

## NOVEL DRUGS – HOW DO THEY WORK?

Saturday 21 May 2016 08:30–10:00

Location: Agora

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### Effects of serelaxin on a systolic cardiac dysfunction induced by isoproterenol in mice with increased cardiac aldosterone

French Federation of Cardiology

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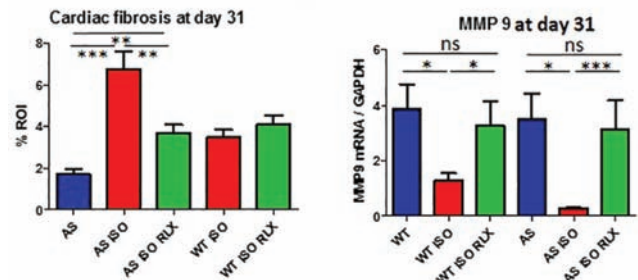
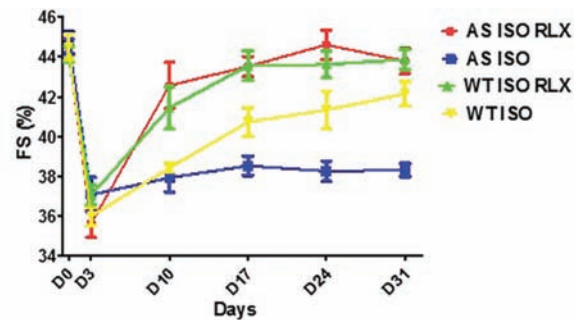
**Background:** Serelaxin (RLX), the recombinant form of human relaxin 2, is a vasoactive peptide hormone with interesting endocrine and paracrine properties, especially for cardiovascular system. Serelaxin is currently tested in clinical trials as a treatment of acute heart failure and may improve the cardiovascular prognosis of patients.

**Purpose:** We aimed to explore the effects of an extended administration of serelaxin in a murine model of chronic heart failure with myocardial injuries resulting from the association of isoproterenol and aldosterone.

**Methods:** Wild type (WT) or transgenic Aldosterone synthase (AS, overexpressing cardiac aldosterone synthase) 3-month old FVB male mice, beforehand injected twice a day for 2 days with subcutaneous isoproterenol (150mg/kg/injection) to induce systolic heart failure, were treated for 28 days with continuous serelaxin infusion (24µg/day), released by osmotic minipumps (WT or AS ISO RLX mice). These 2 groups were compared to control mice which were not treated by serelaxin and had been previously injected (WT or AS ISO mice) or not (WT or AS mice) with isoproterenol. Fractional shortening (FS) was assessed by transthoracic echocardiography along the course of treatment. Evaluation of myocardial fibrosis by sirius red coloration and quantification of mRNA expression by quantitative PCR after reverse transcription were performed at day 31.

**Results:** After isoproterenol injections, AS ISO mice developed a cardiac hypertrophy (heart weight/tibia length ratio +9.4% versus AS mice,  $p < 0.05$ ) and a systolic dysfunction (decrease in FS from 44% to 36%,  $p < 0.01$ ), which persisted 28 days later with major myocardial fibrosis (+300% versus AS mice at day 31,  $p < 0.01$ ). Compared to AS ISO mice, a treatment with serelaxin induced in AS ISO RLX mice an early and persistent improvement in FS ( $p < 0.01$  at day 10, 17, 24, 31, FS 44% for AS ISO RLX mice versus 38% for AS ISO mice at day 31), a decrease in cardiac fibrosis formation at day 31 (-46%,  $p < 0.01$ ), a decrease in mRNA overexpression of pro-inflammatory MCP 1 (-60%,  $p < 0.05$ ) and a restoration of altered expression of mRNA of pro-angiogenic VEGFa and anti-fibrotic MMP 9 in AS ISO mice to similar AS mice levels at day 31. WT ISO mice developed a transient systolic dysfunction after isoproterenol. Serelaxin induced in WT ISO RLX mice an earlier recovery of their initial FS at day 10 (versus day 17 for WT ISO mice) and a decrease in mRNA overexpression of ANP at day 31 (-38% for WT ISO RLX versus WT ISO mice,  $p < 0.05$ ).

**Conclusions:** An extended 28-day treatment with serelaxin improved cardiac function in mice with a systolic dysfunction induced by isoproterenol and cardiac overexpression of aldosterone, through anti-fibrotic, anti-inflammatory and pro-angiogenic properties.



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### Why treatment with natriuretic peptide analogs failed to fulfill our expectations? - receptor expression and function in a failing heart.

Institute of Cardiology Research Grant

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**Background:** Natriuretic peptide (NP) receptors are targets for both native NPs and their analogs used in heart failure (HF) therapy due to antifibrotic and antiproliferative actions. However, in large-scale studies BNP analogs failed to reverse cardiac remodeling and improve patient prognosis. Guanylyl cyclase (GC)-bound receptors (NPR-A, NPR-B) mediate the majority of biological actions of NPs, binding peptides with various affinities. NPR-A binds predominantly with ANP  $\geq$  BNP  $\geq$  CNP, while NPR-B affinity is greatest to CNP  $\geq$  ANP  $\geq$  BNP.

**Purpose:** To demonstrate differences in expression of NPs (ANP, BNP, CNP) and their receptors (NPR-A, NPR-B, NPR-C) on the level of transcription and translation, as well as the GC activity in healthy vs. failing hearts.

**Method:** Rt-PCR and ELISA tests were performed on 43 hearts from patients undergoing heart transplantation and 12 healthy donor hearts not allotted to transplantation in order to determine the expressions of natriuretic peptides and their receptors

on mRNA and protein level. GC activity was assessed by stimulating receptors with increasing concentrations of their respective peptides (ANP for NPR-A and CNP for NPR-B).

**Results:** Expression of myocardium-derived natriuretic peptides (ANP, BNP) in the hearts of heart failure patients was increased on the levels of both mRNA (fold change: 24.4,  $p=0.0003$ ; 13.3,  $p=0.0440$ , respectively) as well as protein levels (1.2 vs. 3.4,  $p=0.001$ ; 26.2 vs. 94.1 ng/mg of protein,  $p>0.0001$ , respectively). CNP mRNA level was reduced (fold change: 0.1;  $p=0.019$ ), while protein level was increased in a failing myocardium (7.6 vs. 12.1 ng/mg of protein;  $p=0.01$ ). NPR-A and NPR-B levels remained unchanged on the level of both mRNA (fold change: 0.9,  $p=0.393$ ; and 1.0,  $p=0.444$ , respectively) and protein (22.8 vs. 21.5,  $p=0.579$ ; 11.1 vs. 10.5 ng/mg of protein,  $p=0.168$ ). NPR-C mRNA levels were raised (fold change: 2.9,  $p=0.00001$ ), while protein expression was reduced (7.5 vs. 4.8 ng/mg of protein,  $p=0.001$ ) in myocardium of HF patients. Stimulation of NPR-A and NPR-B revealed reduced activity of NPR-A (0.45 vs. 1.98 pmol/min/mg of protein,  $p=0.022$ ) in failing vs healthy hearts, while NPR-B function remained unchanged (0.87 vs. 1.45 pmol/min/mg of protein,  $p=0.202$ ).

**Conclusions:** While the levels of both NP receptors exhibiting guanylyl cyclase activity remain unchanged in healthy and failing heart tissues, function of NPR-A, the main target of BNP-based therapeutics, is reduced. On the other hand, the activity of its sister receptor, NPR-B, stays the same, indicating that it might be a better therapeutic target. As expected, expression of ANP and BNP is increased in failing myocardium. Level of CNP mRNA is reduced in the disease, while its protein levels are elevated, likely due to increased production outside the myocardium (vessels) or reduced breakdown. NPR-C (clearance receptor) protein levels are reduced despite elevated mRNA expression, suggesting posttranslational alterations.

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### ORM-3819 promotes cardiac contractility on a dual mechanism of action: troponin-C dependent calcium sensitization is supported by selective PDE III inhibition

MEDIA-261409, TÁMOP-4.2.2.A-11/1/KONV-2012-0045, OTKA: K 109083  
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I Edes<sup>1</sup>; JGY Papp<sup>6</sup>; Z Papp<sup>2</sup>

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**Introduction:** ORM-3819 (L-6-[4-[N'-(4-Hydroxy-3-methoxy-2-nitro-benzylidene)-hydrazino]-phenyl]-5-methyl-4,5-dihydro-2H-pyridazin-3-one) is a novel chemical entity with a molecular structure similar to that of levosimendan.

**Purpose:** This study is the first pharmacological characterization of ORM-3819, focusing primarily on its cardiotoxic effects deriving from its binding to the cardiac troponin C (cTnC) and inhibition of phosphodiesterase (PDE) isozymes.

**Methods:** The binding of ORM-3819 to cTnC was followed by nuclear magnetic resonance spectroscopy (NMR). In vitro enzyme assays on purified PDE III and IV isozymes were carried out to reveal the PDE inhibitory effect of ORM-3819. The cardiotoxic effect of ORM-3819 was evaluated in vitro in permeabilized myocyte-sized preparations from guinea pig left ventricles (LV), ex vivo in Langendorff-perfused guinea pig hearts, in vivo after intravenous drug administration in healthy guinea pigs and mongrel dogs with myocardial stunning induced by the ligation and then reperfusion of the left anterior descending coronary artery.

**Results:** NMR spectroscopy confirmed the binding of ORM-3819 to cTnC by detecting chemical shift changes in the presence of ORM-3819. The selective inhibition of the PDE III and IV isozymes (IC<sub>50</sub>: 3.88±0.3 nM for the PDE III and 4.95±0.02 μM for the PDE IV isozyme) was revealed during in vitro enzyme assays. The Ca<sup>2+</sup>-sensitizing effect of ORM-3819 was demonstrated in vitro in permeabilized myocyte-sized preparations from LV of guinea pig hearts (ΔpCa<sub>50</sub>: 0.12±0.01; EC<sub>50</sub>: 2.88±0.14 μM). ORM-3819 increased the maximal rate of LV pressure development (+dP/dtmax) (EC<sub>50</sub>: 8.9±1.7 nM) and LV systolic pressure (EC<sub>50</sub>: 7.63±1.74 nM) in Langendorff-perfused guinea pig hearts. Intravenous

administration of ORM-3819 increased LV +dP/dtmax (EC<sub>50</sub>: 0.13±0.05 μM/kg) and improved the rate of LV pressure decrease (-dP/dtmax); (EC<sub>50</sub>: 0.03±0.02 μM/kg) in healthy guinea pigs. In an in vivo dog model of myocardial stunning, ORM-3819 restored the depressed LV +dP/dtmax and improved % segmental shortening (%SS) in the ischaemic area (to 18.8±3), which was reduced after the ischaemia-reperfusion insult (from 24.1±2.1 to 11.0±2.4).

**Conclusion:** Our data demonstrate ORM-3819 as a potent positive inotropic agent exerting its cardiotoxic effect by a cTnC-dependent Ca<sup>2+</sup>-sensitizing mechanism in combination with the selective inhibition of the PDE III isozyme. This dual mechanism of action results in the concentration-dependent augmentation of the contractile performance under control conditions and in the postschaemic failing myocardium.

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### Vepoloxamer (purified poloxamer-188) improves LV function, limits cardiomyocyte calcium overload and restores integrity of calcium cycling proteins in myocardium of dogs with advanced heart failure

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**Background:** Calcium overload occurs in cardiomyocytes (CMs) of the failing heart and contributes to cell death and progressive LV dysfunction. Vepoloxamer (VEPO), purified poloxamer-188, is a rheologic agent that improves microvascular blood flow and repairs damaged cell membranes. It is under investigation in a phase-3 trial in patients with acute sickle cell crisis and in phase-2a trial in patients with heart failure (HF).

**Purpose:** We examined the effects of multiple acute infusions of VEPO on LV function in dogs with (HF) (LV ejection fraction, EF~30%) and tested the hypothesis that the membrane reparative properties of VEPO attenuate calcium overload in failing CMs by inhibiting unregulated calcium entry into cells and, in doing so, reverses abnormalities of sarcoplasmic reticulum (SR) calcium cycling proteins.

**Methods:** 14 HF dogs were randomized to 2, 2 hrs infusions of VEPO (450 mg/kg, n=7) or saline (control, n=7) given 3 weeks (W) apart. LV EF and plasma troponin-I (TnI) were measured at baseline, at end of infusion and at 1 and 3W after each infusion. LV tissue obtained at end of study was used to assess calcium ATPase activity (CaAA) and protein levels of phosphorylated (p) ryanodine receptors at serine-2808 (p-RYR-s2808) and p-sodium-calcium-exchanger 1 (p-NCX-1) by Western blotting. Tissue from 7 normal (NL) dogs was used for comparisons. Separately, freshly isolated CMs from 6 control dogs were incubated for 2 hrs with VEPO (4.5 mg/ml) or saline and then treated with 10 μM Fura-2 AM to fluorometrically assess intracellular calcium concentration.

**Results:** VEPO increased EF by 6.0±0.7%\* at 2 hrs; 7.0±0.7%\* at 1W; 1.0±0.6% at 3W; 6.0±1.3%\* at 4W and 5.9±1.3%\* at 6W and reduced TnI by 0.02±0.04 ng/ml at 2hrs; 0.18±0.04\* ng/ml at 1W; 0.13±0.03\* ng/ml at 3W; 0.23±0.03\* ng/ml at 4W and 0.17±0.03\* ng/ml at 6W (\*=p<0.05 vs. control). CaAA was reduced and p-RYR-s2808 and p-NCX-1 levels increased in HF-Controls compared to NL. VEPO therapy normalized all SR proteins (Table). Treatment of isolated CMs with VEPO reduced intracellular calcium compared to saline (2.32±0.05 vs. 3.14±0.32 relative fluorometric units, p<0.05).

**Conclusions:** VEPO attenuates calcium overload and normalizes SR calcium cycling. This leads to lowering of TnI along with improvement of LV function. The results support the development of VEPO for treatment of patients with HF.

#### SR Calcium Cycling Proteins

	NL	HF-Control	HF-VEPO
Ca <sup>2+</sup> -ATPase activity (nmols/min/mg)	699 ± 55	378 ± 12*	576 ± 20†
p-RYR-s2808 (du)	0.44 ± 0.04	1.15 ± 0.09*	0.66 ± 0.04†
p-NCX-1 (du)	0.58 ± 0.04	2.07 ± 0.22*	1.57 ± 0.08†

du = densitometric units; \*p,0.05 vs. NL; †p<0.05 vs. HF-Control

# MODERATED POSTER SESSION 1 – ACUTE HEART FAILURE

Saturday 21 May 2016 10:00–11:00

Location: Poster Area

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## Hypochloraemia during hospitalization for acute heart failure is strongly associated with poor decongestion and mortality

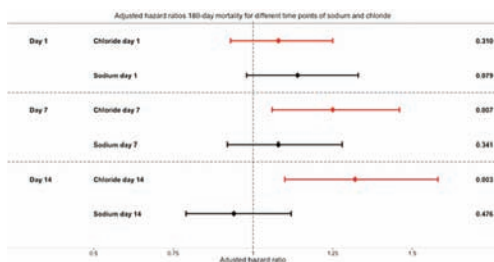
J M Jozine Ter Maaten<sup>1</sup>; K Damman<sup>1</sup>; MM Givertz<sup>2</sup>; M Metra<sup>3</sup>; JG Cleland<sup>4</sup>; DM Bloomfield<sup>5</sup>; P Ponikowski<sup>6</sup>; DJ Van Veldhuisen<sup>1</sup>; JM Testani<sup>7</sup>; AA Voors<sup>1</sup>  
<sup>1</sup>University Medical Center Groningen, Groningen, Netherlands; <sup>2</sup>Brigham and Women's Hospital, Boston, United States of America; <sup>3</sup>University of Brescia, Brescia, Italy; <sup>4</sup>Imperial College London, London, United Kingdom; <sup>5</sup>Merck Research Laboratories, Rahway, United States of America; <sup>6</sup>Wroclaw Medical University, Wroclaw, Poland; <sup>7</sup>Yale University, New Haven, United States of America

**Background:** Chloride plays a key role in renal salt sensing, neurohormonal activation and regulation of diuretic targets and hypochloraemia predicts mortality in acute heart failure (AHF). AHF therapies such as diuretics alter chloride homeostasis.

**Purpose:** We studied the association between (changes in) serum chloride concentration and diuretic responsiveness, decongestion, and mortality in patients with AHF.

**Methods:** Patients hospitalized for AHF in the PROTECT trial (n=2033) who had serum chloride measured within 24 hours of admission and 14 days later were studied (n=1960). Hypochloraemia was defined as chloride <96 mEq/L. Results Median baseline chloride was 101.0 [97.0-104.0] mEq/L. Low baseline chloride was associated with high bicarbonate, poor diuretic response, less haemoconcentration, and more worsening heart failure (all P < 0.01). Newly developed hypochloraemia at day 14 was common and associated with a decline in renal function, and increase in serum urea (P < 0.01). In multivariable analyses, chloride measured at day 14, but not baseline chloride was strongly and independently associated with 180-day mortality (HR per SD decrease: 1.33 [1.17-1.50], P < 0.001). In comparison, sodium was not significantly associated with mortality after multivariable adjustment at any time point. Hypochloraemia at baseline that resolved was not associated with mortality (p = 0.55), but new or persistent hypochloraemia at day 14 was associated with increased mortality (HR: 3.11 [2.17-4.46], P < 0.001).

**Conclusion:** Hypochloraemia at AHF hospital admission was strongly associated with impaired decongestion. New or persistent hypochloraemia 14 days later was independently associated with reduced survival, whereas hypochloraemia that resolved by day 14 was not.



Adjusted HRs 180-day mortality

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## Red cell distribution width (RDW) predicts long term prognosis in patients hospitalized with acute heart failure: the RDW in Acute Heart Failure (REAHF) study.

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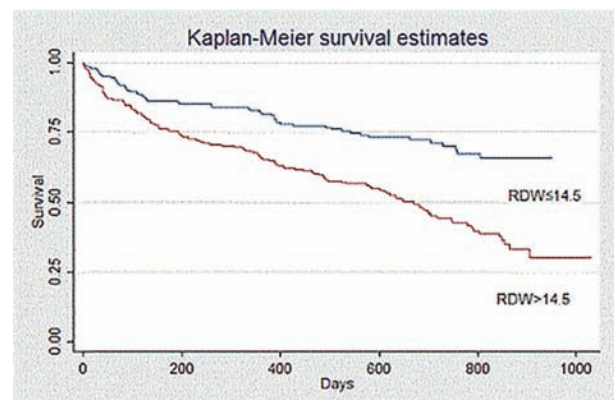
**Background:** RDW has been proposed as a sensitive biomarker of chronic hypoxic burden via the hypoxia-> erythropoietin -> anisocytosis-> RDW model. The role of RDW in predicting prognosis in acute heart failure (AHF) and his relationship with comorbidities is not fully elucidated.

**Purpose:** To evaluate the long-term prognostic value of RDW in a broad population of patients hospitalized for AHF.

**Methods:** in a retrospective cohort observational study, 436 consecutive patients admitted in 2013 for AHF in a urban hospital were categorized in patients with low RDW (<14.5) and high RDW (> 14.5). Hemoglobin, NT-proBNP values along with clinical and biochemical variables were recorded. Charlson comorbidity score was calculated. The rate of death from all causes was determined after a median follow up of 18 months.

**Results:** Overall population has a median age of 80 years (IQR 72-85), 228 patients (52%) were males. At follow up 185 patients (42%) had died: in the cohort with low RDW (n=189) 52 patients had died (27%) whereas in the cohort with high RDW (n=247), 133 patients (53%) had died. The unadjusted risk ratio of patients with high RDW was 2.26 (log rank test p < 0.0001, Figure) In a multivariate Cox regression model, the hazard ratio for death from any cause for the patients with high RDW as compared with those with low RDW was 2.0 (95 percent confidence interval, 1.3 to 2.9; P < 0.001); the RDW added prognostic information beyond that provided by conventional risk factors, including the patient's age; sex; the presence or absence of a history of coronary artery disease, hypertension, diabetes, systolic dysfunction, anemia, hyponatremia; estimated glomerular filtration rate; high NT-pro BNP levels, Charlson comorbidity score.

**Conclusion:** RDW is a powerful marker of long-term mortality in patients with AHF and his prognostic value is maintained beyond that provided by hemoglobin levels, comorbidity score or other well-established risk factors or biomarkers.



Survival curve

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## Admission and discharge prognostic value of Galectin-3 and its relationship with echocardiographic parameters in patients hospitalized for acute heart failure

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**Background:** Galectine-3 (Gal-3), is biomarker involved in different body processes such as inflammation and fibrosis, which play a central role in the development of Heart Failure (HF).



**Purpose:** Aim of this study was to evaluate in patients hospitalized for acute heart failure (AHF), Gal-3 prognostic role also to systolic and diastolic functions related to echocardiographic data.

**Methods:** We enrolled 143 consecutive AHF patients presenting to our emergency department from January 2014 to march 2015. In all studied patients, at hospital admission, together with echocardiographic assessment Gal-3 and Brain Natriuretic Peptide (BNP) were performed and repeated at discharge. A 60 days follow up phone call was made to evaluating cardiovascular events (death and rehospitalization).

**Results:** No statistically significant difference for Gal-3 values at admission and at discharge in patients with events and neither in patients without events and in the whole group. At ROC analysis Gal-3 at discharge showed to be able to predict 60 days events: AUC 0.67, 95% CI 0.533 to 0.793,  $p < 0.05$ . Considering patients with a value of Gal-3 at admission  $> 17.8$  ng/ml, we found a statistically significant correlation with events, while patients who had a Gal-3 median value  $< 17.8$  ng/ml had better prognosis ( $p < 0.001$ ). BNP mean value at arrival was  $1140 \pm 1115$  pg/ml, and at t test it showed prognostic relevance for events (mean value in patients without events  $971 \pm 781$  pg/ml, and  $1644 \pm 1678$  pg/ml in patients with events,  $p < 0.001$ ). At ROC analysis, BNP at arrival showed prognostic value for events (AUC 0.619,  $p < 0.05$ ). The combined ROC curve of BNP and Gal-3 at discharge showed prognostic power for events (AUC 0.75,  $p < 0.05$ ). At echocardiographic assessment, there was no statistically significant difference between patients with reduced and preserved left ventricular ejection fraction in relation with Gal-3. There was a significant inverse correlation between Gal-3 and the deceleration time ( $r = -0.35$ ;  $p < 0.05$ ) in patients with sinus rhythm as result of diastolic dysfunction.

**Conclusions:** In patients admitted with AHF, Gal-3 evaluation at hospital discharge allows to identify those subjects who are at higher risk for events (death and rehospitalization) in the following 60 days; in particular for those ones that presented a value of Gal 3 greater than 17.8 ng/ml. The combined use of BNP and Gal-3 at hospital discharge seems to be useful for predicting future 60 days prognostic value. The prognostic value of Gal-3 could be referred to its effect on left ventricle diastolic function.

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### Acute decompensated heart failure syndrome in patients with myocardial infarction as the predictor of the development of multiple organ dysfunction syndrome

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Myocardial Infarction (MI) complicated with Multiple Organ Dysfunction Syndrome (MODS) is the serious life-threatening condition leading to high mortality.

The purpose of the study was evaluation the cardiologic status of patients with MI due to Acute Decompensated Heart Failure (ADHF) complicated with MODS, investigating the structure of MODS and the contribution of known risk factors to its development. Were examined 76 patients with MI complicated with ADHF syndrome; 48 patients of this group revealed MODS (the 1st group; mean age is 64 (7) years). MODS was not diagnosed in 28 patients (the 2nd group; mean age is 59 (2) years). Heart Function Deficiency (HFD) severity was estimated with the following scales: "CHOCKS" scale, "US" classification, Killip/Kimball scale of 1967, Forrester/Stevenson scale of 1977, patient's model with Heart Failure (HF) "Seattle HF Model", "EFFECT" scale. ADHF Syndrome was revealed in 17 patients in both groups. Severity of Coronary stenosis was estimated by "SYNTAX" scale. Risk factors were estimated with GRACE scale; MODS – with MODS, SOFA scales. The 2,3,4,5 component MODS was determined. Statistical significance was defined at the level of methods for  $p < 0,05$ .

All patients had chronic extra-cerebral pathology prior to the development of severe forms of MI (75% had polymorbidity). 90% of all cases with MODS included the Pathology of the Respiratory system. More often (37%) MODS included 2 components, and only 3% included 5 components. Cardiac Function Deficiency prevailed in patients with MODS ( $p < 0,05$ ). Positive dynamic of HFD was revealed in the 2nd group of patients with all scales ( $p < 0,05$ ). Dependence of the degree of HFD in patients with MODS and severity of coronary atherosclerosis (AS) was assessed as the highest in patients with MI and ACHD in the presence of severe coronary stenosis ("SYNTAX"  $\geq 23$ ) and as the least in patients with moderate coronary stenosis ("SYNTAX"  $\leq 22$ ) ( $p < 0,05$ ). Executing the discriminant analysis had shown the most significant risk factors of MODS: Hypertension, AS, rheumatism, coronary heart disease, chronic intoxication. Carrying out the canon analysis revealed that only hypertension was statistically significant. Defining of the standardized variables for comparison of importance of arterial hypertension as risk factor was found that it contributes to 78% of variability, so, its contribution to the development of MODS is maximal, and then the severity of AH is higher, the more components lead to MODS. Besides AS was found to contribute to 5-component MODS.

Thus, the most common MODS component is the acute pathology of the Respiratory System that does not depend on the MI type with ADHF. More often was found MODS with 3-component. The higher degree of cardiac function deficiency is also found in patients with MODS. Hypertension makes the greatest contribution to the

development of MODS, the severity of hypertension is directly proportional to the number of MODS components.

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### Five years monitoring of pulmonary congestion in chronic heart failure patients in outpatient clinic. Randomized controlled trial (IMPEDANCE-HF).

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Assessment dynamic of pulmonary congestion in patients with congestive heart failure for long period of time by noninvasive technique may help understand mechanisms of Acute Heart Failure development and Heart Failure (HF) associated 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 HF patients. Aim To determine the dynamics of pulmonary congestion development in HF patients.

**Method and Results:** LI change is adequately reflects dynamics of pulmonary congestion and decreasing LI reflects increasing lung fluid. In "Non-invasive Lung IMPEDANCE-Guided Preemptive Treatment in Chronic Heart Failure Patients: a Randomized Controlled Trial (IMPEDANCE-HF trial)" 256 CHF patients with LVEF  $< 35\%$  were randomized (1:1) to a control group treated by clinical assessment and a monitored group whose therapy was also assisted by Lung Impedance (LI). Was found that LI-guided treatment reduced HF hospitalizations by 45% and HF associated death by 58% during 48 months of treatment. Signs, LI and ratio of the instantaneous LI to the calculated baseline LI ( $\Delta LI/R$ ) were monitored monthly in the outpatient clinic. 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 256 study patients, 190 were admitted for HF, 31 for non-AHF causes only and 35 were not hospitalized at all during the follow up period. The average number of HF hospitalizations was 1.05/year. 221 of 256 patients had follow up period  $> 5$  years. Results calculation DLIR/year were for patients without HF hospitalizations (-11%; -8%; -8%; -7%; -8%), (group 1), for patients with HF hospitalizations  $< 1.05$ /year (-17%; -15%; -16%; -15%; -16%), (group 2) and for patients with HF 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 multiple HF hospitalizations.

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### Management of heart failure in the real-world: does the setting make the difference? Findings from the ARNO administrative database.

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**Background:** The natural course of patients with chronic heart failure (HF) is characterised by frequent rehospitalisations that are cause of morbidity and mortality and are responsible for a large part of HF costs. Patients included in randomized clinical trials and registries are generally enrolled in cardiology wards, but in the real-world these patients are frequently managed also in non-cardiology settings.

**Purpose:** The purpose of this study is to describe the real world clinical epidemiology of acute heart failure analysing a large administrative database and describing the main differences in terms of clinical characteristics, treatments, one-year outcomes and costs across the different settings of care.

**Methods:** Data came from the ARNO Observatory that includes nearly 3,000,000 inhabitants of 7 Local Health Authorities of the Italian National Health Service (NHS). Patients with HF were selected when discharged for HF (from January 1, 2008 to December 31 2012) and prescribed on at least one specific HF treatment. We compared patients managed in cardiology vs those managed in internal medicine/geriatric wards. Results. The study population was composed by 37,242 patients discharged alive for HF from the above described specific settings and prescribed on HF treatments. Just 26.6% were managed in a cardiology setting and nearly two thirds of the patients (63.3%) were managed in internal medicine (49.7%) and geriatrics (13.6%) wards. Compared to those discharged from internal medicine/geriatrics settings, HF patients managed in cardiology setting were younger (mean age 73 vs 80 years), with a lower prevalence of females (39.8% vs 56.6). Less co-morbidities such as COPD (26.3 vs 32.0%)



or depression (12.9 vs 24.4%) were reported as well as a higher prescription rate of ACE-inhibitors/Angiotensin Receptor Blockers, Beta-Blockers and Mineralocorticoid antagonists (72.2 vs 63.9 %, 68.6 vs 46.6% and 47.3 vs 40.4%). During the 1-year follow-up, patients managed in cardiology had at least one re-hospitalization in 57.4% vs 56.8% and less frequently due to non-cardiovascular causes (31.1 vs 53.5%). NHS's total direct cost per year were higher in cardiology (15,664€) than in the internal medicine/geriatric wards (10,516 €). p values for all above differences < 0.01.

**Conclusions:** Real world evidence show that only a minority of patients are managed in a cardiology setting and that, according to management setting, patient's characteristics are very different in terms of clinical characteristics, treatments, costs and outcomes.

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### Risk assessment of re-hospitalizations for heart failure during 30 days after discharge for heart failure in randomized controlled IMPEDANCE-HF trial

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**Background:** Prevention of re-hospitalization for heart failure (HF) is an unresolved issue. Aim Evaluate the ability of a new non-invasive method for lung impedance monitoring to predict HF re-admissions within 30 days after previous HF hospitalization.

**Methods:** In "Non-invasive Lung IMPEDANCE-Guided Preemptive Treatment in Chronic Heart Failure Patients: a Randomized Controlled Trial (IMPEDANCE-HF trial)" 256 CHF patients with LVEF<35% were randomized (1:1) to a control group treated by clinical assessment and a monitored group whose therapy was also assisted by Lung Impedance (LI). Was found that LI-guided treatment reduced HF hospitalizations by 45% and HF associated death by 58% during 48 months of treatment. There were 211 and 386 HF hospitalizations in monitoring and control group within 48 months of follow up. LI was measured in all patients at admission and discharge and calculated as a part from normal LI impedance for each patient and presented in percent. Improvement in LI impedance at discharge (decreasing in pulmonary congestion) in compare with admission was divided in 4 categories: A: 0< DLI< 5%; B: 5 < DLI < 10%; C: 10 < DLI < 20% and D: DLI > 20%. Results We found that percent of re-admissions for HF was in categories A: 60 and 64% (NS), B: 30 and 35% (NS), C: 10 and 27% (p < 0.05), D: 6 and 6.1days (NS) in monitored and control group correspondingly. Length of hospital stay was in categories A: 5.4 and 4.9 days (NS), B: 3.7 and 5 days (p < 0.05), C: 5.2 and 5 days (NS), D: 4 and 19% (p < 0.05) in monitored and control group correspondingly.

**Conclusions:** Noninvasive LI monitoring may be used to evaluate effectiveness of therapy in hospitalized HF patients. Small (less 5%) improvement in LI during hospitalization is a very strong predictor for re-hospitalization during next month in both groups. LI improvement in categories A and B was so small that even LI-guided treatment was ineffective to prevent re-admissions during next month. On the other side, LI improvement in categories C and D was enough powerful to enable to LI-guided treatment significantly improves rate of HF hospitalizations.

# CLINICAL CASE CORNER 1: HEART FAILURE UNTOLD: THE CUTTING EDGE OF HEART FAILURE MANAGEMENT

Saturday 21 May 2016 10:00–11:00

Location: Poster Area

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## Dynamic transcatheter mitral valve repair: first in man experience with a novel concept to treat patients with severe heart failure and functional mitral regurgitation

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**Introduction:** We report the case of a 58-year-old man, transferred to our centre following an out of hospital cardiac arrest with acute ST-elevation myocardial infarction and cardiogenic shock. An Impella was inserted and primary percutaneous intervention performed using two drug-eluting stents into left anterior descending and right coronary artery. The patient had a prolonged stay on intensive care unit. Echocardiography demonstrated a significantly impaired left ventricular ejection fraction (LVEF 20%) and severe functional mitral regurgitation. The patient remained hypotensive and dialysis-dependent making treatment with heart failure medication challenging. He was not suitable or ineligible for alternative treatments, including percutaneous edge-to-edge mitral valve repair, re-synchronisation therapy and heart transplantation. Therefore, approval was sought from the Medicine and Health Care Products Regulatory, to insert a spacer balloon, a new device, on compassionate grounds.

**Device Procedure:** This spacer balloon is a novel device for dynamic transcatheter mitral valve repair (DTMVR). It is a fluid-filled balloon, implanted via transapical access into the mitral valve orifice, and aims to improve leaflet coaptation during systole. Its size is adjustable after implantation through a subcutaneous port to enable optimal performance. The patient underwent implantation under general anaesthesia, guided by echocardiography and fluoroscopy. The balloon was filled stepwise, until Swan-Ganz catheter measurements confirmed optimal haemodynamics and echocardiography showed optimal reduction of MR. Post procedure, the patient was no longer dialysis dependent and was discharged home. Improved blood pressure allowed for initiation of heart failure medication. While LVEF improved to 45% and the patients NYHA status increased to II, MR decreased to moderate degree. Thus, at six months, the balloon was topped up (+2.5ml) under echocardiographic guidance during an outpatient appointment, which reduced MR to mild degree. At seven months, the patient developed some small thrombi on the device. Given that his surgical risk had dramatically decreased, mitral valve replacement was performed and the device explanted. The patient had an uneventful postoperative course, has been discharged home and is stable in NYHA class I.

**Conclusion:** This spacer balloon offers a new treatment option of dynamic TMVR. Patients with acute heart failure and MR may benefit as demonstrated. How the spacer balloon would perform as destination therapy in patients with chronic heart failure, remains to be seen.

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## Avoiding heart failure admission - high dose bolus IV Furosemide & CKD stage 4/5

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Heart failure is one of the most common causes of admission to hospital. Studies have demonstrated day case IV Furosemide to be a successful treatment in avoiding admission to hospital. This case study demonstrates high dose IV Furosemide in a complex heart failure patient with chronic kidney disease stage 4/5 can be effective in avoiding admission.

**Background:** An 82 year old male had a past medical history of CKD stage 4/5, COPD, CRTP, EF 10-15%, PAF, Type II DM chronic back pain. He would be outside criteria for many IV Furosemide regimes due to renal failure, GFR 18 and the dose

required. He had 5 admissions over the past year due to heart failure. The patient presented with SOB, weight gain of 4lbs, ankle oedema and abdominal distention. He no longer responded to oral titrations of diuretics. He was on maximum tolerated medication. He was aware of his prognosis, however he valued any time which he could have at home. Day case diuretics within the cardiology department were administered by a heart failure specialist nurse and with support from the cardiology team if required. The dose was determined by previous admission requirements. Furosemide 240mg was administered over 2 hours via syringe driver. Observations were monitored every 15minutes until 1 hour post infusion. Renal function was checked the following morning.

**Results:** The patient required IV diuretics Monday, Thursday & Friday and achieved dry weight, without any deterioration in blood pressure or renal function. The patient was able to go home each evening. This regime was successful because of early implementation of IV Furosemide at large doses. Average duration of previous admissions were 7 days at a cost of £2000 approx. Conclusion : High dose day case IV Furosemide should be considered for complex heart failure patients with stage 4/5 renal disease. Regimes need to be flexible to adapt to individuals requirements, however this needs to be within an environment where the expert clinicians are well known to the care needs of the patient.

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## Gene expression profiling to identify giant cell myocarditis in a patient with clinical suspicion but no histological evidence of the disease

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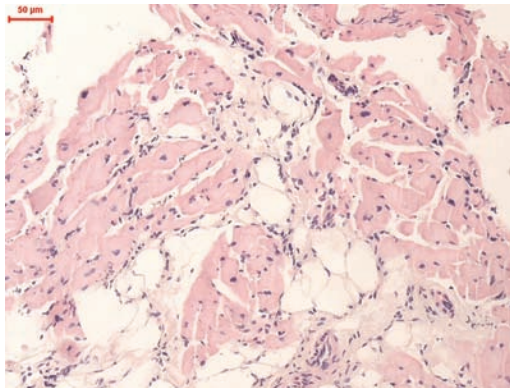
A previously healthy female (26 years) was admitted due to sudden onset of massive dyspnoea, nausea and vomiting following a respiratory infection two weeks ago. At admission the patient had no fever. Due to the acute beginning of dyspnoea pulmonary embolism was excluded by computed tomography. The patient was then admitted to the intensive care unit for treatment. She was intubated and mechanically ventilated with initially high positive end expiratory pressure (PEEP) which led to respiratory stabilisation. However, she was catecholamine-dependent (norepinephrine). Echocardiography revealed a massive depression of left ventricular function with an ejection fraction (LV-EF) of 25%.

Endomyocardial biopsy (EMB) was taken the following day under the suspicion of giant cell myocarditis. After EMB echo showed an even more depressed LV-EF (15%), the patient was even more norepinephrine-dependent and cardiogenic shock was deteriorating as well (INTERMACS-1). This prompted the implantation of an extracorporeal membrane oxygenation (ECMO) in a veno-arterial manner. After five days on ECMO preliminary results of EMB showed no infection of viral genome, no giant cells in histology (although lymphocytes and macrophages were present) while immunohistological staining showed a massive elevation of lymphocytes and macrophages. However, due to the suspicion of giant cell myocarditis a gene expression profiling was done which confirmed the suspicion.

With this information a high-dose cortisone-therapy was started at 10mg/kg body-weight for 3 days followed by 4 weeks at 1mg/kg bodyweight. This was supported by cyclosporine. After 3 days of high-dose cortisone LV-EF increased from 15% to 55% and ECMO was explanted. The patient was extubated and transferred to the normal ward after another 4 days. Overall, the patient left the hospital after 4 weeks to start cardiac rehabilitation. Treatment at discharge consisted of methylprednisolone (1mg/kg for 4 weeks, followed by a decline of 10mg every 2 weeks until 10mg will be reached), cyclosporine (trough level 100-150), pantoprazol 40mg, calcium plus vitamin D, ramipril, eplerenon and bisoprolol.

Giant cell myocarditis is a rapid progressive disease with an enormously high mortality due to pump failure or arrhythmias. Immunosuppression including cortisone

and cyclosporine is the treatment option saving lives. Therefore, every effort must be made to get a definite diagnosis out of the EMB-specimen as soon as possible. In cases where no focal granulomas of giant cells can be found in histology these findings may oppose the clinical suspicion. Therefore, gene expression profiling as reported earlier is an excellent tool to identify the disease and get certainty about the underlying disease.



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#### Life-saving role of ECMO in aggressive multidisciplinary treatment strategy for catastrophic antiphospholipid syndrome

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**Introduction:** Catastrophic antiphospholipid syndrome (CAPS) is a rapidly progressive life-threatening disease characterized by multiple organ failure in presence of antiphospholipid antibodies. Therapy is based on anticoagulation with intravenous (IV) heparin, immunosuppressors, IV immunoglobulins, and plasmapheresis. Nevertheless, the course of the disease is sometimes hyperacute and the high mortality rate is primarily due to acute cardiopulmonary failure. Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) may effectively support cardiorespiratory function and acts as a bridge to recovery.

**Description:** A 29-year-old woman with history of Antiphospholipid Syndrome (APS), past pulmonary, cerebral and skin vasculitis, presented to our hospital with epigastric pain and fever. After 7 days she had chest pain with ECG sinus tachycardia, anterolateral ST segment depression, serum Troponin T elevation and global hypokinesia with 40% left ventricular ejection fraction (LVEF) on echocardiography. The clinical scenario rapidly deteriorated with severe acute respiratory failure with cardiogenic shock (LVEF 20%) and acute kidney injury with anuria, refractory to mechanical ventilation, inotropes, and diuretics. Coronary angiography yielded normal results and myocardial biopsy was performed. Femoro-femoral VA-ECMO was initiated. Blood flow was 2.5 L/min/m<sup>2</sup>. After initial hemodynamic stabilization, we tried to identify the heart failure (HF) etiology. Differential diagnosis included lupus myocarditis, infective and Libman-Sacks endocarditis, thrombotic thrombocytopenic purpura and CAPS. We diagnosed CAPS on the basis of the following criteria: evidence of involvement of 3 or more organs, systems, and/or tissues (pulmonary, cardiac and kidney); development of manifestations simultaneously in a week; confirmation by histopathology of small vessel occlusion in myocardial biopsy; and laboratory confirmation of the antiphospholipid antibodies presence. Pulse steroid therapy with intravenous (IV) methylprednisolone, 1 g daily for 3 days, and IV immunoglobulin 1 mg/kg/d, for 3 days were given. She also underwent 3 plasmapheresis cycles. Heparin infusion, started before ECMO administration, was continued to maintain constant anticoagulation. The patient progressively recovered and ECMO was stopped 10 days later. Steroid therapy was tapered to 120 mg daily associated to immunosuppression with mycophenolate mofetil 1 g twice/daily. Warfarin was started for oral anticoagulation. The patient was discharged 4 weeks after ECMO interruption with specialist follow-up from cardiologists and rheumatologists.

**Conclusion:** CAPS has a high mortality rate, requiring early aggressive treatment managed by a multidisciplinary team. In this case, ECMO device played a key role as a bridge to recovery of cardiac function in a heart failure rare etiology.

### 34

#### Hemodynamics and cerebral oximetry in a case of severe heart failure based on amyloidosis

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**Introduction:** We report a 65-year-old male diagnosed with heart failure in 2011. The ultrasonic cardiography (UCG) showed a left ventricular ejection fraction (LVEF) of 40%. Examination with magnetic resonance tomography (MRT), cardiac and subcutaneous biopsies revealed cardiac AL-amyloidosis. The patient was discharged in New York Heart Association (NYHA) class 3a, mean arterial pressure (MAP) 75 mmHg and heart rate (HR) 71 bpm. UCG in 2013 was unchanged. In 2014 the patient was readmitted because of pleural effusion. The UCG was unchanged. Hemodynamic parameters were stable, NYHA class worsened to 3b. The patient was discharged in NYHA class 3a. In October 2014 the patient was examined with head-up tilt test (HUT) and absolute cerebral oximetry. Two weeks later the patient received emergency treatment due to hyper dynamic sepsis. MAP at admission was 58 mmHg, NYHA class 4. Despite adequate treatment with antibiotics and inotropes the patient remained hemodynamically unstable. LVEF was stable. Even with ventilation and hemofiltration the hemodynamic parameters were unchanged with insufficient circulation and vasoplegia. The patient died in hemodynamic shock after 25 days at the ICU.

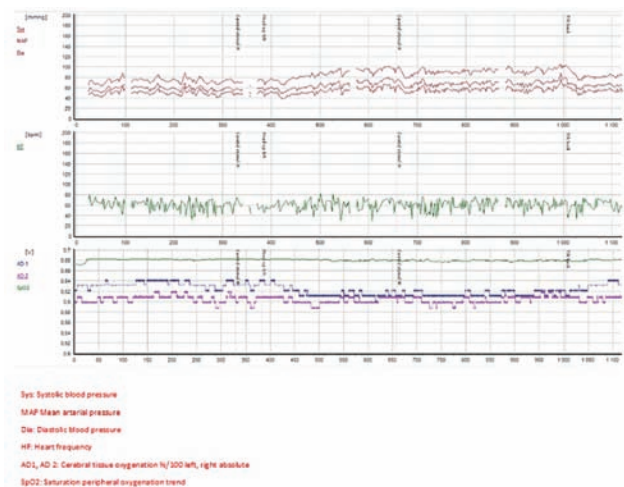
**Objectives:** The patient showed an unexpected BP response during HUT. During postural change induced by HUT, MAP increased from 59 mmHg at base line in supine position to 68 mmHg in 60 degrees HUT where it remained stable until it returned to base line level after tilt back. HR (atrial fibrillation) was unchanged during HUT. Absolute cerebral tissue oxygenation (SctO<sub>2</sub>) decreased slightly during HUT parallel to increasing MAP. Peripheral oxygen saturation (SpO<sub>2</sub>) remained stable during HUT. Two weeks later the patient died in hemodynamic shock despite adequate treatment for sepsis and stable LVEF. HUT was performed according to a protocol adopted from current guidelines. SctO<sub>2</sub> was assessed by an absolute cerebral oximeter. BP and SpO<sub>2</sub> were recorded by a beat-to-beat monitor.

**Clinical question:**

Does cardiac AL-amyloidosis cause pathological changes in BP and HR response, not explained by heart failure, leading to an impaired ability to adequately respond on hemodynamic challenges?

**Discussion:** The increase of MAP from hypotension to normal values during HUT was unexpected. SctO<sub>2</sub> decreased with increasing MAP, which might reflect impaired end organ perfusion, HR did not change notably. This might reflect the patients inability to respond to hemodynamic challenges which might have caused circulatory failure during sepsis.

**Conclusions:** Cardiac AL-amyloidosis might lead to pathological hemodynamic patterns. Amyloid infiltration into the subendocardium is discussed to be the pathophysiological mechanism. Dysautonomia may contribute. HUT could be used to identify patients with autonomic and hemodynamic failure. We promote close follow-ups and generous hospitalization for these patients to early detect and avoid hemodynamically challenging situations.



Cerebral oximetry and hemodynamics

### 35

#### Total circulatory support using isolated left ventricular assist device in a patient with acquired Fontan physiology

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RV failure remains an important cause of increased morbidity and mortality following LVAD implantation and management includes volume optimization, inotropic and mechanical RV support. 55 year female, blood group O, 36% Class I and 93% Class II PRA, with 1year history of DCM was referred for consideration of advanced



therapies in the context of progressive symptomatic deterioration, deranged liver enzymes and high BNP (2012 pg/ml). Her coronaries were unobstructed; cardiac MRI showed nonspecific delayed enhancement with LVEF of 13%, and moderate RV impairment, her QRS was narrow and primary prevention ICD was put in place. Resting hemodynamics were left-sided limited (table 1). Isolated continuous-flow left ventricular assist device was implanted as a bridge to transplant with successful discharge on postoperative day 25. 18 days later, she developed progressive RV failure requiring IV diuretics and milrinone and was listed high status for heart transplantation.

ECG's showed progressive QRS widening and, 30 days after admission, asystole with failure to capture by the pacemaker. Echocardiogram confirmed cardiac standstill. Flow was non-pulsatile and hemodynamics were in keeping with Fontan physiology (table 1). There was no evidence of end organ damage and she was supported on LVAD alone. She was physically active until her transplant 22 days following cardiac standstill. She is well post-transplant with no significant rejection and normal graft function.

To the best of our knowledge only one case has previously been reported using LV assist device alone to provide total circulatory support for 7 days. We considered additional RV mechanical support, but, with satisfactory hemodynamics and no end organ damage, it was felt that the additional risk of surgery for RV support was not warranted. The LVAD alone was providing satisfactory circulatory support in the context of acquired Fontan physiology.

We highlight the difficulties in deciding between isolated LVAD and BiVAD support and demonstrate that total circulatory support with isolated LV assist device is possible in the context of low trans pulmonary gradient and pulmonary vascular resistance.

Hemodynamic parameters							
	RAP€	RV€	PA€	PCW€	TPG€	CO	PVR§
Pre-LVAD	8		43/32 (36)	26	11	2.6	4.2
Cardiac standstill	22	21	(18)	12	6	6.02	1

€: mmHg; : L/Min; §: Woods Units



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#### Untreatable amyloidosis? Definitive therapy with double transplantation.

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We report the case of a young female patient, born in 1966, lived an active life, without any symptoms. Her medical history is negative. In September, 2014, she was admitted with progressive fatigue. Echocardiography showed severe left ventricular wall wall thickening (septal and posterior wall thickness 16 and 15 mm, respectively) and granular myocardial pattern with signs of restrictive cardiomyopathy. A cardiac MRI was performed, which confirmed the diagnosis of cardiac amyloidosis. Her heart failure rapidly progressed, and she was hospitalized in October 2014. The indication for heart transplantation was established, but her untreatable disease contraindicated her transplantation.

Further investigations of the etiology of amyloidosis revealed kappa light chain producing multiple myeloma (MM). After a multidisciplinary consultation including cardiologists and hematologists, the decision for a double, heart and bone marrow transplantation was made. In November 2014 a dose reduced chemotherapy was started and patient reached partial remission of MM. In March 2015, a successful

heart transplantation was performed. She was discharged home after an uneventful postoperative period in April 2015 without any signs of rejection in a good overall condition. After the complete recovery from the cardiac transplant, the hematologist performed a successful autologous stem cell transplantation in September 2015.

Now our patient is in an excellent medical condition. Her routine biopsies revealed no rejection and echocardiography examinations showed good left ventricular function. The multiple myeloma is in complete remission as confirmed by immunoserology and bone marrow biopsy tests.

In conclusion we can say that the multidisciplinary cooperation was able to develop an effective treatment plan to save a patient with a mostly untreatable disease.

### 37

#### An unusual approach in a patient with pacemaker lead-related tricuspid regurgitation

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There are few data in the literature regarding severe tricuspid regurgitation induced by RV pacemaker leads, although such cases are not rare in clinical practice. PM and ICD leads may be the cause of tricuspid regurgitation or may worsen existing tricuspid regurgitation. Severe tricuspid regurgitation is an independent predictor of mortality. The treatment of choice is surgical tricuspid valve repair. A 61 year old female was referred to our hospital with shortness of breath and peripheral edema. Her history revealed that a single chamber transvenous permanent pacemaker had been implanted 4 years before for third degree atrio-ventricular block. The ECG showed AFib and VVI pacing. TTE revealed mild LV systolic dysfunction (LVEF 40-45%) and severe tricuspid regurgitation with right heart dilation and volume overload. 2D and 3D TTE showed that the RV lead (active fixation in the basal septum) was responsible for the severe tricuspid regurgitation (due to interference with septal leaflet coaptation). Our strategy was RV lead extraction and re-implantation in a low septal position under TTE guidance, thus reducing the tricuspid valve closure impairment and upgrade to resynchronization therapy device. Medical treatment included loop diuretic, ACE inhibitor, beta-blocker and vitamin K antagonist. Follow-up at one month showed NYHA class II, normal LVEF (55%) with improved mobility and coaptation of the tricuspid leaflets, moderate tricuspid regurgitation and decreased right ventricular pressures compared with the previous examination.

**Conclusion:** This case reveals the importance of careful risk-benefit estimation when establishing the management of pacemaker lead induced tricuspid regurgitation. Complete assessment of valve anatomy is important to decide whether it is better to extract the pacemaker lead or to repair the tricuspid valve without lead extraction. Upgrading to CRT due to LV systolic dysfunction was an argument towards interventional treatment in this case.



