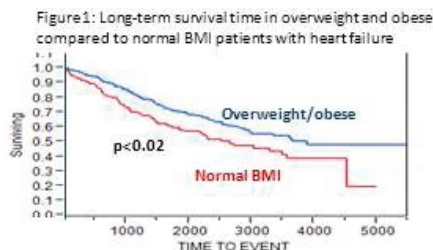
Results: Long-term survival was better in patients who were overweight or obese compared to normal weight patients ($p < 0.02$). See Figure 1. These differences could not be accounted for by differences in age, gender, disease type or ventricular size or function. In addition there was no significant difference in the treatment regime used in both groups. See table 1

Conclusion:

These data highlight that higher weight is beneficial in heart failure patients' survival. Identification of specific obesity related protective factors or simply better nutrition may underlie these benefits.

Table 1: Shows patients characteristics

	no. pts(n)	Male	Mean Age	DCM	Mean NYHA	LViDd	EF%
Normal	124	72%	66 ± 1	46%	1.8 ± 0.06	6.7 ± 0.3	31 ± 1
Overweight/Obese	205	75%	64 ± 1	50%	1.7 ± 0.05	6.5 ± 0.4	32 ± 1
Significance (p-value)	<0.05	ns	ns	ns	ns	ns	ns



P1940

Long-term prognosis and related factors in dilated cardiomyopathy

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Purpose: Classical studies estimate five years mortality rate for heart failure over 50%. Nevertheless, prognosis has improved by the addition of new therapeutic options. Our aim is to know the current prognosis of patients with dilated cardiomyopathy (DCM) as well as to identify prognosis-related factors.

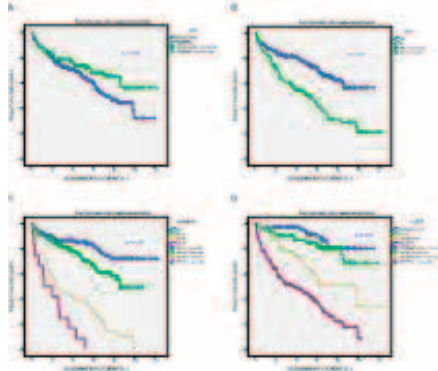
Methods: Retrospective study of a cohort of 387 consecutive outpatients with the diagnosis of DCM. Clinic, electrocardiographic, therapeutic and image techniques data were obtained. Death, heart transplantation and heart failure hospitalization during the follow-up were considered cardiovascular events.

Results: Mean age was 64.5 ± 12.1 years and female gender was 25.6%. Mean follow-up period was 50.4 ± 28.4 months. Death or cardiac transplantation occurred in 25.6% of patients. 23% of patients had at least one hospitalization; 14.7% was hospitalized at least twice and 9.8% of patients had three hospitalizations or more. Mean number of hospitalization per patient was 0.68. Combined event occurred in 37.7% of population.

Factors independently related to bad prognosis were male gender ($p = 0.029$ HR 3.4 IC 95% 1.12-8.33), presence of chronic kidney disease ($p < 0.001$ HR 6.23 IC

95% 2.84-13.67), severe NYHA-FC at the end of the follow-up period ($p=0.005$ HR 2.33 IC 95% 1.29-4.23), lower LVEF at the end of the follow-up ($p=0.039$ HR 1.63 IC 95% 1.02-2.59) and longer time until improvement of LVEF ($p=0.002$ HR 1.04 IC 95% 1.01-1.06).

Conclusions: A quarter of patients died or needed heart transplantation while almost two fifths of patients had at least one event during the follow-up period. The best set of factors for predicting prognosis for DCM was gender, chronic kidney disease, NYHA class at the end of the follow-up period, LVEF at the end of the follow-up and time until improvement of LVEF.



Prognosis in DMC

P1941

Clinical, biochemical and echocardiographic phenotyping of patients with cardiac dysfunction stratified according to prescription of loop diuretics

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Background: Congestion due to cardiac dysfunction is an important cause of symptoms and signs of heart failure. Diuretics are the mainstay of treatment for congestion. Patients treated with loop diuretics have a worse prognosis but whether this is because of their association with congestion or because they cause adverse neuroendocrine activation is uncertain.

Aim: to explore whether the relationship between loop diuretic use and outcome is explained by underlying evidence of congestion amongst patients referred for diagnosis and management to a heart failure clinic.

Results: Of 1190 patients enrolled, 979 (82%) had cardiac dysfunction [either a reduced left ventricular ejection fraction (LVEF <50%) or raised plasma NTproBNP (>400 ng/l)] and 209 (18%) did not. Of those with or without cardiac dysfunction, 71% and 37% respectively were prescribed loop diuretics.

Patients with cardiac dysfunction taking diuretics were older, had more evidence of congestion [more severe symptoms and signs, higher NTproBNP plasma levels, larger left atrial volumes and IVC diameter, more impaired right ventricular function and higher systolic pulmonary artery pressure], lower LVEF, worse renal function, more anaemia and hyponatraemia.

During a median follow-up of 934 (IQR: 513 - 1425) days, 450 patients were hospitalized for HF or died. Compared to patients with cardiac dysfunction not taking loop diuretics, those treated with higher doses of loop diuretics (Furosemide or equivalent >80 mg/day) had a 3.5-fold greater risk of an adverse event (HR: 3.50, 95% CI: 2.49-4.93). However, in multi-variable models, clinical, echocardiographic (IVC diameter), and biochemical (NTproBNP levels) evidence of congestion were strongly associated with an adverse outcome but not the use of loop diuretics or their dose.

Conclusions: Prescription of loop diuretics identifies patients with more advanced features of heart failure and congestion. This association appears to account for the worse prognosis of patients treated with loop diuretics.

HFpEF – HEART FAILURE WITH PRESERVED EJECTION FRACTION

P1942

Results of 3-week rehabilitation in patients with heart failure with reduced and preserved ejection fraction

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Objective: to evaluate the impact of 3-week cardiac rehabilitation (CR) program on the exercise tolerance, lipid blood profile, blood pressure in patients with heart failure and reduced ejection fraction (HFrEF) and in patients with heart failure and preserved ejection fraction (HFpEF).

Methods: 26 patients with HFrEF (mean age - 57.3 ± 11.2 years; men - 80.8%, women - 19.2%) and 94 patients with HFpEF (mean age - 59.2 ± 6.1 years; men - 70.2%, women - 29.8%) were underwent an inpatient 3-week CR program. The CR program consisted of physical exercise, lifestyle modification, and pharmacotherapy. Exercise tolerance, serum lipoproteins, blood pressure were assessed at baseline and follow-up.

Results: Patients with HFrEF compared to those with HFpEF more often had risk factors such as diabetes mellitus (23.1% vs. 11.7%, $p < 0.0001$) and smoking (57.7% vs. 22.3%, $p < 0.0001$). The rate of patients that achieved lower LDL cholesterol (<100 mg/dl), total cholesterol (<200 mg/dl) and triglyceride (<150 mg/dl) values at discharge was high in patients with HFrEF compared to those with HFpEF (88.5% vs. 75.5%, $p < 0.05$). There was no difference in blood pressure between two groups at baseline. At discharge systolic blood pressure was substantially lower in the HFrEF group compared to the HFpEF group (115.6 ± 27.2 vs. 127.1 ± 14.2 mmHg, $p = 0.01$). Maximal power during exercise test improved substantially both in HFrEF group (from 89.8 ± 21.2 to 127.4 ± 34.0 Watts, $p < 0.01$) and in HFpEF group (from 99.7 ± 12.1 to 130.2 ± 16.8 Watts, $p < 0.001$). The distance covered in the 6-min walk test was significantly greater after the 3-week cardiovascular training both in patients with HFrEF (393.4 ± 78.7 vs. 452.9 ± 92.5, $p < 0.05$) and in patients with HFpEF (420.7 ± 48.6 vs. 474.6 ± 57.1, $p < 0.05$).