Rx

### 38

#### Therapeutics alternatives in failing Fontan

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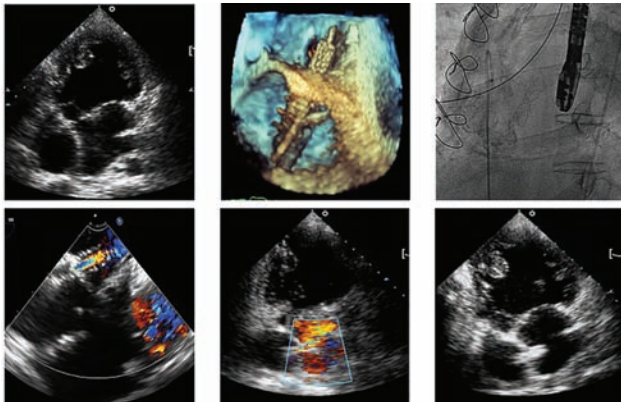
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A 40-year-old woman, who had undergone to total cavopulmonary connection (TCPC), was admitted with severe heart failure. She had a history of double inlet left ventricle with normally-related great vessels. She underwent pulmonary artery banding at 4 months old and Glenn procedure when she was 12 years old. Total cavopulmonary anastomosis with an intra-atrial lateral tunnel was completed at 26 years old.

She kept in functional class (FC) II until one year ago, however during last year she significantly worsened, remaining in FC IIIb. At admission the patient was in anasarca, showing massive pleural effusion, ascites and generalized edema. She weighed 4 Kg more, liver was enlarged and jugular venous pressure was elevated. Her legs were absolutely swollen and oxygen saturation was 81%. Transthoracic echocardiogram showed a single ventricle with mildly decreased ejection fraction (46%). There were no stenosis nor images suggesting thrombi and cardiac magnetic resonance confirmed complications absence. Thoracentesis and paracentesis were required; however, right pleural effusion soon reappeared. After high doses of intravenous diuretics, peripheral edema persisted and kidney function was impaired, requiring veno-venous hemofiltration with slight edema improvement. Protein-losing enteropathy was diagnosed and treatment with corticoid therapy was started. High transpulmonary pressure gradient was confirmed in cardiac catheterization, and pulmonary vasodilators were initiated.

After 20 days on optimum medical treatment, situation was not improved. Then a fenestration of the intracardiac tunnel Fontan was proposed. Percutaneously, an intraatrial tunnel puncture with Brockenburg needle was performed and a stent was implanted to maintain open the new right-to-left shunt. Systemic arterial desaturation was remote and venous pressure significantly decreased.

In "single ventricular physiology", chronic elevation of the pulmonary pressures leads to significant venous congestion. When medical treatment is ineffective, creation of right-to-left shunt could be considered in order to decompress venous system and to increase ventricular filling pressure, improving cardiac output. However, fenestration relieves one of the main aims of Fontan circulation, keeping away circulations, impairing systemic arterial oxygenation. Protein-losing enteropathy is a major complication of total cavopulmonary anastomosis, related to chronically-elevated venous pressures and associated with high mortality. Clinically it could present as peripheral edema, pleural effusions, ascites, dyspnoea and chronic diarrhea. Usually, response to medical treatment is poor, and percutaneous fenestration is a valid alternative prior to heart transplantation.



decided to stop further attempts of RFA. Bilateral renal denervation was performed 2 days after procedure. Further 10 nonsustained VT episodes occurred within the next 48 h. During next 3 months an ICD interrogation showed nonsustained VTs, terminated by ATP, no documented episodes of syncopal VT/VF with ICD shocks occurred with oral Amiodarone (200 mg/day). Discussion. In our patient we can see decreasing amount of VTs and no recorded ICD shocks after RDN. VT in this case was developed on dilated myocardium of LV, and has multiple sites of origin and was difficult to map, which greatly hinders its approach. It remains unclear the question of the primacy of heart failure in this patient, because when ICD was implanted 2 years ago the Echo showed a slight decrease in ejection fraction and moderate enlargement of the heart chambers. On the one hand the progression of heart failure may cause recurrent VT and ICD shocks as a consequence, but on the other hand a frequent occurrence of the VT itself may worsen heart failure. It is possible that, to the effect on the autonomic tone, RSD may result in beneficial effects by improving heart failure, because after procedure there were no symptoms of pulmonary congestion/edema, which suggests that arrhythmia reduction was probably related to heart failure improvement.

**Conclusion:** VTs with multiple ICD shocks might be controlled by renal sympathetic denervation. In our patient with ICD and electrical storm renal sympathetic denervation reduced the arrhythmia load and consequently ICD shocks.

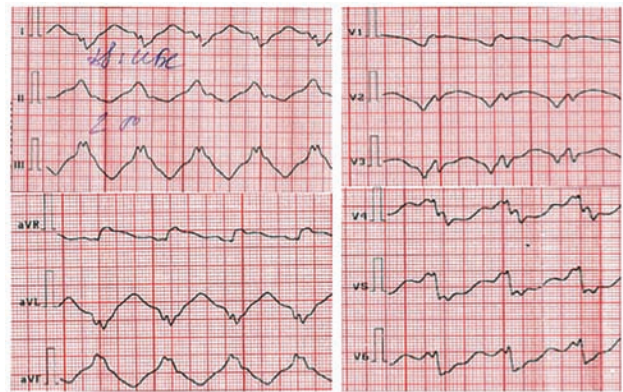


Fig.1 Sustained ventricular tachycardia

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#### Renal sympathetic denervation for electrical storm as polymorphic ventricular tachycardia in dilated cardiomyopathy

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**Introduction:** Despite a continuous improvement in technology, patients with ICDs can experience frequent ICD shocks, delivered for recurrent ventricular tachycardia (VT) or VF. Activation of the autonomic nervous system contribute to the increased mortality in these patients. A 59-year-old male was admitted to the hospital after several episodes of syncope and multiple ICD shocks (around 20 a day). 12 lead ECG was done showing VT (Fig.1). Coronary artery disease had been excluded previously. At admission to the hospital ICD interrogation revealed a plenty of episodes of VTs terminated by a multiple shocks 17 J as cause of the syncope. The Echo showed severely reduced systolic LV-function (EF 37%) and dilated left ventricle (LV). Reversible causes were excluded. Intravenous treatment with amiodarone (1.2 g per day) was initiated. Despite the heart-failure therapy, device reprogramming, recurrent episodes of VT occurred. Patient was taken to EP study. Several sustained polymorphic VTs were induced, activation mapping for first VT morphology revealed the earliest site at the LVOT, the zone was treated with RF, the next slow VT (130/bpm) with another morphology was induced with the earliest ventricular activation at the basal lateral part of the LV, which was also exposed by RFA. Then again VT with another morphology and ongoing changing of cycle was induced. Considering high amount of VTs like electrical storm was

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#### Best management of aortic root thrombus in LVAD patients?

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**Introduction:** Success obtained with bridge-to-transplant and destination therapy has established left ventricular assist devices (LVAD) as an important option for treatment of advanced heart failure. However, LVAD generate significant pathophysiological changes that can interfere with their benefits. One of these changes is permanent closure of the aortic valve (AV) and aortic root thrombus formation. The aim of our study was to review the patients with aortic root thrombus formation early after LVAD implantation for better clinical understanding and to develop strategies to prevent unfavorable outcome.

**Description:** A review of our patients identified 3 cases with aortic root thrombus early after LVAD implantation.

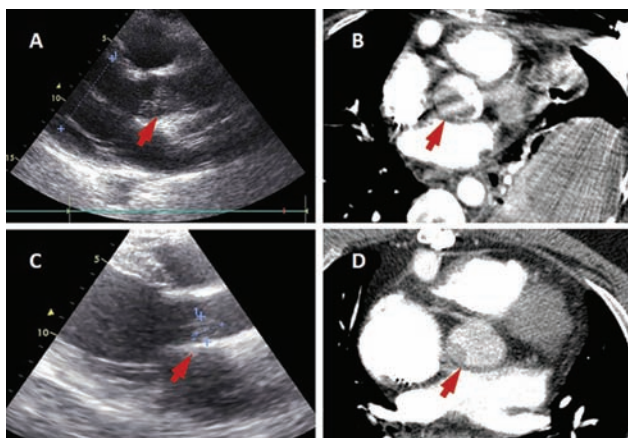
**Case 1:** A 49 years old patient developed a "hyper dense image" suggesting thrombus in the non-coronary sinus on transthoracic echocardiography (TTE) 72 hours after LVAD implantation. Anticoagulation was initiated at h 12 and reached target level at h 48. AV was not opening. A decrease in pump speed allowed partial AV opening at every third beat and the image was no longer present at the next TTE. Patient had an uneventful postoperative course.

**Case 2:** A 65 years old patient developed a "hyper dense image" in the non-coronary sinus on TTE 24 hours after LVAD implantation. Anticoagulation was initiated at h 12 and reached target level at h 24. AV was not opening. A decrease in pump speed allowed partial AV opening every forth to fifth beat. At h 48, while awake and in good condition, the patient experienced sudden unconsciousness, hemodynamic deterioration and abrupt increase in pump power. TTE showed decreased LV unloading with AV opening at every beat and disappearance of the non-coronary sinus image, suggesting the thrombus has been aspirated in the LV and into the pump. A "ramp test" confirmed pump thrombosis. Patient underwent emergently pump exchange and a subsequent CT scan confirmed multiple ischemic strokes.



**Case 3:** A 44 years old patient developed a "hyper dense image" in the non-coronary sinus on TTE 48 hours after LVAD implantation. Anticoagulation was initiated at h 12 and reached target level at h 72. AV was not opening. An increase in pump speed insured good LV unloading. TTE showed a permanently closed AV without aortic insufficiency. A CT scan performed 2 weeks later confirmed a large thrombus in the non-coronary sinus, without obstruction of the coronary ostia (Figure 1). Patient had uneventful postoperative course. Two months later patient underwent cardiac rehabilitation and TTE showed thrombus regression and partial AV opening (Figure 1 C, D)

**Conclusion:** A permanently closed AV early after LVAD implantation is not uncommon and exposes patients to risk of aortic root thrombus with subsequent thrombo-embolism and pump obstruction. If valve opening can't be obtained and development of an aortic root thrombus can't be prevented, complete LV unloading by increased pump speed might be a safer option.



Aortic root thrombus - red arrow

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##### Managing patients with advanced heart failure: the importance of the heart team in a case of severe functional mitral regurgitation

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In 2003, a man experienced his first episode of congestive heart failure (HF) with diagnosis of idiopathic dilated cardiomyopathy, and he was implanted ICD for primary prevention. Therapy up-titration was regularly scheduled, with subsequent upgrading of ICD to cardiac resynchronization therapy (CRT/D). The patient (pt) persisted in good conditions until 2011 (NYHA II), when one episode of acute HF occurred. After stabilization, he persisted in good conditions until the beginning of 2014, when two subsequent episodes of acute decompensation occurred. Following these events, he progressively deteriorated, with NYHA class persistently worsened to III-IV. Eccentric hypertrophy with severe LV dilation, ejection fraction (EF) 27%, pseudo-normalized diastolic pattern, mild aortic and tricuspid regurgitation, and severe mitral regurgitation (MR) with leaflets tethering were the main echo findings. Surgical correction of MR was discussed, but logistic EuroScore and STS scores were 29.40% and 8.17% respectively, so the pt was excluded from surgery by the Heart Team. The percutaneous edge-to-edge correction of MR was proposed after trans-oesophageal echocardiography (TOE) confirmed suitability of the MV for the procedure. Inclusion criteria as requested by the EVEREST II trial were fulfilled, so the intervention was performed in September 2014 (pt aged 79). Swan-Ganz catheterization at the beginning of the intervention showed cardiac output (CO) 2.5 l/min, cardiac index (CI) 1.3 l/min, pulmonary capillary wedge pressure (PCWP) 22 mmHg, pulmonary artery pressure (PAP) systolic/diastolic 35/20 mmHg. The procedure was successfully performed under general anaesthesia and TOE guidance, with deployment of one clip; a total of 1300cc of saline solution and 40 mg of intravenous furosemide were administered, in three hours. At the end of the procedure MR was mild (1+). No mitral stenosis occurred. The following clinical course was regular: three days in the intensive coronary care unit and four days in the cardiology ward. Daily haemodynamic evaluation showed improvement in CO and CI (2.97 l/min and 1.87 l/min respectively), and reduction in PCWP (13 mmHg), with no significant difference in PAP (36/16 mmHg) and systemic and pulmonary vascular resistances. The patient was discharged home without changes in home therapy, with ambulatory follow up planned within a month. Three months later he was

re-hospitalized for acute HF, because of severe MR. He was treated with continuous infusion of intravenous furosemide 1 ml/h and 24-h levosimendan with slow but constant improvement. Two weeks after this re-admission, MR again improved to mild, and he was discharged home in good and stable clinical conditions. Few days after ambulatory visit in late January 2015, the patient experienced several sub-episodes of ventricular tachycardia and ventricular fibrillation. Conducted to the emergency room, he required hospitalization for arrhythmic storm, but died 10 days later.

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##### Unconventional cannulation strategy in peripheral ECMO to prevent differential hypoxia

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<sup>1</sup>Catholic University of the Sacred Heart, cardiovascular department, Rome, Italy

**Introduction:** Veno-arterial extracorporeal membrane oxygenation (VA ECMO) is a therapy in cardiac and respiratory failure, refractory to conventional treatment. But, when the heart recovers and lung function remains poor, may present differential hypoxia with insufficient oxygen supply to the brain and the heart. To solve this problem many strategies have been suggested. We report an unconventional cannulation way. **Description:** A young woman, with history of mitral valve replacement was admitted to our hospital with chest pain and dyspnea. Echocardiography showed mitral valve prosthesis dysfunction caused by a thrombus with reduced left ventricular function, severe pulmonary hypertension and tricuspid regurgitation. An emergent mitral valve replacement and tricuspid annuloplasty were performed. After a few hours she developed severe hypoxemia due to massive pulmonary edema, with cardiogenic shock, refractory to inotropes and ventilation. We decided to put her on ECMO. Peripheral cannulation could be rapidly achieved and re-sternotomy avoided, limiting infections and major bleeding complications. However central cannulation could provide higher circuit blood flow and oxygen delivery, avoiding differential hypoxia. Axillary or subclavian artery cannulation was impossible for their small caliber. We performed a peripheral VA ECMO with a 19 Fr drainage venous cannula through right femoral vein and, to prevent differential hypoxia, a 17 French venous long cannula was inserted into the left femoral artery and advanced until the distal aortic arch, under ecocardiographic guidance. A back flow femoral cannula was placed to avoid limb ischaemia. With ECMO hemodynamic stabilized. Peripheral oxygen saturation measured at the right arm was 100%. Mean cerebral tissue oxygen saturation measured by near infrared spectroscopy was 60% bilateral. Cardiac function gradually recovered. By day seven, she was successfully weaned from ECMO. Mechanical ventilation was removed 18 days later. After 46 days she was discharged from the intensive care unit with no neurological sequelae.

**Discussion and conclusion:** Potential solutions to prevent upper body hypoxemia in peripheral VA ECMO include: (1) increasing pump flows (2) switching to VV ECMO, (3) adding an additional return cannula to the internal jugular vein, (4) switching to central placement of the arterial cannula. In our case axillary or subclavian artery cannulation was impossible, there was a high bleeding risk for a re-sternotomy. We then decided to undertake an unconventional arterial cannulation for ECMO through a long venous cannula inserted in the femoral artery and placed in the proximal descending thoracic aorta. In this way, proximal perfusion was achieved despite a distal cannulation site being used. The main contraindication to the use of the long cannula is severe atherosclerotic disease of the aorta, but in a young woman with no atherosclerosis it can represent a viable option.

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##### a case of severe functional mitral regurgitation in patient with left ventricular non-compaction treated by mitral repair using minimally invasive approach

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**Introduction:** Noncompaction of the left ventricle is a rare congenital cardiomyopathy characterized by prematurely arrested compaction of myocardial fibers. The prognosis is poor when the left ventricular function deteriorates.

**Case report description:** A 18-year-old woman presented with a 6-month history of severe cough, nausea, vomiting and dyspnea despite of maximal medical therapy. Chest X-ray revealed marked cardiomegaly with consolidation of right lower lung field (Figure, left upper). Transthoracic echocardiography revealed multiple prominent left ventricular trabeculations with deep recesses, marked mitral annular dilatation with coaptation failure causing very severe functional mitral regurgitation and depressed left ventricular ejection fraction of 38% (Figure, right). Computed tomographic coronary angiography revealed normal coronary anatomy and confirmed the diagnosis of isolated noncompaction of the left ventricle (Figure, left lower). The patient refused cardiac transplantation due to poor economic status but was amenable to nontransplant surgical options.

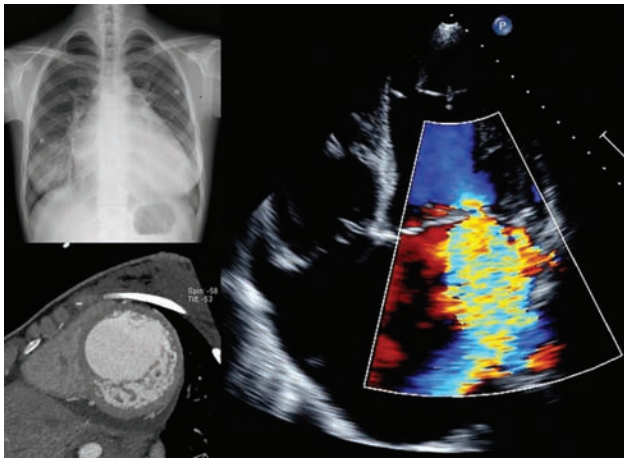
**Question:** What can be offered as an option for the treatment of this patient?

**Answer and discussion:** Mitral repair with ringed annuloplasty was planned for this



young women. Mitral exposure was obtained through right anterolateral minithoracotomy via 4th intercostal space and a left atriotomy. Mitral annuloplasty with 28 mm Physio ring and left atrial reduction by left atrial inferior wall resection were done. Postoperative transesophageal echocardiography demonstrated no mitral regurgitation. The patient was discharged on postoperative day 7 after an uneventful hospital stay. Her ejection fraction decreased to 20%, but estimated systolic right ventricular pressure also markedly decreased from 98 to 26 mm Hg. The patient's symptoms improved to New York Heart Association functional class II by her clinic visit at postoperative month 6. Clinical and echocardiographic follow-up was performed every 6 months thereafter has shown gradual improvement in ventricular function. The latest echocardiogram at 5 yrs postoperatively revealed trace mitral regurgitation and an ejection fraction of 30%. The patient's symptom improved to New York Heart Association functional class I and she can go exercise to the gym.

**Comment:** In this case, the 5-year results of sustainable clinical improvement supports that correction of mitral regurgitation by annuloplasty alone may result in progressive ventricular remodeling. In patients with left ventricular noncompaction and severe mitral regurgitation, mitral annuloplasty using minimally invasive approach might be a surgical alternative to traditional medical therapy or transplantation.



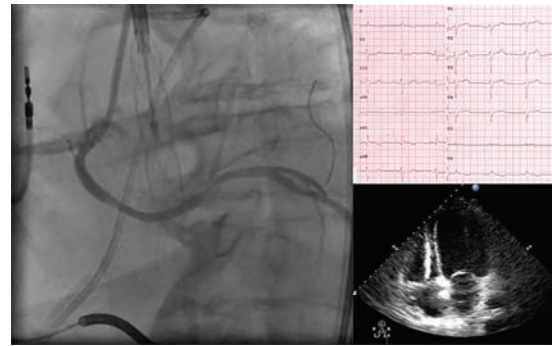
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#### Percutaneous LVAD for high risk angioplasty. Why use support?

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<sup>1</sup>Institute of Cardiology, Intensive Cardiac Therapy Clinic, Warsaw, Poland; <sup>2</sup>Institute of Cardiology, Department of Interventional Cardiology and Angiology, Warsaw, Poland; <sup>3</sup>Institute of Cardiology, Coronary Artery and Structural Heart Disease Department, Warsaw, Poland

A 62-year-old patient with severe post infarction heart failure (CHF) due to previous anterolateral STEMI complicated by cardiogenic shock treated with primary PCI of LAD with DES implantation one year before, post ICD implantation, was admitted with NSTEMI. His additional risk factors included obesity, DM and AF. Patient status on admission to CCU was poor. Symptoms of CHF were dominant, with dyspnea, bilateral rales, peripheral edema and recurrent chest pain. Signs of pulmonary congestion were noted on chest X-ray. Heart rate on admission was 80/min and blood pressure 110/70 mmHg. ECG showed sinus rhythm of 78/min, precordial Q waves and signs of lateral ischemia (Fig.1). Echocardiography revealed dilated left ventricle-62 mm with severely impaired contractility and EF of 15%. Non-significant mitral regurgitation was present (Fig.2). Coronary angiography showed borderline LAD lesions distally to previously implanted stents, borderline lesion in mid-RCA and tight lesion in mid-LCx originating from RCA. The patient was primarily treated conservatively for HF according to ESC guidelines and dual antiplatelet therapy was introduced. Due to severely impaired LV systolic function in our patient, PCI was associated with significantly increased periprocedural risk. Thus, the periprocedural support with Heart Mate PHP was decided. The device was introduced through right femoral access and the PCI procedure was performed through right radial access. The pump was run at 2.5 l/min. Direct implantation of Xience Pro DES (3,0x18 mm) into mid-LCx was performed. Right femoral access was closed with the ProStar system. The patient's hemodynamic status promptly improved. He was discharged at day 10 post procedure. No major adverse events were observed during 13-months follow-up.



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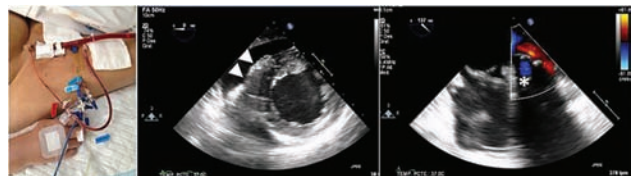
#### Crossing all bridges after acute myocardial infarction

E Zatarain<sup>1</sup>; I Sousa-Casasnovas<sup>1</sup>; P Navas Tejedor<sup>1</sup>; M Martinez-Selles<sup>1</sup>; J Velasquez Rodriguez<sup>1</sup>; M Ruiz Fernandez<sup>2</sup>; A Villa-Arranz<sup>1</sup>; J Hortal-Iglesias<sup>3</sup>; A Gonzalez-Pinto<sup>2</sup>; F Fernandez-Aviles<sup>1</sup>

<sup>1</sup>University Hospital Gregorio Maranon, Cardiology, Madrid, Spain; <sup>2</sup>University Hospital Gregorio Maranon, Cardiac Surgery, Madrid, Spain; <sup>3</sup>University Hospital Gregorio Maranon, Anaesthesiology, Madrid, Spain

**Description:** A 49 years-old woman, smoker and overweighted, was admitted to ER due to atypical chest pain that had started with short episodes one week ago. Her EKG showed extensive ischaemia with RBBB and she was referred to our center for primary PCI. At the cath-lab she presented signs of cardiogenic shock. Norepinephrine, dobutamine and IABP were started at the time of PCI. A thrombotic obstruction in main-left artery was observed and a drug-eluting stent was deployed 8h after the onset of symptoms. Before transfer, she suffered an electrical storm refractory to antiarrhythmic drugs requiring several electric shocks. Treatment, problems and techniques used: Mechanical ventilation (MV) and percutaneous VA-ECMO were started in the cath-lab by the hemodynamist as a bridge to decision (Picture, left). She arrived at the cardiology intensive-care unit with hemodynamic stability, the VA-ECMO was set at 3200 revolution-per-minute giving 2.5-3 L/min outflow and normal pressures. After 12h of support, the flow started to decrease, lactic acid to rise up and deep-negative pressure was registered in the inner cannula. Transesophageal echocardiography revealed heart tamponade with complete collapse of right ventricle (picture middle, arrows). She underwent surgical replacement of VA-ECMO with a short-term centrifugal LVAD (left ventricular assist device) and drainage of pericardial effusion. Due to broad extension of necrosis the inner cannula was placed in the left atrium (picture right, asterisk). Neither suction nor thrombotic or hemorrhagic events were registered. Anticoagulation was achieved with non-fractionated heparine controlled by activated clotting time test (range 180-200 s). Successfully assisted, the LVEF did not recovered during next week and several attempts failed to wean her from LVAD. After heart transplant (HT) work-up without contraindication and favourable sedation window the patient was listed for urgent heart transplantation. The 9th day after LVAD, HT was successfully performed. No significant surgical bleeding occurred and the main complication was weaning from MV due to delirium and sedation requirements. After 18 days in postoperative intensive care unit she was discharged to hospitalization area and 54 days after admission she was discharged home. After HT she has suffered a citomegalovirus reactivation that need valganciclovir 900 mg tid. Today she continues ambulatory follow-up without complications.

**Conclusion and clinical implications:** VA-ECMO can be safely implanted by percutaneous approach, specially in emergency situations in the cath-lab as a bridge to decision. Short-term centrifugal LVAD can successfully rescue the patient from ECMO support when it fails. LVAD cannulation through left atrium is a good choice in those short-term centrifugal devices when extensive necrosis affects LV apex. Short-term centrifugal LVAD can be used as a bridge to recovery or a bridge to transplant in those acute heart failure settings.



## CLINICAL CASE COMPETITION

Saturday 21 May 2016 11:00–12:30

Location: Agora

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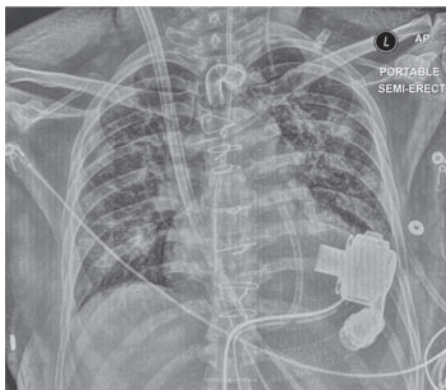
**Supporting the right heart in pulmonary oedema post-LVAD implant**H S Hoong Sern Lim<sup>1</sup>; A Ranasinghe<sup>1</sup><sup>1</sup>Queen Elizabeth Hospital, Birmingham, United Kingdom

A 44-year old man with dilated cardiomyopathy presented with 2 weeks of cough and breathlessness. He was hypoxemic with pulmonary oedema on X-ray. Echocardiogram showed LV ejection fraction of 10% but normal right ventricular (RV) function. Over the ensuing 2 days, he became hypotensive and worsening of oxygenation. Pulmonary artery (PA) catheter data: right atrial pressure (RAP) 8, PA systolic/diastolic/mean pressure 56/28/35, pulmonary artery wedge pressure (PAWP) 25mmHg, cardiac output (CO) 3.9L/min on inotropes. He underwent an uncomplicated left ventricular assist device (LVAD) implant in view of the deterioration. The patient was extubated 12 hours later but remained hypoxemic, albeit hemodynamically stable on enoximone. However, his gas exchange worsened (FIO<sub>2</sub> 0.6, PO<sub>2</sub> 8.4kPa, PCO<sub>2</sub> 7.8kPa) on post-operative day 6 and was re-intubated. Chest X-ray showed bilateral infiltrates and low tidal volume ventilation was adopted (tidal volume 380ml, peak airway and end-expiratory pressure 27 and 8cmH<sub>2</sub>O). He deteriorated further on post-operative day 7: heart rate 148/min, mean BP 56mmHg (non-pulsatile), LVAD flows 3.3L/min with recurrent 'suction' events and oliguria. Pulmonary hemodynamics were: RAP 18, PAP 52/25, mean 32, PAWP 14mmHg and CO 3.6L/min. Echocardiogram showed RV dilatation, small LV cavity, no aortic valve opening and normal cannula Doppler flow. He failed to respond to escalating noradrenaline, adrenaline and enoximone, nitric oxide and pump speed adjustments. With progressive RV failure and acute respiratory distress syndrome (ARDS), a dual lumen cannula was inserted percutaneously via the right internal jugular vein and positioned in the PA [FIGURE], connected to a centrifugal pump for right ventricular support. He improved and vasopressors were weaned off within 24 hours. As oxygenation improved, the percutaneous right ventricular assist device was removed after 7 days without complications.

**Problems:** 1) Assessment/management of RV failure and selecting the modality of RV support in RV failure post-LVAD implant. 2) Differentiating cardiogenic and non-cardiogenic pulmonary oedema

**Discussion:** 1) Percutaneous RV support (which obviates the need for re-sternotomy) may be delivered via a microaxial catheter-mounted pump, a dual cannula system or dual-lumen single cannula system. The latter was chosen to minimise vascular access and allows extracorporeal oxygenation if required. 2) PA catheter may differentiate cardiogenic from non-cardiogenic pulmonary oedema; and aid in the assessment of RV failure post-LVAD. In this case, increased RV afterload from ARDS (evidenced by low pulmonary capacitance and high pulmonary vascular resistance) as the likely cause.

**Conclusion:** ARDS-related RV failure post-LVAD can be effectively supported by a dual-lumen single cannula extracorporeal right ventricular assist device. PA catheters can differentiate the aetiology of pulmonary oedema and define nature of RV failure post-LVAD.



Percutaneous RVAD (dual lumen cannula)

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**Transseptal implantation of a balloon-expandable transcatheter heart valve in a native mitral annulus for treatment of radiation-induced valvulopathy**F Praz<sup>1</sup>; T Suter<sup>1</sup>; A Moschovitis<sup>1</sup>; D Reineke<sup>2</sup>; S Windecker<sup>2</sup><sup>1</sup>Bern University Hospital, Department of Cardiology, Bern, Switzerland; <sup>2</sup>Bern University Hospital, Cardiovascular Surgery, Bern, Switzerland

A 49-year old patient was admitted because of recurrent episodes of left heart decompensation (New York Heart Association class IV) and paroxysmal nocturnal dyspnea requiring home oxygen therapy. He was previously followed in our cardio-oncology clinic for radiation-induced coronary and valvular heart disease, consecutive to treatment of Hodgkin's lymphoma in 1983 (cumulative mediastinal dosis 46 Gray). In 2002 endocarditis of the aortic valve was diagnosed and the patient underwent mechanical aortic valve replacement combined with coronary artery bypass grafting. Twelve years later, mitral stenosis due to progressive thickening of the mildly calcified leaflets was diagnosed and a percutaneous balloon mitral valvuloplasty was attempted. Despite technical success, the transvalvular gradient remained elevated and the patient experienced progressive heart failure. A consecutive transesophageal echocardiography showed severe mitral stenosis with a mean transvalvular gradient of 13mmHg and an effective orifice area ranging between 0.9cm<sup>2</sup> and 1.1cm<sup>2</sup>. In addition, moderate mitral regurgitation was observed. After discussion in the Heart Team, the patient was rejected for open-heart surgery or transapical valve implantation due to "hostile chest" and numerous comorbidities including severe vascular calcification, post-radiation pneumopathy, chronic renal disease (GFR 32ml/min) and hepatitis C with subsequent cirrhosis (Child-Pugh A) contracted because of intravenous drug abuse. A detailed anatomic evaluation showed mild calcification of both leaflets. The mitral annulus dimensions were deemed amenable to the implantation of a 29mm balloon-expandable bioprosthesis with the mechanical aortic valve serving as additional anchoring structure (Figure 1 E). The delivery catheter could successfully be advanced through the previously dilated interatrial septum (Figure 1 A-B) and the valve correctly positioned into the native mitral annulus under echocardiographic guidance (Figure 1 C-D). After deployment, minimal para- or transvalvular regurgitation was observed (Figure 1 E-F) and the mean gradient was acutely reduced to 5mmHg. A transthoracic echocardiography one day after the intervention confirmed normal valve function and excluded a relevant LVOT obstruction or valve migration. The patient was discharged after 5 days and was alive at 30 days reporting symptomatic improvement with complete resolution of the nocturnal dyspnea, but persistent dyspnea on exertion (NYHA II-III). This case report shows the feasibility of the transseptal implantation of a balloon-expandable transcatheter heart valve in a minimally calcified mitral annulus for treatment of radiation-induced mitral stenosis. This technique represents a promising minimal-invasive treatment option for selected inoperable patients.

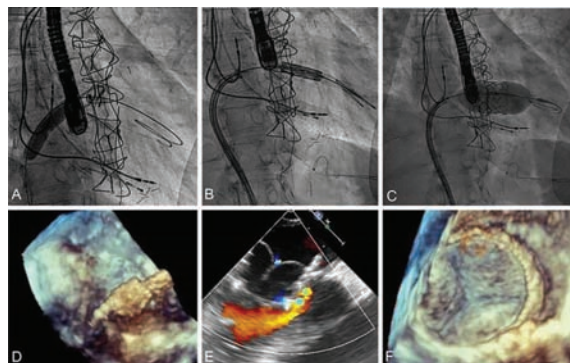


Figure 1



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### Constrictive pericarditis with large multiloculated pericardial effusion as a tuberculosis and HIV co-infection presentation: the role of multimodality imaging

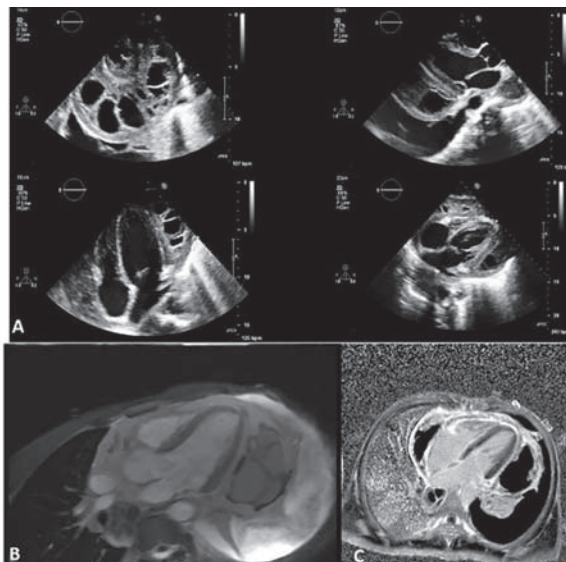
Al Ana Isabel Azevedo<sup>1</sup>; J Goncalves Almeida<sup>1</sup>; N Ferreira<sup>1</sup>; M Ponte<sup>1</sup>; R Fontes-Carvalho<sup>1</sup>; J Ribeiro<sup>1</sup>; A Dias<sup>1</sup>; M Mota<sup>1</sup>; V Gama Ribeiro<sup>1</sup>  
<sup>1</sup>Hospital Center Vila Nova Gaia, Porto, Portugal

**Introduction** Pericardial tuberculosis (TB) is common among TB and HIV co-infected patients and is associated with high morbidity and mortality. Large pericardial effusion can develop, leading to heart failure. Accurate diagnosis is crucial and different imaging techniques have an important role in the evaluation and management of these patients.

**Case report:** A 28-year-old man, natural from Guinea-Bissau, presented with cough, low grade fever, increasing dyspnoea and a weight loss of 15Kg over the previous 3 months. On initial assessment he was diaphoretic, hypotensive (109/62mmHg), tachycardic (122bpm) and tachypneic. Pulmonary auscultation revealed severely diminished breathing sounds at the lower third of the left hemithorax. Chest X-ray showed left pleural effusion and an enlarged cardiac silhouette. The patient was admitted for further evaluation. He was diagnosed with HIV infection (CD4 cell count=202cells/uL). Sputum smear was positive for acid-fast-bacilli and a positive culture for *M. tuberculosis* complex confirmed the diagnosis of TB. Transthoracic echocardiography (TTE) showed pericardial thickening and a large multiloculated pericardial effusion, with no signs of hemodynamic compromise (panel A). Chest computed tomography (CT) showed a large pericardial effusion, with pericardial thickening and a large left pleural effusion. Cardiac magnetic resonance (CMR) confirmed signs of constrictive acute pericarditis with large, multiseptated pericardial effusion (panels B and C). The patient was started on standard treatment regimen for tuberculosis and referred to initiate antiretroviral therapy.

**Discussion:** Clinical manifestations of pericardial TB may overlap with other diseases in HIV-patients and a high index of suspicion for pericardial disease is required. TTE, the first-line imaging modality, may reveal signs of pericardial effusion of tuberculous etiology (thickened pericardium with echogenic coating and fibrin strands) and of hemodynamic compromise. On contrast-CT imaging, enhancement of a thickened pericardium points to an inflamed pericardium and density measurements can characterize pericardial fluid accurately. CMR with high-resolution gradient-echo cine-images allows accurate measurement of pericardial thickening and effusion. Real-time cine imaging enables assessment of ventricular interdependence, and late gadolinium enhancement is seen in inflammatory pericarditis. Antituberculous therapy should be started as soon as the diagnosis is made, with the same treatment regimens recommended for pulmonary TB. Antiretroviral therapy is indicated regardless of CD4 count.

**Conclusion:** Pericardial TB is a common manifestation of HIV and tuberculosis co-infection. Imaging techniques are essential for the diagnosis and patients' management. An analysis of their strengths and limitations is required in order to select their appropriateness in each clinical scenario.



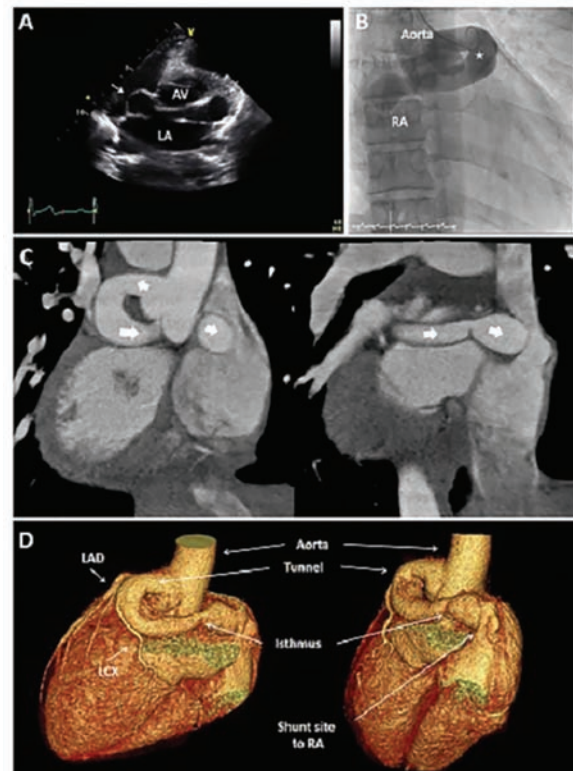
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### Aorta right atrial tunnel : do always need surgical correction?

SK Sunki Lee<sup>1</sup>; HS Yong<sup>2</sup>; CW Choi<sup>1</sup>; HE Lim<sup>1</sup>; JO Na<sup>1</sup>; EJ Kim<sup>1</sup>

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An asymptomatic 31-year-old was referred to our hospital for evaluation of a heart murmur. The patient had no family history of congenital heart disease or collagen vascular disease. Cardiac auscultation revealed a grade 3/6 continuous murmur at the right parasternal border. Transthoracic echocardiography (TTE) revealed a round, tunnel-like structure from the left aortic sinus to the right atrium (RA) (Figure A, arrows) without any evidence of right atrial or ventricular enlargement. Cardiac catheterization showed a normal pulmonary artery pressure (systolic/diastolic: 24/7 mmHg), normal mean RA pressure (4 mmHg) and the Qp/Qs ratio was 1.3:1. Aortography confirmed a large tunnel beginning in the left aortic sinus and ending into the RA (Figure B, asterisk) with normal looking left coronary arteries arising independently from different proximal portions of the tunnel. For better visualization of shunt anatomy, computed tomographic (CT) angiography was performed. CT angiography (Figure C) and 3D reconstructed images (Figure D) delineated the extracardiac structure, showing a large, tortuous, tunnel-like structure originating from the left sinus of Valsalva, running through the posterior side of the aortic root, and terminating in the RA. Based on multiple imaging studies, we could confirm the diagnosis of aorta-right atrial tunnel (ARAT). The patient was asymptomatic, the Qp/Qs ratio was less than 1.5:1, and he showed no evidence of right heart overload; therefore, we decided to observe the patient closely without surgical treatment. At 12 and 24-months follow up of TTE, the size of ARAT diameter was still unchanged without any hemodynamic alterations. During 36-months of follow up period, the patient is still asymptomatic and shows a good performance state without any complications.



Figure



# RAPID FIRE 1 – ACUTE HEART FAILURE

Saturday 21 May 2016 14:15–15:45

Location: Agora

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## Twenty five years of acute heart failure in 1800 consecutive patients: no short- and long-term survival improvement.

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**Introduction:** Acute heart failure has a poor prognosis. However, limited data is available regarding the long-term mortality of such patients. Purpose – We investigated the trends in short- and long-term mortality of patients with acute heart failure in the period 1985 thru 2008. We also determined the influence of major prognostic factors.

**Methods:** In this prospective consecutive registry, we included patients admitted for acute heart failure at the Intensive Coronary Care Unit of our tertiary referral hospital in the period of 1985 until 2008. Patients were classified into four aetiology categories: ischemic cardiomyopathy, other cardiomyopathy, valvular heart disease, and other/unknown. The time window was split up in periods of 1985-1989, 1990-1999 and 2000-2008.

**Results** We identified 1810 patients (age 64 years, 64% male). In the last decade, the number of patients with a history of myocardial infarction, revascularization therapy and diabetes mellitus increased significantly. The overall cumulative mortality at one and ten years was respectively 31% and 71%. Over time, no overall change in mortality rate was found (Figure). After adjustment, compared to valvular heart disease, ischemic cardiomyopathy was associated with a higher mortality (HR 1.25; 95% CI 1.08-1.47). Other parameters associated with poor outcome were advanced age (HR 1.027; 95% CI 1.022-1.031), male sex (HR 1.27; 95% CI 1.13-1.43), previous heart failure (HR 1.58; 95% CI 1.41-1.76), and diabetes (HR 1.20; 95% CI 1.05-1.36).

**Conclusions:** Patients admitted with acute heart failure continue to have very high short- as long-term mortality, identical between the different decades. The prognosis of patients with heart failure due to ischemic cause was worst.

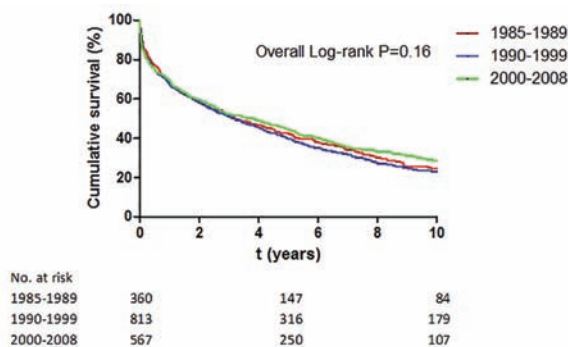


Figure. Kaplan-Meier

Kaplan-Meier

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## Noradrenaline combined with either dobutamine or levosimendan - similar outcome and cardiac biomarker evolution in cardiogenic shock

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<sup>10</sup>Helsinki University Central Hospital, Emergency Care, Helsinki, Finland

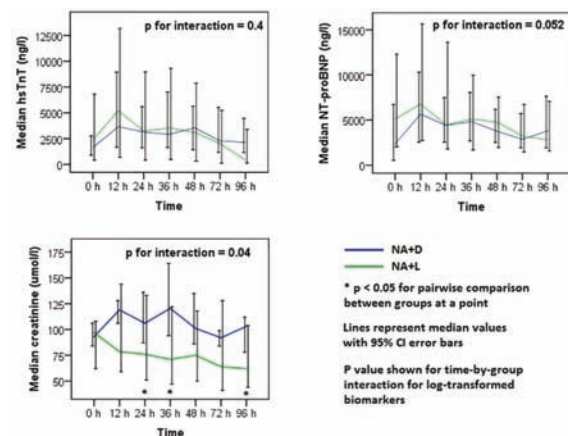
**Background:** In cardiogenic shock (CS), an inopressor-inodilator combination has been proposed to be a more beneficial, or less harmful, alternative than using inopressors alone. However, little data exists to guide clinicians in the choice of specific agents.

**Purpose:** To assess whether there are differences in outcome, or evolution of cardiac and renal biomarkers between two commonly used inopressor-inodilator combinations in CS: noradrenaline either with dobutamine (NA+D) or levosimendan (NA+L).

**Methods:** The CardShock study is a prospective European multicenter study including 219 patients with CS. Serial plasma samples were collected in 178 patients, of which 95 had samples taken until 96 hours from the study baseline. The samples were immediately frozen at -80°C. Creatinine, high-sensitivity troponin T (hsTnT) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) were analysed centrally. Use of vasoactive medications was registered until 96 hours from baseline. Patients who received adrenaline were excluded. Association with mortality was analysed with propensity score adjustment. Biomarker differences at each time point between groups were analyzed with Mann-Whitney U test. Linear mixed modeling was used to analyse differences in changes of biomarkers between groups over time.

**Results:** Of the patients with baseline plasma samples collected, NA+D and NA+L were administered to 38 and 28 patients, respectively. In this cohort of 56 patients, mean age was 66 (SD 13) years, 79% were men and 82% had acute coronary syndrome as CS etiology. Overall 90-day mortality was 38%. No difference between the two treatment groups appeared in mortality after propensity score adjustment. Levels of cardiac biomarkers were similar in the two groups during the initial 96 hours, but there was a trend towards higher creatinine levels in NA+D group (figure).

**Conclusions:** No significant differences between NA+D and NA+L appeared in mortality or in evolution of cardiac biomarkers during the initial 96 hours of CS. There was a trend toward higher creatinine levels in NA+D group.



figure

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**Prognostic significance of multi-organ dysfunction/damage in acute heart failure**

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**Background:** Presence of end-organ dysfunction/damage during early phase of acute heart failure (AHF) is associated with poor outcome. In this context, however, clinical relevance of the inter-organ crosstalk has not been evaluated. This study was designed to assess prognostic consequences of the interplay between impaired function/damage of different organs in AHF.

**Methods:** Consecutive patients hospitalized for AHF between September 2010 and July 2012 were studied (those with clinical diagnosis of concomitant acute coronary syndrome were excluded). The organ dysfunction/damage on admission was diagnosed with the following criteria: a. cardiac damage – as troponin I (TnI) increase above the upper normal limit (>0.056 ng/ml); b. renal dysfunction – as the estimated glomerular filtration rate below 60 mL/minute/1.73 m<sup>2</sup>; c. liver dysfunction – as at least one of the following abnormal liver function tests: AST/ALT above the 3 times of the upper normal limit (114 IU/l, 105 IU/l, respectively), bilirubin above the upper normal limit (>1.3 mg/dl), albumin below the lower normal limit (< 3.8 mg/dl). The primary endpoint was all-cause mortality during 12-month follow-up.

**Results:** We recruited 316 patients with AHF (mean age 66 ± 12 years, 73% men). At baseline, renal dysfunction, myocardial damage and liver dysfunction were present in 54%, 41% and 61% of patients, respectively. Only 39 (12%) patients did not show any evidence of organ dysfunction/damage. Patients were classified into 2 subgroups: those with 2 or 3 organs dysfunction/damage (159 [50%]) vs those without or with only single organ dysfunction/damage (157 [50%] patients). The former group comprised older patients (68 ± 11 vs 65 ± 12 years), with lower systolic blood pressure (125 ± 31 vs 134 ± 34, mmHg), higher level of urea (40 [27–67] vs 30 [19–44], mg/dL), NT-proBNP (7309 [4169–13104] vs 4302 [2305–6947], pg/mL), CRP (11 [5–30] vs 8 [4–21], mg/L) and lower level of sodium (138 ± 5 vs 139 ± 4, mmol/L), who more often required inotropic support during in-hospital stay (14% vs 4%) (P < 0.05 in all comparisons). The 1-year mortality rates were 43% in former vs 17% in the latter group, respectively (P < 0.0001). Importantly there was no statistically significant difference in 1-year mortality between patients without vs with only single organ dysfunction/damage (10% vs 19%). The multivariable analysis revealed that dysfunction/damage of 2-3 organs predicted higher mortality after adjustment for the other prognosticators.

**Conclusion:** In patients with AHF, presence of multi-organ dysfunction/damage on admission carries relevant prognostic information. Interestingly, the number of affected organs (rather than the organ itself) seems to be crucial to identify those at high risk of poor outcomes (similarly to the multi-organ dysfunction syndrome).

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**Clinical characteristics and prognosis of patients hospitalized for heart failure depending on ejection fraction: analysis of administrative data of a nationwide population**

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**Introduction:** Multiple studies have evaluated the different profile and prognosis of heart failure (HF) patients with reduced (HF-ref) or preserved (HF-pef) ejection fraction, with heterogeneous results. We present, for the first time, the clinical characteristics and prognosis of HF-ref and HF-pef patients in a whole country (Spain, 46.77 millions population).

**Methods:** All the discharges from Spanish hospitals corresponding to 2012–2013 with a primary diagnosis of HF, according to the ICD-9-CM classification, were analyzed. Codification as HF-ref or HF-pef was taken into account, discarding those with other codifications. In-hospital mortality and readmissions rate at 1 year were analyzed.

**Results:** 400,861 hospital admissions were recorded. 77,652 of them had HF as primary diagnosis (4,241 HF-ref and 1,752 HF-pef). HF-ref were mainly hospitalized in Cardiology (45.4%) or Internal Medicine (47.3%), with different proportions in HF-pef (65.4% Internal Medicine, 22.9% Cardiology). In the index episode, the

average stay was 9.7 ± 8.3 days vs. 9.2 ± 7.2 (p < 0.01) and in-hospital mortality 6.1% vs. 4.5% (p < 0.001) in HF-ref and HF-pef, respectively. At 1 year, readmissions rate was 37.9% vs. 32.9% (p < 0.001) and in-hospital mortality 12% vs. 10% (p < 0.01) also in HF-ref and HF-pef, respectively. In the multivariate analysis, at 1 year the odds ratio of HF-ref (considering as reference HF-pef) was 1.52 (95% CI, 1.27–1.84) for in-hospital mortality and 1.09 for readmissions (95% CI, 0.97–1.23).

**Conclusions:** In our nationwide study, patients hospitalized for HF showed different medical department of admission depending on ejection fraction. At follow-up, patients with HF-ref had higher annual mortality than HF-pef, without differences in readmissions rate.

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**Combined measurement of sST2 and NT-proBNP is a very early marker of severity in cardiogenic shock complicating acute coronary syndromes**

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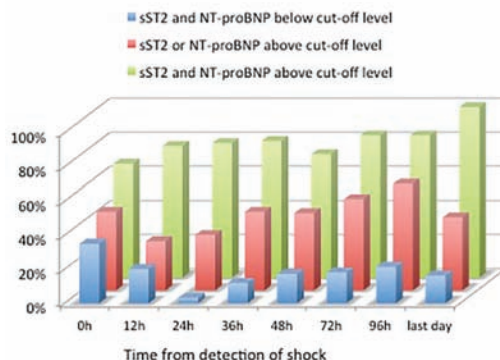
**Background:** The short-term mortality in cardiogenic shock (CS) complicating acute coronary syndromes (ACS) is high, and risk stratification is needed for rational use of advanced therapies. To date, in the absence of prognosticators of poor outcome, risk assessment is based on clinical findings. In patients with myocardial infarction and acute heart failure, soluble ST2 (sST2), a marker of adverse cardiac remodeling and fibrosis, has been shown to have strong prognostic value, which is additive to natriuretic peptides.

**Purpose:** The aim of this study was to evaluate the added value of sST2 and NT-proBNP to clinical variables for risk stratification in patients with CS complicating ACS.

**Methods:** CardShock study was a prospective, observational, European multinational study of CS. The main study introduced CardShock risk score including 7 clinical variables available at baseline, which showed good discrimination for short-term mortality. In this sub-study serial plasma samples at 8 time-points from baseline to the last day of intensive care were analyzed from 145 patients with CS caused by ACS. The cut-off values for sST2 (470 ug/mL) and for NT-proBNP (4800 ng/L) were evaluated with receiver operating characteristic curves for 30-day mortality at 24 hours.