Conclusion: patients with HFrEF and HFpEF both benefited from participation in 3 week CR program, as their lipid profile, blood pressure and exercise tolerance improved.

P1943

The prevalence of obstructive sleep apnoea in patients with chronic heart failure and preserved ejection fraction

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Purpose: To assess the prevalence of obstructive sleep apnoea (OSA) in patients with clinical manifestations of heart failure (HF) and preserved ejection fraction (EF).

Methods: The study included patients with clinical manifestations of chronic heart failure (CHF) with preserved ejection fraction of left ventricle (EF > 50%). Causes of CHF were ischaemic heart disease and essential hypertension. Patients were underwent cardiorespiratory monitoring with the calculation of the index of apnea / hypopnea (IAH). Echocardiography investigations were also performed.

Results: We examined 31 patients (8 women and 23 men), mean age 67+9 years, BMI = 30,6+5,7 kg/m². 22 (70%) patients had CHF of 2 functional class by NYHA, 9 (30%) patients - CHF of 3 functional class. The most frequent clinical manifestations of heart failure were dyspnoea (100%), peripheral edema of the lower extremities (52%) and hepatomegaly (29%). Congestive bibasal rales in the lungs were heard in 2 patients (6,5%). According to the results of cardiorespiratory monitoring during sleep 26 (84%) patients with CHF had respiratory disorders with signs of obstruction. 8 (30%) patients had IAH<15 episodes per hour (e/h), 9 (35%) - IAH 15-30 e/h and 9 (35%) - IAH>30 e/h. It was found that IAH depended on the severity of CHF. In group of patients with 2 functional class of NYHA 3 (14%) of them had IAH 5-15 e/h, 7 (32%) patients - IAH 15-30 e/h, 4 (18%) patients - IAH>30 e/h. 2 (22%) patients with NYHA class 3 had IAH 5-15 e/h, 2 (22%) patients - IAH 15-30 e/h and 5 (56%) patients - IAH>30 e/h. There were no statistically significant differences in echocardiographic parameters between groups of patients with and without OSA.

Conclusions: The findings suggest that the high prevalence of obstructive sleep apnea in patients with chronic heart failure and preserved ejection fraction. The most significant clinical manifestations observed in patients with severe OSA (IAH > 30 e/h). Symptoms of right-sided heart failure were dominated in clinical manifestations in this group of patients.

P1944

Correlations of atrial fibrillation with structural and functional changes of the left atrium in patients with diastolic heart failure

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Objective: Heart failure with preserved ejection fraction (HFpEF) is common, particularly among elderly, female, and hypertensive patients (pts), and is frequently associated with atrial fibrillation (AF). Left atrial (LA) enlargement is a recognized marker for left ventricular (LV) diastolic function and independently associated with an increased risk for morbidity and mortality.

Aim: the purpose of this study was to determine whether the short-standing paroxysmal AF influences structural and functional disorders of LA in patients (pts) with AH.

Methods: Study included 74 pts (40% male) with mild-to-moderate AH and diastolic HFpEF ($\geq 50\%$), mean age 63 ± 9.5 years: 44 pts with paroxysmal AF of less than 1 year arrhythmic anamnesis and paroxysms frequency 1 for 3 months (G1), 30 pts without AF (G2). The groups were similar in terms of age, body mass index, heart rate (HR), blood pressure (BP) and antihypertensive therapy. Standard echocardiography with Doppler technique was performed. LA enlargement was defined as LA volume index (LAVI) ≥ 29 mL/m². LA active emptying fraction (LAEF) $\leq 45\%$ and LA expansion index (LA exp inx) $\leq 90\%$ were categorized as LA phasic dysfunction.

Results: G1 and G2 groups did not differ on LA, MMI, ESV, EDV, EF ($p = NS$ for all cases). There were no significant differences in groups in E, A, e', a', E/e', in both groups 1 type of diastolic dysfunction was prevalent. LAVI was significantly higher in G1 vs G2 (32,1 (28,3; 35,7) vs 24,7 (23,2; 27,2) mL/m², $p < 0.0001$). 23 (52%) pts in G1 and 12 pts (40%) in G2 had LAVI ≥ 29 mL/m² ($p = 0.02$). LAEF was comparable in groups (46,9 (46; 48) vs 45,9% (45,3; 46,6)) as well as reduced LAEF (9 (19%) vs 9 (26%) pts). LA exp inx was significantly higher in G1 (88,5 (85,3; 92,3) vs 85,1% (82,8; 87,3), $p = 0,004$). Decreased LA exp inx was observed more frequently in G2 than in G1 group (24 (80%) vs 20 (46%) pts, $p = 0,003$). In G1 group LAVI significantly ($p < 0,05$) correlated with LA size (0,65), MMI and E/e' ($r = 0,37$ for both cases). There was significant correlation LAVI with LA size ($r = 0,57$), MMI ($r = 0,42$) in G2. In both groups LAVI has directly correlated with diastolic dysfunction type ($r = 0,55$ and $r = 0,44$, respectively), but there were not significant correlations between LAEF and LA exp inx with diastolic function parameters.

Conclusion: Changing of LA structure is highly associated with presence of AF in pts with HFpEF compared to pts without arrhythmia. There was moderate correlation between LAVI and diastolic dysfunction. Short-standing intermittent AF did not significantly influence on LA phasic function in pts with HFpEF.

P1945

Preliminary study on diastolic stress echo: left atrial 3D longitudinal strain as a good descriptor of stress induced diastolic changes

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PURPOSE Analysis of left atrial (LA) longitudinal strain (LS) in diastolic dysfunction (DD) can provide information of pathophysiological relevance. Aim of the study is to assess whether there is any variations in LA mechanics during a diastolic stress test that can help in DD identification.

METHODS 24 symptomatic pts (17 fully analysed, 66 ± 6 years) with normal ($>50\%$) ejection fraction (EF) and various grading of DD underwent a graded effort diastolic stress echo test using both 2D and 3D approach. Left ventricular (LV) and atrial volumes, besides EF, E, A, E/A, DT, e', a', E/e' during basal, stress (around 100/min) and recovery phases were noted.

RESULTS No changes were observed in LV EF or LV and LA volumes (see table), but an important direct relation was found between LA LS and DT ($p < 0.002$), absent using E/e'. In particular, the depression of LA LS during exercise seems to be matched by an increase in LA pump function, as expressed by an increase in a'.

CONCLUSIONS In patients with DD and a normal EF, LA 3D LS seems to be related with changes in DT, reflecting LV operative stiffness. The stiffer is the ventricle, the worst is the atrial behaviour, with progressively loss of atrial deformation (and likely increased atrial stiffness) induced by higher degrees of DD along with stress phase. In this condition, LA pump contribution to LV filling represents the keystone to support the system during stress.

PARAMETERS	REST	STRESS	RECOVERY	ANOVA
HR (beat/min)	66 ± 9.2	101 ± 9.7 †	77.8 ± 9.9 ‡†	<0.001
LV volume MAX ml	92.5 ± 18.1	94.3 ± 27.7	99.5 ± 19	NS
LV volume MIN ml	40.7 ± 11	41.6 ± 11.1	45.4 ± 12.1	NS
LV EF	0.57 ± 0.06	0.55 ± 0.12	0.55 ± 0.05	NS
LA volume MAX ml	43.6 ± 12.3	44.5 ± 17.8	37.9 ± 7.8	NS
LA volume MIN ml	29.5 ± 8.9	28.6 ± 10.5	25.5 ± 7.2	NS
E/A	0.84 ± 0.2	1.01 ± 0.21 †	0.86 ± 0.17	< 0.05
e' cm/s	8.38 ± 2.2	10.3 ± 2.33 †	9.01 ± 2.05	< 0.007
a' cm/s	11.03 ± 1.73	14.15 ± 2.8 †	11.56 ± 2.08 ‡	< 0.002
E/e'	7.69 ± 1.85	9.64 ± 2.57 †	8.06 ± 2.28	< 0.03
DT msec	249.9 ± 51.2	167.3 ± 67.3 †	249.8 ± 56 ‡	< 0.002
LA longitudinal strain 3D	0.091 ± 0.02	0.028 ± 0.036	0.034 ± 0.034 †	< 0.05

† $p < 0.05$ versus rest ‡ $p < 0.05$ versus stress

P1946

Does the isometric stress affect left ventricle filling in heart failure with preserved ejection fraction patients

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Purpose: heart failure with preserved ejection fraction (HFpEF) diagnosis frequently have to be confirmed by physical diastolic stress, but isometric stress was not yet tested as a effective stress maneuver. So the study aims to assess the left ventricular filling indexes in subjects with HFpEF undergoing isometric stress maneuver.

Methods: we allocated 35 patients with ESC criteria for HFpEF diagnosis and underwent them to a handgrip maneuver (50% of the maximal strength during 3 minutes or as the maximal time they could perform) during echocardiogram. The left ventricle (LV) structure, systolic and diastolic indices were analyzed before and after the stress. To detect differences between the indices we performed Student T test. A P value < 0.05 was considered statistically significant.

Results: The population were 64.9 ± 8.1 years old, 68% female and 97% had hypertension. The left ventricular ejection fraction was $69.6 \pm 7.6\%$ and the cardiac volumes were normal. There were significant modification of diastolic indexes, including the E/e' after isometric stress.

Conclusion: the strategy of isometric stress by handgrip maneuver determined significant differences in indices of LV diastolic function, including in non-invasive LV diastolic pressure E/e' in patients with previous diagnosis of HFpEF. It probably could be useful in future studies about diastolic stress.

LV diastolic indices on isometric stress			
LV diastolic indices	Before isometric stress	After isometric stress	P
E/e'	9.46 ± 2,77	10.96 ± 4,05	0.029
E (m/s)	0.77 ± 0,22	0.91 ± 0,28	0.001
A (m/s)	0.77 ± 0,24	0.86 ± 0,82	0.035
e' (m/s)	0.08 ± 0.016	0.09 ± 0.02	NS
a' (m/s)	0.11 ± 0,02	0.11 ± 0,03	NS

E/e' - non-invasive LV diastolic pressure index; E-early diastolic flow velocity; A-late diastolic flow velocity; e' - early anular diastolic velocity; a' late anular diastolic velocity; m/s: meter per second.

P1947

Arterial stiffness indices are not blood pressure dependent in patients with heart failure with preserved ejection fraction contrary to patients with arterial hypertension

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The **Aim:** to evaluate the changes of arterial stiffness and peripheral vascular resistance in patients with arterial hypertension (AH) and heart failure with preserved ejection fraction (HFpEF) on the optimal medical therapy.

Methods: 32 patients with AH (41% men; mean age 58.9 ± 15.5 years) and 41 patients with HFpEF (24% men; mean age 70.2 ± 7.2 years) were consequently enrolled in the study. Pulse-wave characteristics were measured using finger photoplethysmographic device at the baseline and then after adjustment of medical treatment and follow up. Augmentation index (Alx,%), augmentation index, corrected for a heart rate of 75 beats/min (Alx75,%), stiffness index (SI,m/s) and reflection index (RI,%), were assessed. The mean follow-up was 254.3 ± 84.5 days in HF-PEF group and 223.0 ± 30.4 days in AH group. Statistical analysis included ANOVA with repeated measures.

Results: Baseline blood pressure did not differ significantly in patients with HFpEF and AH (SBP = 152.9 ± 25.1 vs 150.1 ± 18.7 mmHg and DBP = 87.2 ± 13.2 vs 89.1 ± 10.2 mmHg respectively). Alx was higher in HFpEF group but SI, RI and Alx75 were similar in both groups. After the follow-up SBP significantly decreased in both groups of patients. In patients with AH Alx and Alx75 correlated with SBP and their decrease after a follow up was SBP-dependent, whereas in patients with HFpEF changes of Alx75 were not linked with the improvement in BP (see table). **Conclusions:** relationship between arterial stiffness and blood pressure lowering on treatment was demonstrated in patients with AH, but not in patients with HF-PEF, possible due to advanced vascular remodeling.

Changes in BP and pulse-wave indices			
	HF-PEF	AH	p-value
ΔSBP, mmHg	9.2	30.4	<.05
ΔAlx75,%	2.6	4.1	NS
ΔAlx75/ΔSBP,%/mmHg	-0.55	0.26	<.04

P1948

Improvement of left ventricular diastolic function as a result of optimization of rate-adaptive algorithm in patients with permanent cardiac pacing

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Objectives and purpose: Heart failure (HF) is well known complication of permanent right ventricular apical pacing. Chronotropic incompetence is considered as one of the main causes of HF in pacemaker-dependent patients. The aim of this study was to work out an algorithm of optimization of programmed rate adaptation in HF patients with permanent pacing.

Methods: 52 patients with HFpEF, permanent atrial fibrillation and cardiac pacing in mode VVIR were studied. The patients were divided in the intervention group (n = 30) and the control group (n = 23). The maximum sensor rate (MSR) was determined using non-invasive pacemaker stress-echocardiography. MSR was programmed 5 bpm below the threshold of stress-induced myocardial wall motion impairment. The heart rate response to exercise was assessed using cardiopulmonary exercise testing (CPET) on a treadmill according to CAEP protocol. The sensor threshold and slope were programmed to achieve an adequate increment of HR up to 3-7 beats per minute (bpm) for 1 ml/kg/min of oxygen consumption (VO₂). In the control group the settings of rate-adaptive pacemaker algorithm were programmed automatically and then were corrected by experienced specialists. The echocardiography, peak oxygen consumption (VO₂peak) and 6-minute walk distance were assessed before and after 3 months after pacemaker's adaptation.

Results: In the intervention group the patients had significant improvement in left ventricular diastolic function. The E/E' ratio decreased from 11,7 ± 3,2 to 10,3 ± 2,9 (p = 0,019), systolic pulmonary artery pressure decreased from 44 ± 13,6 to 39,5 ± 12,4 mm Hg (p = 0,006). There was also reduction of left atrial volume index from 68,14 ± 44,6 to 64,6 ± 42,5 ml/m² (p = 0,072). The patients also had an increase in VO₂peak (from 12,5 ± 2,87 to 14,3 ± 2,82 ml/kg/min, p < 0,0001) and 6-minute walk distance (from 354 ± 72 to 423 ± 52 m, p < 0,0001). There were no any significant changes in the control group.

Conclusions: In patients with HFpEF optimization of rate-adaptive algorithm of permanent pacemaker using non-invasive pacemaker stress-echocardiography and CPET provides improvement of diastolic function, hemodynamic parameters and physical tolerance.

P1949

Insulin resistance as a risk factor for progression of chronic heart failure with preserved systolic function

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Background: Insulin resistance (IR) is identified as a marker for the progression of atherosclerosis and it is often matched in patients with chronic heart failure (CHF). However, the role of IR in progression of CHF with preserved systolic function have not been fully defined.

Objective: we aimed to establish the role of IR in progression of CHF with preserved systolic function.

Methods: 34 patients (21 M, 13 F, mean age - 74,97 ± 2,75 years) with CHF NYHA I-III class and preserved left ventricular ejection fraction (LVEF > 45%) without diabetes mellitus were enrolled. Insulin, total cholesterol, serum triglycerides and high-density lipoprotein cholesterol levels were determined in the blood and HOMA index was calculated as insulin (μU/ml)*glucose (mmol/l)/22,5.