**Results:** Patients' mean age was 68 years, 78% were men, and all-cause 30-day mortality was 44%. The levels of both sST2 and NT-proBNP were higher in non-survivors compared to survivors at each time point measured (all p-values < 0.01). The combination of sST2 and NT-proBNP showed excellent discrimination for 30-day mortality when measured at 24 hours or later (AUC from 0.83 at 24 hours to 0.93 at last sample). Patients with both biomarkers above the cut-off level (470 ug/mL for sST2 and 4800 ng/L for NT-proBNP) had markedly higher mortality compared to those with either or both biomarkers below the cut-off level when measured at any time point (figure; all p-values < 0.05). The combination of sST2 and NT-proBNP measured at 24 hours was independent of and gave added value to CardShock risk score and peak value of troponin T (likelihood ratio 45.5 vs. 27.0, p < 0.001).

**Conclusions:** The combination of sST2 and NT-proBNP is an early, accurate, and independent marker of severity in patients with CS complicating ACS. The combined measurement may help the risk stratification of these patients and support clinical decision for advanced therapies.



30-day mortality

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### Short and long-term prognostic value of hyponatremia in heart failure with preserved ejection fraction versus reduced ejection fraction: An analysis of the Korean Acute Heart Failure (KorAHF) Registry

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**Purpose:** Hyponatremia is a well-known risk factor for worse outcomes in acute heart failure (HF) patients. The impact of hyponatremia on short and long-term clinical outcomes according to the ejection fraction is unknown.

**Methods:** From March 2011 through December 2013, a total of 5,620 acute HF patients have been consecutively enrolled in ten regionally-representative tertiary university hospitals. Serum sodium level was measured at the hospital admission. Hyponatremia was defined as serum sodium level <135 mmol/L, and heart failure with preserved ejection fraction (HFpEF) and reduction ejection fraction (HFrEF) as EF  $\leq$ 40% and  $\geq$ 50%, respectively. The primary endpoint was in-hospital and 1-year all-cause mortality stratified by the serum sodium level.

**Results:** The mean age was 69  $\pm$  15 years and 46% were female. Three thousand two-hundred fourteen patients had HFpEF and 1,359 patients HFrEF. There was no difference in serum sodium level (HFrEF: 134.5  $\pm$  47 mmol/L vs. HFpEF: 137.5  $\pm$  5.0 mmol/L,  $P = 0.966$ ), nor in the prevalence of hyponatremia (HFrEF: 21.6% vs. HFpEF: 21.2%,  $P = 0.782$ ) between both groups. As for short-term outcomes, hyponatremic patients had higher in-hospital mortality in all (11.3% vs. 4.5%,  $P < 0.001$ ), in HFrEF (13.3% vs. 5.3%,  $P < 0.001$ ), and in HFpEF (6.9% vs. 2.1%,  $P < 0.001$ ). After adjustment for significant clinical variables, hyponatremia was independently associated with an increased risk for in-hospital mortality (all: HR, 2.46; 95% CI, 1.78-3.43; HFrEF: HR, 2.51; 95% CI, 1.71-3.68; HFpEF: HR, 2.42; 95% CI, 1.07-5.47). Regarding long-term outcomes, hyponatremic patients had higher 1-year all-cause in HFrEF group (log-rank  $P < 0.001$ ), but not in HFpEF patients (Log-rank  $P = 0.074$ ). After adjustment, hyponatremia was associated with increased mortality in patients with HFrEF (HR, 1.85; 95% CI, 1.26-2.01), but not in those with HFpEF (HR, 1.04; 95% CI, 0.60-1.82).

**Conclusions:** Hyponatremia is a significant risk factor for in-hospital outcomes in all AHF patients regardless of EF. But its prognostic value on long-term outcomes is only valid in patients with HFrEF, not in those with HFpEF.

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### Monitoring of pulmonary congestion in chronic heart failure patients with multiple re-hospitalizations for acute decompensation - randomized controlled (IMPEDANCE-HF) trial.

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 M Kazatsker<sup>1</sup>; D Blondheim<sup>1</sup>; A Asif<sup>1</sup>; S Meisel<sup>1</sup>  
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Prediction and prevention of re-hospitalizations for heart failure (HF) in patients with congestive heart failure 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 HF. Aim To determine the dynamics of pulmonary congestion at admission for AHF during long-term follow-up in HF patients.

**Method and Results:** In "Non-invasive Lung IMPEDANCE-Guided Preemptive Treatment in Chronic Heart Failure Patients: a Randomized Controlled Trial (IMPEDANCE-HF trial)" 256 CHF patients with LVEF <35% were randomized (1:1) to a control group treated by clinical assessment and a monitored group whose therapy was also assisted by Lung Impedance (LI). Was found that LI-guided treatment reduced HF hospitalizations by 45% and HF associated death by 58% during 48 months of treatment. Decreasing LI reflects increasing lung fluid. Signs, LI and ratio of the instantaneous LI to the calculated baseline LI ( $\Delta$ LIIR) were monitored monthly. Initial NT-proBNP level was 3594  $\pm$  5114 pg/ml. Of 256 study patients, 190 were admitted for HF, 31 for non-HF causes only and 35 were not hospitalized at all during the follow up period. Of the 190 HF patients who were admitted for HF, 156 were followed for more than 4 years, with at least one admission each year of follow up. Mean  $\Delta$ LIIR values at admission for HF 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 HF.

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### Characterisation of a hypercoagulable phenotype with increased thrombin generation in acute heart failure

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**Aims:** Subjects with heart failure (HF) are at higher risk of developing thrombosis. We determined the thrombin generating capacity in patients with acute decompensated heart failure (ADHF).

**Methods and Results:** Our prospective study included 34 ADHF patients and 19 control inpatients without HF. In vitro thrombin generation and its downregulation by activated protein C (APC) was monitored by calibrated automated thrombography at hospital admission, at the day of discharge and after at least six weeks of clinical stability. Concentrations of circulating microparticles (MPs) were determined by flow cytometry. Compared to controls, endogenous thrombin potential (ETP) was higher in ADHF patients at admission using platelet-rich plasma. Thrombin generation remained increased during the hospital course. After six weeks of clinical stability, ETP values were lowered to values of controls. The APC concentration inhibiting thrombin generation by 50% was higher at admission compared with the post-discharge period. ADHF patients had higher von Willebrand factor and endothelial protein C receptor plasma levels at admission. Significantly higher concentrations (3 to 5-fold increase) of annexin-V and tissue factor (TF)-positive MPs whatever their cellular origin were also found in ADHF patients at admission but not at the post-discharge point compared to controls. The concentration of TF-positive endothelial or platelet MPs were positively correlated with ETP.

**Conclusion:** The hypercoagulable state at the acute phase of decompensated HF results from increased procoagulant circulating MPs and dampened dynamic anticoagulant APC activity. Our findings demonstrate that thrombin generation assays and MP signatures are sensitive to the temporal evolution of this disease.

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### Relationship of ventricular conduction defects, angiographic findings and mortality in cardiogenic shock

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**Background:** Ventricular conduction defects, such as bundle branch blocks, hemiblocks and non-specific intraventricular conduction defects (IVCD), are frequently present in cardiogenic shock (CS), but their relationship with angiographic findings and mortality is not clear.

**Purpose:** The aim of this study was to investigate whether ventricular conduction abnormalities are associated with specific angiographic findings and increased mortality.

**Methods:** We analysed the baseline electrocardiogram (ECG) of patients who underwent angiography in a multinational prospective cohort study of CS (n=219) conducted in 2010-2012 with one-year follow-up. In total 182 (83.1%) patients underwent angiography. The baseline ECG was available for 164 (74.8%) of these patients. The patients with ventricular conduction defects (n=80; 48.8%) were compared with those who had other ECG pattern (n=84; 51.2%). The multivariate models were calculated with logistic regression adjusted for age, previous myocardial infarction and the CardShock risk score. The risk score takes into account age, confusion at presentation, previous myocardial infarction or coronary artery bypass graft, acute coronary artery syndrome aetiology, left ventricle ejection fraction, serum lactate and estimated glomerular filtration rate.

**Results:** Nearly half of the patients had a ventricular conduction defect (LBBB 2.4%, RBBB 12.2%, LAHB 14.6%, LPHB 3.7% or non-specific IVCD 15.9%). Most of the patients had significant coronary artery stenosis (n=152; 92.7%) and the prevalence did not differ between the groups (95.0% vs 90.5%;  $p = 0.27$ ). In the patients with conduction defects the culprit lesion was more often in the left main (LM) coronary artery (25.0% vs. 9.5%;  $p = 0.008$ ). There was no difference between the groups in three vessel disease (25.0% vs. 32.1%;  $p = 0.31$ ) or in the finding of TIMI flow grade 0 (64.9% vs 71.6%;  $p = 0.38$ ). One-year mortality was higher in patients with ventricular conduction defects (Figure). In the multivariate model ventricular conduction defects independently predicted mortality (OR 1.79; 95% CI 1.07-3.01;  $p = 0.027$ ). When we further adjusted mortality rates for the prevalence of the LM coronary artery disease, ventricular conduction defects



were still an independent predictor of mortality (OR 1.73; 95% CI 1.02-2.93; p=0.043).

**Conclusions:** In CS ventricular conduction defects in baseline ECG are associated with increased mortality and higher incidence of the LM coronary artery disease. However conduction abnormalities do not associate with three vessel disease or TIMI flow grade 0. Conduction defects are an independent risk factor also after eliminating the effect of LM disease. This study suggests that in CS ventricular conduction abnormalities predict mortality regardless of the severity of the coronary artery disease.

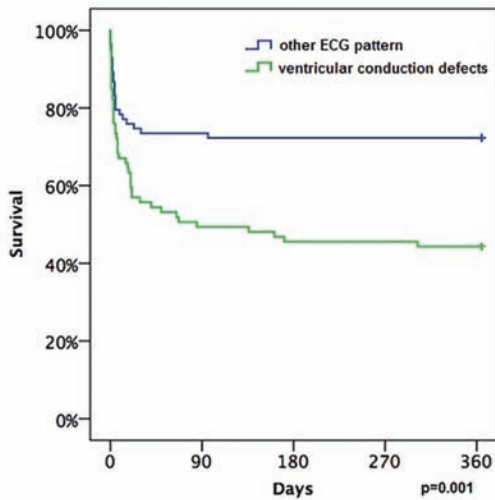


Figure: One-year mortality

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**Application of a simplified risk score derived from cardshock score for prognostic stratification in patients with cardiogenic shock**

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**Background:** Cardiogenic shock (CS) is a severe state of systemic hypoperfusion due to cardiac failure, often resulting in multiorgan dysfunction with rate of death ranging from 50 to 90% of cases. Recently a Cardshock score (CSS) was developed to improve early decision-making and prognostic stratification in CS patients.

**Purpose:** to evaluate the feasibility of the CSS for risk stratification of patients with CS.

**Methods:** we retrospectively evaluated 66 patients admitted for CS in our cardiac intensive care unit over 3 years (2012-2015). At first evaluation, CSS was calculated for each patient. We also evaluated which of the Cardshock variables best predicted mortality.

**Results:** Our population (72.8 ± 12.7 years, 61% men) presented a mean MAP of 61.9 ± 14.4 mmHg, severe LV dysfunction (LVEF 31.1 ± 9.9 %) and moderate to severe renal failure (eGFR(CKD-EPI): 43.7 ± 24.2 ml/min/1.73m<sup>2</sup>). Lactates were 6.64 ± 4.5 mmol/l. 98% of patients received IABP. The mean CardShock risk Score was 5.0 ± 2 with an in-hospital mortality of 55%. Among Cardshock variables, at Cox multivariate analysis (table 1), age and lactates best correlated outcomes and when considering a simplified score, with age and arterial lactates evaluation, it predicted in-hospital mortality well (area under the curve 0.79) as the CSS (area under the curve 0.71).

**Conclusions:** The CSS well stratified the risk and short-term mortality in CS patients. We developed a simplified risk score that equally well stratifies the risk and short-term mortality of our patients as the CSS.

Variable	HR	95%CI	P
Age	1.05	1.02-1.09	0.005
Age score	2.22	1.07-4.60	0.032
Previous PTCA-CABG	0.79	0.32-1.95	0.618
LVEF	0.97	0.94-1.01	0.180
LVEF<40	2.38	0.72-7.88	0.155
GFR	0.98	0.97-1.01	0.188
GFR score	1.27	0.79-2.04	0.324
Lactate	1.17	1.08-1.23	<0.001
Lact score	1.90	1.004-3.59	0.049
Global score	1.43	1.08-1.89	0.012
Simplified score	2.23	1.42-3.59	0.001

Tab 1: Cox multivariate analysis LVEF: left ventricular ejection fraction; GFR: glomerular filtration rate

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**Sleep-disordered breathing is associated with impaired left ventricular function and heart failure after acute myocardial infarction**

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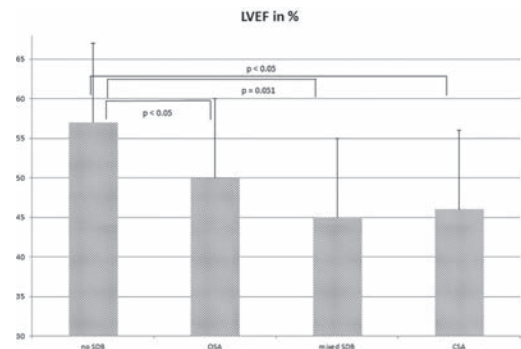
**Background:** Heart failure after acute myocardial infarction (AMI) remains a denotative topic today and routes to identify factors increasing myocardial salvage after infarction are of great interest. Recent literature has indicated an association between sleep-disordered breathing (SDB) and the degree of myocardial salvage after AMI, but only few data is available yet.

**Purpose:** This study investigated the relationship between left ventricular ejection fraction (LVEF) and SDB in patients with AMI.

**Methods:** 223 patients (age 63.3 ± 11.2 years, 81.6% male, BNP 296.7 ± 547.8 pg/ml, CK max 2376.5 ± 2646.6 U/l) were enrolled and underwent multichannel cardiorespiratory polygraphy (PG) after revascularization of myocardial infarction (ST elevation myocardial infarction and non-ST elevation myocardial infarction). None of the patients was treated with ventilation therapy and all patients were naïve to ventilation therapy. The prevalence of SDB (apnea-hypopnea index [AHI] ≥ 5/h) was 86 % (40.8 % had central sleep apnea and 42.2 % had obstructive sleep apnea, rest mixed SDB). Mean AHI was 25.7 ± 19.7/h and mean LVEF after AMI was 49.4 ± 12.5 %.

**Results:** The presence of SDB worsened LVEF after AMI, an association which showed statistical significance, for both presence of OSA or CSA versus no SDB (p < 0.05, graph 1). There was also a trend for worsened LVEF and resulting heart failure for mixed SDB versus no SDB (p = 0.051), as depicted in graph 1.

**Conclusions:** In conclusion, SDB (CSA and OSA) is associated with worsened LVEF after AMI and SDB seems to impair myocardial salvage after AMI. Further studies to investigate this relationship are needed and ongoing.



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**Comparison of treatment response by cardiac and lung ultrasound with symptomatic status - impact on prognosis in patients hospitalized for acute heart failure**

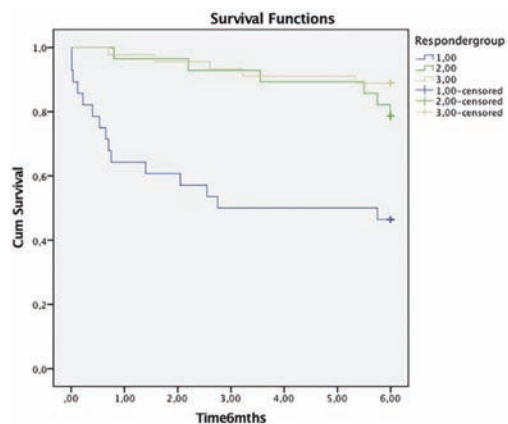
J Jonas Oehman<sup>1</sup>; V-P Harjola<sup>2</sup>; P Karjalainen<sup>1</sup>; J Lassus<sup>3</sup>

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**Introduction:** Poor treatment results remain a major concern in patients hospitalized for acute heart failure (AHF) and has been associated with poor prognosis

**Objectives:** To evaluate the impact of treatment response defined by residual congestion on lung ultrasound (LUS) and symptomatic status on mortality in hospitalized AHF patients -To evaluate the correlation between residual congestion and symptomatic status to cardiac filling pressures (E/e')

**Methods:** We included 101 dyspneic hospitalized AHF patients who were to receive standard in-hospital AHF treatment -We followed these patients daily using a focused thoracic ultrasound protocol combining E/e' and LUS with simultaneous symptom assessment using visual analog scale (VAS) for dyspnea -Patients who were asymptomatic (VAS 0) and non-bedridden at the day of discharge were defined as symptomatic responders -Patients who had no residual congestion on LUS at the day of discharge were defined as sonographic responders -LUS was considered congestive if presenting bilateral B-lines and/or right sided- or bilateral pleural fluid -Patients with both a sonographic- and symptomatic treatment response were considered complete responders, whereas patients with neither treatment response were considered non-responders and patients with either sonographic- or symptomatic treatment response were considered partial responders Results -Only 44.6 % of the patients were complete responders, 27.7 % partial responders and 27.7 % non-responders -Only 54.5 % of the patients had a sonographic treatment response, with 46.5 % having residual congestion at the day of discharge -Sonographic treatment response significantly predicted symptomatic treatment response (PPV 70.3 %, NPV 75.7 %,  $p < 0.001$ ) -6 month mortality was 53.6 % in non-responders (group 1), 21.4% in partial responders (group 2) and 11.1 % in complete responders (group3) ( $p < 0.001$  for comparison of group 1 to group 2 or 3,  $p = NS$  for comparison of group 2 to 3) -Mean E/e' at the day of discharge was 21.1 (SD 6.1) in non-responders (group 1), 18.90 (SD 5.7) in partial responders (group 2) and 15.6 (SD 4.0) in complete responders (group 3), ( $p < 0.001$  between group 1 and 3,  $p = 0.005$  between group 2 and 3,  $p = NS$  between group 1 and 2) with no significant difference in E/e' on admission -Mean decrease ( $\Delta$ ) E/e' during treatment was 0.8 (SD 4.5) in group 1, 1.5 (SD 4.2) in group 2 and 4.5 (SD 4.4) in group 3, ( $p = 0.001$  for group 1 vs. group 3,  $p = 0.006$  for group 2 vs. group 3,  $p = NS$  for group 1 vs. group 2) -Mean final E/e' or  $\Delta E/e'$  during treatment did however not have a statistically significant impact on prognosis ( $p = NS$  for both) **Conclusions** -Poor treatment response was common and associated with an increased short-term mortality -Sonographic- and symptomatic treatment responses correlated well with each other -Responsive patients had a greater  $\Delta E/e'$  during treatment and a lower E/e' at discharge -E/e' per se did not have prognostic significance



Survival according to treatment response

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**Management of heart failure in the real-world: does gender make the difference? Findings from the ARNO administrative database.**

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Reno, Italy; <sup>4</sup>Azienda Ospedaliero-Universitaria Careggi, Department of Heart and Vessel, Section Internal Medicine and Cardiology, Firenze, Italy; <sup>5</sup>Accademia Nazionale di Medicina, Roma, Italy; <sup>6</sup>ANMCO Research Center, Florence, Italy

**Background:** Among patients with heart failure (HF), female gender has generally been shown to be associated with more favourable outcomes. Females are frequently excluded from randomized clinical trial and to some extent from cardiology registries. Purpose. The purpose of this study is to describe gender differences in terms of clinical characteristics, treatments, one-year outcomes and management costs in a real world setting of acute heart failure analysing a large administrative database.

**Methods:** Data came from the ARNO Observatory that includes nearly 3,000,00 in-habitants of 7 Local Health Authorities of the Italian National Health Service (NHS). Patients with HF were selected when discharged for HF (from January 1, 2008 to December 31 2012) and prescribed on at least one HF treatment. We compared patients according to gender. Results. The total study population was composed by 41,413 patients discharged alive and prescribed on HF treatments. Female gender accounted for 51.4%. Mean age was higher among female patients (80.4 vs 75.5%), with increasing number of females particularly among the "very elderly" (> 85 yrs: 66.3% vs 33.7%). Comparing co-morbidities we found a lower prevalence of COPD (27.4 vs 33.7%) and diabetes (29.5 vs 31.9%) in females and a higher prevalence of depression (26.1 vs 15.5%). Females were less frequently managed in a cardiology setting (20.6 vs 32.9%) and more frequently in internal medicine (54.6 vs 44.6%) and geriatric (15.2 vs 12.0%) wards. During the 1-year follow-up, prescription rate of ACE-inhibitors/Angiotensin Receptor Blockers and Beta-Blockers was lower in females (63.5 vs 68.3 % and 45.9 vs 53.6% respectively), as well as for Mineralocorticoid antagonists (41.9 vs 42.3%) and higher for digoxin (29.3 vs 24.2). During the 1-year follow-up, males had a higher re-hospitalisation rate (at least one re-hospitalisation during follow-up) 60% vs 53.3% and less frequently due to non-cardiovascular causes (47.9% vs 50.4%). NHS's total direct cost per year were higher in males that in females, 13,273 vs 10,451 €. p values for all above differences < 0.01.

**Conclusions:** Real world evidence show a gender-related high variability in both clinical epidemiology and management of patients with HF. Females are older, have a different co-morbidity pattern, are less frequently treated in cardiology setting and with HF guidelines recommended drugs.

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**Bioactive adrenomedullin: a novel prognostic marker in cardiogenic shock**

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<sup>1</sup>Hospital de la Santa Creu i Sant Pau, Cardiology Department, Barcelona, Spain; <sup>2</sup>Helsinki University Central Hospital, Cardiology department, Helsinki, Finland; <sup>3</sup>Inserm UMR-S 942, Paris, France

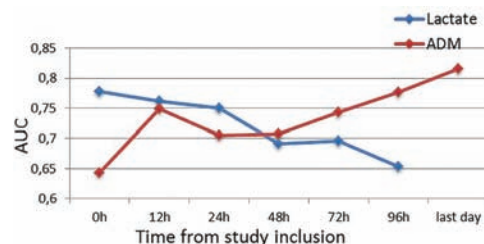
**Background:** The short-term mortality in cardiogenic shock (CS) is high, and risk stratification is needed for rational use of advanced therapies.

**Purpose:** The aim was to evaluate the prognostic value of bioactive adrenomedullin (bio-ADM) and lactate in CS.

**Methods:** CardShock study was a prospective, observational, European multinational cohort of CS. This is a sub-study of 178 patients with serial plasma samples.

**Results:** Both lactate and bio-ADM levels were higher in non-survivors compared to survivors at all time points ( $p < 0.05$ ). Lactate levels fell to normal ( $\leq 2\text{mmol/L}$ ) within the first 24 hours in most patients regardless of outcome. Lactate had good prognostic value during the first 24 hours, whereas bio-ADM showed incremental prognostic value starting at 48 hours (Figure). The addition of bio-ADM at 48 hours to the baseline lactate levels re-stratified the patients in 3 risk groups with 90-day mortality of 8.1%, 35.4%, and 61.1% ( $p < 0.001$ ). Prognostic value of serial measurement of lactate and bio-ADM were independent of conventional risk factors. High bio-ADM levels were associated with persistently impaired hemodynamics (cardiac index, mean arterial, central venous, and pulmonary arterial pressures) and end-organ dysfunction.

**Conclusions:** Bio-ADM is a valuable prognostic marker after the initial phase of management in CS. Combining bio-ADM with early lactate measures may help the recognition of high-risk patients and support clinical decision for the use of advanced therapies in CS.



Evolution of AUC of lactate and bioADM

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### Management of heart failure following primary PCI after st-elevation myocardial infarction: a large UK tertiary centre experience

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<sup>1</sup>Bristol Heart Institute, NIHR Bristol Cardiovascular Biomedical Research Unit, Bristol, United Kingdom

Patients presenting with ST-segment elevation myocardial infarction (STEMI) represent 30% of all acute coronary syndromes (ACS). Even with successful and timely primary percutaneous coronary intervention (PPCI) development of heart failure is a frequent adverse consequence. Local follow up of these patients is often challenging due to the centralisation of acute PPCI services.

**Purpose:** To evaluate the: i) Prevalence of left ventricular systolic dysfunction (LVSD) following PPCI, ii) Predictors for development of heart failure, iii) Prescription of Mineralocorticoid Receptor Antagonist (MRA) as per ESC guideline iv) Number qualifying for primary prevention ICD.

**Methods:** This retrospective observational study was performed at a large tertiary centre in the South-West of England. Data were collected on consecutive patients who underwent PPCI (Jan 2013 -Dec 2013). Echocardiography was used to assess of LV function. Ejection fraction <40% was defined as significant LVSD. Fisher's exact test and student-t test were used to establish statistical significance. P-value of < 0.05 was considered significant.

**Results:** Of the 573 patients who underwent PPCI, 73.8% were male and the median age was 64 years. 9 patients died prior to formal assessment of LV function and were excluded. 42% (n = 231) of patients with a recorded EF had LVSD. Such patients had a significantly greater median length of hospital stay (4 vs 3, P < 0.0001) and 30-day mortality rate (17 vs 9, P = 0.01). Patients with LVSD also had a significantly higher peak troponin level (5981 vs 2816, P < 0.0001) and were more likely to have the LAD as their culprit artery (138 vs 104, P < 0.0001) than patients without LVSD. 83.5% (n = 193) of patients with LVSD qualified for an MRA; however, only 47% (91/193) of these patients received this medication. 214 patients had LVSD on initial assessment and were alive after 40 days. 29.0% (62/214) patients were lost to follow up and hence excluded from further analysis. 76% (115/152) had a repeat assessment of their EF. 29% (33/115) patients qualified for an ICD under ESC guidelines. On the contrary, only 3% (3/115) qualified under the NICE guidelines, as only 3 patients had a QRS > 120ms with or without LBBB.

**Conclusion:** Significant heart failure following STEMI is still a major health problem even after timely and successful PPCI. It is associated with a significantly higher mortality and increased length of hospital stay. Higher troponin level and LAD culprit artery are predictors of severity of LV impairment. Use of MRA is moderate. Heart Attack Centres and local heart failure teams need to coordinate follow up echo and clinical care. This remains challenging. Moreover, adoption of ESC guideline leads to a significantly higher number qualifying for an ICD when compared to NICE guidelines. Further research into the impact of adoption of NICE vs ESC guideline on primary prevention ICD post STEMI is urgently required.

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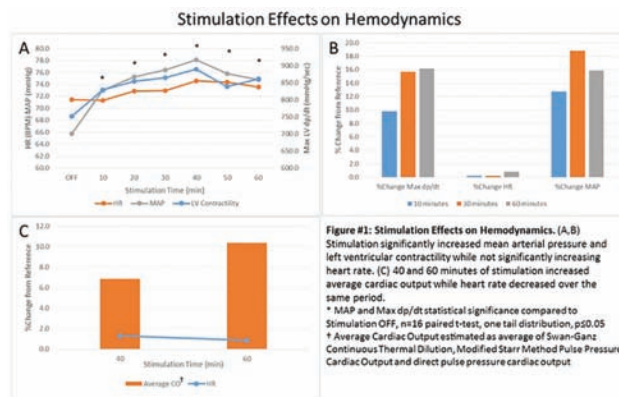
### Transvenous stimulation of cardiac autonomic nerves improves hemodynamics

MPC Michael Cuchiara<sup>1</sup>; CM Marin Y Kall<sup>2</sup>; MP Penn<sup>3</sup>; AE Ebner<sup>4</sup>

<sup>1</sup>NeuroTronik, Clinical Research, Durham, United States of America; <sup>2</sup>University of Miami, International Medicine Institute, Miami, United States of America; <sup>3</sup>Summa Cardiovascular Institute, Akron, United States of America; <sup>4</sup>Facultad de Ciencias Medicas UNA Paraguay, Asuncion, Paraguay

Despite advances in therapies for the management of heart failure, Acute Heart Failure Syndrome (AHFS) is a leading cause of mortality and morbidity. An electrically

active, catheter-based technology is being investigated to transvenously stimulate cardiac autonomic nerves to control left-ventricular contractility and heart rate in order to improve hemodynamics. The purpose of this study was to investigate cardiac autonomic nerve stimulation effects on acute hemodynamics. The present study was a single center feasibility study performed in patients undergoing cardiac catheterization. The study protocol was approved by the Republic of Paraguay, National Council of Health, Bioethics Committee and was conducted in our institute. All subjects signed a written informed consent in order to participate in the study. Purpose built electrical stimulation catheters were percutaneously inserted into an upper venous structure near the heart via either right femoral vein and or left subclavian vein access using standard introducers. All subjects were instrumented with solid state pressure catheters in the left-ventricle and the femoral artery to measure left ventricular and femoral artery pressure respectively. Cardiac output was estimated using an average of three methods: modified Starr Pulse Pressure Cardiac Output, direct pulse pressure method and continuous thermal dilution method. Sixteen (16) subjects were stimulated for one hour and hemodynamics were continuously measured during stimulation. Changes in hemodynamics during stimulation were determined by comparison to a pre-stimulation, reference period when stimulation was off. Statistics were calculated using a single tail paired t-test of the means compared to the reference period. After only 10 minutes of stimulation, left ventricular contractility (maximum first derivative of left ventricular pressure) and mean arterial pressure were increased by +9.8% and +12.7% respectively. After 1 hour of stimulation, left ventricular contractility and mean arterial pressure continued to increase to 16.2% (p = 0.005) and +15.9% (p = 0.0003) respectively. During this time, heart rate increased by 0.8% (p = 0.346) while average cardiac output increased by 10.7%. Increases in left ventricular contractility, mean arterial pressure and cardiac output coupled with small changes in heart rate suggests stimulation preferentially increases cardiac contractility over heart rate. Furthermore, increases in cardiac output that exceed increases in heart rate suggest that left ventricular contractility and subsequently stroke volume drove increased cardiac output. Further potential likely exists to develop the therapy such that increased cardiac output is achieved in the presence of lowered heart rate. In conclusion, we believe this study demonstrates the promise of transvenous cardiac autonomic nerve stimulation therapy to improve hemodynamics.



Stimulation Effects on Hemodynamics



## DIRECTIONS IN HFpEF RESEARCH

Saturday 21 May 2016 14:15–15:45

Location: Barcelona

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**Na<sup>+</sup>/Ca<sup>2+</sup> Exchanger (NCX) inhibition with ORM 11035 improves cardiac function and remodeling without lowering blood pressure in a model of heart failure with preserved ejection fraction**U Primessnig<sup>1</sup>; T Bracic<sup>2</sup>; P Pollesello<sup>3</sup>; B Pieske<sup>1</sup>; FR Heinzel<sup>1</sup><sup>1</sup>Charité - Universitätsmedizin Berlin, Campus Virchow-Klinikum, Department of Cardiology, Berlin, Germany; <sup>2</sup>Medical University of Graz, Department of Cardiology, Graz, Austria; <sup>3</sup>Orion Pharma, Critical Care, P.O. Box 65, Espoo, Finland, Espoo, Finland**Background:** Heart failure with preserved ejection fraction (HFpEF) is increasingly common but there is currently no established pharmacological therapy. We could demonstrate that in a rat model of HFpEF cardiomyocyte dysfunction is associated with impaired cardiomyocyte Ca<sup>2+</sup> handling and altered Na<sup>+</sup>/Ca<sup>2+</sup> exchanger (NCX) function. Therefore we investigated the effects of chronic inhibition of the NCX with ORM 11035, a new NCX inhibitor, on cardiac function and remodeling in HFpEF.**Methods:** Young male Wistar rats were subjected to subtotal nephrectomy (NXT, n=24) or sham operation (SOP, n=24). 8 weeks after intervention chronic treatment for 16 weeks with the novel NCX inhibitor ORM 11035 (1mg/kg body weight) or vehicle was started. At 24 weeks non-invasive blood pressure measurements, echocardiography, pressure-volume loops (PV) and LV morphometry were performed. LV cardiomyocytes were isolated and contractile function and Ca<sup>2+</sup> transients were measured. NCX-mediated Ca<sup>2+</sup> extrusion was quantified from the caffeine-induced Ca<sup>2+</sup> transient. Results NXT rats (untreated) showed signs and symptoms of HFpEF (hypertrophied LV, left- and upward shift of end diastolic pressure (EDP) volume relationship (EDPVR), increased lung weight/body weight ratio (LW/BW) indicating pulmonary congestion and preserved LV systolic function (EF, dP/dt). In LV cardiomyocytes from untreated NXT early relaxation was prolonged and NCX-mediated Ca<sup>2+</sup> extrusion was decreased. ORM 11035 treatment reduced heart weight/BW ratio and LW/BW significantly as well as LV mass without effects on systolic blood pressure (157 ± 1 vs. 158 ± 1, mmHG in NXT, p=ns). LVEDP (13 ± 1 vs. 8 ± 1, mmHG in NXT, p < 0.05) and EDPVR were reduced after chronic treatment with ORM 11035 in NXT. LV cardiomyocytes from ORM-treated rats showed improved diastolic cytosolic Ca<sup>2+</sup> decay as well as restored NCX-mediated Ca<sup>2+</sup> removal indicating specific NCX inhibition as a promising target in the treatment of HFpEF patients.**Conclusion:** Chronic inhibition of the Na<sup>+</sup>/Ca<sup>2+</sup> exchanger with ORM 11035 significantly attenuated cardiac remodeling and diastolic dysfunction without lowering systemic blood pressure in this model of HFpEF.

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**A restrictive pattern of LV filling is only present in one third of cardiac AL amyloidosis patients**S Perlini<sup>1</sup>; F Musca<sup>2</sup>; F Salinaro<sup>1</sup>; R Mussinelli<sup>1</sup>; T Perrone<sup>1</sup>; E Binot<sup>1</sup>; M Boldrini<sup>1</sup>; G Gioia<sup>1</sup>; G Palladini<sup>3</sup>; G Merlini<sup>3</sup><sup>1</sup>Dept. Internal Medicine, University of Pavia, Amyloidosis Research and Treatment Center, IRCCS S.Matteo, Pavia, Italy; <sup>2</sup>IRCCS Fondazione Ca' Granda Ospedale Maggiore Policlinico, Cardiology, Milan, Italy; <sup>3</sup>Amyloidosis Research and Treatment Center, Dept. Molecular Medicine, IRCCS S.Matteo, University of Pavia, Pavia, Italy**Background:** Cardiac amyloidosis represents an archetypal form of restrictive heart disease, characterized by profound diastolic dysfunction, associated with a "normal" ejection fraction (EF) that is preserved until the late stage of the disease in the vast majority of patients. Therefore cardiac amyloidosis patients typically fulfil the definition of heart failure with preserved ejection fraction (HFpEF). A restrictive pattern of transmitral left ventricular (LV) filling is often reported as a typical hallmark of diastolic dysfunction in these patients.**Objective and Methods.** In order to evaluate the extent of diastolic dysfunction in cardiac light-chain (AL) amyloidosis, we enrolled 221 consecutive never-treated subjects, in whom a first diagnosis of cardiac AL amyloidosis was concluded

between 2007 and 2010, according to the International Society of Amyloidosis criteria. Further inclusion criteria were EF&gt;50%, and the absence of significant valve disease, previous myocardial infarction, atrial fibrillation, or chronic obstructive lung disease. The extent of diastolic dysfunction was graded according to the ESC guidelines. To this aim, transmitral Doppler early (E) and atrial (A) velocities, E deceleration time, pulmonary venous flow velocity, early diastolic tissue Doppler peak velocity (E') and E/E' ratio were recorded at diagnosis. Survival was assessed over a median follow-up of 35.8 months (range, 19-60 months).

**Results:** Quite surprisingly, grade III diastolic dysfunction was only present in 37.1% of the whole cardiac AL population (82/221), grade II and grade I diastolic dysfunction being evident in 84 (38.0%) and 55 (24.9%) patients, respectively. The extent of amyloid deposit, as assessed by interventricular septal thickness, was slightly lower in grade I than in grade III diastolic dysfunction groups (14.2 ± 2.0 vs. 14.7 ± 2.1 mm; p < 0.05). Both left atrial dimensions and estimated systolic pulmonary pressure progressively increased from grade I to grade III diastolic dysfunction (p < 0.01 for both). At variance with EF, the grade of diastolic dysfunction was a significant predictor of survival after a 3-year median follow-up (p < 0.001).**Conclusions:** A clear-cut restrictive LV filling is only present in one third of patients with overt cardiac AL amyloidosis, grade I diastolic dysfunction being present in almost one fourth of patients. Despite being an important prognostic factor, the presence of a restrictive pattern of transmitral LV filling cannot be viewed as a "red flag" diagnostic marker in cardiac AL amyloidosis.

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**Dipeptidyl peptidase 4 inhibitor sitagliptin reduces oxidative stress, endothelial dysfunction and preserves diastolic function in a rat model of heart failure with preserved ejection fraction**K Urbanek<sup>1</sup>; D Donato Cappetta<sup>1</sup>; E Piegari<sup>1</sup>; G Esposito<sup>1</sup>; R Russo<sup>1</sup>; LP Ciuffreda<sup>1</sup>; A Rivellino<sup>1</sup>; L Berrino<sup>1</sup>; F Rossi<sup>1</sup>; A De Angelis<sup>1</sup><sup>1</sup>Second University of Naples, Department of Experimental Medicine - Section of Pharmacology, Naples, Italy**Background:** Heart failure with preserved ejection fraction (HFpEF) appears to be a systemic syndrome driven by risk factors and co-morbidities and its pathophysiology is poorly understood. Interstitial fibrosis, myocyte hypertrophy and altered intracellular calcium homeostasis trigger diastolic dysfunction by impairing relaxation and increasing ventricular stiffness. HFpEF associates with diabetes when systemic proinflammatory state and endothelial dysfunction influence patient's cardiovascular profile. Several studies suggesting that dipeptidyl peptidase 4 (DPP4) inhibitors (DPP4i) cardiovascular safety and potential benefits. DPP4i may have effects on cardiovascular system as DPP4 reduces the biological activity of peptides with cardio-, vaso- and reno-protective actions. In addition, DPP4 may exert pro-fibrotic and inflammatory effects, but the possible underlying mechanisms are not clear.**Objective:** To determine whether inhibition of DPP4 affects the progression of HFpEF independently from the effects on a glycemic control and to identify mechanisms involved in the potential cardioprotection.**Methods:** Non-diabetic seven-weeks old Dahl salt-sensitive rats were fed a high salt diet (8% NaCl) for 5 weeks to induce hypertension. Afterwards, rats continued with a high salt diet and were administered either with vehicle or sitagliptin (SITA, 10 mg/kg/die, oral) for the following 8 weeks. Control rats were maintained on a low salt diet (0.3% NaCl).**Results:** Treatment with SITA significantly attenuated diastolic dysfunction ameliorating hemodynamic indices (decreased dP/dt min, increased LVEDP, longer time constant and steeper slope of the end-diastolic pressure-volume relationship). SITA significantly reduced mortality, arterial blood pressure and improved general conditions. Myocardial levels of pro-inflammatory tumor necrosis factor- $\alpha$  and monocyte chemoattractant protein-1 were reduced. It was associated with decreased markers of oxidative stress, nitrotyrosine and oxidized dihydroethidium. Moreover, SITA

reduced the levels of eNOS monomer, responsible for ROS generation, and elevated the amount of NO-producing dimeric form. Finally, increase of collagen deposition and activation of pro-fibrotic TGF- $\beta$ /SMAD3 signaling that leads to elevated myocardial stiffness and diastolic compliance were attenuated by SITA.

**Conclusions:** SITA positively modulates active relaxation and passive diastolic compliance interfering with inflammatory-related endothelial dysfunction and fibrosis associated with HFpEF.

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### HFpEF and HFrEF display different anabolic phenotypes as assessed by IGF-1 and IGFBP-1

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<sup>1</sup>Karolinska Institutet, Department of Medicine, Stockholm, Sweden; <sup>2</sup>Karolinska Institutet, Department of Clinical Science and Education, Stockholm, Sweden;

<sup>3</sup>Karolinska Institutet, Division of Family Medicine, Department of Neurobiology, Care Sciences and Society, Stockholm, Sweden; <sup>4</sup>University Hospital of Rennes, Département de Cardiologie & CIC-IT U 804, Rennes, France

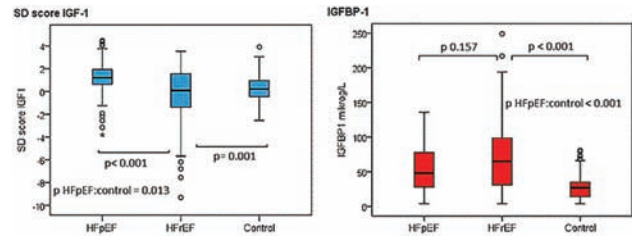
**Background:** Anabolic drive is impaired in heart failure with reduced ejection fraction (HFrEF) but has been insufficiently studied in HF with preserved EF (HFpEF). Insulin-like growth factor 1 (IGF-1) mediates growth hormone effects and IGF-1 binding protein 1 (IGFBP-1) regulates IGF-1. Both can be used as markers of anabolism.

**Purpose:** We tested the hypothesis that HFpEF and HFrEF are similar syndromes with regard to IGF-1 and IGFBP-1 by assessing concentrations, correlations with natriuretic peptides, and prognostic impact.

**Methods:** Concentrations of IGF-1 and IGFBP-1 were measured in patients with HFpEF (n=79), HFrEF (n=85), and controls without cardiovascular disease (n=136); and analysed, logarithmically transformed (ln) with ANOVA, Pearson's r and Cox regression. In HFpEF the composite endpoint was hospitalisation due

to HF and death and in HFrEF, implantation of left ventricular assist device, heart transplantation, or death. Results Age standardized scores of IGF-1 (SD score IGF-1) were increased in HFpEF; median arbitrary units (interquartile range) 1.21 (0.57-1.96), vs controls, 0.22 (-0.47-0.96); p=0.013 and reduced in HFrEF, 0.09 (-1.40-1.62) vs controls; p=0.001. IGFBP-1 was increased in HFpEF, 48 (28-79) and HFrEF, 65 (29-101) vs. controls, 27 (14-35)  $\mu$ g/L, p overall <0.001. These patterns persisted after adjusting for metabolic and severity confounders. High levels of IGFBP-1, but not IGF-1, were associated with high levels of NT-pro-BNP in both HFpEF, r=0.458, p<0.001; and HFrEF, r=0.533, p<0.001. IGF-1 was protective in HFrEF; adjusted hazard ratio per ln increase in IGF-1 SD score, 0.31 (95% confidence interval 0.13-0.77, p 0.011) but not in HFpEF. IGFBP-1 neither predicted outcomes in HFpEF nor HFrEF.

**Conclusion:** HFpEF and HFrEF were similar with regard to IGFBP-1 elevations but differed regarding IGF-1 levels and prognostic impact. HFrEF may be associated with a syndrome-specific impairment in anabolic drive, whereas IGFBP-1 activation in HFpEF may be less specific and related to comorbidities.



Levels of SD score IGF-1 and IGFBP-1

# RAPID FIRE 2 – IMAGING IN CHRONIC HEART FAILURE

Saturday 21 May 2016 16:00–17:30

Location: Agora

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### Extracellular volume fraction for characterization of patients with heart failure and preserved ejection fraction

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<sup>1</sup>Heart Center of Leipzig, Internal Medicine / Cardiology, Leipzig, Germany; <sup>2</sup>Heart Center of Leipzig, Radiology, Leipzig, Germany

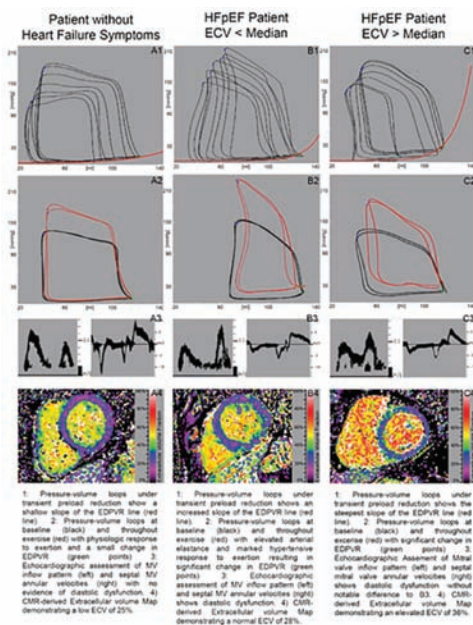
**Background:** Optimal patients characterization in Heart Failure with Preserved Ejection Fraction (HFpEF) is essential to tailor successful treatment strategies. Cardiac magnetic resonance derived T1-Mapping allows for non-invasive quantification of diffuse myocardial fibrosis as extracellular volume fraction (ECV).

**Objectives:** We aimed to elucidate the diagnostic performance of T1-Mapping in HFpEF by examining the relationship between ECV and invasively measured parameters of diastolic function and investigated the potential of ECV to differentiate between different pathomechanisms in HFpEF.

**Methods:** We performed T1-Mapping in 21 patients with HFpEF and 11 patients without heart failure symptoms. Pressure-volume-loops were obtained with a conductance catheter during basal conditions and handgrip exercise. Transient preload reduction was used to extrapolate the diastolic stiffness constant.

**Results:** Patients with HFpEF showed a higher ECV ( $p=0.001$ ), an elevated load-independent passive left ventricular (LV)-stiffness-constant Beta ( $p<0.001$ ), and a longer time constant of active LV-relaxation  $\tau$  ( $p=0.04$ ). ECV correlated highly with Beta ( $r=0.75$ ,  $p<0.001$ ). Within the HFpEF cohort, patients with ECV > median showed a higher LV-stiffness-constant ( $p=0.05$ ) whereas ECV < median identified patients with a prolonged active LV-relaxation ( $p=0.01$ ) and a marked hypertensive reaction to exercise due to a pathologic arterial elastance ( $p=0.05$ ). On multiple linear regression analyses, ECV independently predicted intrinsic LV stiffness ( $B=0.75$ ;  $p<0.01$ ).

**Conclusion:** Diffuse myocardial fibrosis, assessed by CMR derived T1-Mapping, independently predicts invasively measured LV stiffness in HFpEF. In addition, ECV helps to non-invasively distinguish the role of passive stiffness and hypertensive exercise response with impaired active relaxation. Thus, ECV facilitates refinement of patients characterization, which is a prerequisite for any successful therapy in the future.



Results for ECV groups and controls

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### Exercise-induced B-lines identify worse functional and prognostic stage in heart failure patients with depressed left ventricular ejection fraction

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**Background:** Exercise stress echo (ESE) is recommended by latest European Society of Cardiology guidelines for evaluation of heart failure (HF) patients. Recently, lung ultrasound (LUS) has been proposed for dynamic assessment of extravascular lung water through B-lines.

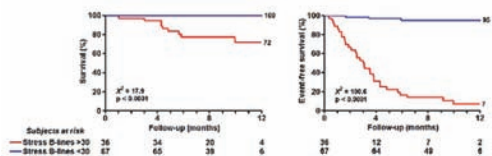
**Aim:** To assess B-lines during ESE in HF.

**Methods:** We performed standard transthoracic and LUS evaluation during semi-supine ESE in 103 NYHA class I-III HF patients (76 males; age  $64 \pm 12$  years) with depressed left ventricular ejection fraction ( $35 \pm 8\%$ ). B-lines were measured by scanning 28 intercostal spaces on anterior chest, both at rest and peak stress. Resting plasma BNP levels and exercise capacity during cardiopulmonary testing with peak oxygen uptake ( $VO_2$  max) were assessed in all patients. All patients were followed-up for a median of 8 months (first quartile, 6; third quartile, 11).

**Results:** LUS was feasible and interpretable in all subjects, with additional scanning time < 3 minutes. The overall B-lines number increased from  $7 \pm 9$  (mean  $\pm$  SD) at rest to  $24 \pm 24$  at peak stress ( $p<0.0001$ ). The number of stress B-lines was more closely correlated with resting BNP ( $r=0.79$ ,  $p<0.0001$ ) than resting B-lines ( $r=0.69$ ,  $p<0.0001$ ). Stress B-lines were also significantly correlated with stress  $E/e'$  ( $r=0.22$ ,  $p=0.03$ ), stress pulmonary artery systolic pressure ( $r=0.42$ ,  $p<0.0001$ ), stress left ventricular ejection fraction ( $r=0.86$ ,  $p<0.0001$ ) and  $VO_2$  max ( $r=0.87$ ,  $p<0.0001$ ). During follow-up, 37 events occurred: 10 cardiac deaths, 22 re-hospitalizations for acute heart failure, 1 sustained ventricular tachycardia, 4 nonfatal myocardial infarctions. Twelve-month event-free survival was 95% in the 36 patients with stress B-lines < 30 (best cut-off identified by Receiver Operating Curve analysis) vs. 7% in patients with  $\geq 30$  B-lines ( $p<0.0001$ ). When only death was considered, survival was 100% vs. 72%, respectively ( $p<0.0001$ ). At multivariable analysis for all spontaneous events, only resting BNP values and stress B-lines (HR 1.04, 95% CI 1.01-1.06,  $p=0.004$ ) were independent prognostic indicators.

**Conclusion:** B-lines are easy to obtain, frequent in HF patients and often increase during ESE. Exercise-induced B-lines are associated more closely than resting B-lines to higher natriuretic peptides plasma levels. Spontaneous events were more frequent in patients with more B-lines during ESE. LUS expands the information provided by standard transthoracic echocardiography, and might be easily incorporated in ESE for direct imaging of functionally and prognostically meaningful extra-vascular lung water accumulation.

Figure 5



Kaplan-Meier survival curves.

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### 4D flow cardiovascular magnetic resonance parameters represent novel imaging biomarkers in heart failure and correlate with conventional prognostic remodelling parameters and myocardial energetics

Dr V. Stoll was funded by the British Heart Foundation (Ref FS/12/14/29354).

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**Introduction:** Cardiac remodelling is initiated by a myocardial insult and causes progression to heart failure. Insights into multidimensional flow patterns and kinetic energy within the left ventricle (LV) are now afforded by the use of 4D flow MRI.

**Purpose:** We hypothesised that in heart failure derangements in 4D flow measures would relate to decreased mechanical function, increased biochemical remodelling markers, worsening symptoms, including reduced exercise capacity and impaired myocardial energetics.

**Methods:** 34 dilated cardiomyopathy (DCM) patients, 30 ischaemic cardiomyopathy (IHD) patients and 36 controls underwent cardiovascular 4D flow MRI. The LV volume was analysed as functional flow components including the direct flow (LV inflow that passes directly to ejection), and the residual volume (resides within the LV for >2 cardiac cycles). The kinetic energy (KE) was measured throughout the cardiac cycle. Assessment of functional capacity (6 minute walk test), biochemical remodelling (B-Type Natriuretic peptide) and patient symptoms was additionally performed. A subgroup of 25 DCM patients and 10 controls underwent phosphorus spectroscopy for quantification of myocardial energetics.