Results: 45% of patients had High insulin levels and HOMA index (mean level 26,19 ± 2,79 μU/ml and 3,5 ± 0,19 respectively). High insulin levels and HOMA index correlated to NYHA functional class (r = 0,25; p < 0,05 and r = 0,27; p < 0,05 respectively), total cholesterol (r = 0,28; p < 0,05 and r = 0,25; p < 0,05 respectively), serum triglycerides (r = 0,34; p < 0,01 and r = 0,32; p < 0,01 respectively) and high-density lipoprotein cholesterol levels (r = -0,22; p = p < 0,05 and r = -0,25; p < 0,05 respectively).

Conclusion: Our results provide suggestive evidence that the IR is not only a predictor progression of atherosclerosis but also CHF with preserved ejection fraction.

BASIC SCIENCE: ISCHEMIA AND MYOCARDIAL INFARCTION

P1952

Yuzu and its major compound hesperidin treatments prevented left ventricular remodelling and dysfunction after myocardial infarction

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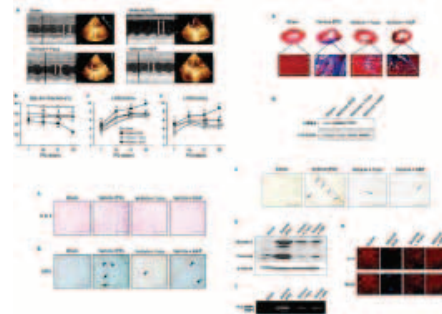
Yuzu and its major compound hesperidin treatments prevented left ventricular remodelling and dysfunction after myocardial infarction

Purpose: Yuzu is a citrus plant originating in East Asia, and has a number of cardioprotective properties such as hesperidin. The aim of this study was to determine yuzu's effects on HF and its potentially related impact on the LV remodelling process after MI.

Methods: The rats were divided 3 subgroups at the beginning of the study: group I, vehicle treatment (PEG, 0.3 ml/day, n = 13); group II, yuzu treatment (100 mg/kg/day, n = 10); and group III, hesperidin treatment (30 mg/kg/day, n = 10). Oral treatments with these agents were repeated each day and were continued for 5 weeks. The rats were administered the oral treatments for 1 week before they were subjected to a sham operation or LAD occlusion. The rats were examined with echocardiography every weeks after LAD occlusion (during 5 weeks). Histological, immunohistochemistry, Gelatinase zymography and western blot analysis was also performed.

Results: LV function and dimensions were preserved more markedly in the yuzu- and hesperidin-treated groups up to the termination of the study (Figure). In vivo studies using the permanent left anterior descending coronary artery (LAD) occlusion model also showed that pre-treatment with yuzu and its major compound hesperidin treated cardiac dysfunction, attenuated myocyte apoptosis, decreased inflammation, and dramatically reduced interstitial fibrosis (figure).

Conclusions: Yuzu and hesperidin prevent post-MI structural remodeling of the myocardium and ventricular dysfunction. These findings may have important implications for designing future therapies for myocardial performance during LV remodeling after MI, affecting the clinical management of patients with HF.



figure

P1953

Cardioprotective role of genistein on cardiomyoblast

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Heart disease (HD) is great associated with gender and menopausal status because of estrogens. In addition, clinical evidence shows that increased level of serum norepinephrine is found in patients with HD. Therefore this study aimed to investigate the cardio-protective effect of genistein, a selective estrogen receptor modulator (SERM) from soy bean extract, in H9c2 cardiomyoblast cells treated with isoproterenol (ISO, a norepinephrine analog). In this in vitro model, image data and results from western blotting shown that ISO treatment was capable of inducing cellular apoptosis, especially mitochondrial dependent pathway. Treatment of genistein could suppress the expression of mitochondrial pro-apoptotic proteins including Bad, caspase-8, caspase-9 and caspase-3 in H9c2 treated with ISO. By contrast, several survival proteins were expressed in H9c2 treated with genistein, such as phosphor (p)-Akt, p-Bad and p-Erk1/2. Furthermore, we confirmed that the protective role of genistein was partially mediated through the expression of Erk1/2, Akt and NF-κB proteins by adding several pathway inhibitors. These in vitro data suggest that genistein may be a safe and natural SERM alternative to hormone therapy in cardio-protection.

P1953

Gelsolin (GSN) enhance cardiomyocyte apoptosis during hypoxia via reducing survival protein p-Akt

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Cytoskeletal filaments play an important roles in cells such as cell shape, cell motility, intracellular transport and cellular division. Actin binding proteins (ABPs) have a lot of functions one of that is regulate the structure formation of actin to filament nucleation, elongation, severing, capping, crosslinking and actin monomer

sequestration. Gelsolin (GSN) is one of actin binding proteins and it regulate actin filament formation and disassembly such as severing, capping, uncapping, nucleation of actin filament, and it regulate by pH, Ca²⁺, phosphoinositides (PIP₂). Moreover, GSN also regulates cell morphology, differentiation, movement, and apoptosis.

In our study, we used H9c2 and H9c2-GSN stable clones, in an attempt to understand the mechanisms of GSN overexpression in cardiomyocytes. This data showed that overexpression of GSN in H9c2 reduces the expression of survival markers p-Akt and Bcl-2. In hypoxia condition, overexpression GSN further reduce p-Akt expression and increase GSN, cleavage-GSN and HIF-1 α expression more obviously. Moreover, overexpression GSN was more serious apoptosis compare with H9c2 cell during hypoxia.

P1954

Long term prognosis of patients with different types of myocardial infarction (NSTEMI and STEMI) with similar left ventricular systolic function and moderate to severe sleep apnea

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Purpose: Sleep apnea (SA) is characterized by repetitive cessation of breathing during sleep, which is associated with intermittent hypoxemia leading probably to ischemic preconditioning in the myocardium. This potential cardioprotective effect of SA may play role in the development of non-ST-elevation myocardial infarction (NSTEMI) rather than ST-elevation myocardial infarction (STEMI) during acute ischemia. There is limited evidence about the occurrence of NSTEMI and STEMI on dependence of having SA. Outstanding issue remains also at what point do the risks associated with SA outweigh the benefits of ischemic preconditioning? We therefore prospectively investigated the prevalence and prognosis of these two types of MI in different SA categories among acute MI patients.

Methods: We prospectively studied 782 consecutive patients admitted to the hospital with the diagnosis of acute MI (both NSTEMI and STEMI). 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 mean follow-up of 19 months.

Results: Almost all patients (98%) underwent urgent coronary angiography and 91% of patients underwent primary PCI. Moderate to severe SA was present in 33.1% of patients after acute MI. Increasing severity of SA was associated with increasing incidence of NSTEMI and conversely with decreasing incidence of STEMI ($p < 0.001$). Relative frequency of NSTEMI was in the moderate to severe SA group 40.6% while STEMI 29.9%. Left ventricle ejection fraction (LV EF) was in these groups (NSTEMI and STEMI) 49.07 (± 13.43)% vs 47.60 (± 11.53)% ($p = 0.413$) respectively. There was a higher total mortality in NSTEMI than STEMI patients in the group of moderate to severe SA ($p = 0.004$).

Conclusion: There was an increasing incidence of NSTEMI associated with increasing severity of SA. There was also a significant difference between relative frequency of NSTEMI and STEMI in the group of moderate to severe SA patients with similar left ventricular systolic function. It may suggest a cardioprotective role of SA during acute MI through ischemic preconditioning, but NSTEMI patients with moderate to severe SA had worse long term prognosis than those with STEMI. Whether diagnosis and treatment of SA after MI will significantly improve outcomes in these patients remains to be determined.

P1955

The effect of opioid receptor stimulation on function of human ischemic myocardium in vitro

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Purpose: Early restoration of myocardial perfusion remains the important way to reduce infarct size. Reperfusion has also been shown to induce myocardial necrosis in the mechanism known as ischemia-reperfusion (I/R) injury and it manifests as decrease the potential benefits of reperfusion. Opioids have been shown to confer protection in vitro and in vivo studies. Several investigators demonstrated that beneficial effect is mediated via Δ -opioid receptors in an animal model of I/R injury but the class of opioid receptors responsible for this effect in humans remains unknown. Aim of the study was to assess the influence of opioid receptor modulators (morphine, selective Δ -opioid receptor agonist D-Ala D-Leu-enkephalin, DADLE) on simulated I/R injury outcomes in the human myocardium.

Methods: Experiments were performed on trabeculae obtained from right atrial appendages of consecutive patients subjected to the coronary artery bypass surgery. Patients with a severe valvular disease or heart failure were excluded. Trabeculae were incubated in organ bath and exposed to protocol including 60 min of hypoxia with subsequent 60 min of reoxygenation. Morphine (10-6, 10-5 or 10-4M) or DADLE (10-8, 10-7 or 10-6M) was used at the time of reoxygenation. Systolic function was assessed by measurement of maximal amplitude of systolic peak (Amax), slope of leading edge of the peak (Slope L), diastolic function was assessed by measurement of slope of trailing edge of the peak (Slope T). Local Bioethics Committee approval for the use of human tissue was obtained all experiments were performed according to the Declaration of Helsinki.

Results: Parameters of systolic and diastolic function for morphine 10-4M were significantly higher vs. control. In the lower morphine concentration group parameters were not significantly different vs. control. Amax was significantly lower for DADLE 10-6, 10-7M vs. control, but Slope T was not significantly different than control for DADLE despite its concentration.

Conclusions: Previous studies utilized mainly the animal models to describe the influence of opioids on I/R injury. Our study is the first to assess the effect of opioids on systolic and diastolic function in hypoxic human myocardium in vitro. The main finding of our study demonstrate protective mechanism of morphine is present in the human myocardium and morphine improves systolic and diastolic function of myocardium in the dose dependent manner. Δ -opioid receptor stimulation attenuates systolic function of heart muscle what remains in the contrast to the previous reports with animal model of I/R injury.

P1956

Myocardial apoptosis associated with the expression of mitochondrial chaperonin HSP 60 during the course of myocardial infarction

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Introduction: Mitochondria participate in apoptotic pathway by providing many important factors. There are multiple cellular pathways triggering apoptosis: intrinsic, for which mitochondrion is the central organelle governed by pro- and antiapoptotic bcl-2 family members, and extrinsic, consisting of cell surface TNF-related family of receptors, their inhibitory counterparts and cytoplasmic adapter or death inhibitory molecules. The heat shock protein 60 (HSP 60) is a mitochondrial chaperonin characterized by antiapoptotic effect. In recent studies was observed that HSP60 decrease with hypoxia and that lead to bax protein translocation to the mitochondria and activate the apoptosis pathway. The aim of the present study was to investigate the expression of HSP60 in myocardial infarction and the relation with apoptotic proteins.

Methods: We studied myocardial samples of hearts with histologic findings of acute myocardial infarction (group A, n=100), old myocardial infarction (group B, n=100) and myocardial samples of normal heart (control group, n=20). An immunohistochemical method was performed with the use of HSP60, Bax, Bcl-2 antibodies, in order to investigate the expression of HSP60 and apoptosis-related proteins bax, bcl-2 in ischemic cardiac disorders.

Results: HSP 60 expression was intensive in the normal myocardial cells and the levels were unchanged at the risk areas of samples with acute myocardial infarction. In old myocardial infarction the HSP60 levels decreased and the positive samples demonstrated weak staining. Bcl-2 positive expression was moderate at the risk areas in 75% of samples with acute myocardial infarction. In old myocardial infarction the bcl-2 positive samples demonstrated weak staining as in the control group. Bax staining was weak in 80% of samples with acute myocardial infarction and intensive in 60% of samples with old myocardial infarction. Bax positive expression was weak in 50% of samples of the control group.

Conclusions: Increased levels of HSP60 were associated with intense expression of antiapoptotic bcl-2 protein in acute myocardial infarction. Decreased levels of HSP60 and intensive expression of proapoptotic bax were found in cases of old myocardial infarction. The above data suggest that the chronic hypoxia induces reduction of HSP60 levels and increased expression of bax. HSP60 play a key role in regulating the function of apoptosis.

Methods: We studied all patients hospitalized for acute coronary syndrome over a period (15) fifteen month from (1 October 2010) to (31 December 2011). We compared the frequency of occurrence of complications during hospitalization and at follow-up of patients who have experienced heart failure to the remaining patients.

Results: In this 15 months, 507 patients were admitted because of an ACS. Among those patients, 69 (13,6%) developed an acute heart failure at presentation or during hospitalization. The rates of in-hospital mortality and cardiogenic shock of acute HF patients were significantly higher than patients without HF (respectively 4.43% vs 0.45%, $p=0.002$ and 10.14% vs 0%, $p=0.000$). Regarding the average length of hospitalization, a significant prolongation was noted in patients with acute heart failure (12.46 days \pm 11.22 vs 6.9 days \pm 5.3, $p=0.000$). During follow-up of our patients, we also found a higher mortality (1.38% vs 5.79%, $p=0.014$) and higher rate of postoperative death (0.45% vs 2.89%, $p=0.033$).

Conclusion: The occurrence of heart failure is a predictor of a higher rate of in-hospital and after discharge mortality in the studies patients hospitalized for acute coronary syndrome.

P1961

Assessment of mitochondrial dysfunction and monoamine oxidase contribution to oxidative stress in coronary patients with and without diabetes

This study was supported by the university grant PIII-C1-PCFI-2014/2015-04 O M Duicu¹; R Lighezan²; R Balica³; A Sturza¹; A Vaduva⁴; H Feier⁵; M Gaspar⁵;

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In the past years the contribution of monoamine oxidases (MAOs) with two isoforms, A and B, as novel sources of mitochondrial oxidative stress in the cardiovascular system has been unequivocally demonstrated. The role of oxidative stress in the pathogenesis of diabetes mellitus (DM) and of its cardiovascular complications is widely accepted.

Purpose: The aims of the present study were: i) to characterize the mitochondrial dysfunction and ii) to assess the contribution of MAOs to oxidative stress in coronary patients in the presence vs. the absence of DM. Methods. Sixty consecutive patients with preserved ejection fraction (EF) that underwent non-emergency cardiac surgery were randomized in 3 groups: (1) Controls (CTRL), valvular patients with no documented coronary heart disease (CHD), (2) CHD, patients with documented CHD without DM, and (3) CHD-DM, patients with documented CHD and DM. Mitochondrial respiration of permeabilized atrial fibers was measured by high resolution respirometry at 37°C in the presence of complex I and II substrates. MAOs expression was determined in atrial samples by qRT-PCR plus immunohistochemical staining and the H₂O₂ content was assessed by means of dichlorodihydrofluorescein assay. Results. Complex I-supported respiration was depressed in all CHD patients with and without diabetes, whereas complex II-dependent respiration was found to be decreased only in diabetic patients. MAO B (not MAO A) was the predominant isoform in the human diseased heart as assessed by qRT-PCR and immunohistochemical assay. However, despite an increase of MAO-B mRNA in the CHD-DM group, no significant difference among the groups was found in protein expression of MAO-B and H₂O₂ production in atrial samples. Conclusion. Our data show a predominance of the MAO-B isoform in non-diabetic and diabetic coronary patients and the impairment of mitochondrial respiration irrespective of the substrate used in the latter group.