**Results:** DCM and IHD patients demonstrated adverse cardiac remodelling with ventricular dilatation, and impaired systolic function (DCM LVEF  $36 \pm 11\%$ , IHD LVEF  $39 \pm 12$ , control LVEF  $67 \pm 4\%$ ). Both patient groups had reduced direct flow proportion (DCM  $11 \pm 6\%$ , IHD  $14 \pm 9\%$ , control  $38 \pm 4\%$ ,  $P < 0.0001$ ) and KE (DCM and IHD 59% decrease in average kinetic power compared to controls,  $P < 0.0001$ ); whilst residual volume proportion (DCM  $51 \pm 11\%$ , IHD  $49 \pm 10\%$  and controls  $30 \pm 4\%$ ) and KE values were increased (DCM by fivefold, IHD by fourfold compared to controls,  $P < 0.0001$ ). Both direct flow KE and residual volume KE correlated, though in opposite directions, with left ventricular end diastolic and systolic volumes, systolic function, BNP, functional capacity and symptoms (All P values  $< 0.0001$ ). In a multiple linear regression model the average kinetic power of the direct flow was predictive of the patient's 6 minute walk test result ( $\beta = 0.279$ ,  $P = 0.039$ , overall model  $R^2 = 0.464$ ,  $P = 0.003$ ), whereas LV EF was not. DCM patients had impaired myocardial energetics compared to controls (PCr/ATP  $1.54 \pm 0.38$  DCM vs  $1.95 \pm 0.25$  control,  $P = 0.004$ ). The PCr/ATP ratio correlated with the proportion of the direct flow ( $r = 0.415$ ,  $P = 0.013$ ) and the KE of the residual volume ( $r = -0.52$ ,  $P = 0.001$ ).

**Conclusions:** Heart failure patients demonstrated less efficient blood flow patterns with deranged kinetic energy profiles compared to controls. The greater the derangement of 4D flow parameters the worse the conventional markers of cardiac remodelling, patient symptoms and myocardial energetics. 4D flow parameters represent a novel biomarker of disease severity and may provide additive value in monitoring novel heart failure therapies and predicting prognosis.

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### Relative prognostic importance of longitudinal strain of right ventricle and tricuspid annular plane systolic excursion in systolic heart failure

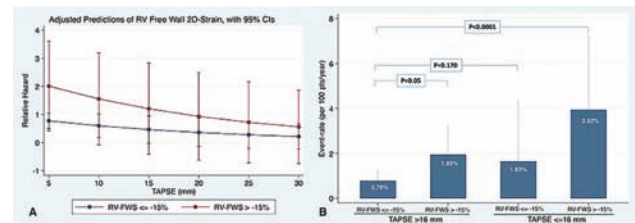
C Riccini<sup>1</sup>; E Erberto Carluccio<sup>1</sup>; P Biagioli<sup>1</sup>; G Bardelli<sup>1</sup>; R Lauciello<sup>1</sup>; A D'antonio<sup>1</sup>; MF Cerasa<sup>1</sup>; A Mengoni<sup>1</sup>; G Alunni<sup>1</sup>; G Ambrosio<sup>1</sup>

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**Background:** Right ventricular (RV) systolic dysfunction, either assessed by tricuspid annular plane systolic excursion (TAPSE) or longitudinal 2D-strain of the RV free wall (RVFWS), is a strong prognostic predictor in chronic heart failure (HF). However, the relative prognostic importance of these two parameters is not known. In particular, it is not clear whether assessment of RVFWS could provide additive prognostic information over TAPSE.

**Methods and Results:** We prospectively enrolled 150 stable HF patients (age  $65 \pm 11$  months; mean EF  $29 \pm 7\%$ ). RV function was assessed using standard and Speckle Tracking echocardiography to measure both TAPSE and 2D longitudinal strain of the RV free wall. Patients were followed-up for a median time of 13 months (IQR 5-30). Cox regression hazard model was used to assess association of clinical and echocardiographic parameters with the composite end-point of all-cause death/HF re-hospitalization. In the whole population, mean value of TAPSE was  $19.7 \pm 4.5$  mm, and mean value of RVFWS was  $-18.4 \pm 6.2\%$ . During the follow-up, 42 patients experienced the primary outcome. By Cox analysis, both TAPSE  $< 16$ mm, and RVFWS  $> -15\%$  were independently associated with outcome. Figure A and B respectively show the adjusted prediction and the event-rate (per 100 pts/year) when patients were grouped by TAPSE and RVFWS. As shown, the relative contribution of RVFWS in predicting prognosis increases in the presence of progressively low values of TAPSE. Patients with normal TAPSE but impaired RVFW had worse outcome than patients with normal RVFWS ( $p < 0.05$ ).

**Conclusions:** Right ventricular longitudinal 2D-strain of the RV free wall seems to have additive prognostic value over TAPSE, mainly in patients in whom TAPSE is impaired.



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### Extracellular volume is an independent predictor of outcome in heart failure with preserved ejection fraction

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<sup>1</sup>Medical University of Vienna, Cardiology, Vienna, Austria

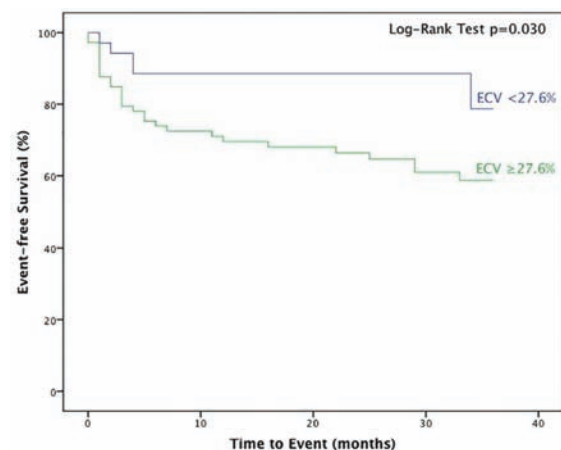
**Background:** Cardiac magnetic resonance (CMR) T1 mapping allows accurate non-invasive quantification of extracellular matrix volume (ECV). Accumulation of extracellular matrix (ECM) is a key pathophysiological mechanism in heart failure with preserved ejection fraction (HFpEF). However, the prognostic relevance and hemodynamic consequences of CMR-ECV in HFpEF are unknown.

**Purpose:** We aimed to elucidate the influence of ECV on the outcome in HFpEF and hemodynamic parameters.

**Methods:** Between January 2011 and August 2015 we prospectively enrolled 108 HFpEF patients. All patients underwent CMR T1 mapping for ECV measurement, using the Modified Look-Locker Inversion recovery (MOLLI) sequence. Furthermore, we investigated the influence of ECV on invasively assessed hemodynamic parameters.

**Results:** The study cohort was prospectively followed for up to three years, during which 33 (30.6%) had a cardiac event (hospitalization and/or death for cardiac reason). Patients in the event group had higher NT-proBNP levels ( $p = 0.001$ ), shorter 6 minute walking distance ( $p = 0.014$ ), were more often in NYHA class III or IV and smoked more frequently ( $p = 0.010$ ). With regards to CMR data, ECV ( $p = 0.006$ ) and right ventricular end-diastolic volume (RVEDV) were higher in the event group. Among clinical parameters NT-proBNP ( $p = 0.001$ ), 6 minute walking distance ( $p = 0.004$ ), NYHA class III or IV ( $p = 0.005$ ) and smoking ( $p = 0.015$ ) were associated with adverse outcome by univariable Cox analysis. CMR parameters predictive of adverse outcome in univariable analysis were ECV ( $p = 0.003$ ), RVEDV ( $p = 0.017$ ) and left ventricular end-diastolic volume ( $p = 0.044$ ). By multivariable Cox analysis only NYHA class III or IV ( $p = 0.015$ ) and NT-proBNP ( $p = 0.026$ ) remained as predictors of outcome among clinical parameters. ECV ( $p = 0.039$ ) and RVEDV ( $p = 0.041$ ) were independent predictors of cardiac events among CMR parameters. ECV significantly correlated with clinical, CMR and hemodynamic parameters: 6MWD ( $R = -0.272$ ,  $p = 0.006$ ), NYHA class ( $R = 0.220$ ,  $p = 0.023$ ), NT-proBNP ( $R = 0.362$ ,  $p < 0.001$ ), right atrial volume ( $P = 0.299$ ,  $p = 0.002$ ), mean right atrial pressure ( $P = 0.246$ ,  $p = 0.020$ ), SvO<sub>2</sub> ( $P = -0.241$ ,  $p = 0.023$ ) and stroke index ( $P = -0.234$ ,  $p = 0.030$ ).

**Conclusions:** CMR-ECV independently predicts outcome in HFpEF and is correlated with severity of symptoms as well as exercise capacity. Reduction of ECV may therefore be a promising therapeutic target.



Kaplan Meier Curves for ECV

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**Comparison between global strain of right ventricle by 2-D speckle tracking (RVGS) and longitudinal strain of free lateral wall (RV-fwLS) in predicting prognosis in chronic heart failure patients.**

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**Background:** The assessment of right ventricular (RV) function still remains a challenge. Two-dimensional (2-D) speckle tracking has recently been proposed in order to evaluate right ventricular systolic function by analysing myocardial deformation. However, it is not clear if the analysis of RV systolic strain should be limited to RV lateral wall or if it should include septum. The aim of this study was to evaluate the role of two different RV strain measures obtained by 2-D speckle tracking analysis in predicting mortality in a group of patients affected by chronic heart failure (CHF).

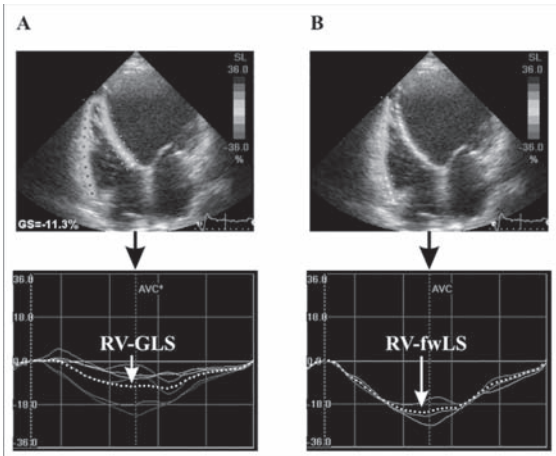
**Methods:** We enrolled 332 outpatients (76% males, 64 ± 14 years, NYHA class 2.2 ± 0.7, left ventricular ejection fraction, LVEF, 33 ± 9%) with CHF (ESC criteria), in stable clinical conditions (> 1 month) and in conventional therapy (86% ACE-inhibitors and/or ARBs, 94% betablockers). By echocardiogram (Echo-PAC, GE) a 4-chamber view (frame rate 50-70/sec) was obtained in order to evaluate by 2-D speckle tracking global strain of right ventricle by 2-D speckle tracking (RVGS) and the longitudinal strain of free lateral wall (RV-fwLS). Figure shows in panel "a" the assessment of RV-GLS; in panel "b" the assessment of RV free wall longitudinal strain (RV-fwLS).

**Results:** During follow-up (36 ± 26 months), 72 patients died (62 for cardiovascular causes and 10 for non cardiovascular causes). Thirteen patients underwent heart transplantation. As shown in the table, at univariate analysis both RV-GLS and RV-fwLS were associated with all cause mortality, but RV-GLS showed a slight greater value of C-index. At multivariate Cox regression analysis, both RV-GLS and RV-fwLS remained associated with events in a model including age, NYHA class, LVEF. AUC of ROC curve for the 12 months occurrence of death of RV-GLS (0.81; 95%CI: 0.72-0.91) was greater than that of RV-fwLS (0.75; 95%CI: 0.65-0.85), but the difference was not statistically significant (p: 0.088).

**Conclusions:** Our findings demonstrate that RV-fwLS and RV-GLS can be similarly used in order to stratify patients' prognosis, although RV-GLS seems to have a slight greater prognostic power. These data strengthen the clinical usefulness of this echocardiographic approach in daily management of CHF outpatients.

Variable	Univariate analysis		Multivariate analysis*			
	HR(95%CI)	p	C-index	HR (95%CI)	p	C-index
RV-GLS	1.20 (1.14-1.27)	<0.001	0.73	1.10 (1.03-1.19)	0.005	0.86
RV-fwLS	1.12 (1.07-1.16)	<0.001	0.70	1.06 (1.02-1.11)	0.005	0.86

\*Multivariate models included separately right ventricular systolic function parameters due to collinearity.



Figure

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**Tissue doppler indexes of diastolic function predict outcome in primary care outpatients**

No sources of financial support

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**Background:** Diastolic dysfunction (DD) provides prognostic information in the general population and has been associated with development of heart failure (HF), increased all-cause and cardiovascular mortality and reduced quality of life. The prognostic relevance of DD detected by Doppler echocardiography in asymptomatic individuals with normal left ventricular (LV) ejection fraction in primary care is unresolved.

**Purpose:** To explore if DD portends independent prognostic information in asymptomatic patients (pt) without normal LV function, in an outpatient clinic.

**Methods:** We performed a retrospective study of clinical and echocardiographic records of pt referred to the Cardiovascular Center of Trieste, between November 2009 and October 2014. Inclusion criteria were age >50 years, sinus rhythm, absence of previous HF, LV ejection fraction ≥50%, no atrial fibrillation or pacemaker, no significant valvular heart disease or prosthesis. The endpoint (EP) was a composite of all-cause mortality and hospital admission for cardiovascular (CV) causes. Diastolic function was assessed by analyzing DTI-derived indices, namely E/e' and e', divided in tertiles estimated in our population. Multivariable Cox regression was applied to evaluate predictors of outcome and Kaplan Meier survival curves were estimated; the Net Reclassification Index (NRI) and the median improvement in risk score for censored data were also computed when adding e' tertiles to standard predictors.

**Results:** 2628pt were included. 52.8% were male, median age 71 years (IQR 63-77), 71% with hypertension, 27% with diabetes, 33% with coronary artery disease and 16% with stroke/TIA. E/e' was ≤8.33 in 35%, 8.34-11.33 in 32%, >11.33 in 33%; e' was ≤6cm/s in 40%, 6.01-8 cm/s in 33%, >8cm/s in 27%. During 26 ± 17months the EP occurred in 392pt: 114(4.3%) deaths and 304(12%) CV hospitalizations. E/e' showed a correlation with EP, from 11.6% in E/e' ≤8.33 to 15.3% in 8.34-11.33 and 18% in E/e' >11.33 (Log rank p < 0.02 vs E/e' ≤8.33). The event free survival at 36 months in the E/e' tertiles were 87% vs 82% vs 78%. E' was related to an increased risk of the EP, ranging from 9.7% in e' ≥8 cm/s, 14% in 6.01-8 cm/s and 19,1% in e' ≤6 cm/s (Log rank p < 0.01 for all contrasts). The event free survival in the e' tertiles were 88% vs 84% vs 77%. After adjustment for clinical and echocardiographic confounders, only e' remained an independent predictor of EP (HR 0.68, 95% CI 0.49-0.94, p = 0.02), while E/e' was no longer significant. A borderline significant value of NRI was found, taking into account the events within 36 months from the visit ('average' NRI = 0.10, 95% CI 0.002-0.203, p = 0.053) and a significant median improvement in the risk score was also observed (0.007, 95% CI 0.001-0.014, p = 0.013).

**Conclusions:** In a large outpatient population without HF, different e' tertiles significantly predict the EP, adjunctively to clinical, therapeutic and echocardiographic variables.

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**Atrial strain analysis and quality of life of heart failure patients**

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<sup>1</sup>University of Siena, Department of Cardiovascular Diseases, Siena, Italy

**Background:** One of the most important keypoint in the analysis of the patients with heart failure is the relationship between instrumental data and quality of life. The Minnesota Living with Heart Failure Questionnaire (MLHFQ) is a disease-specific measure of health-related quality of life. The aim of this study was to evaluate the relationship between noninvasive LV and LA analysis and MLHFQ score in patients with HF and reduced ejection fraction.

**Methods:** 235 consecutive ambulatory heart failure patients with reduced LV ejection fraction (<50%) were studied. Patients underwent clinical and echocardiographic examination, both standard transthoracic echocardiography (TTE) and speckle tracking echocardiography (STE) and were asked to perform the MLHFQ. Results Patients were in NYHA Class I (24%), NYHA class II (45%) and NYHA class III (31%). The mean LV ejection fraction was (41.5 ± 9.8%). Strong correlations were obtained between global LA strain and MLHF Score (r = -0.83 p < 0.0001) and NYHA Class (r = -0.74 p < 0.0001). Poorer correlations were found between MLHF Score and LV ejection fraction (r = -0.31; p = 0.05), LV global longitudinal strain (r = -0.28; P = ns). Not significant correlation with MLHF score was found for LA indexed volume (r = 0.19; P = ns) and E/E' ratio (r = 0.09 P = ns). In multivariate analysis, global LA strain emerged as a determinant of MLHF Score, independent on other confounding factors.

**Conclusions:** LA function analysis by STE appears to be a mirror of patients symptoms and quality of life in patients with heart failure and reduced LV ejection fraction.

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**Prognostic value of left atrial structure and function in patients with heart failure. A report from SICA-HF study (FP7/2007-2013/ 241558)**

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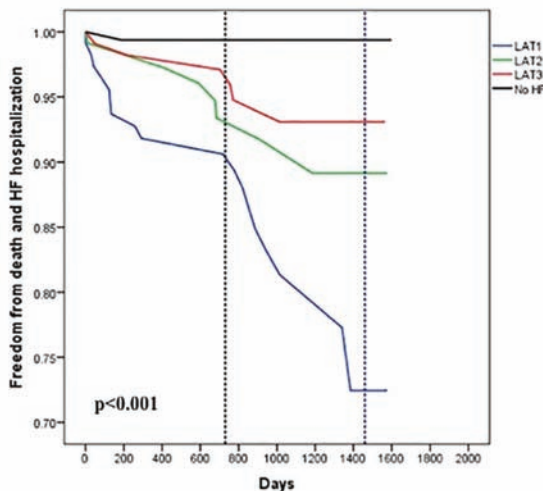
<sup>1</sup>Sapienza University of Rome, Department of Cardiovascular, Respiratory, Nephrological, Anesthesiological, and Geriatric Sciences, Rome, Italy; <sup>2</sup>Castle Hill Hospital, Department of Academic Cardiology, Hull, United Kingdom; <sup>3</sup>Imperial College London, National Heart and Lung Institute, London, United Kingdom

**Background:** Left atrial (LA) dilatation is an established marker of adverse outcome in patients with heart failure (HF), but the prognostic utility of left atrial function assessed by transthoracic echocardiography is still unclear.

**Methods:** Ambulatory patients with HF and control subjects enrolled in the SICA-HF study were assessed if they were in sinus rhythm. Left atrial emptying function (LAEF) was measured as [(maximal LA volume–minimum LA volume)/maximal LA volume] \*100.

**Results:** Of 500 patients, 341 fulfilled the criteria for HF; 49% had left ventricular ejection fraction (LVEF) <40% and 51% had LVEF >40%. Compared to controls, patients with HF were younger (69 ± 11 vs 71 ± 9 years, p=0.04) and had lower LAEF (50 ± 14% vs 62 ± 11%, p < 0.01). Compared to patients in the higher tertiles of LAEF, those in the lowest tertile (worst LAEF) had more severe symptoms, higher jugular venous pressure, higher plasma NTproBNP (1100 (410-2838) vs 452 (214-1192) and 444 (211-907)ng/L, respectively, p < 0.001) and lower LVEF (39 ± 14 vs 43 ± 11 vs 44 ± 12% respectively, p=0.02). Log[LAEF] and log[NTproBNP] were inversely correlated (r -0.33, p < 0.001). During a median follow-up of 943 (IQR 604-1229) days, 84 patients (25%) with HF died or were hospitalised for HF. LA structure and function were associated with this outcome in univariable analysis. However, only worse symptoms and increasing age, NTproBNP and inferior vena cava diameter independently predicted adverse prognosis.

**Conclusions:** In ambulatory patients with HF and in sinus rhythm, LAEF measured by echocardiography is associated with an adverse outcome but in multivariable analyses adds little prognostic information to biochemical or other echocardiographic measures of congestion.



Kaplan-Meier curves for primary EP

characteristics of patients

	No definite evidence of HF (159)	Evidence of HF (341)	p value	LAEF4C tertile 1 (114)	LAEF4C tertile 2 (114)	LAEF4C tertile 3 (113)	p value
LAEF4C - %	62 ± 11	50 ± 14	<0.001	34 ± 8	51 ± 3	64 ± 6	NA
Max LAV 4ch - ml	48 (38-62)	63 (46-81)	<0.001	74 (56-93)	62 (47-86)	57 (36-88)	<0.001
LVEF - %	60 ± 6	42 ± 13	<0.001	39 ± 14	43 ± 11	44 ± 12	0.02
NTproBNP - ng/L	108 (47-200)	567 (256-1362)	<0.001	1100 (410-2838)	452 (214-1192)	444 (211-907)	<0.001
IHD - no. (%)	17 (11)	236 (69)	<0.001	86 (75)	74 (66)	76 (66)	0.21
Age - years	71 ± 9	69 ± 11	0.04	71 ± 11	69 ± 11	68 ± 10	0.14
Sex - no. male (%)	82 (53)	256 (76)	<0.001	85 (75)	87 (77)	84 (74)	0.84
Furosemide ≥ 40mg/die	7 (4)	163 (48)	<0.001	66 (58)	51 (45)	46 (41)	0.02

Abbreviations: HF: Heart Failure; LAEF: Left Atrial Ejection Fraction; LAV - Left Atrial Volume; LVEF - Left Ventricular Ejection Fraction; NT-proBNP - N-terminal B-type natriuretic peptide; IHD - Ischemic Heart Disease.

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**Diffuse myocardial fibrosis of non-infarcted myocardium correlate with biomarkers of cardiac stretch and remodeling in patients with heart failure**

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**Purpose:** Biomarkers are commonly used in heart failure (HF) for risk stratification but it has been debated if they reflect cardiac remodeling. Myocardial fibrosis plays a role in (pathological) cardiac remodeling, and can be assessed by cardiac magnetic resonance imaging (MRI). We examined whether circulating biomarkers are associated with MRI-assessed myocardial fibrosis, i.e either to myocardial scarring (measured by late gadolinium enhancement, LGE) and/or diffuse myocardial fibrosis (measured by T1 time).

**Methods:** In a tertiary referral academic hospital, we routinely measured galectin-3 (whenever NT-proBNP was assessed) and included patients in this study if they also underwent a cardiac MRI with administration of gadolinium (n = 129). All MRI studies were performed on a 1.5-T scanner. Focal myocardial scar, usually a myocardial infarction, was assessed by LGE. Subsequently, diffuse ("interstitial") myocardial fibrosis of the non-infarcted myocardium was quantified by the myocardial post-contrast T1 time, using a cine Look-Locker sequence. Patients were categorized based on the presence or absence of LGE, and by the median of the post-contrast T1 time (shorter T1 times reflect increased interstitial fibrosis).

**Results:** Mean age of the 129 patients was 58 (± 14) years, 55% of the patients were male, and mean LVEF was 37% (± 14). NT-proBNP levels were higher in the LGE positive patients compared to the LGE negative patients (1155pg/mL vs. 484pg/mL p=0.007), whereas LVEF was not (34% vs. 37% p=0.62). In the LGE positive patients (n=52) both NT-proBNP and galectin-3 were significantly higher in subjects with short T1-time, when compared to patients with long T1-time, reflecting the presence of diffuse myocardial fibrosis (NT-proBNP: 1186pg/mL vs. 469pg/mL p=0.026; galectin-3: 20ng/mL vs. 15ng/mL p=0.004). On the other hand, in the LGE negative patients (n=77), no relations between NT-proBNP, galectin-3 and T1 time were observed, which could implicate that these biomarkers reflect active remodeling of the non-infarcted tissue of patients with a scar.

**Conclusion:** In HF patients with an old myocardial infarction and a scar on MRI, significantly elevated NT-proBNP and galectin-3, markers of cardiac stretch and remodeling, are observed in those who have diffuse myocardial fibrosis of the non-infarcted myocardium, suggesting ongoing adverse pathological remodeling.

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**Utility of cardiovascular magnetic resonance imaging in heart failure with preserved ejection fraction for diagnostic and prognostic evaluation**

NIHR Comprehensive Local Research Network and the NIHR Leicester Cardiovascular Biomedical Research Unit.

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**Background:** Heart failure with preserved ejection fraction (HFPEF) is poorly characterised, confers poor prognosis and definitive therapies are lacking. Transthoracic echocardiography (TTE) currently remains the primary imaging choice in HFPEF. Purpose We aimed to evaluate the diagnostic and prognostic utility of cardiovascular magnetic resonance imaging (CMR) in HFPEF.

**Methods:** Patients were recruited as part of Developing Imaging And plasma biomarkers in Describing-HFPEF (DIAMOND-HFPEF): a prospective, single-centre study. Inclusion criteria were: clinical or radiographic evidence of heart failure (HF)



and ejection fraction >50% on TTE. Exclusion criteria were: myocardial infarction (MI) in the preceding 6 months, suspected or confirmed cardiomyopathy, constrictive pericarditis, non-cardiovascular life expectancy <6 months and severe valve/ lung/ renal disease. The CMR protocol comprised cine, adenosine stress/rest perfusion and late gadolinium enhancement imaging on a 3-Tesla scanner. Both TTE & CMR were performed during the index study visit and reported independently. Follow-up outcome data was collected at a minimum of 6 months post-enrollment for the composite endpoint (death and/or re-hospitalisation with HF). Results 154 patients (mean age  $72.4 \pm 10.0$  years, 51% Male) underwent both CMR and TTE. The following previously unknown diagnoses were identified by CMR: significant coronary artery disease (n=20, including 14 with 'silent' MI), hypertrophic cardiomyopathy (n=10) and constrictive pericarditis (n=5). During follow-up (median = 623 days, interquartile range 455 – 753), there were 53 primary outcome events. Kaplan-Meier survival analysis (see Figure 1) revealed worse outcomes in the 'new diagnoses group' (Log Rank test  $p = 0.046$ ). In a multivariate Cox Regression model comprising significant independent predictors during univariate analysis (diastolic blood pressure, NHYA class, urea and log BNP), only the 'new diagnoses group' (hazard ratio [HR]: 1.999; 95% confidence interval [CI]: 1.078 to 3.709;  $p = 0.028$ ) and urea (HR: 1.068; CI: 1.000 to 1.141;  $p = 0.049$ ) were significant predictors of outcomes.

**Conclusions:** In HFPEF, CMR identifies previously unknown pathologies in a significant proportion. This group of 'new diagnoses' is associated with worse outcomes and is an independent predictor of death and/or re-hospitalisation with HF.

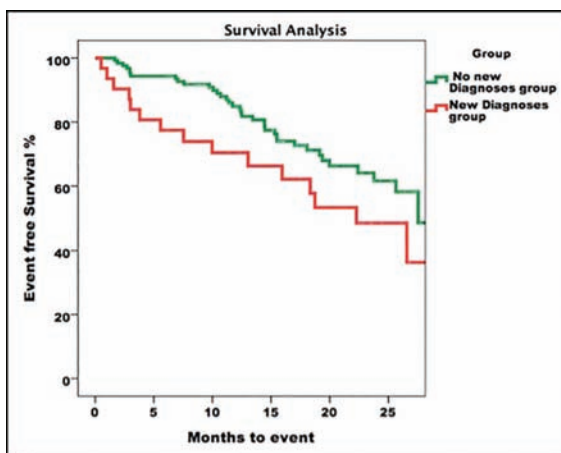


Figure 1: Survival analysis

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#### Right ventricular dysfunction in heart failure with preserved versus reduced ejection fraction

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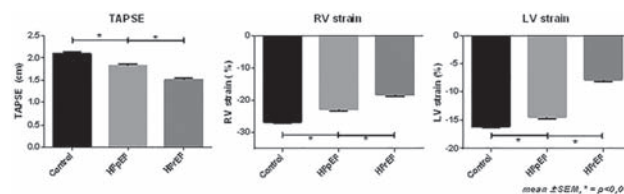
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**Background:** Right ventricular (RV) dysfunction is recognized as a major pathophysiological factor in heart failure (HF). However, the relative contribution of RV dysfunction in preserved versus reduced ejection fraction HF (HFpEF vs HFrEF) is unclear.

**Methods:** Echocardiographic speckle tracking was used to determine global longitudinal RV strain, along with tricuspid annular plane systolic excursion (TAPSE) in HFpEF (EF ≥ 50%; n = 219), HFrEF (EF < 50%; n = 219) and controls without HF (n = 219), all recruited in a prospective longitudinal population-based study and followed for the composite outcome all-cause death and HF hospitalization (174 events over a median of 2 years).

**Results:** Across groups from controls to HFpEF to HFrEF, both RV strain and TAPSE decreased (figure; all  $p < 0.001$ ). LV strain similarly decreased across groups. These differences remained significant after adjusting for clinical covariates, E/e' ratio, LVEF, pulmonary artery systolic pressure (PASP) and NT-proBNP ( $p < 0.001$ ). With increasing PASP, TAPSE, and to a lesser extent RV strain, increased in controls and HFpEF, but decreased in HFrEF. In patients with HF, TAPSE, but not RV strain, was related to outcomes ( $p = 0.018$ ), regardless of HF group (Pinteraction = 0.488), and even after multivariable adjustment (adjusted  $p = 0.035$ ).

**Conclusion:** RV dysfunction parallels LV dysfunction in HFpEF and HFrEF, suggesting a concomitant myocardial process involving both ventricles. Right-sided arterioventricular coupling is preserved in HFpEF but reduced in HFrEF. The potent impact of TAPSE on outcomes, independent of LV dysfunction, suggests that RV dysfunction may be a pathophysiologic target in HF regardless of EF.



TAPSE, RV strain and LV strain

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#### Congenitally Unguarded Tricuspid Orifice Presenting as Heart Failure in Adults

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**Background:** Congenitally unguarded tricuspid orifice (CUTO) with patent right ventricular outflow, a rare form of extreme tricuspid valve dysplasia, is reported in fetuses and in neonates. Very few survive to adulthood. However CUTO is not so rare in adult life and several patients survive to middle age and present with right heart failure, atrial fibrillation or portal hypertension secondary to cardiac cirrhosis. Such cases need to be differentiated from unguarded tricuspid orifice caused by carcinoid disease, infective endocarditis and traumatic tricuspid regurgitation. Purpose. The purpose of this study is to report demographics of CUTO in adult life, their clinical and echocardiographic features, management and follow-up.

**Methods:** Echocardiography enables accurate evaluation of the morphology and function of valve leaflets, chordae tendineae, and papillary muscle. CUTO has been defined as severe low-pressure tricuspid regurgitation due to a large regurgitant orifice secondary to absent or rudimentary tricuspid valve leaflets and subvalvar apparatus. This report describes 18 adult patients of CUTO observed over year 2000-2015, their clinical and echocardiographic features, management and follow-up.

**Results:** Over a period of 15 years, 18 adult patients (age 18-57 years, 6 females) met the criteria of an unguarded tricuspid valve. All presented with right heart failure of variable duration with massively dilated right ventricular outflow tract, dilated and severely hypokinetic right ventricle and right atrium without evidence of infective endocarditis, carcinoid disease or trauma. Atrial fibrillation was present in five and two patients had right atrial thrombi. Two patients underwent tricuspid valve replacement and three underwent Fontan operation. None showed any improvement in symptoms.

**Conclusion:** Dysplasia of the tricuspid valve is probably the most common cause of isolated tricuspid regurgitation and the unguarded tricuspid orifice is its most extreme form. Because of the poor right ventricular contractile function, the pulmonary circulation is maintained by the pumping action of the right atrium or the outflow tract. Some such patients survive into adulthood, present with refractory right heart failure and present therapeutic dilemma.

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#### Clinical predictors and prognostic significance of right ventricular dysfunction in systolic heart failure

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**Background:** Right ventricular (RV) dysfunction is an acknowledged determinant of clinical deterioration and worse prognosis in systolic heart failure (HF). Little is known about clinical and neurohormonal features of this subgroup of patients. Aim of this study was then the clinical, neurohormonal and prognostic evaluation of HF patients with RV dysfunction.

**Methods:** the study evaluated patients with systolic HF (left ventricular ejection fraction [LVEF] < 50%) on guideline directed medical therapy. All patients received a comprehensive clinical evaluation, including assessment of plasma renin activity (PRA), aldosterone, N-terminal pro-brain natriuretic peptides (NT-proBNP) and norepinephrine. All patients underwent transthoracic echocardiography; only patients with a comprehensive RV morphology and function (with evaluation of tricuspid annular plane systolic excursion [TAPSE], Doppler tissue imaging [DTI] of tricuspid

lateral annular systolic velocity [S'] were included. RV dysfunction was defined as TAPSE <17 mm or S' <9.5 cm/sec. Follow-up evaluated cardiac mortality as endpoint.

**Results:** three-hundred and fifty patients met inclusion criteria (LVEF  $34 \pm 9\%$ , mean  $\pm$  SD, age  $66 \pm 13$  years, NYHA class III-IV 29%, beta-blockers 96%, angiotensin converting enzyme inhibitors [ACEI] or angiotensin receptor blockers [ARB] 92%, mineralocorticoid receptor antagonists 71%; 7% implantable cardioverter defibrillator [ICD], 18% resynchronization therapy with ICD). RV dimension was  $28 \pm 4$  mm (parasternal long axis view); mean TAPSE was  $19 \pm 5$  mm, S'  $11 \pm 3$  cm/sec, pulmonary artery systolic pressure (PAPs)  $40 \pm 11$  mmHg. RV dysfunction was present in 95 patients (27%; TAPSE  $11 \pm 3$  mm, S'  $7.6 \pm 1.1$  cm/sec, RV diameter  $29 \pm 5$ , PAPs  $41 \pm 12$  mmHg). They were older ( $69 \pm 12$  vs  $66 \pm 13$  years,  $p < 0.05$ ) and less frequently in ACEi/ARB therapy (96% vs 86%,  $p < 0.05$ ); they had worse LV dysfunction (LVEF  $31 \pm 9$  vs  $35 \pm 9$ ,  $p < 0.05$ ), increased LV end-diastolic pressure (E-wave/e' wave ratio at DTI  $16 \pm 7$  vs.  $13 \pm 6$ ,  $p < 0.05$ ) and left atrial volumes ( $43 \pm 12$  ml vs.  $38 \pm 12$  ml,  $p < 0.05$ ), increased neurohormonal activation: NT-proBNP: median 2202 ng/L, interquartile range 1082-5362 vs. 956 ng/L, 347-2341,  $p < 0.01$ , PRA: 0.8 ng/ml/h, 0.2-2.3 vs. 0.5 ng/ml/h, 0.2-1.7,  $p < 0.05$ ; aldosterone: 134 ng/L, 69-200 vs. 99 ng/L, 52-175,  $p < 0.05$ . At follow-up (28 months, 13-41), 32 cardiac events (23 HF progression, 6 sudden cardiac deaths, 3 myocardial infarction) were recorder. At Kaplan-Meier analysis, RV dysfunction was associated with worse prognosis (log-Rank 6.5,  $p = 0.01$ ). At Cox regression analysis, PRA, NT-proBNP, E/e' and RV dysfunction were predictors of cardiac events. At paired multivariate analysis, RV dysfunction resulted independent predictor of cardiac events.

**Conclusions:** RV dysfunction occurs in a significant proportion of patients with systolic HF and is associated with neurohormonal activation (renin-angiotensin system and natriuretic peptides); its occurrence is also independently associated with worse prognosis.

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### Prognostic value of myocardial fibrosis assessed by cardiac magnetic resonance in patients with idiopathic dilated cardiomyopathy with left ventricular systolic dysfunction

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**Background:** The prognosis of patients (pts) suffering from idiopathic dilated cardiomyopathy (DCM) has improved significantly through the use of the current guidelines for the treatment of heart failure (HF); however in a high proportion of cases, mortality and morbidity remain high. The role of multiple prognostic indicators since the early stage of disease remains limited. The assessment of myocardial fibrosis by cardiac magnetic resonance (CMR) might allow the identification of patients with poor prognosis but its role is still debated.

**Purpose:** to evaluate the prognostic role of myocardial fibrosis assessed by CMR in patients with DCM and left ventricular systolic dysfunction.

**Methods:** We enrolled retrospectively pts suffering from DCM with left ventricular ejection fraction (LVEF)  $\leq 45\%$  underwent CMR with administration of paramagnetic contrast agent followed at our HF Department from January 2012 to December 2014. We evaluated demographic, laboratoristic, therapeutic and imaging parameters (presence of late gadolinium enhancement (LGE), as indicator of fibrosis, LVEF, right ventricular ejection fraction, ventricular volumes and myocardial mass). The composite endpoint was death from any cause and hospitalization for cardiovascular (CV) causes or HF.

**Results:** We enrolled 109 pts (68% male, mean age  $52 \pm 3$  years). 54 pts (49%) showed left ventricular LGE. The parameters that were predictive for the composite endpoint at univariate and multivariate analysis were evidenced in Table 1. At multivariate analysis, only the presence of LGE confirmed its prognostic value (HR 8,009; IC 95% 2,504–25,621;  $p = 0,0001$ ).

**Conclusions:** Myocardial fibrosis is an independent predictor of death and CV and HF hospitalization in pts affected by DCM and may allow early detection of pts at high risk of poor prognosis, needing more aggressive treatment and closer follow-up visits.

Table 1

Univariate	Multivariate		p value	p value
	EVENTS (38, 34%)	NO EVENTS (71, 66%)		
Atrial fibrillation, n (%)	14 (36)	12 (17)	0.01	0.1
Diabetes, n (%)	16 (42)	15 (21)	0.04	0.09
eGFR, ml/min/1.73m2	$62 \pm 26$	$73 \pm 32$	0.01	0.08
Serum Hemoglobin, g/dl	$12.7 \pm 1$	$13.2 \pm 1$	0.02	0.3
LGE, n (%)	33 (86)	21 (29)	< 0.0001	0.001
LVEF, %	$34 \pm 3$	$38 \pm 2$	0.0492	0.06

eGFR: Glomerular filtration rate, LGE: Late Gadolinium Enhancement, LVEF: Left Ventricular Ejection Fraction

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### Relationship between left ventricular myocardial longitudinal mechanics and in-hospital heart failure in patients with acute myocardial infarction: a two-dimensional speckle-tracking study

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<sup>3</sup>Pharmaceutical Science University of Mongolia, Ulaanbaatar, Mongolia;

<sup>4</sup>The State Third Central Hospital, Department of Angiography, Ulaanbaatar, Mongolia

**Background:** In-hospital heart failure during acute myocardial infarction is associated with adverse outcome. However, data about relationship between left ventricular longitudinal myocardial mechanics and in-hospital heart failure with normal left ventricular ejection fraction in patients with acute myocardial infarction is limited.

**Aim of study** In this study, we hypothesized that speckle-tracking derived global longitudinal strain parameter is independent associated with in-hospital heart failure.

**Material and methods:** We prospectively included patients who presented acute myocardial infarction and treated by primary PCI. In-hospital heart failure is defined by Killip class during admission. Multiple logistic regression analysis was used to reveal relationship between left ventricular global longitudinal strain and in-hospital heart failure. Separate multiple logistic regression model constructed for patients with preserved left ventricular ejection fraction (LVEF  $\geq 55\%$ ). The incremental value of global longitudinal strain was tested by assessment of model c-statistics.

**Results:** A total of 414 patients (mean age  $60 \pm 13$ , 84% male) were included and 93 patients (22.5%) presented in-hospital heart failure. Left ventricular global longitudinal strain (GLS) was significantly impaired in patients with in-hospital heart failure compared patients without in-hospital heart failure ( $-16.1 \pm 3.7$  vs.  $-11.6 \pm 3.1$ ,  $p < 0.001$ ). After adjustment of possible predictor of in-hospital heart failure such as age, clinical, biochemical and echocardiographic parameters, global longitudinal strain was independently associated with in-hospital heart failure (odds ratio 1.32, 95% CI 1.16-1.50,  $p < 0.001$ ). In-hospital heart failure presented in 21 patients with LVEF  $\geq 55\%$  and GLS is also significantly impaired in this group ( $-17.7 \pm 3.2$  vs.  $-12.7 \pm 2.2$ ,  $p < 0.001$ ). Separate multiple logistic regression model constructed for this group of patients and global longitudinal strain was still independently associated with in-hospital heart failure. Every 1 unit change of global longitudinal strain is associated with 1.4 fold increased probability of in-hospital heart failure (odds ratio 1.43, 95% CI, 1.31-1.55,  $p < 0.001$ ). Adding global longitudinal strain into model consisting age, clinical, biochemical and echocardiographic parameters associated with increased c-statistics (c-statistic 0.864, 95% CI 0.823-0.905 vs. c-statistic 0.839, 95% CI 0.793-0.885,  $p < 0.001$ ).

**Conclusion:** Left ventricular global longitudinal strain is independently associated with in-hospital heart failure during acute myocardial infarction. This relationship is still evident for group of patients who had preserved LVEF.

# POSTER SESSION 1

Saturday 21 May 2016 8:30–17:30

Location: Poster Area

## ACUTE HEART FAILURE

### P183

#### Systolic time intervals (STI) in acute heart failure(AHF) : comparison between patients with reduced and preserved left ventricular ejection fraction(LVEF)

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<sup>1</sup>fattouma bourguiba hospital, emergency department, monastir, Tunisia

**Introduction:** The distinction between AHF with reduced or preserved LVEF is essential to the early management of patients in the emergency department (ED).

**Objective:** To assess the discriminative value of STI measured by horacioimpedance (TBI) in patients admitted for AHF with and without reduced LVEF.

**Patients and methods:** Prospective study conducted from January 2012 to September 2015 including patients aged more than 18 years old and admitted to the ED for AHF. Reduced LVEF is defined as a LVEF <50 % measured by echocardiography. STI including pre-ejection period (PEP), LV ejection time (LVET) and PEP / LVET ratio are determined by TBI at admission in all included patients (n = 398). **Results:** Mean age 68 ± 14 years, sex ratio (M / F) 1.2 ; 62% of patients have a reduced LVEF. Comparison of patients with reduced and preserved LVEF is mentioned in the table. Area under the ROC curve for: PEP, LVET, PEP/LVET ratio were respectively: 0.66, 0.62, 0.7. **Conclusion:** Only PEP/LVET ratio could be considered as a meaningful non invasive method to help differentiating AHF patients with and without reduced LVEF in ED setting.

Mean (SD)	LVEF<50 n=248	LVEF≥50% n=150	p
PEP (seconds)	0.12 (0.01)	0.11 (0.02)	< 0.01
LVET(seconds)	0.27 (0.09)	0.28 (0.07)	< 0.01
PEP/LVET ratio	0.45 (0.1)	0.39 (0.14)	< 0.01

### P184

#### Diagnostic performance of lung ultrasound in the emergency department in the management of acute dyspnea

NIZAR Fredj<sup>1</sup>; KAOUTH Beltaief<sup>1</sup>; HBIB Grissa<sup>1</sup>; INES Elidi<sup>1</sup>; LASSAA Bouraoui<sup>1</sup>; ADEL Sekma<sup>1</sup>; HAMD I Boubaker<sup>1</sup>; WAHID Bouida<sup>1</sup>; SEMIR Noura<sup>1</sup>  
<sup>1</sup>fattouma bourguiba hospital, emergency department, monastir, Tunisia

**Objective:** To evaluate the performance of lung ultrasound (LUS) in the diagnosis of heart failure (HF) in patients with acute dyspnea.

**Methods:** Prospective observational study performed in the emergency department including all patients aged over 18 years admitted to the emergency department for acute non-traumatic dyspnea. The diagnosis of acute dyspnea of cardiac origin was based on clinical, laboratory (BNP), cardiac ultrasound and expert opinion. LUS was performed at admission and pulmonary congestion score (PC score) is calculated according to B-lines number (range 0 -80). A PC score > 15 defined the presence of HF.

**Results:** 78 patients were included in this study. Mean age 69 ± 11 years and sex ratio (M / F) 1.17; HF was demonstrated in 36 (46%) patients. The area under ROC curve of the PC score was 0.81 with sensitivity 91%, specificity 62%, positive predictive value 68% and negative predictive value 89%. **Conclusion:** In patients admitted to the emergency department for acute dyspnea, LUS was a valuable aid in ruling out HF.

### P185

#### Atrial fibrillation stroke and bleeding risk scores can also predict admissions for acute decompensated heart failure

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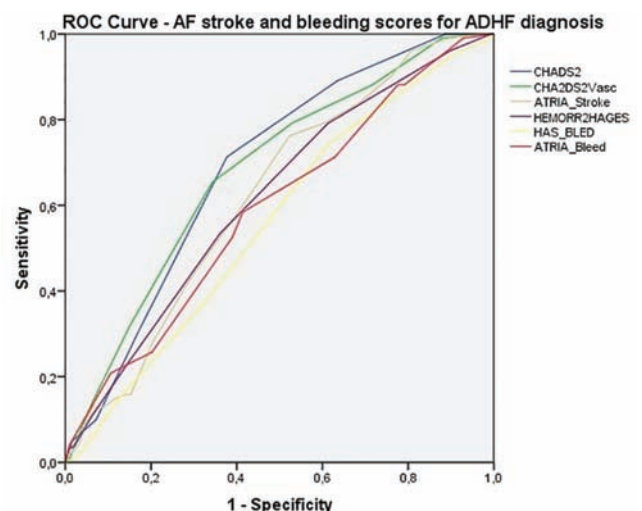
**Background:** Atrial fibrillation (AF) is a frequent comorbidity in patients with heart failure (HF). There are many tools for prediction of hospital readmission for acute decompensated heart failure (ADHF).

**Purpose:** We aimed to evaluate the diagnostic value of well-known AF stroke and bleeding risk scores in the prediction of hospital admissions due to ADHF.

**Methods:** 2181 consecutive patients with AF who were evaluated in our Emergency Department (ED) in a 12 month period were included retrospectively in our study. Among them, 423 patients were admitted for in-hospital management. All patients underwent routine clinical and laboratory exams. We evaluated medical charts in order to identify patients with ADHF and to calculate each score: AF stroke (CHADS2, CHA2DS2-VASc, ATRIA Stroke) and bleeding (HEMORR(2)HAGES, HAS-BLED, ATRIA Bleeding) risk scores.

**Results:** 101 patients were admitted with both AF and ADHF (mean age of 77.2 ± 9.6 years, 40.6% males). In receiver-operating characteristic (ROC) analyses (figure) CHADS2 score performed better than other scores in predicting ADHF (CHADS2 – c-index 0.688, p < 0.001; CHA2DS2-VASc – c-index 0.682, p < 0.001; ATRIA Stroke – c-index 0.624, p < 0.001; HEMORR(2)HAGES – c-index 0.617, p < 0.001; ATRIA Bleeding – c-index 0.591, p = 0.006; HAS-BLED – c-index 0.560, p = 0.067). A CHADS2 > 2 has a sensitivity of 71.3% and specificity of 62.3% (negative predictive value = 68.9%, positive predictive value = 65.7%) in prediction of ADHF.

**Conclusion:** CHADS2 proves an easy and simple tool with modest performance which can predict the risk of admission due to ADHF in patients with AF.





## P186

**Acute heart failure in the course of a suicide attempt by intoxication with *Taxus baccata* leaves.**

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**Background:** *Taxus* (yew) is one of the most frequently reported plants causing potentially fatal outcome when taken incidentally or for suicidal reasons. A fast and reliable method of detection of poisonous compounds or their metabolites is critical in life-saving procedures in cases of yew ingestion. Previously, several chromatographic analytical procedures have been described usually taking longer than one hour of total analysis time.

**Case presentation:** In this report we describe a suicide case study and an ad hoc developed fast method of detection and quantitation of 3,5-dimethoxyphenol – the main taxane metabolite in the blood plasma from the patient as well as the determination of major taxane components in the plant material (*Taxus baccata*). At present, there is no reasonable alternative for mass spectrometry that could match its high sensitivity and accuracy, and Multiple Reaction Monitoring could be adequate and useful mass spectrometry technique in analyzing and identification of plants material compounds that cause severe poisoning in humans. In the reported case, intensive cardiac care together with the astuteness of the treating physicians not only saved the patient's life, but also allowed for his complete recovery and return to work.

**Conclusion:** The developed of ultra fast liquid chromatography tandem mass spectrometry UFLC-MS/MS method provides a fast means to confirm yew alkaloids and their metabolite in various material. The applied analytical procedure allows early detection of main metabolite in patient material as well as comparing to those extracted from the plant. In our study, the taxanes remained undetected, probably due to the time elapsing from the patient admittance and collection of plasma. In cases like reported in this study, retaining the gastric material should be obligatory to confirm the ingestion of yew. The possibility of using this approach in detection of native taxane compounds in human plasma remains to be verified.

## P187

**Advanced peripheral endothelial dysfunction predicts future cardiovascular events in patients with acute decompensated heart failure**

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**Introduction:** Early post-discharge rehospitalization and mortality rates in patients with acute decompensated heart failure (ADHF) continue to be high. To achieve the better postdischarge outcomes in patients hospitalized for ADHF, optimizing treatments in the early post-discharge period will require the improvement of risk stratification and patient triage during the compensated condition of HF symptoms. Endothelial dysfunction plays an important role in the pathogenesis of HF. We previously reported that endothelial dysfunction could predict future cardiovascular events in patients with chronic HF with reduced or preserved ejection fraction. However, clinical significance of peripheral endothelial dysfunction in ADHF has not been determined.

**Purpose:** The purpose of this study was to investigate whether peripheral endothelial dysfunction could predict occurrence of future cardiovascular events in patients with ADHF.

**Methods:** We conducted a prospective cohort study of 95 patients with ADHF who were referred in a University Medical Center between July 2011 and November 2013 (age: 71 ± 11 years, male: 60%, left ventricular ejection fraction (LVEF): 38 ± 16%). We non-invasively assessed peripheral endothelial function by reactive hyperemia peripheral arterial tonometry (RH-PAT) as RH-PAT index (RHI) in patients with ADHF. ADHF patients were followed until January 2015 or an endpoint occurred. The endpoint was a composite of cardiovascular death, nonfatal myocardial infarction, or HF re-hospitalization)

**Results:** A total of 40 patients had a cardiovascular event (median follow-up period: 16 months). Kaplan-Meier analysis demonstrated a significantly higher probability of cardiovascular events in the low-RHI group than in the high-RHI group (a cut-off value 0.46, median, log-rank test, P = 0.05). Multivariate Cox hazard analysis including LVEF and B-type natriuretic peptide levels on admission identified RHI (hazard ratio 0.40, 95%-confidence interval 0.18-0.89, P = 0.03) and serum creatinine levels (hazard ratio 2.46, 95%-confidence interval 1.64-3.68, P < 0.001) as independent predictors of the future cardiovascular events.

**Conclusions:** Peripheral endothelial dysfunction independently correlated with the future cardiovascular events, adding incremental clinical significance for risk stratification in patients with ADHF.

## P188

**Acute heart failure admissions should a plasma NT-proBNP of 300ng/litre or 400ng/litre be the threshold for ruling out the diagnosis of heart failure**

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**Background:** The recently published National Institute of Clinical Excellence (NICE) guidelines on the management of acute heart failure recommended using a plasma NT-proBNP threshold of 300ng/litre to assist in ruling out the diagnosis of heart failure, updating previous guidelines recommending using a threshold of 400ng/litre.

**Purpose:** We reviewed all the plasma NT-proBNP results in our institution over one year to see how many additional patients with heart failure presented with plasma NT-proBNP 300-399ng/litre. In our hospital all patients presenting with possible heart failure undergo NT –proBNP testing. Those with results above 400ng/l automatically receive an echocardiogram with a dedicated heart failure sonographer, if no study has been done within 6 months, and a heart failure consultant review.