BASIC SCIENCE: ISCHEMIC PRECONDITIONING

P1962

Characterization of the effects of novel ATP-sensitive potassium channel openers in isolated rat heart mitochondria

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Purpose: There is substantial experimental evidence that opening of the mitochondrial ATP-sensitive potassium channels (mKATP) protect the heart in conditions associated with ischemia-reperfusion injury. The aim of the present study was to characterize the dose-dependent effect of four novel pharmacological openers of the mKATP, namely KL-1487, KL-1492, KL-1495, and KL-1507 on mitochondrial

respiratory rates and reactive oxygen species (ROS) production in isolated rat heart mitochondria. Methods. Mitochondrial respiratory function was assessed by high-resolution respirometry and H₂O₂ production was measured by the Amplex Red fluorescence assay in the presence of complex I and II respiratory substrates. Four concentrations were tested: 50, 75, 100 and 150 microM, respectively. Results. When used in concentrations of 100 and 150 microM all investigated compounds exerted an uncoupling effect as shown by a significant increase in state 2 and 4 respiratory rates and a decrease in the respiratory control ratio, respectively. The highest concentration also elicited an important decrease of oxidative phosphorylation and electron transport system capacity, respectively. Both above mentioned concentrations in the case of KL-1487, KL-1492, and KL-1495, and only the concentration of 150 microM in the case of KL-1507 also induced a significant reduction of mitochondrial H₂O₂ production. Conclusion. In isolated rat heart mitochondria these novel mitochondrial KATP openers are able to elicit mild uncoupling and decrease in oxidative stress, properties that are likely to be effective in cardioprotection.

P1963

Early and late cardioprotective effects of intracoronary administration of 4-chlorodiazepam in a rat model of ischemia/reperfusion

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Background: The Translocator Protein of the outer mitochondrial membrane has been recently recognized as a potential therapeutic target for the mitigation of ischemia/reperfusion injury in heart. A ligand of this receptor, 4-chlorodiazepam (4-CLD), increases cardiomyocyte resistance to oxidative stress. We examined the effects 4-CLD, administered at the onset of reperfusion, on the severity of microvascular damage and the recovery of systolic function in a rat model of ischemia-reperfusion.

Methods: Acute myocardial infarction was induced in 32 (weight 300-350 gr) Wistar rats by ligation of the mid portion left anterior descending coronary artery for 45 minutes, followed by 1 hour of reperfusion. Five minutes before the onset of reperfusion the animals were randomly assigned (1:1) to either intraventricular infusion of 200 µL of 4-CLD (1%) or control. Infusion was performed during temporary obstruction (20sec) of blood flow in inferior vena cava and ascending aorta sequentially, insuring the selective intracoronary delivery of the administered agent. At the end of reperfusion, animals were randomly reassigned (1:1 in each group) to either microvascular obstruction (MVO) and area at risk of the left ventricular myocardium (AR) planimetry [acute protocol] or to left ventricular end-diastolic (EDV) and end-systolic volumes (ESV) and ejection fraction (EF) at 2 and 60 days post-intervention measurements [chronic protocol].

Results: Although the myocardial area at risk did not differ significantly between the 2 groups in the acute protocol (22.7% \pm 6.3% vs 21.4% \pm 6.3% $p=0.695$ for 4-CLD and control, respectively), there was a significant reduction of MVO in 4-CLD group, 15.1% \pm 5.6% of the area at risk vs 23.5% \pm 8.3% in the control group ($p=0.034$). EDV and ESV did not differ significantly between the two groups at 2 days post-MI echocardiography, whereas EF was significantly higher in the 4-CLD group compared to the control group (58 \pm 9 vs 45 \pm 8%, $p=0.03$). At 60 day ultrasound study, cardiac volumes were significantly higher in the control group when compared to the 4-CLD group (EDV: 432 \pm 102 ml vs 273 \pm 120 ml, $p=0.045$, LVESD: 198 \pm 98 ml vs 95 \pm 45 ml, $p=0.003$). LV systolic function recovered in both groups but remained significantly higher in the 4-CLD group (66 \pm 8% vs 49 \pm 11%, $p=0.018$).

Conclusions: In experimental model of myocardial ischemia/reperfusion, intracoronary administration of 4-CLD just before the onset of reperfusion reduces the extent of no-reflow phenomenon and leads to early and sustained enhancement of LV systolic function and abolishment of adverse cardiac remodeling.

P1964

Exenatide prevents morphological and structural injury of mitochondria in ischemia-reperfusion injury

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Background: Exenatide exerts cardioprotective effects by activating the opening of adenosine triphosphate (ATP)-sensitive mitochondrial potassium channels in order to attenuate ischemic reperfusion (IR) injury. We used atomic force microscopy (AFM) to investigate changes in mitochondrial morphology and properties in order to assess exenatide-mediated cardioprotection in IR injury.

Methods: We used an in vivo Sprague-Dawley rat IR model and ex vivo Langendorff injury model. Using a left anterior descending artery (LAD) occlusion model, animals were randomly divided into three groups: sham-operated rats (Sham, n = 5), IR-injured rats treated with placebo (IR, n = 6), and IR-injured treated with exenatide

(IR + EXE, n = 6). Using the Langendorff model, rats were randomly divided into two groups: IR injury with placebo (IR, n = 4) and IR injury with exenatide (IR+EXE, n = 4). Morphological and mechanical changes to mitochondria were analyzed by AFM.

Results: Exenatide improved cardiac function as evidenced by improvement in left ventricle fractional shortening (LV FS) and LV ejection fraction (EF). The ratio of infarct area to risk area (IA/RA) was significantly reduced in exenatide-treated rats. According to AFM, IR significantly increased the area of isolated mitochondria, indicative of mitochondrial swelling. IR + EXE reduced mitochondrial area and ameliorated the adhesion force of mitochondrial surfaces.

Conclusion: Our results suggest that exenatide provides cardioprotective effects against IR injury by improving the morphological and mechanical characteristics of mitochondria.

P1965

An impact of remote ischemic preconditioning on ischemia-reperfusion injury in the isolated diabetic rat heart

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Purpose: Remote ischemic preconditioning (RIP) is a potential strategy of endogenous cardioprotection against ischemia-reperfusion (IR) injury. This protection can be induced by brief episodes of non-lethal IR applied to an organ or tissue distant from the heart. It was demonstrated in many experimental studies that acute diabetes mellitus induces, besides damaging effects, partial adaptation of the heart to hypoxia and Ca²⁺ overload that leads to increased resistance against IR. However, the relationship between remote ischemic preconditioning and diabetes mellitus is still little understood. The aim was to investigate the impact of remote ischemic preconditioning on ischemia-reperfusion injury in healthy non-diabetic and diabetic rat heart.

Methods: We used 9-10 weeks old male Wistar rats in our experiments. They were kept on standard pellet diet at 22-23°C in 12/12 day/night regimen with free access to food and water. Acute diabetes mellitus was induced by a single dose of streptozotocin (STZ, 65 mg/kg, i.p.). Experiment was finished on the 8-day after STZ application. At that day, diabetic animals exhibited significantly increased blood levels of glycohemoglobin, glucose, cholesterol, triglycerides, as well as decreased insulin. Diabetic and non-diabetic rats were subjected to remote ischemic preconditioning induced by 3 episodes of 5 minutes ischemia (occlusion of the femoral artery) / 5 min reperfusion in right hind limb. Subsequently, the hearts were removed and Langendorff-perfused. After 15-min stabilization perfusion they were subjected to 30 min global ischemia and 40 min reperfusion. Cardiac functional parameters (HR, CF, LVSP, LVDiP, LVDP, +dP/dtmax, -dP/dtmax) were recorded during the protocol of IR.

Results: Baseline pre-ischemic parameters did not differ between the groups. However, we noticed a significantly better post-ischemic recovery of systolic and diastolic function in all three adapted groups relative to non-adapted controls. Moreover, recovery of cardiac function did not differ between these groups indicating that application of RIP in the diabetic hearts did not result in further increase in their resistance against IR.

Conclusions: The results suggest that RIP provides an effective protection in healthy non-diabetic myocardium, but confers only partial further protective effect in diabetic myocardium. This indicates that similar protective mechanisms as in the myocardium exposed to RIP are apparently involved in reduced sensitivity against IR in the diabetic hearts.

P1966

Diabetic heart influenced by remote ischemic preconditioning and pharmacological preconditioning: functional alterations of cardiac mitochondria

VEGA SR 2/0101/12, 2/0133/15, 2/0201/15; APVV-0102-11

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Purpose: Acute diabetes mellitus (DM), pharmacological preconditioning with mitochondrial KATP opener diazoxide (DZX) and remote ischemic preconditioning (RIP) induce adaptation of the heart which is manifested by increased tolerance to acute ischemia.

Structural and functional alterations of heart mitochondria is an important factor leading to preservation of energy function in myocard affected by pathological stimulus. Aim of these work was contribute to elucidation of processes by which heart mitochondria are involved in preconditioning.

Methods: Male Wistar rats (9-11 weeks) were divided into healthy (n = 49) and diabetic groups (n = 49). RIP was induced by three 5-min occlusions of the right hind limb. Acute DM was induced by a single dose of streptozotocin (65 mg.kg⁻¹, i.p.). Isolated heart mitochondria were exposed to increasing concentrations of 200 μl DZX (0-7 μmol.l⁻¹). Mitochondrial Mg²⁺-ATPase activity was assessed by ATP splitting. Mitochondrial membrane fluidity was estimated by fluorescence anisotropy with the aid of 1,6-diphenyl-1,3,5-hexatriene.

Results: Exposition of healthy heart mitochondria to DZX (5; 6 and 7 μmol.l⁻¹) and DM both induced an increase (p < 0.05) in Mg²⁺-ATPase activity. However, exposition of diabetic heart mitochondria to the same concentrations of DZX induced only a moderate further elevation of Mg²⁺-ATPase activity. A similar moderate increase of membrane fluidity was also observed in diabetic and the DZX-treated heart mitochondria while RIP induced a significant (p < 0.05) increase in this parameter.

Conclusions: Increase in Mg²⁺-ATPase activity and membrane fluidity of mitochondria observed in the experimental models employed seem to belong to basic mechanisms which participate in an increase of cardiac ischemic tolerance. Stimulation of MIT Mg²⁺-ATPase (ATP synthase) plays an essential but not exclusive role in cardioprotective effect provided by both DZX and DM.

P1967

Remote ischemic preconditioning during rehabilitation in coronary artery disease patients after percutaneous coronary interventions

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It is known that moderate ischemia or repeated short-time ischemic interventions are pathogenetic reasonable and clinically perspective for increasing adaptive reserve of the organism, treatment and prevention of pathologic conditions determined by lack of oxygen, as of coronary artery disease (CAD) patients in different stages of management and rehabilitation.

Objective: evaluate the application of remote ischemic preconditioning (IP) in CAD patients with incomplete anatomic revascularization after percutaneous coronary interventions (PCI) during early rehabilitation.

Material and methods: We examined 19 CAD patients (14 men, 5 women) aged 40-65 with incomplete anatomic revascularization after PCI. Instrumental methods of examination included ECG, Holter ECG monitoring, diagnostic treadmill stress-test according the protocol of R.Bruce. Holter ECG monitoring results were used to assess ST index, depth and duration of ST depression, myocardial ectopic activity. Remote IP was performed according to fixed protocol: distal vessels (arm) were cuff compressed with interleaving up to 4 times for 3 minutes and reperused up to 4 times for 3 minutes. Mean duration of the procedure was 24 minutes. Remote IP was performed no less than 5 times with no less than 48 hours between the procedures. Oxymeter was used for oxygenation control on distal vessels. Safety assessment during the whole period of monitoring was performed by markers of myocardial necrosis and ischemia and by results of instrumental examination. Results. Course of 5 remote IP sessions in CAD patients with incomplete anatomic revascularization after 5-8 days of PCI decreased ectopic activity by 1.6 times and decreased the severity of heart rhythm disorders. The courses of remote IP performed according to the protocol in CAD patients with incomplete anatomic revascularization downsized ischemic signs: the depth of ST depression was reduced by 20.5% and ST index - by 17%.

Conclusions: Remote IP on brachial artery in CAD patients with incomplete anatomic revascularization performed in the first week of outpatient recovery period after PCI and repeated no less than 5 times with intervals between them no less than 48 hours shows anti-arrhythmic and anti-ischemic effects.

P1968

Increased post ischemic survival of cardiomyocytes due to rapid coenzyme Q10 accumulation in myocardium after intravenous injection

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Purpose: To evaluate effects of iv administration of CoQ10 on its myocardial levels and early processes of postischemic remodelling of myocardium.

Methods: Concentrations of CoQ10 in rat plasma and myocardium were measured for several days after single iv administration in the dose of 30 mg/kg by HPLC with electrochemical detection. Effects of CoQ10 on correlates of inflammation were studied on the model of myocardial ischemia evoked by the permanent occlusion of left coronary artery. Solubilised form of CoQ10 was administered 10 min after beginning of occlusion. Morphological changes of the early remodelling of myocardium were studied in 72 h of ischemia on the peak of inflammation reaction.

Results: Changes in plasma concentrations of CoQ10 were reflected by the bi-exponential kinetic curve dependent on time after its iv administration. During 16 days plasma levels of CoQ10 were several folds higher than baseline levels. Calculated half-elimination time was equal to 117.5 h. High plasma levels of CoQ10 was followed by the fast and long maintenance of its high concentrations in myocardium. Myocardial levels of CoQ10 increased by 142% in 15 min and reached its maximum (+242%) in 1 h after iv administration. During the following period of 2-48h the level of CoQ10 was higher than baseline by 111-80%. In 4 days the level of CoQ10 was higher by 50%. At the end of 8th day concentrations of CoQ10 returned to the baseline levels.

Morphological studies showed, that increase in CoQ10 levels in myocardium increased the survival of cardiomyocytes and inhibited the inflammation reaction in early periods of ischemia. In CoQ10-treated rats the total zone of damaged myocardium was decreased by 51%, the zone of necrosis - by 84% and zone, infiltrated by the cells of inflammation reaction - by 38.7% ($p < 0.001$). Inhibition of the acute inflammation response of ischemic myocardium is followed by the decrease in fibrotic changes that evoke development of myocardial hypertrophy, increase in rigidity of the myocardium and development of the disturbances in the function of the heart.

Conclusions: I.v. administration of CoQ10 creates high plasma-myocardium concentration-gradient that followed by the fast increase in its myocardial levels. It increases the survival of cardiomyocytes and decreases the inflammation reaction in early phases of myocardial ischemia.

P1969

Inhibition of H₂S formation from L-cysteine provides cardioprotection against ischemia/reperfusion in rats

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Purpose: L-cysteine is a well-known precursor for both glutathione and hydrogen sulfide (H₂S) biosynthesis. The modulation of H₂S production in heart ischemia/reperfusion model was investigated using an inhibitor of cystathionine-gamma-lyase - DL-propargyl glycine (PAG) and an inhibitor of glutathione biosynthesis - DL-buthionine-sulfoximine (BSO).