**Methods:** All consecutive patients who had plasma NTpro-BNP requested between 10/09/2014 and 09/09/2015 were included. Hospital databases and records were used to identify diagnoses, length of stay and inpatient mortality. Outpatient mortality was confirmed using Summary Care Records (follow up range 4 to 16 months). Data was collected as part of our Institution's approved Clinical Audit.

**Results:** In total, 2135 patients had plasma NTpro-BNP tested between 10/09/2014 and 09/09/2015. 1791 patients had NT-proBNP over 400ng/litre compared to 344 patients with plasma NTpro-BNP under 400 ng/litre, of which 71 patients had results 300-399 ng/litre (3.3%). Two patients represented during the year, and so 69 patients were identified with NT-proBNP 300-399ng/litre.

Of these 69 patients, 4 patients had Heart Failure with preserved ejection fraction (HFpEF), two patients had left ventricular systolic dysfunction (LVSD) and one patient had Right Heart Failure (RHF). Three of these patients had previously been seen in cardiology outpatients and one of the patients with HFpEF had presented 6 months previously with known HFpEF. The average length of stay for the HFpEF patients was 5.5 days (SD 4.7), for the LVSD 13 days (SD 5) and right heart failure 6 days.

None of the patients with HFpEF, LVSD or RHF died. The overall inpatient mortality for patients with plasma NTpro-BNP 300-399ng/litre was 2.9% with outpatient mortality was 12.9%. This is compared to patients with plasma NTpro-BNP >400ng/litre, the inpatient mortality was 8.1% and the outpatient mortality was 25.3%

**Conclusions:** In our institution, lowering the plasma NTpro-BNP level from 400 to 300ng/litre would have identified 71 new patients compared to 2135 with levels of over 400. In these 71 patients we only identified three new patients with heart failure over the year (4 patients were already known to cardiology). This real world experience would suggest that the recent updated NICE guidelines to lower the plasma NT-proBNP threshold of 300ng/litre to rule out the diagnosis of heart failure will be relatively inefficient if applied on a large scale.

## P189

**Efficacy of levosimendan after PCI in patients with acute decompensated heart failure and low ejection fraction**

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**Background:** Treatment of patients with acute decompensated heart failure (ADHF) and low ejection fraction is still a field of research. In-hospital death is very high in this group of patients.

**Purpose:** To examine the efficacy PCI followed by 24 hour infusion of inotropic drug levosimendan in patients with very low left ventricle ejection fraction.

**Methods:** In our study 12 patients with ADHF and very low left ventricle ejection fraction (< 25%) were included. All patients were with documented coronary artery disease and myocardial infarction in the past. Coronary angiography with PCI was done for all patients and followed by 24 hour infusion of levosimendan. On admission and after 48 hours echocardiography and levels of NT-proBNP were examined.

**Results:** After 48 hours of treatment in 9 patients ejection fraction improved from 21+/-3.4 to 32+/-4.1% and level of NTproBNP decreased in 8 of these patients from 7643+/-1321 to 5265+/-1018 pg/ml, in one patient NT-proBNP was not changed. In the other 3 patients no any changes in ejection fraction or NT-proBNP were noticed, 2 of these patients died during hospital course. The other patients were discharged from hospital.

**Conclusion:** PCI followed by 24 hour infusion can be considered as effective strategy in patients with ADHF and very low ejection fraction. More studies are needed in this group of patients.

## P190

**Effectiveness and safety of ivabradin use in patients with acute ischemic heart failure (AIHF) requiring inotropic support**O Koval<sup>1</sup>; A Skoromna<sup>2</sup><sup>1</sup>Dnipropetrovsk State Medical Academy, Dnipropetrovsk, Ukraine; <sup>2</sup>Regional Clinical Center of Cardiology and Cardiac Surgery, Dnipropetrovsk, Ukraine

**Background:** Dobutamine (D) is the most used for inotropic support in AIHF, causes tachycardia that in turn results in decrease of its inotropic effect. Ivabradin (I) in addition to suppression of tachycardia ameliorates calcium metabolism in sarcoplasmic reticulum. Albeit such combination therapy seems to be pathophysiologically relevant, the data are very scarce, and in majority of cases include concomitant therapy with beta-blockers (BB). Aim was to assess the effectiveness and safety of simultaneous use of D and I in patients with AIHF requiring inotropic support.

**Material and methods:** 20 pts admitted at Dnipropetrovsk regional emergency centre with acute myocardial infarction (MI) and experienced AIHF with sinus rhythm, arterial hypotension (Killip II-III, mean  $2.7 \pm 0.1$ ) requiring inotropic support during first 24 hrs after admission, despite previous therapy by BB in anamnesis (interrupted at admission in 35%). Pts having cardiogenic shock, ventricular tachycardia/fibrillation (VT/VF), atrial fibrillation (AF), and known severe concomitant pathology were excluded. Investigation was approved by local ethic committee. All patients received standard therapy without reperfusion because of late admission (after 12 hrs, no access to primary PCI) and were subdivided into 2 subgroups: standard therapy with inotropic support (S) – 11 pts and additional ivabradin (I) use: 5 mg/bid with increase dose to 7.5 mg/bid if required (4 pts). Both groups were comparable for gender, age, anterior MI, arterial hypertension, diabetes, prior MI, HF and smoking, initial hemodynamic indexes (APs  $114.0 \pm 12.8$  (S);  $98.9 \pm 11.8$  (I) mmHg); heart rate:  $95.6 \pm 12.7$  (S)  $98.9 \pm 11.8$  b/min (I) and EF  $34.5 \pm 5.7\%$  (S)  $35.6 \pm 6.2\%$  (I). BB therapy renovated/prescribed after 48 hrs after stabilization and up titrated if required without decrease of I dose.

**Results:** Heart rate reliably was lower in I group after D infusion despite dose regimen:  $5 \mu\text{g/kg/min}$  ( $106.8 \pm 15.6$  (S)  $89.8 \pm 10.8$  b/min (I);  $p = 0.05$ );  $10 \mu\text{g/kg/min}$ :  $108.7 \pm 16.7$  (S)  $84.5 \pm 12.6$  b/min (I);  $p = 0.024$ );  $15 \mu\text{g/kg/min}$ :  $115 \pm 14.5$  (S)  $85.5 \pm 10.7$  b/min (I);  $p = 0.0047$ ). There were no bradycardia episodes in I group, less VT/VF (3, one fatal in S group; 1 – nonfatal in I group with  $15 \mu\text{g/kg/min}$  D dose). The difference in heart rate frequency remain significant at 7 days despite latter BB inclusion ( $78.1 \pm 7.5$  (S)  $66.4 \pm 8.2$  b/min (I);  $p = 0.05$ ) and disappeared at discharge ( $65.4 \pm 8.1$  (S)  $63.5 \pm 6.7$  b/min (I) group). In both groups there was death, 3 subacute LV aneurysm formation and 7 huge hypokinetic zones in S group, and no aneurysm formation and 5 hypokinetic zones in I group.

**Conclusions:** In patients with MI and AIHF with sinus rhythm requiring inotropic support with D simultaneous therapy with Ivabradin is safe and effective as for suppression of unwanted tachycardia and for trend of better clinical outcome. In pts, who received I therapy in AIHF period its further constant preservation is recommended.

## P191

**Ivabradine use in acute heart failure: safety and efficacy**I Ilaria Battistoni<sup>1</sup>; M Marini<sup>1</sup>; L Angelini<sup>1</sup>; MV Matassini<sup>1</sup>; M Francioni<sup>1</sup>; A Gili<sup>1</sup>; S Moretti<sup>1</sup>; GP Perna<sup>1</sup><sup>1</sup>University Hospital Riuniti, G.M.Lancisi Hospital, Department of Cardiology, Ancona, Italy

**Background:** Despite novel therapies, acute heart failure syndromes (AHFS) with cardiogenic shock (CS) are characterized by poor prognosis. Tachycardia, early compensatory mechanism, in long term increase myocardial oxygen demand, reduce diastolic coronary perfusion, further impairing cardiac performance.

**Purpose:** to assess clinical and hemodynamic effects of ivabradine in AHFS/CS patients on top of therapy.

**Methods:** 19 patients (14 M,  $61 \pm 12$  years) with AHFS (53%) and CS (47%), severe LV dysfunction (LVEF  $25 \pm 6\%$ ), requiring inotropic and vasopressor drugs, were treated with Ivabradine 5 mg bid and monitored through clinical and non-invasive echocardiographic hemodynamic evaluation at 24, 48, 72, 120 hours.

**Results:** Ivabradine administration was associated with reduction in HR (from baseline  $103 \pm 14$  to  $77 \pm 11$  bpm at 120h,  $p = .04$ ) without negative effects on mean blood pressure (from  $68 \pm 13$  to  $70 \pm 7$  mmHg at 120h,  $p = \text{ns}$ ). Cardiac index increased (from  $1.8 \pm 0.2$  to  $2.2 \pm 0.5$  l/min/mq at 120h,  $p < .001$ ) as stroke volume index (from  $20 \pm 4$  to  $30 \pm 9$  ml  $p < .001$ ), cardiac stroke index (from  $18 \pm 9$  to  $28 \pm 14$  g/m<sup>2</sup> at 120h,  $p = .002$ ) and LVEF (from  $25 \pm 6$  to  $30 \pm 9\%$  at 120h,  $p < .001$ ). No serious side effects ivabradine-related occurred.

**Conclusions:** Ivabradine administration in AHFS/CS patients is safe and effective leading to assume a future promising use in acute ill patients.

## P192

**High incidence of anxiety and depression in in-hospital acute heart failure patients**L Surdi<sup>1</sup>; MC Murru<sup>1</sup>; O Bettinardi<sup>2</sup>; U Corvi<sup>1</sup>; A Verde<sup>1</sup>; S Binno<sup>1</sup>; GQ Villani<sup>1</sup>; M F Massimo Francesco Piepoli<sup>1</sup><sup>1</sup>Guglielmo Da Saliceto Hospital, Department of Cardiology, Piacenza, Italy;<sup>2</sup>Guglielmo Da Saliceto Hospital, Piacenza, Italy

**Introduction:** After acute heart failure event, depression has been estimated to have an incidence of around 20%, to increase significantly the risk of cardiac death, hospitalisation and recurrences and poor compliance to treatments. Therefore recent position papers recommend early screening of symptoms of depression to optimise medical therapy and improve secondary prevention. Aim of the study was to investigate the incidence of markers of anxiety and depression in in-hospital patients after acute heart failure events by an appropriate psychometric screening.

**Materials and method:** All consecutive patients admitted for acute cardiac events during the time interval of June-July 2012 were requested to fill in Questionnaire AD-R (2) for the evaluation of anxiety and depression. The study population included 254 consecutive patients (mean age  $62 \pm 12$  years, 77% male), hospitalised for heart failure secondary to acute coronary syndrome (60%), valve disease (11%), arrhythmic event (19%).

**Results:** The percentages of patients with score above the clinical cut-off were 41% for anxiety (STAI-X3) and 25% for depression (QD-R). The percentages of critical answers to questions "Life is worth living" and "Sometime I wish I were dead" were 2.5% e 8.5% respectively. The presence of anxiety and depression was associated with prolonged hospitalisation ( $11 \pm 3$  days vs  $9 \pm 3$  days), and early (1 month) hospital readmission (19% vs 15%) ( $P < 0.05$ ).

**Conclusions:** The results confirm the importance of the screening for anxiety and depression among heart failure patients and the need to develop adequate strategies of intervention and therapy.

## P193

**Nursing management of acute heart failure: applying the GRADE system to adapting heart failure guidelines for nursing care**

China Medical Board (no. 04-797)

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**Background:** Nurses are key healthcare professionals to provide immediate care of someone who is acutely unwell as a result of heart failure. There has been an increase in the development of clinical practice guidelines (CPGs) to improve standards of care, and yet there are no evidence-based practice guidelines developed for nurses in managing acute heart failure (HF).

**Objective:** The purpose of this study was to rate the quality of evidence based on the GRADE system for adapting generally available HF clinical practice guidelines to nursing.

**Methods:** The databases of Cochrane Library, PubMed, EMBase, SinoMed, CNKI, WanFang and the websites of SIGN, NICE, NGC and so on, were retrieved for systematic review of existing evidence. The quality of all guidelines was critically appraised using the Appraisal of Guidelines for Research and Evaluation II instrument (AGREE II). Clinical Recommendations were analyzed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. All relevant recommendations for management of acute heart failure that nurses can undertake were synthesized.

**Results:** Ten pertinent clinical questions were articulated by panel of experts. Eight evidence-based guidelines with recommendations concerning acute heart failure were included. They were AHA/ACCF 2013, ESC 2012, NICE 2014, SIGN 2007, NHFA 2011, CCS 2013, HFSA 2010, China 2014. Twenty-five recommendations were identified, which were divided into 5 groups (assessment, intervention, medication, education, and document).

**Conclusions:** The format and methodology of the Clinical Guidelines have changed over time. This critical appraisal can assist Chinese nurses to adapt evidence-based clinical practice guidelines to improve outcomes in managing acute heart failure.

## P194

**Nutritional intervention in malnourished hospitalized patients with heart failure and hypoalbuminemia: subanalysis of PICNIC study**JL Bonilla Palomas<sup>1</sup>; AL Gamez Lopez<sup>2</sup>; MC Moreno Conde<sup>1</sup>; MC Lopez Ibanez<sup>1</sup>; E Ramiro Ortega<sup>1</sup>; P Castellano Garcia<sup>1</sup>; Y Pimentel Quezada<sup>1</sup>; AL Villar Raez<sup>1</sup><sup>1</sup>Hospital San Juan de la Cruz, Úbeda, Spain

**Introduction:** Hypoalbuminemia is common in acute heart failure (HF) patients and has been associated with increased hospital mortality and long-term mortality. In this clinical setting, malnutrition is a factor causing hypoalbuminemia. The PICNIC study results show that a nutritional intervention in malnourished hospitalized patients with HF reduces the risks of all-cause death and of readmission for HF.

**Purpose:** We aimed to investigate whether the efficacy of a nutritional intervention is consistent among the subgroups of patients with and without hypoalbuminemia.

**Methods:** In PICNIC study, a total of 120 malnourished hospitalized patients due to acute HF were randomised to conventional HF treatment or conventional HF

treatment combined with an individualised nutritional intervention. The primary endpoint was a composite of all-cause death or readmission for worsening of HF, with a maximum follow-up of 12 months. In this substudy we assessed the interaction of the effects of a nutritional intervention among patients with and without hypoalbuminemia. Analysis was by intention to treat.

**Results:** 59 (49,2%) patients demonstrated hypoalbuminemia and 61 (50,8%) had no hypoalbuminemia. At 12 months, the number of events for the primary endpoint in the intervention group compared with the control group was consistent among patients with hypoalbuminemia (25,8% intervention vs 60% control, hazard ratio 0,35, 95% CI 0,15-0,81,  $p=0,014$ ) and those without (28,6% intervention vs 61,3% control HR 0,34, 95%CI 0,15-0,79,  $p=0,012$ ).

**Conclusions:** There was no evidence that the relative efficacy of a nutritional intervention in malnourished acute HF patients was different between patients who had hypoalbuminemia and those who had no hypoalbuminemia.

#### P195

##### Effectiveness of rotating tourniquets for acute heart failure: a systematic review based on GRADE system

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**Background:** Rotating tourniquets is common traditional treatment for managing people with acute heart failure. Yet this intervention has not been systematically evaluated using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system.

**Objective:** To evaluate the effectiveness and safety of rotating tourniquets for people with acute heart failure.

**Methods:** Evidence-based methodology was performed to form a PICO model. Systematic reviews, RCTs and observational studies concerning rotating tourniquets for the treatment of acute heart failure were searched in Cochrane Library, EMBASE, PubMed, SCI, CINAHL, Chinese Biomedicine Literature Database(CBM), WanFang Database, China National Knowledge Internet Database(CNKI). Studies meeting the inclusion criteria were selected and data were then extracted. The evidence level of outcomes was appraised through the GRADE system. All these procedures were conducted by two researchers.

**Results:** Four observational studies and one RCT were included. Because of bias among the studies, descriptive analysis was chosen. The evidence level of outcomes, including dyspnoea, PaO<sub>2</sub>, right atrial pressure, cardiac output and so on, was rated as low to very low quality according to the GRADE system. There was no improvement in both dyspnoea and PaO<sub>2</sub> with the intervention of rotating tourniquets.

**Conclusions:** This review suggests no effectiveness of rotating tourniquets for the management of acute heart failure, thus don't recommend offering rotating tourniquets for people with acute heart failure routinely, though the evidence level is of very low quality. Besides, studies with large sample and high quality are needed in the future.

#### P196

##### Multi-vessel stenting versus staged revascularization for STEMI with multi-vessel coronary artery disease in cardiogenic shock

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**Introduction:** There are several treatment strategies for non-infarct related artery in ST-elevation myocardial infarction (STEMI) patients with multivessel coronary artery disease (MVCD): multivessel stenting in the primary PCI setting and staged revascularization. We aimed to compare the staged PCI versus multivessel stenting reducing mortality.

**Methods:** From the Korea Acute Myocardial Infarction Registry, 1078 patients with STEMI with MVCD (63.2 ± 12.1 years, 21.8% women) were enrolled between November 2011 and July 2015. The patients were divided into two groups. group I: staged PCI after primary PCI group (n = 600) and group II: multi-vessel PCI group in the primary PCI setting (n = 478). Major cardiovascular events and cardiovascular deaths were compared between two groups.

**Results:** Cardiovascular death (HR, 0.173; 95% CI, 0.092-0.327,  $p < 0.001$ ), major adverse cardiac event (MACE) were significantly lower in staged PCI group (HR, 0.499, 95% CI, 0.345-0.723,  $p < 0.001$ ). After adjusted for clinical variables, although the risk of MACEs were not significantly different between staged PCI group and multi-vessel PCI group ( $p = 0.810$ ), the risk of cardiovascular death were significantly lower in staged PCI group (HR, 0.4335, 95% CI, 0.20-0.94,  $p = 0.035$ ). The beneficial effect of stage PCI is much higher in patients with cardiogenic shock. Cox regression analysis confirmed staged PCI as a negative predictor for cardiovascular death in patient with STEMI undergone primary PCI.

**Conclusions:** This study demonstrates that staged PCI after primary PCI is associated with reduced cardiac death compared to multi-vessel PCI in the primary PCI setting with STEMI.

#### Adjusted Clinical Events between multi-v

	Stable hemodynamics(n = 927)	Cardiogenic shock(n = 151)		
		HR (95% CI) for Staged PCI	P value	HR (95% CI) for Staged PCI
In-hospital mortality	1.019[0.395-1.670]	0.970	0.131[0.041-0.416]	0.001
MACE	1.218 [0.718-2.064]	0.465	0.244 [0.125-0.477]	0.014
Cardiac death	0.462 [0.164-1.299]	0.143	0.161 [0.068-0.384]	0.012
Non-cardiac death	0.261 [0.055-1.247]	0.092	0.255 [0.068-0.384]	0.386
All-cause death	0.404 [0.172-0.950]	0.038	0.345 [0.195-0.612]	0.007

MACE included cardiovascular death, non-fatal MI, non-fatal stroke, Major bleed defined as TIMI major bleeding criteria but not related to CABG. Adjusted for age, sex, smk, HTN, DM, prior HF, prior MI, Hypercholesterolemia, killip class, lesion type

#### P197

##### Intravenous furosemide in a heart failure unit: effectiveness and security in a three days protocol.

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**Introduction:** Intravenous (iv) treatment of congestion in heart failure (HF) is a common issue in clinical practice, but there is not a strong evidence of the most suitable and safe protocol for running it.

**Purpose:** Present our experience in the effectiveness and safety of a three days protocol for intravenous diuretic administration in a HF Unit.

**Methods:** We selected patients with moderate or severe HF decompensation, not requiring urgent admission. Clinical evaluation (weight, abdominal perimeter, signs of congestion...) and also analytic determinations were performed before starting treatment. Two days iv furosemide was administered according to diuretic ambulatory dose and renal function, continuing their habitual oral diuretic dose at home. 24 h after the last administration, clinical and analytic evaluation were repeated. Also, 24 hour diuresis, was registered.

**Results:** We included 29 iv furosemide administrations (63.2% in men). Mean age was 76 ± 8.7 years old and causes of cardiomyopathy were: ischaemic 78.9%, dilated 15.8% and hypertensive 5.3% (mean LVEF 0.51 ± 0.19). All of them had optimal HF treatment, including diuretics. Basal characteristics before administration were recorded in table 1. The mean dose of iv administered furosemide was 56.84 ± 15.29 mg. The 24 h diuresis after first infusion was 1985.3 ± 560.1 mL and after the second one 2125.0 ± 577.6 mL. No adverse effects were reported. The characteristics of the patients 24 h after iv treatment were recorded in table 2.

**Conclusions:** Three days iv furosemide administration in a HF unit, with doctor and nurse supervision, improves clinical status and reduces congestion, without significant renal deterioration or electrolyte disturbances. Because of that, it could be a good option to reduce readmission and improve patient's quality of life.

Table 1. Characteristics of the patients

Characteristic	Basal	24 h after infusion	P value
Domiciliary treatment (mg)	Furosemide 101.1 25.0	101.8 25.0	0.6
Spironolactone/Eplerenone	Thiazides 75.0	44.4	0.11
Body weight (kg)	77.6	76.9	0.006
Abdominal perimeter (cm)	106.2	104.4	0.001
NYHA I-% NYHA II-% NYHA III-% NYHA IV-%	0 21.1 78.9 0	5.0 52.0 26.3 0	<0.01
Incremental dyspnea-%	Orthopnea-% 79 53	13 13	
Incremental oedema-%	Jugular 29.5 28	19.4 0	<0.01
ingurgitation-%			
Creatinine (mg/dL)	CKD-EPI (mL/min) 1.44 50	1.47 48	0.670
Cystatine C (mg/dL)	1.35	1.43	0.199
			0.234
Na (mEq/L)	K (mEq/L) 135.3 4.6	135.5 4.3	0.669
			0.001
NT-pro BNP (pg/mL)	9202	8489	0.204

Clinical and analytic characteristics of patients before and after intravenous furosemide treatment.



P198

**Usefulness of combining admission BNP plus hospital discharge Bioelectrical Impedance Vector Analysis (BIVA) in predicting 90 days cardiovascular mortality in patients with Acute Heart Failure.**

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**Background:** Heart Failure is a disease with high prevalence, mortality, and frequent relapses episodes. Indeed, despite all available therapies and drugs, its incidence remains unacceptably high worldwide.

**Purpose:** Aim of this study was to investigate the prognostic power for death of combining Brain Natriuretic Peptide (BNP) and peripheral congestion detected by Bioelectrical Impedance Vector Analysis (BIVA).

**Methods:** This was an observational, prospective, multicentre study. We performed BNPat arrival and BIVA at discharge. Cardiovascular deaths were evaluated by a 90 days follow up phone call.

**Results:** We enrolled 292 patients. BNP was higher in non survivors (mean value 838 pg/ml vs 515 pg/ml,  $p < 0.001$ ). BIVA at discharge showed statistically significant difference in patients who died than in survivors (respectively: HI 85 vs 74,  $p < 0.001$ ; Xc 26.7 vs 37,  $p < 0.001$ ; R 445 vs 503,  $p < 0.01$ ). Discharge BIVA showed prognostic value in predicting cardiac death (HI: AUC 0.715, 95% CI 0.65-0.76;  $p < 0.004$ ; Xc: AUC 0.712, 95% CI 0.655-0.76,  $p < 0.007$ ; R: AUC 0.65, 95% CI 0.29-0.706,  $p < 0.0247$ ), and when combined with BNP a greater prognostic power was obtained (combined ROC: AUC 0.74; 95% CI 0.68-0.79;  $p < 0.001$ ). **Conclusion:** In AHF, high BNP levels at arrival, and a discharge BIVA assessments showing congestion both have a significant predictive value for 90 days cardiovascular mortality. The combined use of BNP and BIVA increases prognostic power of cardiovascular death.

P199

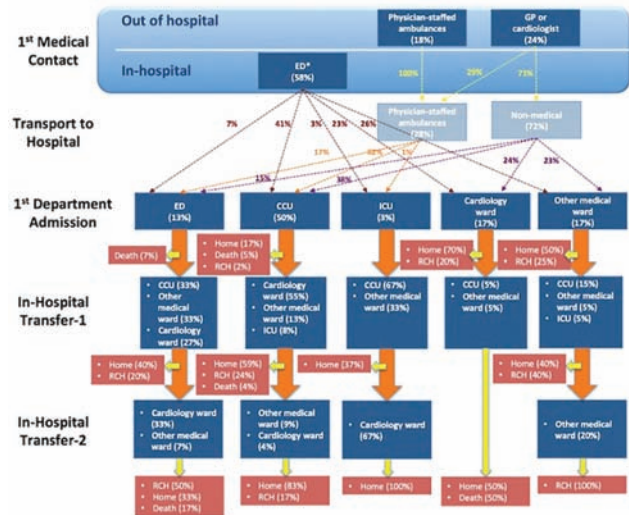
**Pre- and in-hospital course of care for patients with acute heart failure: features and impact on prognosis in the real life**

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**Background:** Acute heart failure (AHF) is a life-threatening medical emergency for which no new effective therapies have emerged during recent decades. No previous studies have exhaustively described the entire course of care of AHF patients from first medical contact to hospital discharge nor assessed its impact on prognosis.

**Methods and Results:** One hundred and nineteen adults with AHF were consecutively enrolled in a multicenter prospective observational cohort study. All of the emergency departments, intensive care units, coronary care units, cardiology wards, and other medical wards participated to the study. The composite primary outcome, including 6-month rate of cardiovascular death, readmission for acute heart failure, acute coronary syndrome or stroke, occurred in 59% of patients. This rate was high and similar regardless the first medical contact, the type of transport, the first medical department of admission, and the number of medical departments involved in the course of care. A cardiologist was involved in the management in 80% of cases and the global median hospital stay was then shorter (7 days [IQR 4-11]) versus 10 days [IQR 7-18],  $P = 0.003$ . History of hypertension ( $P = 0.004$ ), need for non-invasive ventilation ( $P = 0.023$ ), and Lee prognostic score ( $P = 0.028$ ) were independently associated with the primary outcome.

**Conclusions:** Morbi-mortality and readmissions were high regardless of the course of care for patients admitted for AHF in the real life. The reduction of hospital stay when cardiologists were involved in the management encourages the creation of "mobile acute heart failure cardiology teams".



Course of Care for patients with AHF

P200

**Low procalcitonin indicates stable disease after hospitalisation for decompensated systolic heart failure**

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**Background:** Elevated natriuretic peptides are well-established indicators of fluid overload in heart failure, but their utility after cardiac decompensation is limited since the individual baseline level in a single patient is often unknown. Measurement of procalcitonin (PCT) is well established for the management of septicemia. However, elevated PCT levels have also been reported in patients with congestive heart failure and were related to elevated plasma endotoxin concentrations. Increased gut permeability and pulmonary congestion may elicit such PCT response following bacterial challenge under these circumstances. We hypothesized that PCT indicates residual fluid overload at discharge from hospitalisation for cardiac decompensation and thus predicts the risk of re-hospitalisation for worsening heart failure or cardiovascular (CV) death.

**Methods:** PCT was measured prior to discharge in patients hospitalized for decompensated systolic heart failure (left ventricular ejection fraction [LVEF]  $\leq 40\%$ ). According to manufacturer's instruction, cut-off level for normal healthy individuals was  $< 0.05$  ng/ml, and the detection limit of relevant bacterial infection was 0.5 ng/ml. After 6 months, rates of re-hospitalisation and death (all-cause and cause-specific) were evaluated.

**Results:** In 910 patients ( $68 \pm 13$  years; 72% male; LVEF  $29 \pm 6\%$ ), PCT was measured. In the total cohort, levels ranged from 0.00 to 9.77 ng/ml with a median of 0.061 ng/ml (quartiles: 0.039, 0.099). PCT levels were  $< 0.05$  ng/ml and  $< 0.5$  ng/ml in 39% ( $n = 355$ ) and 97% ( $n = 889$ ) of the total cohort, respectively. Within 6 months after discharge, 41% ( $n = 374$ ) of all patients had experienced re-hospitalization or death, and 16% ( $n = 146$ ) had been re-hospitalized for worsening heart failure or had died from CV death. Univariable Cox regression revealed that in patients with PCT  $< 0.05$  ng/ml both, the risk of all-cause re-hospitalisation or death and the risk of re-admission for worsening heart failure or CV death were significantly lower compared to subjects with PCT  $\geq 0.05$  ng/ml: hazard ratio (HR) 0.60 (95% confidence interval (CI) 0.48-0.75) and HR 0.39 (95%CI 0.26-0.57), respectively (all  $p < 0.001$ ). The association of low PCT with low risk of re-admission for worsening heart failure or CV death was not attenuated by adjustment for age, sex, C-reactive protein, white blood cell count, NYHA functional class, N-terminal pro-brain natriuretic peptide, renal dysfunction and diabetes: HR 0.60 (95%CI 0.38-0.93;  $p = 0.024$ ).

**Conclusion:** In systolic heart failure, PCT may be a surrogate marker of residual congestion. After an episode of cardiac decompensation, a PCT level below 0.05 ng/ml indicates a fluid-balanced and therefore stable condition, i.e. at low risk for re-hospitalisation for worsening heart failure or CV death. The clinical utility of such biomarker information deserves to be tested in a controlled trial.

## P201

**Prognosticators of heart failure in patients after treatment because of acute coronary syndrome**

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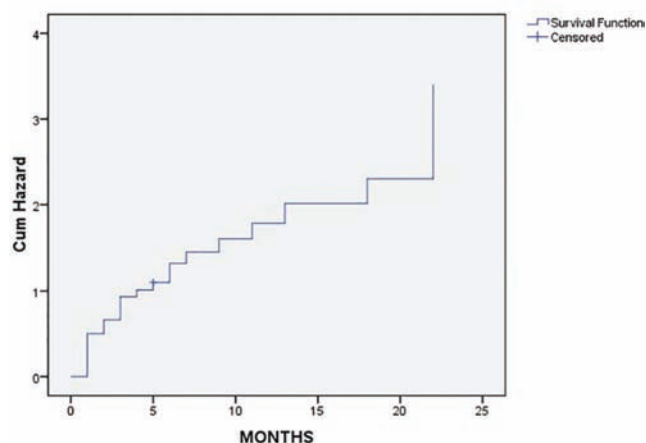
**Aim:** of the study was to identify frequency and predictors of heart failure in patients treated for acute coronary syndrome (ACS).

**Patients and methods:** Patients with ACS treated medically or with PCI, were extracted from the hospital registry. Analyzed variables: age, gender, risk factors, SBP and HR at hospital admission, type of MI, location, CAD severity, LV function, type of treatment, in-hospital morbidity, pharmacologic treatment post discharge, time to event. Statistical analysis: descriptive and comparative analysis, uni and multivariate regression analysis, Kaplan-Meier event free survival analysis.

**Results:** 437 patients treated for ACS, at mean age  $63,2 \pm 11,1$  years, 294(67,3%) males and 143(32,7%) females, were followed up for mean  $17,3 \pm 10,3$  months. A total of 128(29,3%) patients had 136 cardiac events (CE), 32(25%) of whom heart failure (HF). Mean time to HF was  $5,9 \pm 7,4$  (SE), CI(3,3-8,6) (Figure 1). As univariate predictors of HF in ACS treated patients we identified: length of hospitalization (for ACS treatment)  $3,9 \pm 2,2$  vs  $5 \pm 2,5$  days (beta.169,  $p=0,009$ ); diuretic utilization during ACS hospitalization (beta 1.992,  $p=0,001$ ); EF (%) (beta -0.092,  $p=0,001$ ); reduced EF (<40%) had OR for HF 3.282 (CI 1,129-9,542,  $p=0,011$ ); receiving PPCI (beta -1.584,  $p=0,011$ , exp(B) 0.205); known DM (beta0.741,  $p=0,007$ , exp(B) 2,098); previous MI (beta 0.832,  $p=0,068$ , exp(B) 2,297); statin therapy prior ACS (beta-0.955,  $p=0,028$ , exp(B) 0.385); PCI performed (beta-0.990,  $p=0,043$ , exp(B) 0,372); in-hospital morbidity (beta 0.868,  $p=0,028$ , exp(B) 2,382). In multivariate analysis (binary logistic regression) four independent predictors were identified: known diabetes ( $p=0,004$ ), PCI treatment for ACS ( $p=0,006$ ), diuretic therapy during ACS hospitalization ( $p=0,004$ ) and LV function ( $p=0,024$ ).

**Conclusion:** Predictors of HF development in pts. after ACS, seems to be pre-existing DM, need for diuretic therapy during ACS event, and reduced LV systolic function as negative ones, but, receiving PCI (myocardial revascularization) is the most important positive predictor.

Hazard Function



Kaplan-Meier cumulative hazard ratio-HF

## P202

**Impact of acute heart failure: precipitating factors, one-year outcome and risk factors.**

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**Introduction:** Acute heart failure is a frequent condition associated with high morbidity and mortality. Despite advances in its care, the prognosis of patients hospitalized for acute heart failure remains poor and rates of readmissions continue to rise. In order to effectively prevent readmissions and improve overall outcomes, it is important to have a complete characterization of the hospitalized patients and identify prognostic factors.

**Purpose:** This study was performed to analyze patient characteristics, precipitating factors and outcomes of acute heart failure in our population and to determine prognostic factors.

**Methods:** A retrospective observational study was conducted with data prospectively collected in an internal medicine department. All consecutive patients hospitalized with acute heart failure during the year 2014 were included. Demographic, clinical, laboratorial data and parameters from transthoracic echocardiograms were collected. Patients were followed for a period of one year in order to determine the outcomes (rehospitalizations, emergency admissions and death).

**Results:** 255 patients were included, with  $81 \pm 8$  years, 146 women. Hypertension, atrial fibrillation and coronary heart disease were the most common underlying conditions, present in 88.6%, 60.8% and 47.5% of the patients, respectively. Infectious diseases, therapeutic failure/disease progression and arrhythmias were the precipitating factor in 45.5%, 32.9% and 10.6% of the cases, respectively. Preserved left ventricular ejection fraction was observed in 61.5%; valvular disorders were common, especially mitral regurgitation, which was reported on echocardiography in 49.5% of patients. Median length of stay was  $11 \pm 8$  days and the 12-month all-cause mortality was 27.5%. During the one-year follow up period 61.2% of patients needed to be readmitted and 34.1% required treatment in the emergency department due to decompensated heart failure. Univariate statistical analysis determined that coronary heart disease ( $p=0.04$ ), diabetes ( $p=0.05$ ), pulmonary hypertension ( $p=0.03$ ), valvular disorder ( $p=0.04$ ) and hypertension ( $p=0.05$ ) were associated with the need of rehospitalization and mortality.

**Conclusion:** Characteristics and prognosis of an unselected population of acute heart failure patients are presented. Preserved systolic function was found in a substantial proportion of the patients. One-year readmissions and mortality were high. In this population, coronary heart disease, diabetes, pulmonary hypertension, valvular disorder and hypertension were identified as independent risk factors for rehospitalization and mortality.

## P203

**Acute heart failure secondary to cardiac amyloidosis: a case series**

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**Introduction:** Amyloidosis is a disease characterized by the abnormal deposition of protein in visceral organs and soft tissue. Affected organs include the heart, kidney, liver and nervous system. Deposition of amyloid in the heart characterizes advanced stages of the disease and cardiomyopathy due to amyloidosis is the leading cause of morbidity and mortality in patients affected by the disease. Patients can present with signs of right-sided heart failure, including elevated jugular venous pressures and lower extremity edema. While there have been as many subtypes of amyloid proteins identified, the most common subtypes to deposit in the heart are immunoglobulin light chain (AL) amyloid as well as wild-type (wt) and mutant transthyretin amyloid (ATTR). Cardiac involvement occurs in about 50% of patient with AL amyloidosis. Some reports indicate that 4% of African Americans possess a mutant variant of ATTR and 23% of African Americans with cardiac amyloidosis have the Val122Ile mutant variant of ATTR.

**Purpose:** The purpose of this study is to analyze three cases of acute decompensated heart failure due to amyloidosis and compare and contrast each patient's presentation, diagnosis and acute and long-term management of the disease.

**Methods:** Three cases of cardiac amyloidosis were identified in our hospital's advanced heart-failure clinic and analyzed as a part of a case-series.

**Results:** The cases of cardiac amyloidosis in our case study included one patient each diagnosed with AL, wt ATTR and Val122Ile mutant ATTR amyloid. The age of our patients at presentation was 53, 71 and 72 years old. One patient was African American, two were Caucasian and all were male. Each patient presented to our clinic with either symptoms of shortness of breath or volume overload. In each case, diagnosis was made by endomyocardial biopsy and immunohistochemistry. Each patient was treated, when appropriate, for heart failure with a beta-blocker and an ACE-inhibitor or angiotensin receptor blocker as well as a diuretic for volume control. Definitive treatment strategy varied with respect to the patient's subtype of cardiac amyloidosis.

**Conclusions:** The management strategy of acute decompensated heart failure secondary to amyloid deposition in the heart is two-fold: treatment of the symptoms of heart failure as well as the source of the abnormal protein production. Heart failure management is similar regardless of the amyloid subtype. Patients require heart rate and after-load control as well as volume regulation with diuretics. Long term treatment and potential cure is dependent upon the source of amyloid production. AL and ATTR subtypes are synthesized in the bone marrow and liver respectively. Therefore, patients with AL amyloid deposition require chemotherapy and stem cell transplantation while patients with ATTR amyloid are treated with liver transplantation. Novel therapeutic strategies focus on eliminating amyloid from the body.

## P204

**Sex-determined differences of short- and long-term prognosis of mortality in patients hospitalized with acute decompensated heart failure**

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**Purpose:** We evaluate sex-dependent features of acute decompensated heart failure (ADHF) in terms of in- and post-hospital prognoses.

**Methods and materials:** We observed 450 patients, 235 males and 215 females (average age  $69.4 \pm 10.6$  years) hospitalized to cardiological departments or intensive care units with ADHF of ischemic or hypertensive origin. 25 patients (5.6%) died in hospital, 425 (94.4%) were discharged. We obtained 2-years outcome concerning vital status about all of 425 patients discharged, 208 of them died within 2 years. We performed multivariate statistical analyses using t-test at first for independent cohorts, and then binomial logistic regressions were applied stepwise. The regression outcome was taken as in-hospital death (of any cause) for the first series of models, and as post-hospital death after initial discharge for the second series of models.

**Results:** We obtained some significant risk factors for in- and post-hospital mortality for patients who were discharged after ADHF. For in-hospital death these factors were the following: High hs-CRP level ( $> 20$  mg/l; ULN = 5 mg/l), high BNP-level ( $> 1000$  pg/ml; ULN = 100 pg/ml), low LV EF ( $< 33\%$ ), age ( $\geq 75$  years), and sex (male). We revealed certain interactive effects for each sex: higher CRP was more dangerous for males ( $p=0.0001$ ). Higher BNP was a stronger predictor of death for females ( $p=0.003$ ), as well as low EF ( $p=0.0003$ ). All measured values were assessed at hospital admission. For post-hospital mortality patients' data at discharge were analyzed. Significant factors were the following: High hs-CRP level ( $> 20$  mg/l; ULN = 5 mg/l), high BNP-level ( $> 600$  pg/ml; ULN = 100 pg/ml), age ( $\geq 75$  years), and sex (male) raise the probability of death within two-years after discharge. Interactive effects have shown that the higher CRP adds more to male mortality ( $p=0.001$ ), as well as older age ( $p=0.009$ ), and lower EF ( $p=0.02$ ).

**Conclusion:** There are clear sex-dependent differences in a range of significant factors for short-term and long-term prognosis of in-hospital and post-hospital mortality for males and females. Generally, females show better outcomes. Higher BNP levels, and lower LV EF have stronger worsening effect for females than for males. Higher CRP, and older age result in higher probability of death for males. Those differences to be considered when short- and long-term mortality prognoses for patients with ADHF are assessed.

## P205

**Primary valvular non-acute coronary syndrome pulmonary edema-clinical and paraclinical characteristics. Prognosis factors.**

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**Acute:** Pulmonary Edema (APE) represents a severe clinical form of acute heart failure, with high in-hospital (IH) and 1 year mortality. A few data describe APE regarding the etiology and prognosis factors.

**Purpose:** Characterization of a group of patients with primary valvular (PV) non-acute coronary syndrome (non-ACS) APE, regarding demographic, clinical and paraclinical data, the analysis in relation to the other etiologies (hypertensive and ischemic). Identification of short and medium term prognosis parameters.

**Material and methods:** 92pts with non-ACS APE, with polymorphic etiology (23.91% primary valvular, hemodynamic graded at least moderate, 28.26% non-ischemic hypertensive, 44.56% ischemic and 3.26% others), admitted in our clinic, between 01.01-31.12.2013. We analyzed demographic, clinical, biological and echo parameters in relation to etiology and IH and 1 year mortality.

**Results:** In relation with the other two etiologies: equal gender distribution, differences with statistic value ( $p=0.03$ ), similar mean age (75.3 years), same incidence for hypertension (80.56%) and type II diabetes mellitus (27.77%), higher for smoking (19.44%) and lower for dyslipidemia (38.89%). The main valvular diseases (VD) identified were mitral regurgitation (36.11%) and aortic stenosis (13.88%); these two were associated in 31.94% of cases. 19 (20.65%) of 92 pts have mixt etiology (valvular and ischemic). For the entire group, IH mortality (IHM)-23.91%, was not influenced by the etiology ( $p=0.6$ ): 18.18% PV, 23.08% hypertensive and 52.27% ischemic; the results were different from 1 year mortality (28.25%), which was associated with ischemic etiology (ischemic-68.42% vs PV - 31.58%,  $p=0.01$ , RR=1.43). 50% of ischemic death associated a significant VD ( $p=0.001$ ). The next parameters were associated with IHM for PV etiology: urea ( $p=0.004$ ) and sodium ( $p=0.002$ ) at admission, diastolic left ventricular diameter ( $p=0.003$ ), right atrial-ventricular gradient ( $p=0.02$ ), E/E' ( $p=0.06$ ), and with 1 year mortality: pre-therapeutic heart rate (HR,  $p=0.02$ ), LVEF ( $p=0.04$ ), TAPSE ( $p=0.02$ ), PAAT ( $p=0.04$ ).

**Conclusions:** Ischemic etiology is dominant in non-ACS APE. IH and 1 year mortality is not influenced by PV etiology, but the association of significant valvular disease with ischemic etiology rises the 1 year mortality risk ( $p=0.001$ ). For PV etiology a lot of clinical, biological and echo parameters proved to have statistical value for short and medium term prognosis. Early identification of underlying pathology and prognosis factors in non-ACS APE is important for risk stratification.

## P206

**INTERMACS profile predicts in-hospital mortality in cardiogenic shock**

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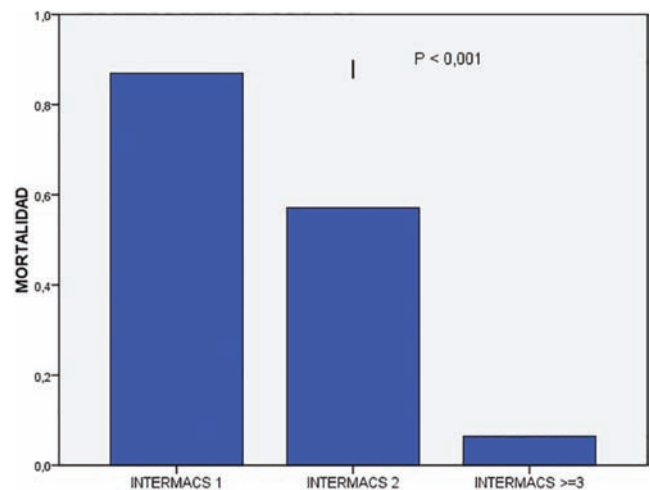
**Background:** Mortality in the setting of cardiogenic shock (CS) is high, but some patient characteristics can stratify this risk. INTERMACS profiles are useful in the characterization of advanced heart failure before ventricular assist device implantation. This classification could be useful as mortality predictor among the patients with CS due to medical conditions admitted to the Cardiovascular Intensive Care Unit (CICU).

**Methods:** We performed a retrospective analysis of all the patients with CS due to medical conditions in our CICU from February 2012 to Sept 2015. We collected base-line characteristics and shock, treatment and mortality data. INTERMACS profile at 24 hours of CS diagnosis was assigned by two cardiologists independently, in case of discrepancy the case was discussed.

**Results:** We collected 196 patients during the study period.

**Etiology:** Acute coronary syndrome 57.7%; Acutely decompensated heart failure 23.4%; Arrhythmias 13.2%; other etiologies 5.6%. Men 70.4%. Age 67.8 (SD 14.3). After INTERMACS classification the groups resulted: INTERMACS1 19.9%; INTERMACS2 23.5%; INTERMACS $\geq 3$  56.6%. The overall in-hospital mortality rate was 32.1%. Regarding to INTERMACS profile, the mortality rate was resulted: INTERMACS1 89.7%; INTERMACS2 39.1%; INTERMACS $\geq 3$  9%. Comparison with univariate logistic regression showed significant differences among the groups ( $p < 0.001$ ). After analysis with multivariate logistic regression and adjusting with traditional predictors (blood pressure, LVEF, glycemia, diabetes, chronic renal insufficiency and age) the signification persisted with worse prognosis as INTERMACS profile decreased: INTERMACS2 vs INTERMACS $\geq 3$  ( $p < 0.001$ ; OR 6.5 [2.7-15.6]); INTERMACS1 vs INTERMACS $\geq 3$  ( $P < 0.001$ ; OR 88.4 [26.0-299.8]).

**Conclusion:** INTERMACS profile at 24h of CS diagnosis was strongly associated with in-hospital mortality. We suggest that it can be a valuable tool in order to stratify the risk of the patient suffering from CS, and thus it can help to guide the need for more aggressive therapies.



## P207

**Acute heart failure and cardiogenic shock are predictors for in-hospital mortality in patient admitted with acute coronary syndrome**

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Despite aggressive intervention, morbidity and mortality of patients with acute coronary syndrome (ACS) remain high. Various clinical condition may contribute to



the outcomes during acute phase. The aim of this study was to analyze clinical parameters that predict in-hospital mortality of ACS patient. We examined 1315 consecutive patients admitted with ACS in CVCU of our National Cardiovascular Center in 2015. Multivariable logistic regression was used to analyze predictors for in-hospital mortality. Among 1315 patients, 786 (59.8%) were STEMI and 529 patients were UA/NSTEMI. Most of them are male (82.4%), below 65 years old and smoker (59.1%). Overall in-hospital mortality were 5.7% (76 of 1315), including 47 patients with STEMI and 29 with UA/NSTEMI. STEMI patients who failed to survive during hospitalization more likely have diabetes, suffered from acute heart failure (AHF) and cardiogenic shock (CS). However, after multivariable risk adjustment, only AHF and cardiogenic shock remain independent predictors for in-hospital mortality (odds ratio 7.64; 95%CI 3.41-17.13 and 11.45; 95%CI 5.61-23.36 respectively). Almost similar findings were observed in UA/NSTEMI population, with CS as strong predictor for in-hospital mortality (odds ratio 24.2; 95%CI 8.5-68.27), and those who underwent early revascularization were survive (odds ratio 0.361; 95%CI 0.131-0.994). We also observed no significant differences in mortality between cardiogenic shock patients who had IABP implantation and those without IABP. In conclusion, we observed AHF and cardiogenic shock as predictors for in-hospital mortality among STEMI patients, and cardiogenic shock in UA/NSTEMI population. Early revascularization but not IABP implantation predicted survival during hospitalization.

## P208

### Predictors of left ventricular systolic dysfunction in patients with first acute ST-segment elevation myocardial infarction undergoing primary angioplasty

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**Background:** The degree of left ventricular systolic dysfunction (LVSD) determines the prognostic outcome of STEMI.

**Purpose:** To define different variables related to LVSD in patients with first STEMI referred for primary PCI.

**Methods:** The sample included 288 patients from January 2013 till December 2014. Demographic, clinical, laboratory and angiographic data were collected prospectively into a computerized registry. Patients were divided into four groups by degree of LV systolic function: normal (EF $\geq$ 50%), mild (EF = 40-49%), moderate (EF = 30-39%), and severe (EF < 30%) and compared for different variables.

**Results:** LVSD was associated more with females ( $p = 0.029$ ), anterior STEMI ( $p = 0.004$ ), longer symptom to door time, longer door to device time, more than Killip class II on presentation (0.001), extend of CAD ( $p = 0.021$ ), and high peak creatine kinase. There were no significant correlations between LVSD and age, DM, hypertension, dyslipidemia, technique of PCI or use of aspiration device. On bivariate analysis, symptom to door time ( $r = -0.312$ ,  $P < 0.001$ ), door to device time ( $r = -0.327$ ,  $P < 0.001$ ) and peak creatine kinase ( $r = -0.202$ ,  $P = 0.003$ ) were the most significant independent predictors of LVSD. Patients with LVSD had higher in-hospital mortality ( $p = 0.001$ ). **Conclusion:** LVSD after first STEMI can be predicted by female gender, anterior STEMI, Killip class on presentation, symptom to door time, door to device time and the size of infarction assessed by peak creatine kinase. Patients with LVSD had higher in-hospital mortality.

## P209

### Hemographic indices are associated with mortality in acute heart failure

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**Background:** Hemographic indices have been associated with clinical outcomes in patients with chronic heart failure. We therefore investigated the prognostic values of hemographic indices in patients hospitalized for acute heart failure (AHF), regardless of left ventricular functions.

**Methods:** Patients hospitalized primarily for AHF were drawn from an intramural registry. Hemographic indices, including white blood cell counts, neutrophil counts, neutrophil-to-lymphocyte ratio, reciprocal of lymphocyte (RL) and platelet-to-lymphocyte ratio were recorded. National Death Registry was linked for the identifications of all-cause mortality, with a follow-up duration of up to 5 years.

**Results:** Among a total of 1923 participants (mean age  $76 \pm 12$  years, 68% men), 875 patients died during a mean follow-up duration of  $28.6 \pm 20.7$  months. All of the hemographic indices were related to mortality, independent of age, sex, mean blood pressure, left ventricular ejection fraction, sodium and hemoglobin level, estimated glomerular filtration rate, and medications. In a forward stepwise Cox regression analysis among hemographic indices, RL was the strongest predictor getting into the model [HR and 95% CI: 1.166 (1.097-1.240)] after accounting for

the confounding factors. RL was consistently correlated with mortality, irrespective of age, gender, diabetes, chronic kidney disease, coronary artery disease, and left ventricular systolic function. However, conditioned on the survivals, the hemographic indices were independently related to mortality within 3 years of follow-up, rather than beyond.

**Conclusions:** Hemographic indices were independent risk factors of mortality in patients hospitalized for AHF, especially in patients with impaired left ventricular systolic function. As an acute presentation of inflammation, hemographic indices might be useful to identify subjects at risk of mortality soon after the index hospitalization.