Methods: Wistar male rats were divided into 5 groups: 1) ischemia/reperfusion (I/R); 2) L-cysteine+I/R (L-cysteine, 121 mg/kg); 3) PAG+I/R (PAG, 11.3 mg/kg); 4) PAG+L-cysteine+I/R, 5) PAG+BSO+L-cysteine+I/R (BSO, 22.2 mg/kg). Rat isolated hearts were Langendorff-perfused and underwent 20-minute total ischemia and 40-minute reperfusion. Contractile function was evaluated as left ventricle developed pressure (LVDP) and its first derivative (dP/dt). Oxygen tension of inflow and outflow perfusate samples was measured with an oxygen electrode of gas analyzer. 'Arterial-venous' difference was calculated and used for oxygen consumption calculation.

Results: L-cysteine alone, as well as PAG, showed slight tendency to improve recovery of LVDP after I/R of isolated rat hearts. However, post-ischemic myocardial contraction was not observed in PAG-pretreated hearts. Combination of PAG and L-cysteine provided more than 90% recovery of LVDP from the onset of reperfusion and throughout the whole period of monitoring ($p < 0.05$). Moreover, PAG+L-cysteine group revealed more effective oxygen utilization by ischemic myocardium. At the 10th min of reperfusion the oxygen cost of heart work has increased only by 34% (by 139% in I/R group) ($p < 0.028$). Pre-treatment of animals with glutathione depletor BSO has completely abolished the cardioprotective effect of PAG+L-cysteine combination.

Conclusions: Inhibition of H₂S synthesis with PAG pretreatment alleviates damaging effect of ischemia. PAG in combination with L-cysteine provides powerful protection from I/R injury and prevents non-effective oxygen utilisation by ischemic myocardium. It could be concluded that observed cardioprotective effect is vastly depended on glutathione formation from L-cysteine.

P1970

Role of inflammasomes and its regulation in the myocardium after ischemia and reperfusion

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Purpose: The adverse ventricular remodeling is used to describe a variety of changes in the myocardium following an infarct that comprises the functionality of the heart, and it is associated with a worse clinical outcome. The advance in the knowledge of this process is critical to design new therapeutic agents to prevent or reverse the heart failure associated. Inflammation is an immune response against tissue injury in order to repair the damage. Different immune cells and inflammatory mediators participate in this process and could result in the activation of the multi-protein complex called inflammasome. However, the molecular events underlying this inflammatory response are incompletely understood. The present study aimed to investigate the role of inflammasomes and its regulation in the myocardium after ischemia and reperfusion.

Methods: Rats were randomly divided into sham operation and myocardial ischemia/reperfusion (MI/R, 30 min ischemia followed by 90 min reperfusion). Real-time PCR was used to study the relative expression of a panel of genes on demand participating in the inflammasome complex.

Results: The ischemic heart exhibited enhanced inflammasome activation showing a significant upregulation of Nlrp3 and Il1b expression. Moreover, significant upregulations in Cd14, Nod2 and Txnip expression suggested that different pathways may mediate activation of the Nlrp3 inflammasome in the ischemic and reperfused heart.

Conclusion: Interventions that block Txnip/Nlrp3, Cd14/Txnip or Nod2/Nlrp3 signalling seem to be candidate target for strategies to prevent the inflammatory response associated to adverse ventricular remodelling induced by MI/R injury.

P1971

The role of remote ischemic preconditioning in the process of improvement of mitochondrial respiration of heart exposed to ischemia/reperfusion injury

Grants: VEGA 2/0101/12, 2/0133/15, 2/0201/15; APVV-0102-11

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Background: Mitochondria play a central role in cardioprotection conferred by remote ischemic preconditioning (RIP). However, the mechanism by which mitochondria mediate this protection has not yet been fully elucidated. For this purpose, we aimed to investigate whether RIP can preserve or improve mitochondrial respiration after ischemia and reperfusion.

Methods: Male Wistar rats were subjected to RIP procedure consisted of 3 cycle of 5-minutes ischemia and 5-minutes reperfusion of descending branches of the right hind limb femoral artery. Not-preconditioned and preconditioned isolated hearts were subsequently tested to ischemia-reperfusion injury (T-IRI): 30 minute ischemia followed by 40 minutes of reperfusion according to Langendorff. Parameters of oxidative phosphorylation (OXPHOS) in the isolated cardiac mitochondria were determined by the method of high resolution respirometry using Oxygraph-2k (Oroboros Instruments, Austria).

Results: Mitochondrial respiration was stimulated by ADP (state III) using glutamate+malate and malate+octanoylcarnitine as substrates. Results of high resolution respirometry showed that RIP enhance ADP-stimulated respiration after ischemic phase of T-IRI: the hearts without RIP exhibited a decrease by 26.7% whereas the hearts with RIP showed an increase by 40.4% in the rate of O₂-consumption in comparison with the hearts in baseline preischemic phase of T-IRI. However, after 40-minutes reperfusion of T-IRI, we did not observe better preserved state III O₂-consumption by hearts with RIP. Interestingly, a decrease in O₂-consumption induced by reperfusion was less pronounced when malate+octanoylcarnitine as a substrates were used instead of glutamate+malate.

Conclusion: Our results revealed that the process of fatty acid oxidation may be involved to the mechanism of cardioprotection by RIP. We assume that the observed immediate effect of RIP will be more developed after 24 hours post stimulus of RIP - the second window of RIP-induced cardioprotection.

P1972

Acute diabetes mellitus and remote ischemic preconditioning: stimuli for initiating processes of endogenous myocardial protection

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Purpose: Diabetic myocardium is constantly in a state of pseudohypoxia, which leads to impaired ability of diabetic heart mitochondria (MIT) to utilize oxygen. In this way, myocardium in acute state of diabetes mellitus acquires characteristics similar to ischemic preconditioning and can stimulate process of endogenous protection leading to adaptation to the stimulus. Aim of the present study is to elucidate the role of cardiac MIT in the process of enhanced myocardial protection in presence of diabetes (DIA) and remote ischemic preconditioning (RIP).

Methods: Male Wistar rats (220 ± 20g) were used in the experiment. DIA was induced by a single dose of streptozotocin (65 mg/kg, i.p.). RIP was induced by 3 series of 5-min. ischemia and 5-min. reperfusion applied on the right hind limb. MIT were isolated by means of differential centrifugation. Mg²⁺-dependent and 2,

4-nitrophenol-stimulated ATPase activity was estimated by measuring of the Pi liberated from ATP splitting. MIT membrane fluidity was assessed spectrofluorometrically by means of 1, 6-diphenyl-1, 3, 5-hexatriene. Conjugated dienes in MIT membrane lipids were estimated spectrophotometrically at 230 nm. Content of oxidized isoforms of coenzyme Q (CoQ9ox and CoQ10ox) in the isolated MIT was estimated by means of HPLC.

Results: MIT from acute (8 days) DIA hearts exhibited significantly ($p < 0.05$) elevated Mg²⁺-ATPase activities without any considerable elevation of conjugated dienes formation. Functional remodeling of DIA heart MIT and also healthy heart subjected by RIP is associated with increase in the fluidity of MIT membranes. It was most expressed in the DIA group. Significant increased of membrane fluidity found in the DIA group is not supported by presence of RIP. MIT from RIP treated

hearts seemed to exhibit relatively high level of CoQ9ox. However, it appears that the RIP prevents the ischemia/reperfusion-associated increase in CoQ9ox oxidation. Investigation of CoQ10ox formation in MIT from control and RIP-treated hearts yielded less marked results.

Conclusions: Diabetes mellitus induced changes in physical parameters as well as in activities of some enzymatic components of MIT membranes. They are involved to compensation and myocardial adaptation processes and lead to endogenous protective mechanisms. It is not observed the additive fluidization effect of combinations DIA and RIP. Changes in functional properties of MIT membranes associated with diabetic- and RIP-induced remodeling are involved in increased ischemia-tolerance of the myocardium.