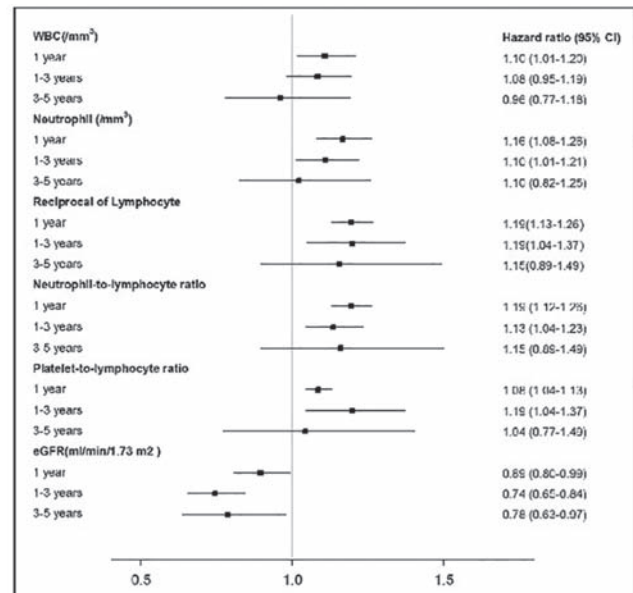


Figure 1

## P210

### The effects of continuous iv furosemide on arterial stiffness and ventricular-arterial coupling in AHF patients

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**Background:** Congestion and fluid overload are the hallmarks of heart failure (HF). Arterial stiffness and ventricular-arterial coupling (VAC) are independent prognostic factors in HF patients. No studies to date have investigated the role of decongestion with continuous iv furosemide regarding these parameters.

**Purpose:** we aimed at evaluating arterial stiffness and VAC at admission and discharge in patients hospitalized for acute HF (AHF) with reduced left ventricular ejection fraction (LVEF).

**Methods:** 26 patients hospitalized for AHF were enrolled. Before the administration of iv furosemide and at discharge they underwent radial artery applanation tonometry to evaluate central blood pressures and augmentation index (AIx@75), and transthoracic echocardiography to assess aortic elastance (Ea), end-systolic left ventricular elastance (Ees) and their ratio, namely VAC.

**Results:** mean age was  $76 \pm 10$  years. 12 (46.2%) were male. LVEF at admission was  $34 \pm 9\%$ . Hemodynamic parameters are reported in Table 1. After iv furosemide there was a great improvement in central pressure. We found that AIx@75 significantly worsened in parallel with decongestion. On the other hand, no effects were seen on VAC and its components. These results are independent from LVEF increasing and weight loss.

**Conclusion:** In patients hospitalized for AHF iv furosemide is associated to an improvement in central pressure, with no effects on VAC. The surprising arterial stiffening in parallel with decongestion can be probably linked to a reduced shear stress due to fluid unloading. Considering the prognostic role of arterial stiffness in patients with HF, our results are contrasting and need further analysis.

Variable	Admission	Discharge	p
Aortic SBP (mmHg)	109 ± 19	105 ± 11	0.211
Aortic DBP (mmHg)	75 ± 5	71 ± 5	0.001
Aortic MAP (mmHg)	89 ± 11	85 ± 6	0.030
Aortic PP (mmHg)	34 ± 17	34 ± 12	0.846
Alx@75 (%)	19 ± 11	27 ± 13	0.006
Stroke volume (mL)	52 ± 17	59 ± 34	0.183
Ea (mmHg/mL)	2.3 ± 0.9	2.2 ± 0.9	0.333
Ees (mmHg/mL)	2.8 ± 1.2	2.8 ± 1.4	0.831
VAC	0.8 ± 0.2	0.8 ± 0.2	0.534

**P211**  
**The impact of admission blood glucose level on clinical picture and prognosis in cardiogenic shock**

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**Introduction:** Critically ill patients often present with hyperglycaemia, regardless of previous history of diabetes mellitus (DM). Stress hyperglycaemia has been associated with adverse outcome in acute myocardial infarction and acute heart failure, but data regarding cardiogenic shock (CS) are sparse.

**Purpose:** To investigate the impact of admission plasma glucose level on clinical picture and short-term mortality in CS.

**Methods:** We enrolled 219 adult CS patients, that were divided into five categories according to admission plasma glucose level (hypoglycaemia (glucose <4mmol/L), normoglycaemia (4-7.9mmol/L) and mild (8-11.9mmol/L), moderate (12-15.9mmol/L) and severe (≥16mmol/L) hyperglycaemia). We compared the clinical picture, biochemical findings and short-term mortality between the groups.

**Results:** Glucose levels were distributed equally between normoglycaemia (26% of patients) and mild (27%), moderate (20%) and severe (25%) hyperglycaemia, while hypoglycaemia (2%) was rare. Severe hyperglycaemia was associated with higher blood leukocyte count (17.3 E9/L), higher plasma lactate level (4.4mmol/L) and lower arterial pH (7.23) compared with normoglycaemia or mild to moderate hyperglycaemia (p < 0.001 for all). The hypoglycaemic patients presented with hyperlactatemia (8.3mmol/L), acidosis (arterial pH 7.19) and high levels of NT-proBNP (26300 ng/L) and alanine aminotransferase (466 U/L). In contrast, the normoglycaemic patients had normal levels of arterial pH (7.35) and plasma lactate (1.8mmol/L). Acute coronary syndrome was the aetiology of CS particularly often in patients with severe hyperglycaemia (92%) in comparison with normoglycaemic (69%) and hypoglycaemic (60%) patients (p = 0.029). 90-day mortality was highest among hypoglycaemic and severely hyperglycaemic patients (60% for both) compared with 26% in normoglycaemic patients (Figure 1.). Severe hyperglycaemia was an independent predictor of in-hospital mortality (OR 3.72, 95% CI 1.18-11.7, p = 0.025), when adjusted for age, gender, LVEF, lactate and DM. Mean glucose level of survivors and non-survivors differed significantly among non-diabetic patients (10.1 vs. 12.9 mmol/L, p = 0.009), but not among patients with prior DM (16.3 vs. 17.4 mmol/L, p = 0.59).

**Conclusions:** Glucose level significantly affects the outcomes in CS, and prior DM status modifies the prognostic value of plasma glucose. Mortality rates are highest among hypoglycaemic and severely hyperglycaemic patients. Moreover, severe hyperglycaemia is an independent predictor of in-hospital mortality in CS and is associated with biochemical findings of hypoperfusion. In contrast, plasma lactate and pH remained within the normal range among normoglycaemic patients, suggesting that tissue perfusion and oxygenation were sufficient to meet the demands despite the clinical manifestation of shock.

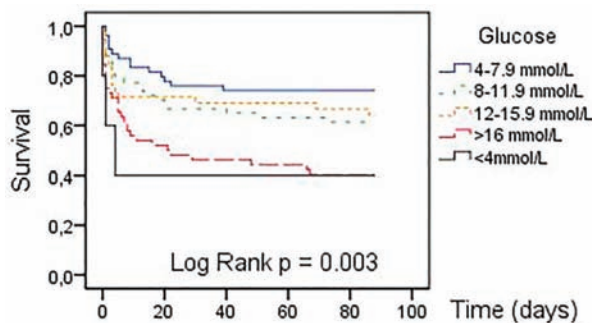


Figure 1. Kaplan-Meier survival curves

**P212**  
**Prognostic value of changes in cardiostrophin-1 levels over time in patients with acute heart failure**

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**Background:** Cardiostrophin-1 (CT-1) is a factor enhancing cardiomyocyte survival and protection in response to biomechanical stress. Data received from rodent and canine models suggest that CT-1 also behaves as a profibrotic cytokine. In rodent myocardial infarction model, CT-1 expression in the late phase of wound healing and the onset of heart failure may also contribute to ventricular dilation by inducing hypertrophy of myocytes. Nevertheless, the role of CT-1 expression at early stages of myocardial remodeling remains unclear. Clinical significance of serial measurements of CT-1 in acute heart failure has not yet been reported.

The purpose of the study was to assess the significance of repeated measurements of CT-1 in patients with acute heart failure.

**Methods:** 172 patients admitted for acute dyspnea aged 39...60 were included in ongoing prospective open local study. The plasma concentrations of CT-1 were determined using available commercial immunoassay kits at baseline and on 7th day since AHF manifestation. For the purpose of the study, results of 72 male patients with acute heart failure were analyzed by categorical and percentage changes in CT-1 level. Patients are followed-up for duration of hospital stay (in-patient), cardiovascular rehospitalization, cardiovascular death and heart failure signs and symptoms (shortness of breath, ankle swelling, weight gain >2 kg within 3 days).

**Results:** Baseline CT-1 was comparatively high: 236.3 (220.4; 263.8) pg/mL. Increasing CT-1 level over time from baseline to 7th day's level was associated with significant increase in baseline levels of RDW (15.3 (14.7; 15.7) vs 14.5 (13.9; 14.8), p = 0.006), left ventricular myocardial mass index (94 (90; 99) vs 82 (75; 95), p = 0.023) and lower baseline CT-1 level (227.0 (213.1; 249.3) vs 256.5 (222.1; 270.2) pg/mL, p = 0.042). In 25% of patients CT-1 increased by > 10%, while deceleration of CT-1 by >10% was in 29.2%. Both increase and decrease of CT-1 by 10% were associated with higher relative hazard of adverse cardiovascular event within one (HR 1.43 (CI 1.01; 2.84), HR 2.34 (CI 1.05; 3.01)) and six months (HR 2.53 (CI 1.71; 3.86), HR 2.14 (CI 1.65; 4.17)) since admittance due to acute heart failure. Categorized changes in CT-1 level correlated with the duration of hospital stay (r = 0.651, p < 0.05).

**Conclusion:** In male adult patients with acute heart failure repeated measurements of cardiostrophin-1 level provide important information on acute heart failure risk stratification.

**CHRONIC HEART FAILURE**

**P213**  
**The role and importance of interleukin investigation in chronic heart failure**

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**Background:** The study of the content immunocytokines in patients with chronic heart failure (CHF) due to the fact that cytokines play a significant role in the formation of myocardial remodeling and progression of heart failure. Purpose of the study. Study of the level of cytokines and their relationship with the course of ischemic CHF.

**Material and methods:** The study included 45 patients with a confirmation of CHD and post myocardial infarction which complicated with heart failure, corresponding to stage II and III CHF. At echocardiography all of patients ejection fraction is below 50%. All participants underwent an electrocardiogram, chest X-ray, general clinical and biochemical studies. We have chosen for the determination of interleukin-6 (IL-6) and tissue necrosis factor-alpha (TNF-α). Thus, in stage II A the concentration of TNF-α and IL-6 was 20.6 ± 3.32 and 34.0 ± 12.3 pg/ml, stage II B stage - 72.1 ± 8.43 and 67.8 ± 11.1 pg/ml and increased to stage III to 172 ± 17.1 and 141 ± 21.2 pg/ml (p = 0.001).

**Conclusions:** Thus, definition of interleukin status in serum of patients with CHF can use as markers of the disease, in combination with a standard inspection. The level of interleukin status had a direct correlation with the stage of heart failure.

**P214**  
**Impaired gas diffusion and RV to pulmonary circulation uncoupling limit exercise performance in heart failure patients**

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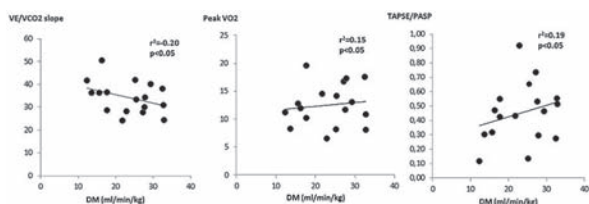
In heart failure (HF) patients, an altered gas diffusing capacity for carbon monoxide (DLCO) is a marker of lung capillary injury that bears relevant clinical and prognostic information. It is unknown whether right heart-pulmonary circulation (RH-PC)

uncoupling abnormalities and gas diffusion are linked and may become synergic in causing exercise limitation and ventilation inefficiency.

**Methods:** 17 HF patients (mean age  $64 \pm 11$ ; male 75%; NYHA II-III; mean left ventricular (LV) ejection fraction  $34 \pm 9\%$ ) underwent DLCO measurements with assessment of membrane component (DM) an capillary blood volume (Vc) and underwent to maximal cardiopulmonary exercise testing (CPET, tilt-ergometer, personalized ramp protocol) combined with Echo-Doppler assessment of right ventricular function by assessing tricuspid annular peak systolic excursion (TAPSE) and pulmonary systolic pressure (PASP).

**Results:** Patients exhibited an abnormal gas diffusion (mean DLCO  $17 \pm 3.9$  ml/min/mmHg) with depressed alveolar-capillary membrane diffusing capacity (DM) component (mean  $23.4 \pm 6.8$  ml/min/mmHg) and elevated capillary volume (mean  $111.2 \pm 64$  ml) along with significant functional limitation (mean peak VO<sub>2</sub>  $12.5 \pm 3.7$  ml/kg/min) and ventilatory inefficiency (mean VE/VO<sub>2</sub> slope:  $34.4 \pm 6.9$  and mean end-tidal of CO<sub>2</sub> mean  $32.1 \pm 5.2$  mmHg).

Significant correlations were found between DM, TAPSE/PASP relationship, peak VO<sub>2</sub> and VE/VO<sub>2</sub> slope at peak exercise (figure).



Gas diffusion and CPET parameters

## P215

### Study of the effect of lisinopril on the kidney functional state in the patients with chronic heart failure

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Purpose of research was study of the effect of lisinopril on the kidney functional state (KFS) in the patients with chronic heart failure (CHF).

**Methods:** This investigation included 86 males with ischemic heart disease associated with II - III FC CHF (mean age  $59.4 \pm 8.9$  years). Control group - 10 healthy persons. The patients received additionally to the standard therapy (spironolacton, beta-blockers, antiagregants) the lisinopril (mean dose -  $8.1 \pm 3.6$  mg/day). The KFS was evaluated by the level of glomerular filtration rate (GFR by MDRD) and the renal blood flow (RBF) assessment was performed by pulse-wave dopplerography. Peak blood flow systolic velocity (Vs), end-diastolic velocity (Vd), resistive and pulse index (RI, PI) were studied at the right and left renal artery.

**Results:** The results of investigation show that in the patients with FC II and III CHF - GFR was  $65.3 \pm 9.8$  and  $57.7 \pm 9.4$  ml/min/1.73 m<sup>2</sup>, respectively. In the patients with CHF at the level of renal arteries there was noted additionally to the increase in parameters of RI and PI with reduction of velocity parameters during systole and diastole periods also increase in comparison with control parameters. During dynamics of treatment of the patients with CHF at the level of right and left renal arteries there was noted tendency to reduction of the parameters of RI by 10,1% and 7,3% and PI - by 12,5% and 11,7%, there was noted increase in velocity parameters during systole period by 9,8% and 11,0% and diastole by 10,5% and 11,5% in comparison with initial parameters.

**Conclusions:** In the patients with CHF the treatment during 6 months with inclusion of lisinopril resulted in improvement of the parameters of renal functional state and renal blood flow that characterizes nephroprotective effect of the therapy performed.

## P216

### Risk stratification of ambulatory patients with chronic heart failure by six-minute walking test and B-type natriuretic peptide: results from the nebula network study group

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**Background:** Reliable assessment of patients with chronic heart failure (HF) is sometimes difficult in an ambulatory setting. Although clinical evaluation still represents a cornerstone of daily practice, such an approach not always allows accurate prognostic stratification. In this scenario, a strategy based on the combination

of simple instrumental and laboratory parameters, such as 6-minute walking test (6-MWT) and B-type natriuretic peptide (BNP), could sharpen the simplistic clinical examination and guide patients' management during follow-up. Aim. This study was designed to assess the value of 6-MWT and BNP assessment in the prognostication of patients with chronic stable HF either with preserved (EF $\geq$ 45%) or reduced ejection fraction (EF<45%).

**Methods:** 641 ambulatory patients (mean age:  $70 \pm 12$  yrs; 31% female) with chronic HF with preserved (HFpEF; n=341) or reduced EF (HFrEF; n=300) were enrolled. They underwent a complete echocardiographic examination. Effort tolerance by 6MWT and BNP plasma levels were evaluated at the time of the index echocardiogram. The end-point was all cause-mortality.

**Results:** During the follow-up ( $30 \pm 18$  months, median: 30 months), there were 86 deaths. The most powerful univariate predictors of all-cause mortality were BNP ( $p < 0.0001$ ), estimated glomerular filtration rate (eGFR) ( $p < 0.0001$ ), etiology ( $p < 0.0001$ ), 6-minute walking distance ( $p < 0.0001$ ), age ( $p < 0.0001$ ), NYHA class ( $p < 0.0001$ ), LV EF ( $p < 0.0001$ ), left atrial diameter ( $p = 0.0001$ ), and restrictive mitral flow ( $p = 0.006$ ). In the multivariate model, etiology ( $p = 0.002$ ), 6MWT ( $p = 0.003$ ), eGFR ( $p = 0.004$ ), gender ( $p = 0.005$ ), age ( $p = 0.022$ ) and BNP ( $p = 0.041$ ) emerged as predictors of outcome. Receiver operating curve analyses showed that 6-minute walking distance of 322 m and BNP of 330 pg/ml were the best cut-off values for outcome prediction. Kaplan-Meier analyses showed a survival free from all-cause mortality at 48-months in 41% of patients with 6-minute walking distance  $\leq$ 322 m and BNP  $>$  330 pg/ml, in 66% of those with 6-minute walking distance  $>$  322 m and BNP  $>$  330 pg/ml, in 86% in those with 6-minute walking distance  $\leq$ 322 m and BNP  $\leq$ 330 pg/ml, and in 93% in those with 6-minute walking distance  $>$  322 m and BNP  $\leq$ 330 pg/ml (Log-rank: 118.7;  $p < 0.0001$ ).

**Conclusion:** In patients with chronic stable HFpEF and HFrEF, 6-MWT and BNP had a strong predictive power for the end-point of all-cause mortality. Our results highlight that 6MWT and BNP may be a first line approach for ongoing monitoring risk stratification of a population of ambulatory patients with HF.

## P217

### 17beta-estradiol reduces endothelin-1 release in women with ischaemic left ventricular dysfunction

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**Objectives:** To assess whether acute administration of 17 $\beta$ -estradiol influences pacing-induced cardiac release of endothelin-1 in female menopausal patients with ischaemic left ventricular dysfunction.

**Background:** Endothelin-1 is a potent vasoactive peptide, estrogens decrease plasma levels of endothelin-1 and improve stress-induced myocardial ischemia in menopausal women with coronary artery disease. Methods. Thirty-two postmenopausal women with angiographically proven coronary artery were screened to enter a double blinded, placebo-controlled study. Selected were those with left ventricular dysfunction (LVEF <40%). Patients were sampled into the coronary sinus and aorta for endothelin-1 at baseline and after incremental pacing. After baseline study patients were randomized to receive either sublingual 17 $\beta$ -estradiol (1 mg) or placebo and underwent the sampling protocol 20 minutes thereafter.

**Results:** The time of onset of myocardial ischemia during pacing (AST > 1mm) was significantly increased by 17 $\beta$ -estradiol (223 $\pm$ 21 versus 296 $\pm$ 15 seconds; The coronary sinus plasma levels of endothelin-1 were significantly reduced by estradiol administration but not by placebo, at each step of pacing protocol. The maximum reduction of endothelin-1 levels after E2 administration was noted at peak pacing (-0.19; -0.08, -0.3; 95% CI) while no changes were noted in patients allocated to placebo (-0.002; -0.06, -0.01; 95% CI). Similarly, aorto-coronary sinus difference was also significantly influenced by estradiol administration but not by placebo.

**Conclusion:** Acute administration of 17 $\beta$ -estradiol reduces pacing-induced cardiac release of endothelin-1 in postmenopausal women with ischaemic left ventricular dysfunction.

## P218

### Plasma volume is normal but heterogeneously distributed and true anemia is highly prevalent in patients with stable heart failure

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**Background:** Both intravascular volume overload and depletion as well as anemia are associated with increased hospital admissions and mortality in patients with heart failure. The purpose of this study was to accurately measure plasma volume and red cell mass (RCM) in stable patients with chronic heart failure with reduced ejection fraction (HFrEF) and gain more insight into plasma volume regulation and anemia in stable conditions of HFrEF.

**Methods and Results:** Plasma volume and RCM measurement based on



99Tc-labeled red blood cells, venous blood samples and clinical parameters were obtained in 24 stable HFrEF patients under optimal medical therapy. Measured plasma volume values were compared with predicted values based on body surface area. Plasma volume was on average normal (99% of predicted) but heterogeneously distributed (variations of 81% up to 133%) (Figure 1). Neurohumoral activation and medication use were not associated with plasma volume status (Table 1). Furthermore, anemia based on measurement of RCM was more prevalent than anemia based on hemoglobin concentration and present in up to 75% of subjects. The origin of anemia was mostly a true anemia while hemodilution was very rare.

**Conclusion:** In stable chronic HFrEF patients under optimal medical therapy, plasma volume is overall normal but heterogeneously distributed. Anticipated factors such as neurohumoral activation and heart failure medication were not associated with plasma volume status. Furthermore, anemia is more common than assessed by hemoglobin in stable HFrEF, but seldom dilutional.

Table 1. Subjects with measured plasma v

	Plasma volume <100% of predicted n = 11	Plasma volume >100% of predicted n = 13	p
Hemoglobin (g/dl)	13.1 ± 1.2	13.5 ± 1.3	0.35
Creatinine (mg/dl)	1.38 ± 0.52	1.57 ± 0.77	0.189
aldosterone (ng/L)	260 (117;438)	129; 306	0.54
PRA (ng/L/h)	11.9 (0.42; 34.2)	1020 (374;1668)	
NT-pro BNP (ng/L)	1025 (457;2590)		
Ratio measured vs predicted plasma volume	+11.2 ± 9.2	-9.6 ± 6.3	< 0.01*
Angiotensin converting enzyme inhibitor (None/<=50%/ > 50%)	2/6/3	1/5/5	0.82
Beta-blocker (None/<=50%/ > 50%)	8/4/1	6/5/4	0.60
Mineralocorticoid receptor antagonist (None/<1 mg/1 -2 mg)			0.47
Loop diuretic			

Loop diuretic dose is expressed in bumetanide equivalent (mg B eq) e.g. furosemide 40 mg = bumetanide 1 mg. Other HF therapy is presented as the number of patients on none, <=50% or >50% of the target dose.

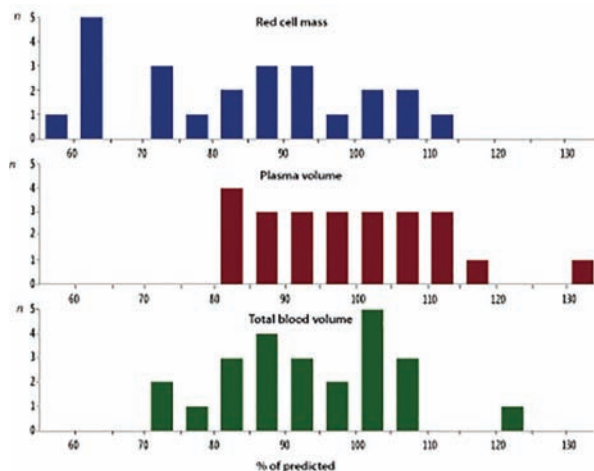


Figure 1: Measured to predicted ratio of

**P219 Integrated approach to the management of heart failure: cardio - nephrology ambulatory.**

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**Background:** Advanced refractory cardiac failure is a chronic condition seriously compromising the patient's quality of life often associated with significant complication, most notably the kidney damage, with high costruzione to National Health

Service. Consequently an increased non hospital care is the focal point in the management of this complex pathology. In our medical center we focus on clinical examination of the patients with refractory cardiac failure and kidney failure, specifically hydration state and non invasive hemodynamic evaluation.

**Purpose:** The main aim of our study is to assess whether early detection of worsening of the cardiac function improve patient's outcome (hospitalization for heart failure, slows the decrease of kidney function, improve the quality of life, improve diastolic function).

**Methods:** We use Bio impedance vector analysis (BIVA), non invasive technique to assess Hydration status and body mass, resistance and reactance measurements. Cardiac non invasive hemodynamic evaluation assess systolic function, ejection fraction, stroke volume and index cardiac output to evaluate diastolic function and semiquantitative estimation of left ventricular end diastolic pressure. The lung-ultrasound with the detection of lung comets is also used to evaluate the interstitial edema. The vena cava excursion during breathing is an indirect index to estimate the central venous pressure. Result: We have observed in over two years of practice activity, patients quality of life improvement and a reduction of 40% in rates of re-hospitalization in this very frail patient.

**Conclusion:** Integrated management model between cardiologists and nephrologists allow to clinically stabilize "frequent flyers" patients through responsible involvement in the disease management of patient and therapy improved.

**P220**

**Tolvaptan is useful and safe for the treatment of very elderly patients with heart failure and chronic kidney disease**

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**Background:** Very elderly patients hospitalized for the treatment of heart failure (HF) are increasing in number. Because of their older age, many of those patients also have chronic kidney disease (CKD). Treatment of very elderly patients with HF and CKD is relatively difficult since those patients tend to be resistant to conventional diuretics treatment and diuretics therapy is frequently associated with further reduction in kidney function. Tolvaptan (TVP) was approved in Japan for the treatment of congestive heart failure 5 years ago. However, the effect of TVP on these patients has not been evaluated.

**Objective:** To investigate whether TVP administration to the very elderly patients with HF and CKD improves HF and the other clinical parameters.

**Methods:** Among very elderly patients (aged 80 or older) with HF and CKD, those who were resistant to conventional treatment or who exhibited impaired kidney function following initial treatment were enrolled. Subjects were additionally given oral TVP (7.5-15mg/day).

**Results:** 45 patients were included in this study and TVP was clinically effective for 41 patients. In the TVP responders, urine volume was significantly increased, and body weight and plasma BNP levels were significantly decreased. There was no significant change in serum sodium and creatinine levels.

**Conclusion:** TVP is useful and safe for the treatment of very elderly patients with HF and CKD.

**P221**

**Treatment with omega-3 PUFAs improves endothelial function and novel echocardiographic indices of left ventricle systolic function**

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**Background:** Omega-3 polyunsaturated fatty acids (PUFAs) improve endothelial function and arterial stiffness in several patient groups and prevent heart failure (HF) progression.

**Purpose:** To evaluate the effects of omega-3 PUFAs on cardiac function and remodeling in patients with HF.

**Methods:** The study was carried out on two separate arms (omega-3 PUFAs-2gr/day- or placebo for 8 weeks), in a cross-over double blind design with an 8-wash out period between the two arms. The study population consisted of 15 systolic stable HF patients of ischemic etiology. All subjects were under optimal medical therapy for a period of 6 months. All subjects were evaluated at baseline and after completion of each treatment arm. Endothelial function was assessed using flow-mediated dilation (FMD) of the brachial artery. Pulse wave velocity (PWV) and augmentation index (AIx) were assessed non-invasively to evaluate arterial stiffness. Left ventricular (LV) function before and after treatment was assessed using LV ejection fraction (LVEF), determined by the biplane modified Simpson method, and LV global longitudinal strain (GLS), using Philips QLAB software.

**Results:** Fifteen subjects (age 65.4 ± 5.9yr) were included in the study. FMD at the end of the treatment period was significantly improved in the PUFA group compared to baseline (4.8 ± 2.2% vs. 2.9 ± 2.3%; p=0.003) but not in the placebo group (3.0 ± 2.3 vs. 2.8 ± 2.2%, p=0.065). PWV and AIx were not significantly

different in either the PUFA or the placebo group ( $p=NS$  for all). A significant improvement in LV function as assessed by LVEF and GLS was observed only after PUFA treatment ( $35.2 \pm 7.7\%$  vs.  $33.9 \pm 7.2\%$ ;  $p=0.039$ , and  $-11.8 \pm 3.1\%$  vs.  $-10.3 \pm 3.1\%$ ;  $p=0.020$ , respectively) as well as a marginal improvement in LV diastolic and systolic dimensions ( $55.6 \pm 5.9\text{mm}$  vs.  $57.0 \pm 6.1\text{mm}$ ;  $p=0.245$ , and  $45.3 \pm 6.4\text{mm}$  vs.  $47.6 \pm 5.5\text{mm}$ ;  $p=0.101$ , respectively).

**Conclusions:** In systolic HF patients, short term treatment with omega-3 PUFAs improves left ventricle function and global longitudinal strain in parallel with benefits on endothelial function. These findings may shed light to the favorable pathophysiological mechanisms of omega-3 PUFAs in heart failure subjects.

## P222

### Profile of our patients with reduced left ventricular fraction (HFrEF) explored in a day care unit

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**Introduction:** Despite the major progress in the field of medical and interventional therapy, we have every day to challenge chronic heart failure patients therapy and hospitalization.

**Purpose:** To describe clinical, and echocardiographic characteristics of patients (pts) with heart failure and reduced left ventricular fraction (HFrEF).

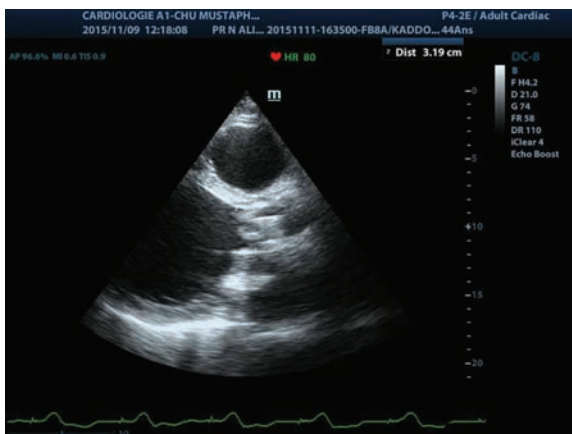
**Methods:** From January 2005 to January 2015, 401 patients, 230 males and 171 females, sex ratio 1.3, mean age  $62 \pm 15$  years with depressed left heart failure were analyzed. Epidemiological, anthropometric, chest radiography, EKG and echocardiographic data in the context of a prospective mono centric observational study were assessed.

**Results:** Association of hypertension and diabetes was found in 30% of the patients. Smoking is present in 40% of the male patients. Right heart failure in 325 (81%), left heart failure in 296 patients (73%). Cardiomegaly in 351 (87%) of the patients. Atrial fibrillation occurs in 99 pts (25%), complete left bundle branch block (LBBB) in 32 pts (8%) and electro stimulated rhythm in 13% of them. Average Left ventricular ejection fraction is present in  $42 \pm 8\%$  and pulmonary arterial hypertension in 190 pts (47%). Regarding medical treatment : 301 pts (75%) were on ACE Inhibitors (Angiotensin Converting Enzyme Inhibitors inhibitors), 100 (24%) on Angiotensin II Receptor Blockers (ARBs), beta blockers: 355 (88%) and spironolactone: 155 (38%). Cardiac resynchronization therapy (CRT/P/D) occurs in 20 pts with LBBB (62%) and failed in 8 of them.

**Conclusion:** In our country, age and etiology for heart failure differs from the European ones: our patients are younger and etiologies are mainly valvulopathies followed by coronary diseases closely related to hypertension and diabetes.

#### Etiology of cardiovascular diseases

Valvulopathies (n, %)	98 (24)
Dilated cardiomyopathy	123 (30)
History of coronary disease (n, %)	88 (21)
Hypertensive cardiovascular disease (n, %)	11 (2.7)
Toxic cardiomyopathy (Anthracyclin) (n, %)	3 (0.7)
Arrhythmogenic right ventricular dysplasia (n, %)	3 (0.7)
Grown up congenital heart disease (n, %)	2 (0.4)
Myocarditis (n, %)	2 (0.4)
Left ventricular non compaction (n, %)	1 (0.02)
Hypertrophic cardiomyopathy (n, %)	1 (0.02)



CRT-P in patient with aortic prothesis

## P223

### Who diagnoses and treats patients with chronic heart failure in Germany? A retrospective study of the health risk institute healthcare claims database

This research was funded by Novartis Pharma AG, Basel, Switzerland  
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**Background:** Little is known about the journey of patients with newly diagnosed chronic heart failure (CHF) in real-world settings in Germany. Therefore, a retrospective study of anonymized healthcare claims data from the Health Risk Institute (HRI) database was conducted.

**Purpose:** The objective was to describe the journey of patients with newly diagnosed CHF in Germany.

**Methods:** Data from patients with at least two recorded CHF-related diagnoses in 2011 (based on ICD-10 German Modification codes for CHF in a hospital or ambulatory setting) were analysed. Further, a subgroup of patients with newly diagnosed CHF was identified based on the absence of a CHF diagnosis in the year before first diagnosis in 2011. All patients were followed for 2 years.

**Results:** CHF was newly diagnosed in 26 368 patients; in 63.2% ( $n=16\,653$ ) the diagnosis was made by an office-based physician, in 36.6% ( $n=9653$ ) the diagnosis was made in a hospital inpatient setting. Among patients diagnosed by an office-based physician, 61.6% ( $n=10\,254$ ) of diagnoses were made by family practitioners and 21.6% ( $n=3595$ ) by specialists in internal medicine; of the latter, 68.5% ( $n=2462$ ) of diagnoses were made by cardiologists. A small proportion (7.0%,  $n=1171$ ) of first CHF diagnoses were made by an office-based physician outside of family and internal medicine. Among patients with a first CHF diagnosis made in a hospital inpatient setting, 70.7% ( $n=6827$ ) of diagnoses were made by internal medicine specialists; 27.3% ( $n=1864$ ) of these were made by cardiologists. There was no information available for CHF diagnosed in a hospital outpatient setting. Of patients surviving the first quarter after CHF diagnosis (95.4%,  $n=25\,155$ ), almost all (98.0%,  $n=24\,641$ ) were treated in primary care in the same quarter; this proportion remained virtually unchanged after 2 years. Of note, 26.0% ( $n=6541$ ) of these patients received additional hospital inpatient care in the first quarter after CHF diagnosis; this decreased to 14.9% after 2 years. A much smaller proportion of patients (4.2%,  $n=1058$ ) received hospital outpatient care; this fraction remained almost unchanged after 2 years.

**Conclusions:** These results demonstrate the pivotal role of family practitioners as the primary point of contact in the diagnosis and management of patients with CHF. Close collaboration and communication between all specialities and sectors is essential for providing optimal care for these patients. Further studies are needed to quantify the effectiveness of patient journeys in terms of costs and patient outcome.

## P224

### Implementation of device therapy in LVSD (HFREF) as per the new UK nice guidelines: real world experience in a UK district general hospital

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**Background/Introduction:** New UK National Institute for Clinical Excellence (NICE) guidelines have been published in June 2014 with respect to device therapy for Heart Failure with Reduced Ejection Fraction (HFREF) and QRS durations of  $>120\text{ms}$ . The Institute has updated the recommendations in the use of Cardiac Resynchronisation Therapy (CRT) with or without an associated Implantable Cardiac Defibrillator (ICD) in Left Ventricular Ejection Fractions (LVEF) of  $<35\%$ .

**Purpose:** This retrospective, observational audit was conducted to evaluate the implementation of the NICE guidelines in real world terms in a UK District General Hospital. In this particular setting, cardiac devices are inserted off-site with the support of a local electrophysiologist.

**Methods:** Electronic patient records for admissions in patients labelled with heart failure over a period of 6 months (Aug 2014 – Feb 2015) were analysed. Patients with  $\text{LVEF} < 35\%$  on Transthoracic Echo with associated  $\text{QRS} > 120\text{ms}$  on surface ECG were identified. Results 226 patients were found to have  $\text{LVEF} < 35\%$ , out of which only 49 patients had  $\text{QRS} > 120\text{ms}$ . This constituted the study population (ie.  $n=49$ ). The ages ranged from 60 to 95 years old with 75% ( $n=37$ ) being in the 70-89 age bracket. 65% ( $n=32$ ) were male. 55% ( $n=27$ ) had underlying AF. 63% ( $n=31$ ) had LBBB with only 1 of these having a  $\text{QRS} > 150\text{ms}$ . 32% ( $n=16$ ) mortality at 6 months with the overwhelming majority (81%,  $n=13$ ) not having a device already in situ. 27% ( $n=13$ ) of patients had a device (CRTp/CRTd/ICD) in situ with a 23% ( $n=3$ ) mortality at 6 months. 8% ( $n=4$ ) of patients who were eligible for a device and did not have any other disqualifying reason (eg frailty, patient choice) were deemed to have been missed, and hence guidelines not been adhered to.

**Conclusions:** The population eligible to receive device therapy in HFREF is ageing, with over three quarters being in excess of 70 years old. Mortality at 6 months appears to be higher if a patient does not have a device. For this particular District

General Hospital, there appears to be good adherence of 92% to new UK guidelines pertaining to device therapy in HFREF.

**P225**

**The use of digoxin and its association with mortality in heart failure patients**

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**Introduction:** Digoxin is a drug use to treat heart failure especially in those with left ventricle ejection fraction (LVEF) reduced and/or atrial fibrillation. It has been reported the risk/benefit of the minimum concentration (0.5-0.9 ng/ml) reducing the mortality. Nevertheless, some studies have report that the mortality increased with concentration above of 1ng/ml.

**Objective:** Assess if the digoxin use in patients with heart failure increase the mortality risk.

**Materials and methods:** Retrospective cohort study carried out in the Heart Failure and Respiratory Clinic in 279 patients on digoxin therapy. The patients were divided in two groups according with the outcome (surviving=255 and death=24). Were analyzed, demographic (sex, gender), anthropometric (BMI, dynamometry, hip and waist circumference), body composition thorough bioelectrical impedance (phase angle) clinics (NYHA), echocardiography characteristics and co-morbidities.

**Results:** The 59.9% were male (167), mean age was 62.6 ± 15.3. The ejection fraction was: 40.1% (112 LVEF), 12.2% (34), and 36.9% (103) right heart failure. To compare the surviving/mortality groups we used a T student independent; significant difference were found between waist (94.7 ± 15.5 vs 87.8 ± 10.9, p=0.02), and hip (100.7 ± 12.4 vs 94.2 ± 6.9, p < 0.001) circumferences, ischemic heart disease (35.9% (80) vs 71.4% (15), p=0.001), NYHA 1: 32.1% (80) vs 25% (6), NYHA 2: 41.4 % (103) vs 29.2% (7), NYHA 3: 21.3% (53) vs 45.8% (11), NYHA 4: 5.2% (13), p=0.04. Respect to other drugs: nitrates 35.3% (90) vs 75% (18), p < 0.0001. A Cox regression model was made to value the risk of digoxin use on mortality adjusted by demographic, body composition, pharmacologic treatment and clinics variables, as well as co-morbidities. A risk of 4.23(IC95 1.12 - 15.8, p=0.03) were found

**Conclusion:** Patients with heart failure had 4 fold risk of die because the digoxin use compare with those with not use. Nevertheless those who died were chaquectic (69.1) and have a worst clinic status, indeed, it could be explain our these results.

**P226**

**Effects of valsartan/sacubitril on parameters of ventricular-arterial coupling in patients with heart failure and reduced ejection fraction**

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**Objective:** Angiotensin receptor-neprilysin inhibition with LCZ696 is a novel approach for the treatment of heart failure with reduced ejection fraction (HFREF). The aim of the study was to assess the effects of valsartan/sacubitril on parameters of ventricular-arterial coupling and left ventricular (LV) work efficiency in patients with stable HFREF.

**Methods:** In the open-label follow-up to PARADIGM HF study 18 patients with stable HFREF (16 male, 69 ± 9 years (M ± SD), arterial hypertension 83%, previous myocardial infarction 89%, diabetes mellitus 39%, dyslipidemia 56%, LVEF 32 ± 4%, serum creatinine 118 ± 21 µmol/l, eGFR 56 ± 13 ml/min/1.73m<sup>2</sup>, potassium 4.45 ± 0.35 mmol/l) were enrolled. Patients received a stable background treatment for at least a month (ACEI 94%, beta-blockers 100%, aldosterone receptor antagonists 83.3%, loop diuretics 72.2%). ACEI treatment was interrupted for 36 h and replaced with LCZ696 100 or 200 mg (11 patients) BID according to baseline brachial BP (mean dose 185.7 ± 36.3 mg BID). 2-dimentional echocardiography was performed to assess arterial (Ea) and end-systolic LV elastance (Ees) baseline and after 6 month LCZ696 therapy. VAC was assessed as the ratio Ea/Ees. Wilcoxon test was considered significant if p < 0.05.

**Results:** Baseline brachial BP decreased from 137.1 ± 22.0/83.4 ± 11.8 to 120.5 ± 13.5/75.1 ± 9.3 mmHg (Δ -16.6 ± 14.2/-8.3 ± 10.3 mmHg, p < 0.05), heart rate did not change (78 ± 12 vs 75 ± 15 beats/min (Δ -2.7 ± 14.7 beats/min, p>0.05). LCZ696 therapy was associated with significant decrease of VAC (2.10 ± 0.55 vs 1.68 ± 0.32, p < 0.05), Ea (2.11 ± 1.04 vs 1.66 ± 0.6 mmHg/ml/m<sup>2</sup> (Δ -0.70 (-0.26%)), p < 0.05), arterial peripheral resistance (0.029 ± 0.016 vs 0.027 ± 0.011 mmHg/ml/min, p < 0.05), increase of stroke volume (63 ± 24 vs 78 ± 26 ml, p < 0.05). Ees remained unchanged (1.11 ± 0.42 vs 1.01 ± 0.52 mmHg/ml/m<sup>2</sup>, p>0.05). LCZ696 therapy was associated with potential energy decrease (8049 ± 2846 vs 5037 ± 2492 mmHg\*ml/m<sup>2</sup>, p < 0.05), stroke work/pressure-volume area index (LV work efficiency) increase (0.48 ± 0.09 vs 0.63 ± 0.05, p < 0.05). There was no statistically significant correlation between decrease of Ea and brachial BP decrease. LCZ696 was well tolerated and there were no BP-related adverse events.

**Conclusion:** In stable patients with HFREF LCZ696 therapy was associated with BP-independent improvement in VAC related with decrease of Ea rather than Ees changes. Treatment with LCZ696 was also associated with decrease of arterial peripheral resistance and improvement of LV work efficiency

**P227**

**Value of right ventricular function measurements in cardiac CT for patients with severe heart failure**

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**Purpose:** Right ventricular (RV) function is a parameter of paramount importance to define and modify treatment in patients with severe heart failure. Since many patients carry non-MR compatible pacemakers or defibrillators, we compared RV function in cardiac CT with echocardiography and invasive catheter as gold standard.

**Methods:** Twenty-six patients with severe cardiomyopathy (EF <35%) underwent 128-dual source ECG-gated cardiac CT with a biphasic contrast agent injection protocol to define RV function (EF, end diastolic and systolic volume). Measurements were compared to transthoracic echocardiography (EF, TAPSE, RA diameters) and invasive catheter (right atrial pressure, right ventricular contractility).

**Results:** While RV-EF in CT showed no significant correlation with TAPSE (r = 0.366, p = 0.94), the correlation to right atrial pressure (RAP) was moderate (r = 0.595, p = 0.006). TAPSE correlated non-significantly with RAP (r = 0.317, p = 0.23). Increasing severity of tricuspid regurgitation in TTE was significantly, inversely correlated with RV-EV in CT (r = 0.44, p = 0.05) and stronger correlated with RAP (r = 0.58, p = 0.02), while TAPSE showed a weaker trend (r = 0.29, p = 0.2). **Conclusion:** RV-EF in cardiac CT may be a better surrogate for right atrial pressure than TAPSE in CMP patients with severe CMP and thus pose a useful alternative to MR in case of incompatibility.

**P228**

**Evaluation of the effect of taurine supplementation in chronic heart failure patients; a new study on old amino acid.**

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**Background/Introduction:** Ample of preclinical studies pointed out a huge benefit of taurine on cardiac functions. There is no recommendation with or against taurine supplementation due to paucity of clinical studies.

**Purpose:** Our aim was to test the effect of taurine on NT-proBNP levels, NYHA class and echocardiographic parameters in chronic heart failure (CHF) patients.

**Methods:** 34 CHF patients admitted to cardiac rehabilitation program were randomized into two groups as follows: -taurine group received 1 gm taurine capsule twice daily and guideline based therapy (beta-blocker, ACE-I or ARB, MRA and diuretics) -control group received only guideline based therapy. Evaluation of patients were performed at baseline and after two months regarding: NT-proBNP, NYHA class and echocardiographic parameters.

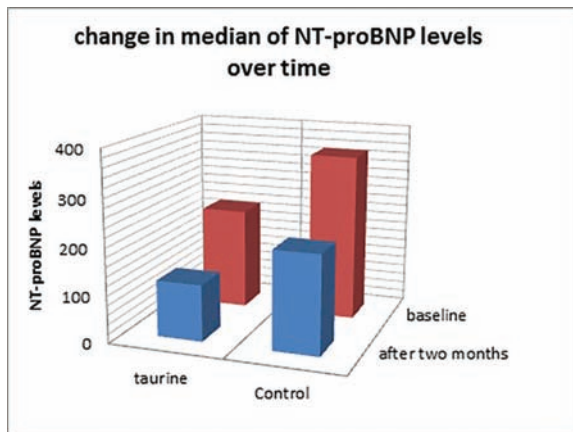
**Results:** All variables were comparable at baseline in both groups except for LVESV which was lower in taurine group. There were a significant reduction in NT-proBNP levels in taurine group (median; from 216.4 to 120.1 pg/ml, p = 0.009) and in control group (median; from 352.7 to 208.8 pg/ml, p = 0.002). However, the percent change between groups was not significant. Regarding NYHA class, taurine group showed significant improvement (median; from 2 to 1, p = 0.002) while control group showed improvement but without statistical significance. Improvement of echocardiographic parameters occurred in both groups but without statistical significance.

**Conclusion:** Despite the early promising results of previous studies on taurine, this study did not show favorable effects of taurine on lab, NYHA class or echocardiographic parameters in CHF patients subjected to cardiac rehabilitation.

	taurine group (n = 16)	control group (n = 18)	P-value
Age (years)	54.06 ± 9.06	54.28 ± 10.31	ns
Gender (M/F), n	13/3	16/2	ns
Etiology of HF (ischemic/non-ischemic), n	13/3	15/3	ns
NYHA class (II/III), n	11/5	12/6	ns
LVEF (%)	35.8 ± 3.9	32.4 ± 6.6	ns
LVEDV(ml)	168 ± 39.6	215 ± 88.7	ns
LVESV(ml)	107 ± 28	146 ± 63.3	0.02

baseline data of the study groups





### P229

#### Role of echocardiography in identifying patient at risk of adverse events in a heart failure reduced ejection fraction (HFREF) population: a single center experience

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**Background:** Heart failure (HF) is still the first cause of hospitalization and death in Western countries, with significant burden of costs for healthcare system. Several clinical parameters, laboratory and instrumental tools have been extensively studied and applied to predict outcome of HF patients. Echocardiography is the most useful tool to achieve this goal, based on its large availability and relative low cost, in the face of the numerosity of information obtained

**Purpose:** Aim of this study is to investigate any association between echocardiographic parameters and adverse events (death and/or hospitalization for HF) in a cohort of HF outpatients, referred to our center as heart transplant (HTX) candidate.

**Methods:** This is a prospective observational study of a single center HF patient population. Between November 2011 and September 2014, all patient with ejection fraction (EF) <35% referred to outpatient clinic of our Institution for evaluation for HTX candidacy have been enrolled in the study. Criteria of exclusion were congenital cardiomyopathy, recent hospitalization (<1 month) for HF, recent myocardial revascularization or cardiac resynchronization device implant (<6 months). At enrollment, clinics and demographics data, labworks, glomerular filtration rate with MDRD formula, 12-leads EKG and transthoracic echocardiogram were recorded. Such evaluation was repeated every six months and events (death and/or hospitalization for HF) registered. Association between clinical, laboratory, echocardiography data and events was analyzed.

**Results:** During the period of observation 217 patients (82% males) were enrolled in the study. Mean age was 59,4 ± 10,2 years, mean EF 27%. Median follow-up was 27 months (range 12-39). During the period of observation we recorded 16 death and 53 hospitalizations for cardiac causes, for a total of 47 patients reaching the end-point. At univariate analysis, a bigger left ventricle end-diastolic diameter (LVEDD, 67 ± 7 vs 62 ± 7 mm, p < 0.0001) and volume (LVEDV, 228 ± 69 ml vs 191 ± 64 ml, p = 0.003), a

lower EF (23 ± 6 vs 27 ± 6%, p < 0.0001), a bigger left atrium diameter (LAD, 51 ± 9 vs 4. ± 7 mm, p < 0.0001) and volume (LAV, 109 ± 46 vs 86 ± 41 ml, p = 0.007), an higher E/e' ratio (17.4 ± 9 vs 13.4 ± 6.5, p = 0.012), a bigger mitral regurgitation vena contracta (2.6 ± 1.2 vs 1.9 ± 1.3 mm, p = 0.002), a lower TAPSE (17 ± 5 vs 19 ± 4 mm, p < 0.04) and a higher estimated central venous pressure (8 ± 4.7 vs 6 ± 3.6 vs, p = 0.01) were associated with combined endpoint. At multiple logistic regression analysis, lower EF (HR 0.937, p = 0.036), higher LVEDD (HR 1.060, p = 0.008) and LAD (HR 1.048, p = 0.011) were associated with combined endpoint

**Conclusion:** Our experience confirms that in a cohort of HFREF patients, most of the parameters currently used has been associated with adverse events (death and/or hospitalization for HF). Moreover, EF, LVEDD and LAD resulted associated with outcome, independently from other clinical and echocardiographic variables.

### P230

#### Exposure to heart failure treatments in newly diagnosed patients in Sweden

This research was funded by Novartis Pharma AG, Basel, Switzerland G Wikstrom<sup>1</sup>; K Boman<sup>2</sup>; M Olofsson<sup>2</sup>; K Lindmark<sup>3</sup>; R Lahoz<sup>4</sup>; S Corda<sup>4</sup>; V Wintzell<sup>5</sup>; R Linder<sup>5</sup>; A Gondos<sup>6</sup>; J Stalhammar<sup>7</sup>

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<sup>3</sup>Umea University, Heart Centre, Department of Public Health and Clinical Medicine, Umea, Sweden; <sup>4</sup>Novartis Pharma AG, Basel, Switzerland; <sup>5</sup>IMS Health Sweden, Stockholm, Sweden; <sup>6</sup>IMS Health Germany, Berlin, Germany; <sup>7</sup>Uppsala University, Department of Public Health and Caring Sciences, Uppsala, Sweden

**Background:** Exposure to heart failure (HF) therapies in newly diagnosed patients is unclear; a better understanding of therapy combinations used may improve treatment.

**Purpose:** To characterize HF therapies for patients with newly diagnosed HF (main ICD-10 code I50) in Sweden.

**Methods:** Primary and secondary care electronic medical records and the Swedish Prescribed Drug Register were used to identify patients and prescribed therapies. Patients (≥18 years) with a first HF diagnosis (index date) from 01/01/10–31/03/15 were included. A 9-year look-back period to exclude prevalent cases and a 2-year follow-up period per patient were applied. A therapy episode was assumed to last from first dispensation to 30 days after last dispensation (≤120 days between dispensations). Predefined therapy groups (including 'no therapy') were analyzed: angiotensin-converting-enzyme inhibitors (ACEi), angiotensin receptor blockers (ARB), beta-blockers (BB) and mineralocorticoid receptor antagonists (MRA) (alone or combined).

**Results:** Of 8777 records, 1885 patients were identified (45% women; mean age: 75 years); 357 (19%) had confirmed HF with reduced ejection fraction (HF-rEF; left ventricular EF ≤50%), 217 (12%) had confirmed HF with preserved EF (HF-pEF; left ventricular EF >50%) and 1311 (70%) had HF of unconfirmed phenotype (HF-unknown). One year after index, triple therapy (any combination) was used more often for HF-rEF than for HF-pEF or HF-unknown (Table 1). Dual therapy was consistently used more frequently than triple therapy. Proportions of patients in the following groups varied from 1 year before index to 1 year after index: ACEi+BB (1 year before index: 14%; at index: 22%; 1 year after index: 21%); ACEi+BB+MRA (1 year before index: 3%; at index: 10%; 1 year after index: 12%); and ARB+BB (1 year before index: 8%; at index: 11%; 1 year after index: 12%). Peak therapy exposure arose 2 months after index in all cases.

**Conclusions:** Patients with HF-rEF were more intensively treated with triple therapy than those with HF-pEF, as per ESC guidelines and evidence. Confirming HF phenotype may optimize HF therapies.

61058. Table 1

Therapy type	HF with reduced ejection fraction (n = 357)		HF with preserved ejection fraction (n = 217)		HF of unknown phenotype (n = 1311)					
	1 year before index	At index	1 year before index	At index	1 year before index	At index	1 year before index	At index	1 year after index	1 year after index
Single	28	25	18	29	28	28	34	29	28	28
Dual	17	30	39	30	41	44	29	41	41	41
Triple	5	19	30	9	16	19	7	15	18	18
Quadruple	0	2	3	0	0	0	0	1	0	0
None	49	24	10	31	14	8	30	14	14	14

## P231

**Effect of ivabradine on functional status and cardiovascular disease risk of mortality, in patients with heart failure and left ventricular dysfunction. A PanHellenic prospective study**

SERVIER HELLAS

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**Background/Introduction:** Heart failure (HF) patients present increased cardiovascular (CV) morbidity and mortality and thus, are classified as high CV risk patients. Medical treatment represents the cornerstone to improve prognosis and reduce rehospitalizations in those patients.

**Purpose:** To record the effect of ivabradine on functional NYHA classification, as well as on the CV risk, in patients with HF and left ventricular systolic dysfunction (LVSD), recently hospitalized (in the last 6 months) for HF decompensation. To record patient's adherence with ivabradine treatment, co-administered medical treatments, as well as co-existing risk factors and comorbidities.

**Methods:** In this observational study, 1603 HF patients with LVSD were prospectively recorded from 140 public or private cardiology departments or practices. The estimation of the 10 year % risk of CV disease mortality was assessed through the FINRISK chart (including the following variables: age, gender, smoking, BMI and resting heart rate (HR)).

**Results:** From 1603 HF patients who participated in the study, 12 patients (0.7%) prematurely discontinued treatment. 67% of the sample were males aged  $69.4 \pm 10.8$  years, while mean HR was  $82.0 \pm 10.9$  bpm. After 4 months treatment, ivabradine addition resulted into an improvement of NYHA functional class; the percentage of patients NYHA I/II increased from 0%/48.5% to 32.7%/57.9%, while the percentage of patients NYHA III&IV decreased from 51.5% to 9.4% ( $p < 0.001$ ). Heart rate was decreased from  $82.0 \pm 10.9$  bpm to  $66.7 \pm 6.4$  bpm ( $p < 0.001$ ), leading to an improvement on 10 year % risk of CV disease mortality score. The percentage of patients with a 10 year % risk  $\geq 10\%$  decreased from 47.6% to 24.4%, while the percentage of patients with a 10 year % risk  $< 10\%$  increased from 52.4% to 75.7% ( $p < 0.001$ ).

**Conclusions:** Ivabradine administration in patients with HF and LVSD improves not only NYHA classification, but also the 10 year % risk of CV disease mortality.

## P232

**Characterisation of circulating hepcidin levels in patients with heart failure**

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**Background:** Anaemia and iron deficiency (ID) are important factors for muscle function and exercise capacity in patients with chronic heart failure (HF). Their interaction in HF remains to be defined.

**Methods:** A total of 253 patients with stable chronic HF (mean age:  $67 \pm 11$  y, 21% female, left ventricular ejection fraction [LVEF]  $39 \pm 13\%$ , body mass index [BMI]  $29.5 \pm 5.5$  kg/m<sup>2</sup>, New York Heart Association [NYHA] class  $2.3 \pm 0.6$ , diabetes mellitus 30%, glomerular filtration rate  $53.7 \pm 15.6$  mL/min) were enrolled from 2010 and followed until April 2014 or until they died. Anaemia was defined according to World Health Organization criteria [Hb  $< 13$  g/dL in men,  $< 12$  g/dL in women]. Iron deficiency (ID) was defined as serum ferritin  $< 100$  µg/L or ferritin  $< 300$  µg/L with transferrin saturation (TSAT)  $< 20\%$ . Exercise capacity was assessed by spiroergometry (peakVO<sub>2</sub>) and 6-minute walk test (6MWT).

**Results:** A total of 72 patients (28%) presented with anaemia and ID was present in 122 patients (48%). Differentiating all patients according to iron status, patients with ID had lower peak VO<sub>2</sub>  $15.5 \pm 5.1$  vs. patients without ID  $17.9 \pm 4.5$  mL/kg/min ( $p = 0.0002$ ). Likewise, hand grip strength was significantly reduced in patients with ID ( $34.3 \pm 11.8$  vs. patients without ID  $39.1 \pm 11.7$  kg,  $p = 0.002$ ) and 6MWT was reduced in patients with ID ( $400.8 \pm 140.1$  vs. patients without ID  $456.2 \pm 129.8$  m,  $p = 0.002$ ). Patients with ID showed significantly lower serum hepcidin ( $11.8 \pm 11.6$  vs. patients without ID  $18.6 \pm 12.4$  ng/mL,  $p = 0.002$ ), lower L-Kynurenin ( $3.6 \pm 1.5$  vs. patients without ID  $3.3 \pm 1.3$  µmol/L,  $p = 0.04$ ) and higher FGF-23 levels ( $216.8 \pm 242.3$  vs. patients without ID  $117.9 \pm 122.2$  RU/mL,  $p < 0.0001$ ), higher PTH ( $61.3 \pm 36.3$  vs patients without ID  $51.0 \pm 30.2$  pg/mL,  $p = 0.02$ ). There were no differences in serum hepcidin between anaemic and non- anaemic patients. Patients with HFpEF showed significantly higher hepcidin levels ( $20.1 \pm 16.2$  ng/mL) than patients with HFrEF ( $14.2 \pm 10.8$  ng/mL,  $p = 0.02$ ). Regardless of HFpEF or HFrEF patients in NYHA I-II had lower levels of hepcidin ( $14.0 \pm 10.9$  ng/mL) than patients in NYHA III&IV ( $18.8 \pm 14.5$  ng/mL,  $p = 0.03$ ).

**Conclusion:** Increased level of hepcidin characterizes an early stage of HF, and is not accompanied by anaemia. The progression of HF is associated with the decline in circulating hepcidin and the development of ID.

## P233

**Systematic assessment of heart failure data sources across 120 countries: analysis of their suitability for real-world evidence research**

This research was funded by Novartis Pharma AG, Basel, Switzerland  
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**Background:** There is a wealth of global real-world data relating to patients with heart failure (HF).

**Purpose:** This study aimed to identify real-world patient-level HF data sources in 120 countries across seven geographical regions that could be used in observational research designed to generate real-world evidence in HF. The study also aimed to critically evaluate data sources completeness to address pre-specified research questions in at least one data source from each country.

**Methods:** A systematic literature review for the period from 1 January 2010 to 7 December 2014 was conducted in Medline and EMBASE. A search of ISPOR databases, a focused Internet search and a survey of Novartis and Mapi colleagues were also conducted. A database abstraction tool was developed to record information on each data source. The value of each source for observational research was scored using 15 criteria relating to data on: patients with acute and chronic HF; five essential variables (including left ventricular ejection fraction); six pre-specified HF real-world evidence research questions (on epidemiology, treatment patterns, predictors of outcomes, safety, effectiveness and burden of illness); sample size of  $> 1000$ ;  $\geq 1$  year of follow up; and accessibility to pharmaceutical companies.

**Results:** Overall, 1034 unique HF data sources were identified. Of these, 150 data sources (24 international and 126 national) covering 103 countries were selected for detailed evaluation. Coverage of variables related to the pre-specified HF real-world evidence research questions varied across sources, with the degree of completeness ranging from 0–97%; the largest number of sources ( $n = 35$ ) had data which were 41–50% complete across variables. Of the variables related to the research questions, the most complete were age and sex (93%) and comorbidities (84%); the least complete were use of procedure codes (7%) and prescription codes (6%) and dates of procedures and prescriptions (6%). All geographical regions had at least one level-3 (high value) data source (44 level-3 sources in total). There were no level-4 (very high value) data sources.

**Conclusion:** There are many data sources containing real-world patient-level data on HF across the globe. However, the data available on real-world safety, effectiveness and burden of illness are limited. These limitations may be overcome by linking sources using patient identifiers. These evidence gaps need to be addressed so that existing data sources can be made suitable for observational studies in HF.

## P234

**Review in a specialist heart failure clinic is associated with reduced hospitalisation in patients with suspected heart failure and raised natriuretic peptides**

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**Introduction:** In the UK, national guidelines (NICE) recommend that patients with suspected heart failure (HF) and raised natriuretic peptides are seen at a specialist clinic for timely echocardiography and assessment. Limited data are available on whether this affects outcome. The aim of this study was to compare outcomes in patients with suspected HF and raised natriuretic peptides who were reviewed in a specialist clinic (HF clinic) to those who were managed in non-specialist primary care settings (No HF Clinic).

**Methods:** Data were collected retrospectively from hospital records. All outpatients with a raised NTproBNP ( $> 400$  pg/ml) from February to September 2014 were included in the study. Outcomes assessed were hospital admissions, length of stay, reason for admission and mortality. Minimum follow up was 6 months from the raised NTproBNP result.

**Results:** 567 consecutive patients were identified: 161 (28%) in the HF Clinic group and 406 (72%) in the No HF Clinic group. All HF clinic patients were seen within 2 weeks (NTproBNP  $> 2000$ pg/ml) or 6 weeks (NTproBNP 400-2000pg/ml) of referral in line with NICE recommendations. Mean follow up was  $8.9 \pm 2.3$  months. Results are shown in Table 1.

**Conclusions:** Hospitalisation rates were extremely high over a relatively short follow up period. Patients reviewed in HF clinic had much higher NTproBNP levels, suggesting they were at higher risk of adverse outcomes, yet also had significantly lower rates of all cause and cardiovascular hospitalisation. The data are observational so causation and association cannot be separated however the magnitude of difference between the two groups suggests referral to HF clinics may improve outcomes. Our findings support national guidelines that patients with suspected HF and raised natriuretic peptides should be seen at a specialist clinic.

Table 1

	HF clinic (n = 161)	No HF clinic (n = 406)	p value
Age	78 ± 9	80 ± 9	0.02
Males	84 (52%)	195 (48%)	0.42
Average NTproBNP	3352	2365	<0.0001
All-cause hospitalisation	37 (22.3%)	180 (44.3%)	<0.0001
CV hospitalisation	4 (2.5%)	57 (14.0%)	<0.0001
Deaths	9 (5.6%)	33 (8.1%)	0.3
Mean hospital stay	4.7 days	5.6 days	0.42

### P235

#### Value of anti-HLA antibodies monitoring during the first year after cardiac transplantation

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**Introduction:** Examination of anti-HLA antibodies (HLAab) by solid base methods (Luminex) before cardiac transplantation (CTX) is useful for screening patients (pts) at risk of antibody-mediated rejection (AMR) after CTX. The value of de novo HLAab developed after CTX is less clear. Purpose Aim of the study was to estimate whether monitoring of HLAab during the 1st year after CTX can be useful for prediction of rejection and mortality of the pts.

**Patients and methods:** Between 1/2011 – 7/2013 CTX was performed in 119 pts. We prospectively studied the group of 97 pts with complete clinical and immunological data, who survived 1st 12 months after the operation. Follow-up was 27-57 months. Examination of HLAab was performed before CTX and in 1st, 3rd, 6th and 12th month after CTX. The results were correlated with clinical events (treated cellular rejection – ACR, AMR, graft dysfunction and death / retransplantation). ACR and AMR were assessed from endomyocardial biopsy (EMB) samples, decrease of left ventricular ejection fraction (LV EF) below 40 % was sign of graft dysfunction. HLAab were investigated by Luminex method. Results HLAab class I (I) were found in 33 % of pts (in 13 % only after CTX – de novo). HLAab class II (II) in 11.8 % (in 7, 5 % de novo). Donor specific ab (DSA) were found in 16 %. ACR occurred in 13 pts, AMR in 6, graft dysfunction in 13 pts. Nine pts died, 6 of them from cardiovascular (CV) cause. Pts with de novo HLAab II had higher rate of (1) ACR (26 % vs 9 %, p=0.042; OR 6.3 [1.2 – 32.5] PPV 43 %, NPV 89 %); (2) graft dysfunction (43 % vs 11 %, p=0.047; OR 6.2 [1.2 – 32.1]; PPV 43 %, NPV 89 %); (3) mortality from CV cause (28.6 % vs 3.6 %, p=0.046; OR 10.8 [1.5 – 80.1]; PPV 29 %, NPV 96 %). Patients with de novo DSA experienced higher rate of graft dysfunction (42.9 % vs 10.0 %, p=0.04; OR 6.8 [1.3 – 35.7]; PPV 43 %, NPV 90 %).

**Conclusions:** Absence of HLAab II during the 1st year after CTX predicted good clinical outcome in middle-term follow up, but positive predictive value was low. Developing de novo HLAab did not allow prediction of AMR in our group of pts.

### P236

#### Cardiac resynchronisation in elderly patients: improvement in left ventricle ejection fraction in real world.

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**Background:** improvement in left ventricle ejection fraction (LVEF) after cardiac resynchronization therapy (CRT) appears in around 57%, when pooled data are analysed. Response in the elderly is poorly defined. We aimed to study echocardiographic response to CRT in a group of elderly patients (≥75 years old).

**Methods:** A total of 45 patients (mean age 79.2 ± 2.9 years; 79.6% men) undergoing CRT implantation between June 2006 and October 2014 were studied. Echocardiographic response was defined by an improvement in LVEF ≥15% (relative).

**Results:** average LVEF was 23.1 ± 6.7% at the time of the implant. The mean QRS duration was 155.4 ± 25 ms and mean left ventricle end diastolic diameter (LVEDD) was of 60.4 ± 6.6 mm. Left bundle branch block (LBBB) was present in two thirds and most of the patients included were in NYHA III-IV functional class (FC) (54.2%). Population was under optimal medical treatment (Beta blockers: 87.5%; ACEI (angiotensin-converting enzyme inhibitors)/ARB (angiotensin II receptor blockers): 64.6/27.1% respectively). After a mean follow up of 37.2 months, a significant improvement in LVEF (mean value: 30.8 ± 13.7%) and FC (NYHA I-II in 60.5% of population) was observed and the mean LVEDD also decreased (57.3 ± 9.3 mm). Response estimated by LVEF improvement of ≥5% was observed in 55.6% of

the sample (25 patients). Responders not only showed significant improvement in LVEF (baseline LVEF 23.3 ± 6.6 and final LVEF 30.7 ± 13.8; p=0.001) compared with non responders (baseline LVEF 22.9 ± 6.7 and final LVEF 24.7 ± 9.6; p=0.297) but also greater reductions in LVEDD (baseline 59.3 ± 7.7 mm and final 53.3 ± 10.1; p=0.014 in responders Vs baseline 61.4 ± 4.6 mm and final 61.9 ± 5.9; p=0.655 in non responders). None of the predictors of response to CRT in general population (gender, non-ischemic etiology, LBBB, QRS duration, sinus rhythm) were useful in our population of elderly patients.

**Conclusion:** echocardiographic response to CRT in old patients was similar than in younger population. Up to 55.6% of elderly patients under optimal medical treatment showed a significant improvement in LVEF after long-term follow up. Indications used for CRT in general population must be also followed in patients ≥ 75 years.

### P237

#### Use and benefit of angiotensin-converting enzyme inhibitors/ angiotensin receptor blockers in senior patients with left ventricular systolic dysfunction

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**Background:** ACE inhibitors and ARBs have been demonstrated to enhance survival in patients with HF and reduced ejection fraction (EF), therefore its use has a class I indication in this patient population according to current guidelines.

**Purpose:** We aim to assess the use and benefit of ACEi/ARB's in the daily clinical practice in elderly patients.

**Methods:** Between 2008 and 2013 we prospectively collected and analysed clinical and technical data of patients over 75 years diagnosed with left ventricular EF < 35% by transthoracic echocardiography in our laboratory. At the end of the follow-up, medical history and test results were completed by a detailed medical report review. We evaluated the rates of mortality and cardiac events, defined as death from cardiovascular cause or hospitalization for Heart Failure.

**Results:** A total of 802 patients were included with a mean age of 82 ± 4.9 years, 33.8% were female and the mean LVEF was 28 ± 6.5% at inclusion. The rate of high BP was 79.2%. Thirty-three percent of the population was diabetic and 35.7% had chronic renal disease. During the follow-up (32.7 ± 22.7 months), 381 patients (47.5%) died and there were 496 cardiac events (61.8%). Regarding anti-remodelling therapy, 73.9% of the study population was on ACEi/ARBs, 69.3% on beta blockers and 45.1% of the patients received aldosterone antagonists. Although the use of ACEi resulted to be associated to a significantly lower mortality (OR:0.66;0.53-0.82) and cardiac event rate (OR: 0.65;0.54-0.79), 26.1% of our patients did not receive this therapy during the follow-up. Chronic renal disease (32.8%), dizziness or hypotension (16.9%), and hyperkalaemia (2.2%) resulted to be the most common causes of not taking ACEi/ARBs. Nevertheless in 28.4% of the patients no formal contraindication was found.

**Conclusions:** In our study population, ACEi/ARBs therapy was associated to a lower mortality and cardiac event rate. However, a significant number of patients did not receive these drugs without having a formal contraindication. Becoming aware of its beneficial effect, and with a more strict adjustment to the current guideline recommendations, ACEi/ARB therapy could improve the prognosis of a particular patient population: the elderly.

### P238

#### Prescription of recommended therapy decreases with the severity of heart failure

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**Aim:** To describe pharmacotherapy of heart failure in stable patients with chronic heart failure treated in specialized cardiology outpatient departments.

**Methods:** Anamnestic data were collected from November 2014 till November 2015 in 7 cardiology outpatient departments in 3 university hospitals in 2 cities. The patients had to be treated for systolic heart failure (EF < 50%) and stable for at least one month.

**Results:** 1121 patients were included mean age 65 years, 80.5% were male. The etiology of heart failure was ischemic heart disease in 49.1%, dilated cardiomyopathy in 41.0% and 9.9% were classified as other. The median of blood pressure was 120/80 mmHg, median of heart rate 72. 149 (13.3%) were classified as NYHA I, 673 (60.0%) NYHA II and 299 (26.6%) as NYHA III and IV. Patients with higher NYHA class had more frequently leg oedema (p<0,001), atrial fibrillation (p<0,001), lower ejection fraction (38% resp. 30% resp 25%) and more frequently co morbidities. They had lower BPs (131 resp. 129 resp. 125 mmHg), but the same BpD 80 mmHg (ns) and more frequently co morbidities. The prescription of ACE-I/AIIA decreased with the severity of the disease (95,3% resp. 88,4% resp. 82,9%, p<0,001), the prescription of betablockers remained stable + 92% and the prescription of furosemide increased (52,3% resp 81,5% resp. 93,6% p<0,001) as well as the prescription of digoxin (16,1% resp. 29,0% resp. 49,8%, p<0,001). Increased prescription with increased



NYHA class was also observed in aldosterone blockers ( $p < 0.001$ ), anticoagulants ( $P < 0.001$ ) on the opposite there was a decrease in the prescription of antiaggregation ( $p = 0.003$ ) or statins ( $p = 0.05$ ).

**Summary:** the trends in pharmacological prescription probably reflex not only the severity of heart failure, but also co-morbidities and complications like renal failure or atrial fibrillation. The data will be further analysed, complete biochemistry (including NT-proBNP) is available in all patients.

## P239

### Effect of long term treatment with trimetazidine on left ventricular systolic function, on quality of life and exercise capacity in patients with chronic heart failure

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**Background:** Metabolic treatment involves the use of drugs that improve cardiomyocyte function. Trimetazidine is one of the most investigated drug in this group with a well-established role in the treatment of chronic angina. The available data suggest that therapy combining trimetazidine and hemodynamic drugs is effective in patients with chronic heart failure.

**Methods:** Patients were randomized to receive either trimetazidine (twice daily) or placebo (twice daily) in addition to optimal standard therapy, and were evaluated at baseline and after 12 months left ventricular function, exercise tolerance and quality of life.

**Results:** we have enrolled fifty patients (30 male, mean  $[+/-SD]$  age  $63 \pm 5.9$  years). NYHA class and left ventricular ejection fraction were comparable between the two groups. At 12 months there was a significant improvement in the number of dyspnea episodes per month in the trimetazidine group ( $-4.1 \pm 2$ ,  $p < 0.05$ ), also the left ventricular ejection fraction increased only in the trimetazidine group from 32.1 % to 34.6 %,  $p < 0.05$  while in the placebo group there are not significant difference (from 31.7 to 32.1 %,  $p > 0.05$ ). For the distance at 6 minutes walking test the patients in the trimetazidine group increased more than the placebo group (respectively from 274 m to 388 m ( $p < 0.05$ ) and 283 m to 301 m ( $p > 0.05$ ). The overall assessment of QoL showed an improvement in patients randomized to trimetazidine at 12 months (from 5.4 to 7.1,  $P < 0.01$ ) and no changes in patients randomized to placebo (from 4.8 to 4.9,  $P > 0.05$ ).

**Conclusions:** In patients with chronic heart failure, trimetazidine improves clinical condition, left ventricular systolic function, quality of life and exercise capacity.

## P240

### Pharmaco-invasive approach aimed at preservation of the left ventricular function in patients with stable coronary artery disease on the top of carbohydrate metabolism disorders

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**Introduction:** the coronary artery disease (CAD) treatment in type 2 DM patients remains a major issue for cardiologists. Despite significant advances in medical and invasive treatment, including implantation of drug-eluting stents, the patients still have high morbidity and mortality due to progression of atherosclerosis and HF even after percutaneous or surgical revascularization.

**Purpose:** the aim of our study was to investigate the effect of the metabolic agent trimetazidine (TMZ) on the left ventricular function in patients with CAD on the top of carbohydrate metabolism disorders, who underwent elective percutaneous coronary intervention (PCI).

**Methods:** an open label, prospective, randomized clinical trial was conducted in 63 patients stable CAD on the top of carbohydrate metabolism disorders. All patients underwent elective coronary stenting. The patients of the main group ( $n = 32$ ) received TMZ 35 mg bid in addition to standard therapy for 2 weeks before and 1 year after the procedure. In control group patients ( $n = 31$ ), PCI and the following follow-up were performed on the top of standard therapy only, without the use of metabolic agents. At baseline, two groups did not differ significantly in terms of the severity of myocardial ischemia, clinical and medical history data, degree of carbohydrate metabolism disorder, as well as concomitant treatments, characteristics of coronary artery lesions and performed PCI. The echocardiography was performed twice: at baseline and at 12 months of follow-up.

**Results:** despite the performed PCI, the carbohydrate metabolism disorders in CAD are associated with a significant deterioration in the regional contractility of myocardium and reduction in the LV pump function at the follow-up (WMSI increase by 8.3% and LV SVI decrease by 7.25% at 12 months after the intervention, compared with baseline). Long-term treatment with myocardial cytoprotector in this patients results in a significant improvement in the contractile function of the LV myocardium in the long-term, according to the EchoCG data (LV EDI decrease by 5.5%, LV ESI decrease by 4.4%, LVEF increase by 2.5% at 12 months after the

intervention, compared with baseline). The improvement in the myocardial function during the long-term treatment with TMZ is evidenced clinically by a longer distance walked during the 6MWT (+18.4% vs. the standard treatment group).

**Conclusion:** the pharmaco-invasive approach, namely the addition of a metabolic agent trimetazidine to the standard therapy in patients with carbohydrate metabolism, undergoing the elective PCI, contributes to the preservation of myocardial function.

## P241

### Ethnic differences in quality of life and its association with survival in patients with heart failure

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**Background:** Optimizing quality of life (QoL), as a patient-centred outcome, is a key priority in the management of heart failure (HF). Aims: To investigate ethnic differences in QoL and its association with 1-year survival among Asian HF patients.

**Methods:** In a prospective nationwide cohort ( $n = 1070$ , mean age 62 years, 24.5% women) of Chinese (61.6%), Malay (27.2%) and Indian (11.1%) ethnicities from Singapore, QoL was assessed using the Minnesota Living with HF Questionnaire (MLHFQ) at baseline presentation and 6 months, and patients were followed for all-cause mortality.

**Results:** At baseline, mean MLHFQ scores for total, physical, and emotional components were  $32.9 \pm 23.1$ ,  $15.4 \pm 11.0$  and  $5.9 \pm 6.0$ , respectively in the entire cohort. Chinese had a lower (better) MLHFQ total score ( $29.1 \pm 21.6$ ) compared with Malays ( $38.5 \pm 23.9$ ) and Indians ( $41.7 \pm 24.5$ );  $p < 0.001$ . Of the 21 MLWHF questions, patients reported the greatest burden in response to "Costing you money for medical care?" (median score: 3). NYHA class was the strongest independent predictor of MLHFQ scores (17.3 additional units for class III/IV vs I/II;  $p < 0.001$ ). After adjusting for NYHA class, demographics, BNP levels, comorbidities and medications, ethnicity remained an independent predictor of QoL ( $p < 0.001$ ). At six months, all ethnicities showed improvement in QoL, with the greatest improvement in Indians (41.7 to 21.2). Crude 1-year mortality was 16.5%. A significant interaction between MLHFQ and ethnicity was found ( $p = 0.019$ ), where poor MLHFQ score predicted higher adjusted mortality only in Chinese (HR 1.2 for total score and 1.4 for physical and emotional score per 10 unit increase). Per 10 unit increment of the physical component (of MLHFQ) was associated with an increased hazard (HR 1.2) of 1-year mortality ( $p = 0.018$ ) in the overall cohort.

**Conclusions:** Ethnicity is an independent determinant of QoL in HF. In spite of better baseline QoL in Chinese, QoL was more strongly related to survival in Chinese compared to Malays and Indians. These findings support an ethnicity-specific approach in the assessment of QoL in HF.

## P242

### Heart failure: predictors of mortality in elderly patients

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**Background:** Heart failure (HF) has a high prevalence in the elderly population and with the expected aging of the population will increase its incidence. This group of patients still needs further characterization.

**Purpose:** To investigate which clinical, biochemical and echocardiographic parameters routinely assessed may affect in-hospital mortality in elderly patients.

**Methods:** We identified all patients admitted for HF in a single center between 01/01/2009 and 31/12/2014. Only the first episode of each patient was included. We selected all patients with 85 years or older. It was evaluated clinical, laboratory and echocardiographic parameters and were compared with in-hospital mortality.

**Results:** During the reporting period, there were 262 patients who met the inclusion criteria. Predominance of females (58.8%),  $88.20 \pm 2.80$  years old and in-hospital mortality was 10.3%. The results obtained are in the table. Conclusion: This study showed that urea is superior to creatinine in predicting in-hospital mortality in

60631. Table 1

	Hemoglobin	Urea	Creatinine	C-reactive protein	BNP	PSAP	Ejection Fraction
No Deaths	12,18 ± 1,92	74,67 ± 36,00	1,36 ± 0,74	2,21 ± 2,77	904,00 ± 1076,62	47,80 ± 14,68	53,77 ± 15,27
Deaths	11,42 ± 1,67	114,38 ± 61,11	2,52 ± 3,69	3,35 ± 2,97	1770 ± 1514,00	59,56 ± 14,14	50,42 ± 15,79
T-test	p=0,760	p=0,000	p=0,124	p=0,058	p=0,013	p=0,038	p=0,461

## Biochemical and echocardiographic results

this age group. The value of the BNP is also a good predictor of mortality. The hemoglobin and c-reactive protein do not appear to correlate with mortality in patients with HF. In the echocardiographic parameters, the PSAP proved to be a good predictor of mortality; however, ejection fraction did not get a statistically significant result as predictor of mortality in elderly patients with HF.

## P243

**Acute effects of positive airway pressure on mitral regurgitation in heart failure patients with reduced ejection fraction**

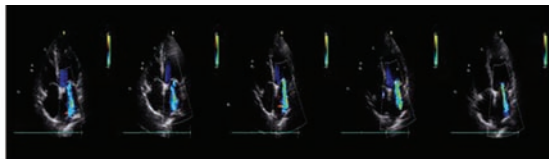
T Kato<sup>1</sup>; T Kasai<sup>2</sup>; S Yatsu<sup>1</sup>; H Matsumoto<sup>2</sup>; A Murata<sup>1</sup>; S Suda<sup>2</sup>; M Hiki<sup>1</sup>; H Daida<sup>1</sup>

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**Background:** Acute effects of positive airway pressure (PAP) on mitral regurgitation (MR) in heart failure patients with reduced ejection fraction (HFrEF) remain controversial. Purpose: We evaluate whether PAP therapy reduce Mitral Regurgitation in patient with heart failure.

**Methods:** Seven HFrEF patients (5 men; EF, 35.5%; BNP, 641pg/ml) with moderate-to-severe MR underwent echocardiogram during 10-min continuous PAP (4, 8 and 12 cmH<sub>2</sub>O) and adaptive servo-ventilation (ASV). MR area defined as a ratio of MR-to-left atrial area. Stroke volume (SV) was calculated from the time-velocity integral and cross-sectional area of aortic annulus.

**Results:** MR area was reduced significantly by the increase in continuous PAP level, and reduced further on ASV (0.38 ± 0.10, 0.38 ± 0.11, 0.37 ± 0.10, 0.34 ± 0.13, and 0.33 ± 0.10, P < 0.05) (Figure) in association with the stepwise increase in SV (P < 0.05). **Conclusion:** In HFrEF with moderate-to-severe MR, PAP, especially ASV, reduced MR in association with the increase in forward SV.



baseline CPAP of 4cmH<sub>2</sub>O CPAP of 8cmH<sub>2</sub>O CPAP of 12cmH<sub>2</sub>O ASV

Comparison of MR during PAP therapy

## P244

**What kind of information does patients with heart failure find interesting - a substudy from paceman-hf?**

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**Background:** OPTILOGG is a home based tool for heart failure (HF) patients, which monitors symptoms, titrates diuretics and educates the patient about HF. Patient Centred Management of Heart Failure (PACEMAN-HF) was a prospective, multi-centre, randomized controlled trial (RCT) that showed significantly improved self-care behaviour and increased knowledge in HF. HF patients currently receive information from various sources but there is a lack of knowledge about what type of information that the patient finds useful.

**Methods:** 32 patients using OPTILOGG were analyzed in the sub study. Mean age was 75 ± 8, 66 % were male, 62 % in NYHA class III, 38 % in NYHA class II. The information is presented in two ways. Either as a short "tip of the day" that is presented automatically every day, and if the patient wants to can select "Read More", or as a "Know More" tab that the patient actively selects. The "Know More" tab has four main categories, with associated sub categories.

**Results:** 100% of patients chose the "Learn More" at least once, and on average the patients chose to immerse one time every 2 weeks. 53% of the tips that often

triggered further need of information belonged to the main category of "What is heart failure?". Under the "Know More" tab "Food and beverages" was most popular with 31% of the elections, the least popular category was "Help, I feel bad!" that accounted for 17% of the elections.

**Conclusion:** The study shows that patients tend to focus their active choices on subjects that are perceived as positive. The study provides insight into how patients seek information, and can provide guidance on how we should formulate individualized patient information. The challenge for health professionals is to create information based on the patient's needs and circumstances.

## P245

**Validity of Zarit Burden Inventory in a sample of caregivers of heart failure patients**

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**Background:** The burden is one of the negative consequences that most reported among caregivers. The Zarit Burden Inventory is the instrument used for measuring the burden, composed of 22 items with Likert scale of 0-4, where 0 is never and 4 is always. It has been proved that caregivers with higher burden, measured by this instrument, show worse health perception and more likely to have emotional disorders.

**Purpose:** Evaluate the psychometric properties of Zarit Burden Scale in a sample of caregivers of heart failure patients.

**Methods:** This study includes a validation sample of 125 caregivers (75.2% females, age 54.8 ± 13.8) of patients with heart failure of Instituto Nacional de Enfermedades Respiratorias "Ismael Cosío Villegas". Reliability analysis and factor was performed using Cronbach's alpha and the variability was calculated using t-student.

**Results:** Six items was eliminated. The final inventory was brief composed of 16 items, on a single factor: burden, with a Cronbach's alpha of 0.907. The variability was statistically significant (p < 0.05).

**Conclusion:** The scale demonstrated adequate psychometric properties comparable to the original. The results support the use of the inventory in caregivers of patients with heart failure in Mexico.

## P246

**Gender differences of biomarkers and damage myocardial mass in patients with a history of myocardial infarction: parallels with post myocardial infarction remodeling**

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**Aim:** To evaluate the risk factors, levels of the blood biomarkers, damage myocardial mass according to magnetic resonance imaging (MRI), their influence on the course of post infarction remodeling in female and male patients. **Methods:** 182 patients (42 women and 140 men) with myocardial infarction (MI) were entered into the study. A part of common standard tests (echo-cardiogram on the 5-7th day, and then again 3 and 12 months later) on the 3-4th day patients were tested for blood serum levels of the following: high sensitivity C-reactive protein (hs-CRP), N-terminal pro B-type natriuretic peptide (NT-proBNP), interleukin-6, metalloproteinases-1 and -9 (MM-1, MMP-9), tissue inhibitor of matrix metalloproteinases-1 (TIMP-1). On the 9-11th day and after 3 months 66 patients were tested for MRI with contrasting.

**Results:** Women enrolled into study were 10 years men's senior (<0.05). Female patients more often presented diabetes mellitus (DM) (23.8 %) and hypertension (AH) (92.0 %), male patients presented smoking (28.5 %) and chronic obstructive pulmonary disease (26.4%). Mostly women have presented the multivessel coronary artery disease (30.9 % vs 15.7 %; <0.05) and the non-Q MI (54.8 % vs 23.5 %; <0.05). An acute left ventricular failure over the 2nd Killip Class more often

complicated MI in women (21.4 %), than in men (6.4 %). In the multivessel coronary artery disease the odds ratio of unfavorable course of remodeling 8.57 (95 % CI 1.31-70.59,  $p=0.02$ ). The gender differences of concentration of hs-CRP, MMP-1, MMP-9, NT-proBNP, interleukin-6, TIMP-1 on the 3-4th day of MI and over the 3 months were not revealed. The unfavorable course of post myocardial infarction remodeling in men was associated with higher concentration of MMP-1 (10.6 (6.5; 15.4) vs 7.1 (4.4; 12.0) ng/ml;  $<0.05$ ). In women the MMP-9/TIMP-1 was lower in unfavorable course of remodeling. Increase of the left ventricular systolic and diastolic volume indexes, damage myocardial mass, percent of damage myocardial mass, as well low ejection fraction were associated with unfavorable course of remodeling both in men and women. The early revascularization supported to protection of the viable myocardium in the peri-infarction zone. According to the MRI the scar myocardial zone's borders have not differences as women as men, however the dimension of the microcirculation obstruction (MVO) was less in female patients.

**Summary:** Women have mostly presented the risk factors as age, AH, DM, as well as multivessel coronary artery disease. Extended volume and size of LV, low EF were as predictors of the unfavorable remodeling and were not depended on the gender. Characteristics of the scar zone were not depended on the gender however the dimension of MVO in women was less than in men. In unfavorable course of post myocardial infarction remodeling as men as women have revealed in blood the high content of interleukin-6, MMP-9, NT-proBNP, and hs-CRP.

**P247**

**Electrical dyssynchrony in LBBB and factors related to its severity**

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Significant impact of left bundle branch block (LBBB) on heart failure (HF) development and progression has been demonstrated in many clinical studies. However, the true incidence of LBBB in a population, and factors related to its severity are not well established.

**Aim:** To evaluate the incidence of LBBB among patients <70 years of age, and to identify factors associated with the severity of electrical dyssynchrony.

**Methods:** 65.397 patients (35.585 male (59%) and 26.812 female (41%)), mean age  $52.7 \pm 12.5$  yrs) underwent annual check-up with ECG screening between February 2008 and December 2012, followed by thorough examination. Congenital heart diseases, valvular diseases, cardiac tumors, and cardiomyopathies were exclusion criteria.

**Results:** During this period 104 (0,16%) patients with LBBB (51 male and 53 female, mean age  $57.5 \pm 8.6$  yrs) have been identified, and 11 of them met exclusion criteria. Among the remaining 93 patients: 35 (37.6%) had a history of coronary artery disease with 34 of them suffered from MI. All of them underwent coronary angiography. Arterial hypertension (AH) has been diagnosed in 67 (72,0%) patients, and left ventricle hypertrophy was revealed in 32 (47,7%) of them. Signs of previous myocarditis have been demonstrated by cardiac MRI with gadolinium in 22 patients (23.7%). Only 4 (4,3%) patients with LBBB had no features of CVD after thorough examination including invasive and noninvasive tests. CHF was observed in 52 (55.9%) patients: NYHA I - 17 pts, NYHA II - 27 pts, and NYHA III - 8 pts. The remaining 41 (44,1%) patient was asymptomatic. The mean duration of the QRS complex was  $148.2 \pm 14.5$  ms, and  $\geq 150$  ms in 52 (55.9%) patients. It was noted that 87 of 93 patients (93.5%) had criteria of LBBB proposed recently by Strauss (2011): duration of complex QRS  $> 140$  ms in men and  $> 130$  ms in women, QS or RS pattern in leads V1 and V2 and QRS notch at least in two of these leads (V1, V2, V5, V6, I, AVL). ST-segment depression was observed in 86 patients (92.5%), negative T waves were detected in 37 patients (39.8%), and 16 (17.2%) patients had left axis deviation  $> 30^\circ$ . Multiple linear regression analysis was used to identify factors associated with the severity of electrical dyssynchrony. Twenty six parameters were analyzed altogether. The severity of electrical dyssynchrony was related to male gender ( $=0,004$ ), CAD ( $=0,011$ ), End Systolic Volume (ESV;  $<0,001$ ), and E wave - early peak LV filling velocity ( $=0,02$ ).

**Conclusions:** The incidence of LBBB among patients <70 years of age was 0,16%. Male gender, CAD, ESV and E wave have the maximal impact on the severity of electrical dyssynchrony.

**P248**

**Improvement of cognitive function in patients with heart failure by cognitive training: first results of the cognitive training in heart failure study (cogtrain-HF)**

Supported by the German Heart Foundation/German Foundation of Heart Research

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**Background/Introduction:** Patients with heart failure show cognitive impairments which are associated with adverse effects. There is an association with higher mortality rates, worse quality of life, poor drug adherence and hospitalization. Cognitive impairment pertains to executive functioning (e.g., initiation and inhibition of actions), episodic and working memory, attention and processing speed. There is evidence for improvement in these areas under computer-based cognitive training in healthy subjects. Training enhances performance both in trained tasks and untrained tasks (transfer effects). However, there are only few studies dealing with cognitive training in cognitively impaired adults and it is unclear whether findings of studies with healthy subjects can be transferred to patient samples.

**Purpose:** The purpose of this study is to investigate the impact of an adaptive computer-based cognitive training on cognitive functioning in patients with heart failure. We assess improvements in three trained cognitive tasks as well as transfer effects on untrained tasks and cognitive abilities, changes in quality of life and drug adherence.

**Methods:** In a pretest-training-posttest design we compared three groups of heart failure patients ( $n=39$ ; left ventricular ejection fraction  $\leq 45\%$ , NYHA classification II-III): an experimental group, which performed a cognitive training over six sessions ( $n=13$ ; mean age=63.76 years,  $SD=11.07$ , 7.1% females), an active control-group, which performed a training of general knowledge over six sessions ( $n=12$ ; mean age=65.33 years,  $SD=9.19$ , 0% females) and a passive control group ( $n=14$ ; mean age=65.96 years,  $SD=7.84$ , 14.3% females). During pretest and posttest all groups completed cognitive tests with untrained tasks to measure transfer effects.

**Results:** Results show a significant improvement in each of the training tasks when comparing the last to the first training session: verbal working memory ( $F(1,9)=14.814$ ,  $p=.004$ ,  $\eta^2=0.622$ ), visual-spatial working memory ( $F(1,9)=18.155$ ,  $p=.002$ ,  $\eta^2=0.669$ ) and cognitive flexibility ( $F(1,12)=5.457$ ;  $p=.038$ ,  $\eta^2=0.313$ ).

**Results:** show no transfer effects.

**Conclusion:** Patients with heart failure can benefit from similar cognitive training tasks as healthy subjects. Results show improvements in cognitive functioning in patients with heart failure after cognitive training. These findings encourage further research to examine whether cognitive training could also lead to improvements in other fields, e.g. drug adherence or quality of life.

**P249**

**Congestive heart failure has differential perioperative risk for myocardial infarction/cardiac arrest (MICA) in geriatrics vs. non-geriatrics patients**

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**Background/Introduction:** Geriatrics Patients have characteristic, progressive constriction of homeostatic reserve that occurs with aging in every organ system. The unique characteristics of this population make them respond differently to known risk factors. CHF is a known risk factor for MICA, however it not known whether geriatrics patients risk is different from the general population and by what extent.

**Purpose:** We aim in this study to examine if CHF has differential risk (ORs) for MICA in Geriatrics vs. Non-Geriatrics Patients. If this theory proves to be valid, then identifying risk factors becomes insufficient and weighting risk factors according to age groups becomes essential.

**Methods:** For testing our theory we utilized the American College of Surgeons National Surgical Quality Improvement Program NSQIP 2012 database, which is a multicenter prospective dataset collected systematically by trained professionals. It contains ( $n=543,885$ ) cases submitted by 374 participating hospitals. After conducting descriptive analysis, we performed multivariate logistic regression analysis on all the variables believed to be risk factor for MICA. The model variables selection was theory driven. We applied the model on all the patients, patients <65 and patients  $\geq 65$ . We compared the odds ratio for these 3 groups.

**Results:** See table 1

**Conclusions:** CHF has differential OR for MICA in geriatrics vs. non-Geriatrics patients. This does not imply increased risk, rather a different risk weight. It proves our theory that risk factor identification should be followed by age group analysis to appropriately weight the risk factor in geriatrics patients.

Table 1

Age group	Overall	Age <65	Age $\geq 65$
Sample N	489,133	314,001	175,132
Adjusted Odds Ratio	1.713	2.039	1.653
P-Value	< 0.001	< 0.001	< 0.001



## P250

**The analysis of efficiency of physical rehabilitation of patients with chronic heart failure**VL Galenko<sup>1</sup>; TA Lelyavina<sup>1</sup>; M Y Sitnikova<sup>1</sup><sup>1</sup>North-west state medical university, Saint-Petersburg, Russian Federation

**Introduction:** In world practice, the selection intensity physical training of patients with CHF on the basis of achievement of anaerobic threshold when you perform cardiorespiratory test (CPET). The majority of patients with severe HF do not reach anaerobic threshold during the CPET that requires the use of certain indicators in the appointment of physical training. This alternative indicator can be lactate threshold, which achieved first during the execution of the CPET.

**Purpose:** To evaluate the effectiveness of aerobic physical exercise in HF patients, selected on the basis of determining the lactate threshold during CPET. Methods. 56 patients, CHF NYHA III (under the supervision of cardiologists-experts in heart failure) were randomized into two groups - primary (aerobic training) and control (standard treatment of heart failure). Main group - 43 patients, mean age  $54 \pm 12.5$  years, body mass index (BMI)  $26.46 \pm 6.4$  kg/m<sup>2</sup>. The control group - 13 patients, age  $53 \pm 17$  years, BMI was  $25.4 \pm 6.8$  kg/m<sup>2</sup>. The original estimated results of physical examination, laboratory parameters. CPET, quality of life (QOL), exercise tolerance (ET) was assessed at baseline and after 1,3,6 months of follow-up. The CPET served on treadmill using hardware "Oxycon ro". Echocardiography (EchoCG) were performed at baseline and after 6 months. The data were statistically processed using software package "Statistika, 6.0".

**Results:** In the main group after 6 months of training EF increased by  $7.5 \pm 0.5\%$  from baseline, QOL was changed by  $17.5 \pm 8$  points (significant regression of symptoms). ET increased by  $9 \pm 1$  points. After 1 month of observation VO<sub>2</sub> peak increased by  $2.6 \pm 0.1$  ml/min/kg after 6 months -  $4.4$  ml/min/kg in the control group showed an increase EF  $4 \pm 1,1\%$ , the change of QOL  $14 \pm 7,22$  points, the increase in ET at 1.5 points. Decreased VO<sub>2</sub> peak in a month  $1.05 \pm 1.2$  ml/min/kg, after 6 months -  $1.7$  ml/min/kg. Revealed a strong positive correlation between the initial values of VO<sub>2</sub> peak and EF ( $r=0,4$ ,  $p$ ), and between baseline levels of sodium, hemoglobin and the effectiveness of physical rehabilitation ( $r_{Na}=0,41$ ,  $p,0,05$ ;  $r_{Hb}=0,45$ ,  $p<0,05$ ).

**Conclusion:** Aerobic physical exercise in CHF patients, selected on the basis of achieving lactate threshold during the CPET effective in improving values of CPET, EchoCG, QOL and increasing ET.

## P251

**The influence of ventilatory disorders and clinical status on the early and late prognosis in patients with recent chronic heart failure exacerbation**

The research was financed by the Ministry of Higher Education allocated to the development of young scientists and doctoral students

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**Purpose:** The aims of the study were to assess: the prevalence of ventilatory disorders in patients with chronic heart failure (CHF) exacerbation, the correlation with clinical status and impact on prognosis.

**Methods:** There were 25 patients-22 (88%) men and 3 (12%) women ( $60 \pm 13$  years) with decompensated CHF recruited for the study. All patients underwent following examinations: medical history, physical examination, laboratory tests (repeated on the lung function tests day), 12-leads electrocardiogram, X-ray, echocardiogram. The spirometry and body plethysmography were performed after patient's clinical haemodynamic stabilization. The following lung function tests parameters were taken into analysis: forced expiratory volume in one second (FEV<sub>1</sub>), Tiffeneau ratio -FEV<sub>1</sub> %VCmax (Maximal Vital Capacity), total lung capacity (TLC), vital capacity (VC), total airway resistance (Rtot). All examinations were repeated 3 months after the discharge. The median follow-up was 61 months. The Student's t-test or Mann-Whitney-U test,  $\chi^2$  test and Pearson correlation were used for the initial statistical analysis.

**Results:** The ejection fraction (EF)  $\leq 35\%$  ( $21,1\% \pm 7,42$ ) was confirmed in all patients on admission and 3 months after the discharge ( $23,3 \pm 8\%$ ,  $p=0,05$ ). The elevated BNP level ( $2131,3 \pm 1096,8$  pg/ml) was revealed in all patients on admission. Both BNP levels after stabilization ( $1192,4 \pm 1070,8$  pg/ml) and 3 months after the discharge ( $745,7 \pm 635$  pg/ml) were lower than initial ( $p<0,0001$ ). The spirometry revealed obstructive disorders in 20 patients (80%) at the discharge and 3 months later. The body plethysmography confirmed restrictive disorders in 2 patients (8%) at the discharge. We revealed the significant correlations between FEV<sub>1</sub> %VCmax and the highest BNP level ( $r=-0,45$ ,  $p=0,027$ ) and BNP level on lung function tests day ( $r=-0,44$ ,  $p=0,03$ ). We also found negative relationships between: EF and FEV<sub>1</sub> ( $r=-0,41$ ,  $p=0,04$ ), EF and TLC ( $r=-0,59$ ,  $p=0,007$ ), EF and FEV<sub>1</sub> measured 3 months after the discharge ( $r=-0,45$ ,  $p=0,04$ ). The mortality rate achieved 44% in 3 and 52%

in 5 year follow-up. There was a significant correlation between BNP level at the discharge ( $p<0,01$ ), EF measured 3 months later ( $p=0,02$ ) and death in 3 year follow-up period.

**Conclusions:** Ventilatory disorders appeared in the majority of patients with CHF exacerbation and 3 months after this episode. There is a significant correlation between maximal BNP level, BNP after the stabilization and FEV<sub>1</sub> %VCmax. There were no correlations between lung function tests parameters and mortality in early and late follow-up in this group of patients.

## P252

**Revascularization type and outcome in patients with multivessel coronary disease and reduced ejection fraction**T Tanja Popov<sup>1</sup>; D Kovacevic<sup>1</sup>; S Susak<sup>1</sup>; A Vulin<sup>1</sup><sup>1</sup>Institute of Cardiovascular Diseases Vojvodina, Novi Sad, Serbia

**Background:** Several studies have compared outcome of coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) in the treatment of multivessel coronary disease, but a few were focused on patients with reduced left ventricular function.

**Purpose:** To compare effectiveness of PCI and CABG in patients with ischemic cardiomyopathy and multivessel coronary disease.

**Methods:** This single-center study, included 178 patients, admitted because of symptomatic multivessel coronary disease, ejection fraction of left ventricle (EF)  $\leq 50\%$ , who underwent PCI or CABG, with two-years follow up of adverse cardiac and cerebrovascular events (MACCE), which included mortality, myocardial infarction (MI), target lesion/vessel revascularisation (TLR/TVR) and stroke.

**Results:** There was higher incidence of MACCE in PCI group (18.1% vs. 9.5%,  $p=0.145$ ). That was mainly because of higher incidence of MI (6% vs. 0%,  $p=0.021$ ) and TLR/TVR (6% vs. 0%,  $p=0.021$ ) in PCI group. There was no difference in mortality rate (9.6% in PCI group vs. 9.5% in CABG group,  $p>0.05$ ). Age, fibrinogen, C-reactive protein were predictors of stent thrombosis, while left ventricular dilatation, EuroSCORE and SYNTAXscore were predictors of mortality in our study.

**Conclusion:** There was no difference in mortality rate during 2-year follow-up after PCI and CABG in studied patients. Incidence of MI and TLR/TVR was higher after PCI comparing with CABG.

## P253

**Recent trends in diagnostic work-up among unselected patients newly diagnosed with heart failure: a Swedish population-based study**

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**Background:** Echocardiography, electrocardiogram (ECG) and natriuretic peptide (NP) testing are recommended by the European Society of Cardiology for the diagnostic work-up of heart failure (HF).

**Purpose:** To describe population-based trends in the use of diagnostic tests in patients newly diagnosed with HF (main ICD-10 code I50) in Sweden.

**Methods:** Patients were identified via primary and secondary care electronic medical records. All patients aged  $\geq 18$  years with a first HF diagnosis from 1 January 2010 to 31 October 2014 were included. A 9-year look-back period to 1 January 2001 was applied for each patient to exclude prevalent HF cases. The use of echocardiography, ECG and NP testing (for brain NP or the N-terminal of the prohormone brain NP [NTproBNP]) in the 6 months before and 6 months after a first HF diagnosis were determined. ECG was captured predominantly during secondary care.

**Results:** Of 8777 records, 3744 patients were identified (46.8% women; mean age: 78 years; mean Charlson comorbidity index: 2.2). Echocardiography had been used in 1605 patients (42.9%), ECG in 1736 patients (46.4%) and NP testing in 3436 patients (91.8%). Of 3071 patients who were tested for NTproBNP within 6 months after first diagnosis, the mean (standard deviation [SD]) NTproBNP level was 5155 (8736) ng/L. The mean (SD) number of days from first diagnosis to receiving NTproBNP results was 15.6 (36.1). First use of echocardiography, ECG and NP testing was stable from 2010–2014. Echocardiography and ECG were much more commonly used in younger patients (echocardiography,  $<75$  years: 61.1%;  $\geq 75$  years: 33.2%. ECG,  $<75$  years: 65.1%;  $\geq 75$  years: 36.5%). The use of NP testing was similar regardless of age ( $<75$  years: 92.0%;  $\geq 75$  years: 91.7%). Men were more likely than women to undergo echocardiography (men: 47.9%; women: 37.2%) and ECG (men: 51.0%; women: 41.2%). The use of NP testing was similar regardless of sex (men: 92.0%; women: 91.6%). The waiting time between patient referral and the patient receiving their first echocardiography varied over time. The mean (SD)

number of days per year from referral to examination was as follows: 2010, 19.5 (41.4); 2011, 22.1 (60.9); 2012, 11.8 (25.7); 2013, 22.5 (49.4); 2014, 36.9 (101.2).

**Conclusions:** In this population, in contrast to NP testing, the use of echocardiography for the diagnosis of HF is low, particularly in patients aged  $\geq 75$  years and in women. Echocardiography is mandatory for the diagnosis of HF phenotype, which influences patient treatment; its use should be increased in clinical practice, especially among women and elderly patients.

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**Assessment of patient selection bias in prospective studies for heart failure**

JJGdV, IS, GG, SCP, JMR and AT are employed by Philips Research. ACG, KMG, JGC and ALC have received departmental research support from Philips. JJG Gert-Jan De Vries<sup>1</sup>; I Sokoreli<sup>1</sup>; G Geleijnse<sup>1</sup>; SC Pauws<sup>1</sup>; JM Riiastama<sup>1</sup>; A Tesanovic<sup>1</sup>; A Crundall-Goode<sup>2</sup>; KM Goode<sup>2</sup>; JG Cleland<sup>3</sup>; AL Clark<sup>2</sup>  
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**Purpose:** Various types of recruitment bias can occur in clinical studies. These may occur deliberately through the use of pre-specified trial inclusion/exclusion criteria, or indirectly as a consequence of the place and method of enrolment; due to a patient's perception of the value, risk and inconvenience of being involved; or pre-selection bias by the clinicians approaching the patient. We set out to explore these biases.

**Methods:** OPERA-HF is a prospective, observational study enrolling patients hospitalized for or with heart failure. Other inclusion criteria are: age  $>18$  years, treatment with loop diuretics and at least one of the following: left ventricular ejection fraction  $\leq 40\%$ , left atrial dimension  $>4.0$  cm or NT-ProBNP  $>400$  pg/mL (if sinus rhythm) or  $>1200$  pg/mL (if atrial fibrillation). Three different study participation levels were possible: full, partial and routine care (via audit). All patients were eligible for the study, but might not be approached if the clinician thought it inappropriate; patients could choose which group to join if they declined to take part in the full study. Relative risk, for binary variables, and Wilcoxon rank-sum tests, for continuous variables, were estimated to compare data at different study participation levels.

**Conclusion:** Patients recruited into the full study had fewer comorbidities and used less medication than those recruited into the partial and routine care arms. They also had a lower risk of readmission and mortality. Trials should be interpreted in the light of possible selection bias for less ill patients. Whether the selection bias was due to clinicians/nurses or patient choice needs further study.

Results	Full Participation (n = 428)	Partial Participation (n = 110)	Routine Care (n = 243)
Age	74 [66 - 81]	77 [68 - 84]*	77 [69 - 83]*
NT-proBNP	4924 [2010 - 10085]	3942 [1962 - 9803]	5288 [2476 - 10912]
Myocardial infarction	45 (10.6%)	21 (19.6%)*	43 (18.4%)*
Cerebrovascular accident	33 (9.1%)	11 (11.0%)	28 (20.9%)*
Ace inhibitor	217 (50.6%)	53 (48.2%)	170 (70.0%)*
Beta blocker	259 (60.4%)	75 (68.2%)	192 (79.0%)*
30 day readmission	8 (3.0%)	3 (2.9%)	15 (7.8%)
1 year death	41 (20.4%)	22 (23.4%)	65 (33.3%)*

Results of key characteristics by study participation level, represented as median [IQR] or # (%). Missing data were excluded. \* Indicates significant ( $p < 0.05$ ) difference compared with Full Participation.

**P255**

**Spinal cord stimulation in heart failure: effect on disease-associated biomarkers**

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**Background:** Experimental studies suggest that spinal cord stimulation (SCS) can reduce neurohormonal activation and reverse remodeling in animal models of heart failure (HF). The mechanism of SCS benefit in experimental HF remains ill defined and human data is limited. PurposeTo test the hypothesis that SCS favorably affects disease-associated biomarkers in patients with systolic HF.

**Methods:** Thirteen patients with systolic HF and narrow QRS, previously participating in the larger DEFEAT-HF clinical trial with SCS treatment for  $\geq 6$  months were included in this cross-over study. Patients were randomly assigned to 6 weeks of SCS-ON followed by 6 weeks of SCS-OFF, or vice versa. Stimulation (aiming at the T2-T4 segments of the spinal cord) was delivered for 12 hours per day (amplitude: 90% of maximally tolerated paresthesia). Following the "ON" and "OFF" periods, peripheral blood samples were drawn for subsequent analysis of circulating biomarkers of neurohormonal activation (norepinephrine - NE, adrenaline ADR, aldosterone - ALDO and renin), inflammation (high-sensitivity C-reactive protein - hs-CRP), cytokine activation (Interleukin 1 and 6 - IL-1  $\alpha$ /IL-6) as well as myocardial stress (NT-proBNP) and injury (high-sensitivity cardiac troponin T-hs-cTnT). In addition, renal function was assessed using plasma cystatin C.

**Results:** Thirteen patients (mean age:  $65.3 \pm 8.0$  yrs, 69% males, 46% ischemic cardiomyopathy) completed the study. The results of SCS on HF-associated biomarkers are shown in table 1.

**Conclusion:** In this small study, SCS was associated with a modest but significant increase in troponin T, which may reflect cardiac injury. The small magnitude of increase is not likely to be clinically relevant, but may offer a novel mechanistic insight into SCS in HF. Furthermore, a trend toward elevated levels of circulating cytokines was found. Whether cytokine activation contributes to SCS-associated cardiac injury warrants further studies.

Biomarker	SCS-ON	SCS-OFF	p-value
P-NE (nmol/L)	3.8 $\pm$ 1.8	4.1 $\pm$ 2.0	0.72
P-ADR (nmol/L)	0.4 $\pm$ 0.1	0.4 $\pm$ 0.1	0.75
P-ALDO (pmol/L)	563 $\pm$ 487	425 $\pm$ 291	0.68
P-Renin (ng/L)	230 $\pm$ 357	172 $\pm$ 212	0.79
P-hs-CRP (mg/L)	3.6 $\pm$ 4.5	3.6 $\pm$ 4.9	0.39
P-IL-1 $\alpha$ (pg/ml)	67 $\pm$ 137	43 $\pm$ 116	0.08
P-IL-6 (pg/ml)	22.4 $\pm$ 48.5	17.9 $\pm$ 40.9	0.09
P-NT-proBNP (ng/L)	565 [273-3110]	464 [146-3400]	1.00
P-hs-cTnT (ng/L)	23 $\pm$ 17	20 $\pm$ 14	0.04
P-Cystatin C (mg/L)	1.2 $\pm$ 0.5	1.2 $\pm$ 0.4	0.24

Table 1

**P256**

**PACEMAN-HF - pooled analysis from two randomized controlled trials.**

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**Background:** OPTILOGG is a home based tool for heart failure (HF) patients, which monitors symptoms, titrates diuretics and educates the patient. Patient Centred Management of Heart Failure (PACEMAN-HF) was a prospective, multi-centre, randomized controlled trial (RCT) that showed significant reduction in-hospital days by 28% and a system compliance of 85% after 6 months. There is a growing need for real-life data. Pragmatic trials are designed to evaluate the effectiveness of interventions in real-life routine practice conditions. Such a trial has been conducted within primary care in Sweden.

**Methods:** 100 patients were enrolled. The mean age was  $78 + / - 9$ , 65% were male, 43% NYHA class III, 48% NYHA class II and 9% NYHA class I. All patients were listed at a HF clinic in primary care, with a confirmed HF diagnosis and recently performed echocardiography. Patients were randomized 1:1 to either receive OPTILOGG (intervention group, IG) or not (control group, CG). The 2 groups were well balanced at randomization. Aside from prescribing OPTILOGG, routine practise remained unchanged. All hospitalizations for the patients were recorded for 6 months. All HF related hospitalizations were adjudicated by a HF specialist.

**Results:** After 6 months, there was a 33% reduction of in-hospital days due to HF [RR: 0.67; 95% CI: 0.45-0.99;  $p < 0.05$ ] in the IG, and the compliance was 97% [IQR: 91% - 99%]. A multiple regression analysis, adjusted for differences in health status, was performed on pooled data from both studies, based on 610 in-hospital days and 172 patients. The adjusted risk ratio with a 95% confidence interval was 29.2% [RR: 0.708; 0.607-0.825], and the median system compliance for the pooled cohort was 94% [IQR: 84% - 98%].

**Conclusion:** Results from pooled analysis are consistent with previously published results, showing a reduction of in-hospital days, indicating that the results are generalizable and reliable.

**P257**

**Mortality and mode of death in chronic heart failure patients**

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**Introduction:** Heart failure (HF) remains a pertinent problem across Europe and it is responsible for high levels of mortality. The heterogeneity of the heart failure population is reflected in the different ways in which these patients die. Mode of death analysis provides an understanding of the clinical course of the disease.

**Purpose:** To evaluate the mode of death in outpatients with chronic HF of different etiologies and to define predictor variables for all-cause mortality.

**Methods:** We evaluate consecutive HF outpatients treated in a HF clinic. Mode of death was classified as cardiovascular (CV), non-CV, or unknown. Non-CV death was defined as a death due to a specific non-CV event; unknown death was defined as a death for which no information surrounding the event was available. CV death comprised pump failure, sudden cardiac death (SCD), acute myocardial infarction (AMI) and stroke. Twenty-one prespecified potential predictor variables were used in a stepwise Cox proportional hazards model for all-cause mortality.

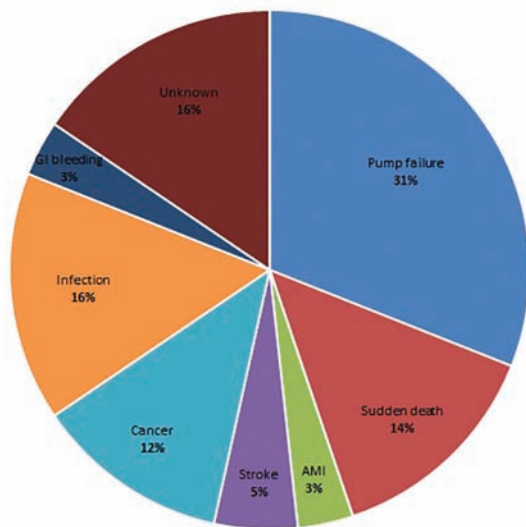
**Results:** Of the 224 patients evaluated, death occurred in 59 (26%) during a median of 51 months. Mean age was  $64.5 \pm 11.4$ ; 74 % were male; mean ejection fraction was 32%; 49% had an ischemic etiology and 50 % were in New York Heart Association (NYHA) functional class II. Of all deaths, 31.0% were due to pump failure, 13.8% due to SCD, 3.4% due to AMI, 5.2 % due to stroke, and 31.0% due to non-CV causes (figure). Age and use of diuretics were associated with significantly increased mortality (table).

**Conclusion:** In our study, cardiac mortality was the leading cause of death. However almost one third of HF patients died from non-cardiovascular causes.

Multivariate analysis of mortality

Variables that remain in the equation	p-value	Cox HR (95% CI)
Age (years)	0,0210	1,0316 (1,0048 - 1,0591)
Use of diuretics	0,0060	1,0098 (1,0028 - 1,0168)

Variables removed from the equation: gender, weight, systolic blood pressure, NYHA functional class, left ventricular ejection fraction, ischemic etiology, total cholesterol, plasma hemoglobin, plasma sodium, lymphocyte's percentage, uric acid, use of angiotensin converting enzyme inhibitors, angiotensin II receptor blockers, betablockers, aldosterone antagonists and allopurinol; implantable cardioresponder-defibrillator and cardiac resynchronization therapy. HR, hazard ratio; CI, confidence interval



Mode of death in heart failure patients

#### P258

##### Heart failure with reduced ejection fraction is associated with the highest visit-to-visit blood pressure variability in complicated arterial hypertension

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**Background:** Visit-to-visit blood pressure variability (BPV) is associated with adverse cardiovascular outcomes in different patients' populations. Mechanisms of visit-to-visit BPV in different groups of patients have not been determined yet. The aim of our study was to assess visit-to-visit systolic BPV in patients with uncomplicated controlled arterial hypertension (AH) and patients with controlled AH and

stable coronary heart disease (CHD) or heart failure (HF) with reduced ejection fraction.

**Methods:** In retrospective study we assessed 3 groups of patients with controlled AH. Group 1 included 52 patients with uncomplicated AH (20 men, age  $58,9 \pm 9,0$  yrs) who achieved target BP on RAAS-inhibitor/amlodipine combination. Group 2 included 40 pts with stable CHD (28 men, age  $69,2 \pm 5,9$  yrs). Group 3 included 100 pts with HF with reduced EF (80 men, age  $64,4 \pm 9,3$  yrs, mean EF  $32,3 \pm 4,3\%$ ). Pts in groups 2 and 3 received stable therapy for CHD and HF. BP was measured with a validated oscillometric device. Visit-to-visit BPV was calculated as SD for 5-7 visits during 8-18 months of stable therapy.  $p < 0,05$  was considered significant.

**Results:** First evaluated BP in group 1 was  $126,4 \pm 7,6/76,7 \pm 7,2$  mmHg, in group 2 -  $125,5 \pm 7,5/75,2 \pm 8,8$  mmHg, in group 3 -  $127,6 \pm 15,1/77,9 \pm 8,3$  mmHg. At final evaluated visit BP was  $123,7 \pm 9,7/76,8 \pm 6,7$  mmHg,  $124,2 \pm 13,4/72 \pm 8,5$  mmHg and  $123,6 \pm 13,6/74,8 \pm 8,9$  mmHg, respectively. Despite stable levels of BP, BPV on stable therapy varied in wide range in all groups: 1,8-16,8 mmHg, 0,7-23,3 mmHg, 2,3-20,0 mmHg for systolic BPV, respectively and 1,0-11,4 mmHg, 0-17,9 mmHg and 1,5-13,1 mmHg for diastolic BPV, respectively. Despite similar levels of final BP, there were significant differences in mean BPV between groups: systolic BPV in group 1 was  $7,2 \pm 3,6$  mmHg vs  $7,8 \pm 6,6$  mmHg in group 2 and  $10,2 \pm 3,8$  mmHg in group 3; diastolic BPV -  $4,8 \pm 2,7$  mmHg vs  $7,0 \pm 4,4$  mmHg and  $7,3 \pm 2,2$  mmHg, respectively ( $p < 0,01$  for trend). No predictors of BPV were found in all groups.

**Conclusion:** Despite similar BP levels HF with reduced EF is associated with the highest visit-to-visit BPV compared to uncomplicated AH and stable CHD. Thus high visit-to-visit BPV may be a marker of the severity of cardiovascular disease.

#### P259

##### Early remodeling of left ventricle after heart valve surgery in patients with chronic heart failure (REVERSE-HF study)

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**Background:** In heart failure (HF) due to chronic volume overload, heart valve surgery determines LV reverse remodeling (LV-R). In aortic regurgitation (AR), LV-R mainly occurs in the early postoperative stage. Entity of early LV-R usually vary among patients with AR or mitral regurgitation (MR). Its pathophysiology and prognostic significance are actually unknown.

**Purpose:** To verify entity, determinants, gender-related differences and impact on long-term outcome of LV-R, occurring early (discharge) after surgery for AR and/or MR.

**Methods:** 52 pts (median age 70 yrs [interquartile range 54–76], 75% male) with HF due to AR and/or MR, underwent echocardiography prior to (baseline) and at  $7 \pm 4$  days after surgery (discharge). LV end-diastolic volume (EDV) and its variation at discharge vs baseline value ( $\Delta$ EDV,%) were analyzed.  $\Delta$ EDV  $\geq -20\%$  indicated LV-R, while  $\Delta$ EDV  $< -20\%$  was considered as No-LV-R. Outcome data were collected in 43 pts at  $13 \pm 6$  month follow-up for an unpowered survival analysis.

**Results:** In the total study population (63% pts with MR, 17% with AR, 19% with MR+AR) median  $\Delta$ EDV was  $-28.71\%$  ( $p < .001$  for discharge vs baseline EDV), without significant differences among valvular diseases ( $-26.32\%$ ,  $-36.81\%$ ,  $-33.13\%$ , respectively). Replacement caused greater  $\Delta$ EDV in MR+AR and AR than MR pts ( $p=.01$  and  $p=.027$ , respectively).  $\Delta$ EDV in MR pts was greater after repair than replacement ( $p=.017$ ). No-LV-R was associated to smaller EDV and LV mass at baseline and more MR than LV-R ( $115$  vs  $165$  mL,  $p=.025$ ;  $241$  vs  $331$  g,  $p=.005$ ;  $86.66\%$  vs  $54.05\%$ ,  $p=.031$ , respectively). Baseline EDV  $\geq 152.5$  mL independently predicted LV-R ( $p=.017$ ) with 60% sensitivity and 73% specificity (AUC 0.70,  $p=.025$ ). No gender-related differences were found in  $\Delta$ EDV. EDV (indexed for body surface area) was smaller in women than men, both at baseline and at discharge ( $p=.001$  and  $p=.031$ , respectively). Mortality was 19% in LV-R and 23% in No-LV-R pts, despite absence of statistical significance. Rehospitalization for HF similarly occurred in LV-R and No-LV-R pts, but seemed more frequent in MR than AR and MR+AR (24% vs 6.66%,  $p=ns$ ) pts. Women apparently had better prognosis than men if remodeled (100% vs 81% survival rate, respectively,  $p=ns$ ) and worse prognosis than men if did not remodeled (50% vs 11.11% mortality, respectively,  $p=ns$ ).

**Conclusions:** In HF due to AR and/or MR, early LV-R is greater in pts with higher baseline EDV. It is not gender-related, but might predict long-term outcome. Pts with MR display smaller EDV at baseline, less LV-R at discharge and might have worse prognosis than pts with AR and MR+AR.

#### P260

##### High red cell distribution width is able to predict hospitalisation for heart failure in patients with coronary artery disease

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**Background:** Red Cell Distribution Width (RDW) is the measure of the range of variation of red blood cell volume and it is found to be a very strong independent predictor of morbidity and mortality in patients with chronic heart failure.

**Purpose:** We aimed to analyse whether RDW was a predictor of hospitalization for heart failure in patients with CAD, with or without systolic dysfunction. Method: we prospectively enrolled patients with stable Coronary Artery Disease (CAD) from our Outpatient Clinic from 2009 to 2013. We enrolled patients with or without left ventricular dysfunction. Each patient underwent clinical evaluation and biochemical measurements and a telephone follow-up was planned to register the long term outcomes. Sensitivity/specificity ratio for RDW was analysed with ROC analysis and the independent role of RDW was evaluated with Cox regression model of analysis. The survival rate was represented by Kaplan Meier curves.

**Results:** 152 patients were enrolled with mean age  $69.1 \pm 10.8$ ; the mean left ventricular systolic function was  $43.9 \pm 14.9\%$ . Mean time follow up was  $1340.9 \pm 803.7$  days, mortality rate was 20.9% (32 deaths) and hospitalization for heart failure rate was 27.5% (42 events). Mean value of RDW was  $14.8 \pm 3.0\%$ ; the analysis of the ROC curve identified a RDW cut-off level of 13.2% (AUC 0.767;  $p < 0.0001$ ). Patients with RDW  $> 13.2\%$  had significant independent (adjusted for age, sex, NYHA class, NT-proBNP, Ejection Fraction and eGFR) higher risk of hospitalization for heart failure (HR=6.50; 95% CI: 2.40-17.70) and of composite outcome (hospitalization and mortality) (HR=0.87; 95% CI: 0.31-2.44). Its predictivity remained significant either in patients with left ventricular systolic dysfunction and in those without.

**Conclusions:** in patients with CAD with or without heart failure, RDW value of  $> 13.2\%$  independently predicts increased risk of hospitalization for heart failure and composite outcome.

## P261

### Need for support for patients with chronic heart failure, the development and implementation of self management strategies at home- A qualitative research study in Switzerland

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**Introduction:** Chronic heart failure (CHF) is characterized by a wide range of symptoms, high prevalence in the elderly, poor (quality of life QoL) and frequent hospitalisations. Managing one's condition at home is important to successful treatment. Multiprofessional patient education programs have shown positive effects on self management strategies (SMS), QoL, mortality and costs although a lack of congruency exists in methods, quantity and duration of programs. It is unclear what support these patients need to integrate and maintain SMS at home. This survey explored the support needed to maintain SMS at home for CHF patients who have completed a self-management (SM) course during hospitalisation. Additionally, it evaluated which available social networks support SMS at home.

**Methods:** A qualitative study was utilized to explore the subjective perspective of patients. Grounded theory was chosen to examine patients' perspectives in SM at home. Twenty two interviews were conducted at the participants' homes after hospital discharge. Various methods of coding, open, axial and selective were used. The process was completed after the main phenomenon has been identified.

**Results:** The results show intrinsic motivation as the main phenomenon. This motivation gives patients strength and energy to develop SMS for achieving a good QoL. SM is influenced by the patient's relationship with the health care providers, and their personal experiences shape their behaviour. Confidence is the key factor for cooperation between patients and health care providers. It results from behaviours such as reliability, feeling encouraged to ask questions, listening, attentiveness and friendliness, being able to talk to each other and taken seriously, knowing each other and more. In the critical event of transitions from inpatient to outpatient, the social network and the collaboration between the patient and the health care provider may be the key element for successful SMS at home.

**Conclusion:** Results show a wide range of factors influence intrinsic motivation for effective SMS at home with the aim of a high QoL and preventing hospitalisation. Professionals need to be aware of influencing factors and should build networks to provide patient support. Each patient situation requires a comprehensive assessment to provide individualised help with SMS at home and to establish a supportive social network.

## ADVANCED HEART FAILURE

## P262

### The Impact of optimized care on heart transplant outcome in high-risk patients at Germanys First advanced Heart Failure Unit

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Hospitalizations for acute and advanced heart failure are increasing, with patients presenting in complex conditions affecting multiple organs. Optimized medical and interventional therapies have led to a better survival even in severe heart failure. Consequently more patients with very advanced disease have to be treated in cardiology units by sophisticated medical and interventional strategies. To our knowledge there is so far no ward that will meet these high expectations in the European hospital system. Here we report our 3-year experience with a dedicated advanced heart failure unit (AHFU) in Germany, with special focus on its impact on outcome in high-risk heart transplant candidates. The AHFU is an intermediate care facility with 8 treatment units established as an extension of our intensive care unit (14 beds) and our coronary care unit (10 beds). The eight beds unit was established as an extension of the cardiologic intensive care (14 beds) and coronary care (10 beds) units in an intermediate care setting. Each bed was equipped with 24 hours hemodynamic, respiratory and arrhythmia monitoring. The unit is served 24 hours/7 days a week by 5 residents in cardiology, one staff cardiologist specialized in medical and interventional heart failure care and 10 intensive care nurses. The cardiology team is supported by colleagues from cardiac surgery, sports medicine, psychosomatics and the internal medicine departments with routine interdisciplinary conferences and rounds. Due to this unique interdisciplinary therapeutic approach under the leadership of the cardiologic department special tailor-made treatment plans are elaborated for each patient. The cohorts of patients undergoing high risk heart transplantation from HU status before (pre AHFU 2008-2011) and after establishment of the AHFU (AHFU 2012-2014) were studied and compared to test intensified advanced heart failure care on the AHFU. Interestingly, post-heart transplant survival was comparable in both cohorts, despite significant increase in morbidity and comorbidity as assessed by the Index for Mortality Prediction After Cardiac Transplantation (IMPACT) model in the AHFU group. AHFU being the first in Germany is improving the care of patients with advanced HF. The evaluation of the AHFU in Heidelberg shows that patients with advanced heart failure benefit from the high degree of expertise, the experienced team and the outstanding interdisciplinary cooperation at the AHFU. From our perspective, the AHFU represents a milestone in the treatment of these critically ill patients.

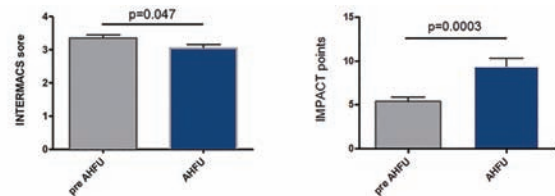


Figure 2: IMPACT score, IMPACT score. Means±SEM or absolute numbers and %, Mann-Whitney-test.

## P263

### Cardiac resynchronisation therapy in the treatment of end-stage inotrope-dependent class IV heart failure

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**Background:** Currently, cardiac resynchronisation therapy (CRT) is recommended only for New York Heart Association (NYHA) class IV ambulatory patients. However, some recent reports have suggested that CRT could also be beneficial for end-stage inotrope-dependent heart failure (HF) NYHA class IV patients. In this report, we summarise the results of CRT implantation in a group of 11 HF inotrope-dependent patients. Orthotopic heart transplantation (OHT) and Left ventricular assist devices were not available in many developing countries.

**Methods and results:** Between March 2005 and December 2014, 11 end-stage inotrope-dependent HF patients with wide QRS complex, ineligible for urgent OHT, were implanted with CRT. Dependence on inotropic therapy was defined as an inability to stop the infusion of the drug without the occurrence of hypotension, oligo or anuria and/or hypoxemia. All patients were successfully implanted with CRT. Rapid haemodynamic amelioration allowed the withdrawal of inotrope support gradually within the median time of two (1,17) days. Mean QRS duration shortened from  $143, 6 \pm 17$  ms at baseline to  $102, 7 \pm 15$  ms ( $p < 0.001$ ) after the procedure. All patients were discharged from hospital. Median hospital stay after the procedure was ten (5,3) days. During the median follow-up of 534 (range : 180 - 1500) days, LV volumes decreased (end-diastolic from  $334, 3 \pm 48$  to  $222 \pm 53$  ml;  $p = 0.07$ ; end-systolic from  $251 \pm 25$  to  $135 \pm 98$  ml;  $p < 0.01$ ). LV ejection fraction increased ( $21.72 \pm 6\%$  to  $29.9 \pm 12\%$ ;  $p < 0.05$ ). Three patients died (one because of arrhythmic

storm, one because of infective endocarditis and another because of progressive pump failure).

**Conclusion:** CRT can be safe and effective and can be an alternative for end-stage inotrope-dependent HF patients with wide QRS where heart transplantation is not available. CRT should be considered relatively early in the course of sustained inotropic therapy.

#### P264

##### Percutaneous valve-in-valve implantation in tricuspid position as an alternative for very high surgical risk patients with refractory heart failure symptoms.

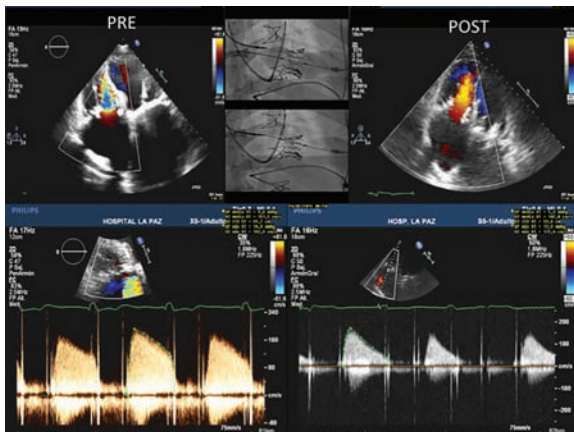
FJ Francisco Javier Irazusta Cordoba<sup>1</sup>; O Gonzalez Fernandez<sup>1</sup>; SO Rosillo Rodriguez<sup>1</sup>; A Sanchez-Recalde<sup>1</sup>; AM Iniesta Manjavacas<sup>1</sup>; P Meras Colunga<sup>1</sup>; V Rial Baston<sup>1</sup>; D Gemma<sup>1</sup>; F Gutierrez-Larraya<sup>1</sup>; JL Lopez-Sendon<sup>1</sup>  
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**Background:** Redo valve surgery for failure of a tricuspid bioprosthesis is recommended in symptomatic patients when optimal medical therapy becomes unsuccessful, but still represents a challenge. Transcatheter valve-in-valve implantation has emerged as a new valid technique for these patients, yet experience is very limited. Previously reported cases have described the use of valves designed for pulmonary position, although their maximum available size of 22mm results in a significant limitation. Transcatheter aortic valves (TAVI) may then be a useful alternative.

**Methods:** We present a series of percutaneous valve-in-valve implantation of TAVI in tricuspid position performed at our center in patients with refractory heart failure symptoms due to stenotic tricuspid bioprosthesis and high risk for surgical intervention.

**Results:** A total of three cases were performed and described as follows: 14-year-old female with a 25 mm tricuspid bioprosthesis due to repaired complex congenital heart disease; 38-year-old male with Ebstein's anomaly corrected with a 31 mm bioprosthesis, and a 73-year-old male with rheumatic valve disease and a 31 mm bioprosthesis. In all cases implantation was performed under general anesthesia in the catheterization laboratory; two through a transfemoral approach and one transjugular. Only one procedure required pre-stenting. Two TAVI of 29 mm and one of 23 mm were implanted in opposite direction of the aortic valve. Transoesophageal echocardiographic assessment after implantation revealed normal valvular function and ruled out further complications. Mean transvalvular gradient decreased from 11.1 to 6.7 mmHg at discharge. Improving of heart failure symptoms at mid-term follow-up (2,4 and 12 months), was confirmed in all patients with a mean reduction of one level of their baseline NYHA class.

**Conclusions:** Percutaneous TAVI implantation in failing bioprosthetic tricuspid valve seems to be a valid alternative in very high risk surgical patients with refractory heart failure symptoms. More cases and longer follow-up are required to confirm our results.



#### P265

##### Feasibility of the first year post-heart-transplantation follow-up in a cardiology day hospital

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**Introducción:** First year post-heart transplantation (HTx) follow-up consists of a close monitoring of the graft function, immunosuppression and related complications. It requires multiple tests, some of them invasive like endomyocardial biopsy, right heart catheterization or coronariography, so classically the patient was admitted in the cardiology ward. In the last decades the experience in ambulatory procedures has offered the possibility of a fully outpatient follow-up. The feasibility and security of this strategy is not well known.

**Methods:** From 2007 we transitioned from an inpatient to an outpatient follow-up in the first year post-HTx through a cardiology hospital day. We have retrospectively reviewed the clinical course during the first year post-HTx of the outpatient group (2007 to 2014) and an immediately prior inpatient group (2000-2006). Patients with postoperative death or mixed follow-up were excluded. Data collected were: basal characteristics, hospital stay, infections, rejection episodes and invasive tests performed during the first year.

**Results:** During the period of study 87 patients had an Inpatient Follow-up (IF) and 99 patients had an Outpatient Follow-up (OF). Basal characteristics were similar in both groups: Male sex 79.3% in IF, 67.7% in OF (ns); Hypertension 39.1% vs 35.7% (ns); Diabetes 65% vs 71.7%; IgG-CMV negative 18.4% vs 12.2%. We found significant differences in immunosuppression and age due to historical comparison: tacrolimus 44.8% vs 90.8% ( $p < 0.001$ ); mycophenolate 86.2% vs 100% ( $p < 0.001$ );  $52 \pm 11.5$  vs  $56.1 \pm 11$  ( $p = 0.014$ ).

More clinical visits were performed in the OF group ( $10.4 \pm 2$  vs  $13.1 \pm 3.7$ ,  $p < 0.001$ ). Hospital stay (postoperative stay excluded) was lower in the OF group ( $27.8 \pm 14.8$  vs  $12.4 \pm 18.2$ ,  $p < 0.001$ ). A similar percentage of patients presented infection, rejection or vascular complications. No difference was either in mortality in the first year: 2 patients IF and 1 patient in OF (2.3% vs 1%, ns).

**Conclusion:** The first year post-HTx follow-up seems to be feasible and safe in terms of infection, rejection, vascular complications and mortality. It offers the benefit of more frequent clinical visits and lower hospital stay.

#### P266

##### Clinical aspects of continuous intravenous morphine for palliative care in patients with advanced heart failure from experience with 55 cases

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**Background:** Heart failure is epidemic in developed countries and approximately 5% of patients with heart failure are refractory to medical therapy. Palliative care for those patients is recommended for relief of symptom and patient satisfaction. However, we could not intervene enough because of insufficient evidence and experience including pharmacotherapeutic intervention.

**Methods:** We experienced continuous intravenous infusion of morphine for palliative care in 55 patients with advanced heart failure from March 2011 to December 2015. We reviewed our experience and evaluate safety and efficacy of morphine administration. Intensity of symptoms was evaluated by Visual Analogue Scale (VAS).

**Results:** Morphine hydrochloride was administered for 55 patients among 2042 patients (male 51%, aged  $79 \pm 12$  yrs) for palliation of dyspnea (85%) and pain (15%) during  $6.5 \pm 6.0$  days. LVEF was  $35.8 \pm 14.4\%$ , estimated glomerular filtration rate (eGFR) was  $32.7 \pm 36.0$  ml/min/1.73m<sup>2</sup>, BNP level was  $1855 \pm 1546$  pg/ml. Inotropic agents, diuretics, and sedative medication were administered in combination with morphine in 75%, 92%, 35%, respectively. Systolic blood pressure, heart rate, respiratory rate were  $101.0 \pm 23.7$  vs  $97.9 \pm 24.6$  mmHg ( $p = 0.51$ ),  $95.0 \pm 22.7$  vs  $92.3 \pm 19.9$  beats per minute ( $p = 0.52$ ),  $26.8 \pm 7.2$  vs  $18.2 \pm 4.3$  breaths per minute ( $p < 0.001$ ) at baseline and 24 hours after administration respectively. Mean dosage of drug was 7.2 at initiation and 10.5 mg/day at maintenance. Dyspnea was significantly improved after morphine administration (VAS  $6.0 \pm 1.8$  vs  $2.7 \pm 1.9$ ,  $p = 0.0008$ ).

For patients discharged after discontinuation of morphine due to amelioration of symptoms. No patients discontinued morphine due to adverse events. ICD was deactivated in 7 among 11 implanted patients (64%).

**Conclusion:** Low dose morphine hydrochloride was relatively safe and effective even though for the patients with advanced heart failure.

	Baseline	24 hours after administration	p value
Dosage amount (mg/day)	$7.0 \pm 5.0$	$11.0 \pm 7.4$	0.0008
Systolic blood pressure (mmHg)	$101.0 \pm 23.7$	$97.9 \pm 24.6$	0.51
Heart rate (bpm)	$95.0 \pm 22.7$	$92.3 \pm 19.9$	0.52
Respiratory rate (bpm)	$26.8 \pm 7.2$	$18.2 \pm 4.3$	0.0001
SpO2 (%)	$95.7 \pm 4.1$	$95.9 \pm 4.7$	0.84
Intensity of symptoms (Visual Analogue Scale)	$6.0 \pm 1.8$	$2.7 \pm 1.9$	0.0008

Effect of intravenous morphine for palliative care in patients with advanced heart failure

## P267

**Tricuspid valve regurgitation after heart transplantation: does it really have a poor prognosis?**

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**Introduction:** Tricuspid regurgitation (TR) is the most common valvular abnormality after orthotopic heart transplantation (OHT). Although endomyocardial biopsy is responsible for the majority of cases (chordal damage), there are others causes: Shumway technique, pulmonary hypertension, cardiac allograft rejection ...

Some studies show that TR is a significant clinical finding and has an important impact on the long-term clinical progress of the OHT patients.

**Purpose:** Analyse the patients with severe TR after OHT in our Advanced Heart Failure and Heart Transplant Unit.

**Methods:** A retrospective single-centre study. Patients with severe TR after OHT from January 1992 to December 2015 were enrolled. Clinical and echocardiographic variables were collected.

**Results:** 25 patients (92% male) were analysed. The etiology of cardiomyopathy before OHT was 48% ischemic, 32% idiopathic dilated, 12% valvular and 8% congenital. 84% were performed by Shumway technique and 16% by bicaval technique. 56% of the cohort remained asymptomatic despite the severe TR, although 28% developed left ventricle failure symptoms, 8% showed systemic congestive symptoms and only 8% had global heart failure symptoms. The 40% of our population were diagnosed with allograft vascular disease.

About TR etiology, a flail leaflet was found in 18 cases (72%); functional TR with right ventricle dilatation in 6 cases (24%) and infective endocarditis was described in one case (4%). None of the patients underwent tricuspid valve surgery. Freedom from severe TR is described in the figure 1a.

For a follow-up of  $13,3 \pm 6,8$  years, the cumulative survival is described in the figure 1b. 33% died of sudden death, 25% of advanced heart failure and 42% of non-cardiac causes.

**Conclusion:** Although many studies in the literature correlate severe TR with a poorer prognosis, our series showed a high survival rate, which suggests that TR is not related with a worst prognosis. The 5 years survival rate in our serie (88%) is higher than the XXV Spanish Registry of Heart Transplant (65%), published in December 2015. This may be caused by the small size of our series and by missed cases (early deaths after the OHT).

None of our patients underwent tricuspid valve surgery. Recipients with significant TR are more symptomatic in the reviewed literature but in our series more than a half remained asymptomatic.

Many patients died of non-cardiac causes, as infection or cancer.

A larger comparative study in our population is needed to obtain further information.

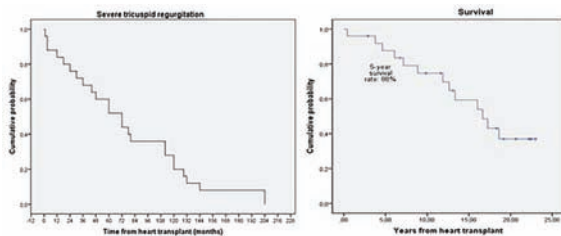


Figure 1

## P268

**The criterion of unfavorable postoperative period in patients with ischemic cardiomyopathy**

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**Objective:** to study preoperative perfusion and metabolism of left ventricular (LV) myocardium in patients with ischemic cardiomyopathy (ICMP) for the further prognosis and evaluation of possible postoperative repeated heart remodeling.

**Methods:** The study included patients with ICMP (n = 32) of  $56 \pm 7$  years old, subjected to Triple V type surgical treatment (CABG, SVR, MVR). Inclusion criteria: obliterating atherosclerosis of coronary arteries (CA) (stenosis of the left main CA  $\geq 75\%$  or proximal stenosis of the anterior descending CA, and/or more than 75% stenosis of two and more CAs); previous myocardial infarction; chronic HF NYHA II-IV; LVEF  $< 40\%$ ; LV ESVI over 60 ml/m<sup>2</sup>; presence of akinetic and dyskinetic areas of LV by echocardiography. SVR was performed by L. Menicanti technique. Exclusion criteria: organic heart diseases; acute myocardial infarction; right ventricular

failure; acute cerebrovascular disease; absolute contraindications to surgical treatment. Prior to the surgery myocardial scintigraphy with 99mTc-MIBI at rest was performed to evaluate perfusion and with 123I-MIBG to evaluate metabolism of fatty acids in the myocardium. Scintigraphy results were presented as a median of lower/higher quartiles (Me (IQ/hQ)). Clinical status of LV and EchoCG data were evaluated before the surgery, 1 month after the surgery and 1 year after the surgery.

**Results:** One year after the intervention the patients were allocated into two groups: (Group 1) patients (n=18) with a positive effect from the surgery, in which LV repeated postoperative remodeling process was not noticed: ESVI decreased, remained at the same postoperative level or increased  $< 15\%$  if compared with that in the early postoperative period; (Group 2) patients (n = 14) in which, despite successful surgery, repeated LV remodeling took place: ESVI increased  $\geq 15\%$  in comparison with that in the early postoperative period. The groups were comparable by their LV volumes and clinical status prior to the surgery and in the immediate postoperative period. Significant preoperative differences were revealed by the following baseline scintigraphy data: defect of metabolism in the delayed images (26.5% (20.6%; 32.4%) and 38.2% (16.2%; 44.1%),  $p = 0.02$ , respectively), perfusion-metabolic mismatch in the early (5.9% (-5.9% 7.4%) and -1.5% (-7.4% 1.5%),  $p = 0.02$ , respectively) and delayed (14.7% (5.9%; 27.9%) and 4.4% (2.9% 7.4%),  $p < 0.0001$ ) images. The largest area under the ROC curve was found to be for the method of identification of perfusion-metabolic mismatch in the delayed scans (AUC = 0.778,  $p < 0.0001$ ).

**Conclusion:** The size of the perfusion-metabolic mismatch  $\geq 12\%$  predicts positive effect of surgical treatment with sensitivity and specificity of 100% and 56%, respectively.

## P269

**Application of the new classification of primary graft failure in a contemporary heart transplantation series**

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**Introduction:** Primary graft failure (PGF) is a severe complication in the initial post-transplantation period. There is significant discrepancy in the definitions used by the different studies. In 2014 the International Society of Heart and Lung Transplant (ISHLT) established new criteria for the diagnosis of PGF and proposed a severity scale in the left ventricle (LV) PGF. The utility of this classification to predict postoperative mortality is not fully evaluated.

**Methods:** We analysed retrospectively all heart-transplantation patients in our department between January 2005 and December 2014. We collected basal characteristics and data of the initial postoperative period (echocardiogram, hemodynamics, cardioactive drugs). The application of the ISHLT classification was determined independently by two cardiologists, discussing the data in case of disagreement. Finally, the combined event postoperative death and graft loss was analyzed.

**Results:** During the study period 165 heart-transplantations were performed. We excluded from analysis 14 patients, not fulfilling the PFG criteria (due to pulmonary hypertension with PSAP  $> 50$ mmHg, GTP  $> 15$ mmHg and RVP  $> 4.5$ UW, or technical complications). The basal characteristics of the remaining 151 patients were: Age  $55.1 \pm 11.8$ y; Male 66.9%; diabetes 41.7%; hypertension 37.7%; positive CMV-IgG 88.1%; urgent status listing 31.1%. The global incidence of PGF was 60.3%, with the following distribution: Isolated right ventricle (RV) PGF 30.5%; Isolated LV-PGF 1.3%; Biventricular PGF 28.5%. The severity in the LV-PGF group resulted: mild 17.7%; moderate LV-FPI 53.3%; severe LV-PGF 40%.

The analysis of the combined event resulted: non-PGF 3.3%; Isolated RV-PGF 10.9%; mild LV-PGF 0%; moderate LV-PGF 8.3%; severe LV-PGF 94.1%. Logistic regression analysis showed statistically significant difference only in the severe LV-PGF in comparison with the non-PGF group ( $p < 0.001$ ; OR 464 [IC95 39.5-5449.7]).

**Conclusion:** With the application of the new ISHLT classification to a contemporary heart-transplantation series we found that any kind of PFG was frequent (60.3%). There was similar proportion of isolated RV-PGF and biventricular-PGF (30.5 and 28.5%), with a very low proportion of isolated LV-PGF (1.3%), so LV-PGF was mostly combined with RV dysfunction. In terms of mortality or graft loss, the only group with a significant higher risk was the severe LV-PGF.

## P270

**LVAD bridge to recovery**

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 M Mustafa Alrefai<sup>1</sup>; MUSTAF Refae<sup>1</sup>

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We reported three cases with non ischemic cardiomyopathy with chronic heart failure symptoms recovered their lv systolic function after LVAD implantation and lv recovered to have LVAD explanted case 1-20year female presented with severe left ventricular failure with lvef 10% with failure of medical therapy case discussed



in our cardiac meeting then decision for LVAD implantation. LVAD implanted without complication with regular follow up with 2dechoardiography lvef improve from 10% to 55% LVAD explanted after one year of implantation. Case 2- 40y male patient with chronic heart failure secondary to non ischemic dilated cardiomyopathy with lvef 15% with narrow qrs complex with failure of medical therapy LVAD implanted at our center with regular fu with transthoracic echo cardiography lvef improve from 15% to 50% over 1 year period with recovery of lv function so LVAD explanted case-3 36y male patient diagnosed with dilated cadiomyopathy lvef 20% with repeated hospitalisation with left ventricular failure so LVAD implanted at our center with regular follow up with transthoracic echo cardiography lvef improve from 20% to 60% so improvement in clinical and surgical expertise in LVAD has improved the quality of life in well selected patient and to be as bridge to recovery.

## ATRIAL FIBRILLATION

### P271

#### Atrial fibrillation does not impair functional performance in patients with chronic stable heart failure.

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**Background:** Atrial fibrillation(AF) is commonly observed in patients with Heart failure and may impair their functional capacity. We evaluated this by comparing functional performance in patients with chronic stable heart who were in AF with those in Sinus rhythm (SR).

**Objective:** To assess if there is a significant differences in measured functional capacity between patients with chronic heart failure whether they were in AF or SR.

**Methods** 95 consecutive patients with chronic Heart failure were enrolled. 33 with AF and 62 in SR (controls). Functional performance was assessed using New York Heart Association (NYHA) class, 6 minute Walk Test and 3 Day FitBit Activity tracker.

**Results:** AF patients were older (73.15 ± 2.10) compared to patients in sinus rhythm (63.20 ± 1.54) and their mean heart rate was higher; 78.09 ± 2.34 vs 66.85 ± 1.68. Results are summarized in the table below. **Conclusion:** Our results highlight that in patients with chronic stable heart failure, the presence of atrial fibrillation and higher heart rates did not significantly impair their objectively measured functional capacity compared to those in sinus rhythm. These observations cast doubt on strategies to revert these patient to sinus rhythm.

	Atrial fibrillation	Sinus rhythm	p-value
No. pts (n)	33	62	< 0.0001
Male (%)	72.73	64.52	0.416
Age (Yrs ± SD)	73.2 ± 2.1	63.2 ± 1.6	0.0002
Mean heart rate(beat/min)	78.1 ± 2.3	66.9 ± 1.7	0.0002
Body Mass index(kg/m2)	29.0 ± 1.0	28.8 ± 0.7	0.480
Left ventricular function(cm)	41.1 ± 2.1	37.86 ± 1.72	0.237
Left ventricular diameter (cm)	6.3 ± 0.2	6.6 ± 0.6	0.2
Functional performance			
New York Heart Association score	1.3 ± 0.1	1.3 ± 0.1	0.767
6 min walk distance(m)	389 ± 211	386 ± 120	0.956
Activity tracker (FitBit) (mean steps)	4928 ± 749	6263 ± 590	0.165

### P272

#### Ivabradine improves heart rate control and exercise tolerance in patients with heart failure with preserved ejection fraction and atrial fibrillation.

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**Purpose:** to evaluate the impact of Ivabradine administration on heart rate control and exercise tolerance of patients with heart failure with preserved ejection fraction (HFpEF) and permanent atrial fibrillation (PAF).

**Methods:** 11 subjects with of HFpEF and PAF, age 74.5 ± 21 years, M/F = 9/2, ejection fraction 56.5 ± 8.3, resting heart rate > 100 bpm were included. all subjects performed 24/h ambulatory ECG monitoring (AEM), six minute walking test (6MWT) and cardiopulmonary test, at baseline and after two months of treatment with ivabradine. The dose of ivabradine was 5 mg/bid. We defined patients as responders to ivabradine if their mean heart rate at 24/h AEM decreased at least of 15% at two

months. According to the observed response, patients were divided in two groups as responders (group 1) or not responders (group 2).

**Results:** After two months seven out of 11 patients (63.6%) were responders. Group 1 had a significant reduction of mean heart rate at 24/h AEM compared to group 2 (-37.5 ± 11% bpm vs -8.6 ± 3.1 bpm, p 0.003) After two months 6MWT distance (group1 = 97 ± 28 m; group 2 = 41 ± 19 m; p0.0002) and VO2 peak(group1 = 19.8 ± 5.3 %; group 2 = -2.3 ± 1.4 %; p0.004) increased significantly in group 1 compared to group 2.

**Conclusions:** Ivabradine improved heart rate control in more than half patients with HFpEF and PAF. The decrease of heart rate was associated with an improvement of exercise tolerance.

### P273

#### Left atrial longitudinal strain for discrimination of thromboembolic risk in patients with atrial fibrillation

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**Background:** According to the results of a retrospective study patients (pts) with atrial fibrillation (AF) and CHA2DS2-VASc score of 1 may be at lower risk for thromboembolic events than previously reported. Consideration of additional factors can provide a more comprehensive assessment of an individual's suitability for anticoagulation treatment.

**Purpose:** To evaluate whether left atrial (LA) speckle tracking measurements improve risk discrimination in pts with AF and CHA2DS2-VASc score of 1 in whom it is unclear if treatment with anticoagulants is beneficial.

**Methods:** Sixty pts [mean age 65 (60; 72) yrs, 45% men] with AF were divided into three groups based on CHA2DS2-VASc score: the score of 1, the score of 2, the score of ≥3. All pts underwent conventional and speckle tracking echocardiography. 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) in the reservoir (r) and contractile (c) phase.

**Results:** In nonlinear logistic regression analyses, only higher PALSr was significantly associated with lower CHA2DS2-VASc score (OR 0.61; 95% CI 0.38-0.97; p=0.03). The ROC curve showed the optimal PALSr cut-off point for prediction of CHA2DS2-VASc score of 1 was 16.7%. This had a sensitivity of 62.5% and a specificity of 39.0% and an area under the curve of 0.85 (95% CI 0.72-0.98; p=0.002).

**Conclusions:** PALSr was independently associated with CHA2DS2-VASc score in pts with AF. Use of a PALSr threshold may be clinically available instrument for decision making to initiate anticoagulation treatment based on the risk versus benefit of therapy in pts with AF and CHA2DS2-VASc score of 1.

### P274

#### Relationship between central blood pressure and left atrial remodeling in patients with diastolic heart failure

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**Objective:** Left atrial (LA) remodeling is associated with left ventricular (LV) diastolic dysfunction that could cause diastolic heart failure (DHF). Arterial stiffness is elevated in patients with arterial hypertension, atherosclerosis, diabetes mellitus, but it's relations with HF and atrial fibrillation (AF) is not well known.

**Aim:** to compare central blood pressure in patients with recurrent AF and DHF in dependence of structural and functional changes of LA.

**Methods:** The study included 55 hypertensive patients (40% men) aged 66 (62; 73) years with recurrent AF and DHF (EF>50%). Standard echocardiography with Doppler technique and applanation tonometry were performed. LA structural abnormalities were defined as LA volume index (LAVI) ≥ 34 mL/m<sup>2</sup>. LA emptying fraction (LAEF) ≤ 45% and LA expansion index (LA exp inx) ≤ 90% were categorized as LA phasic dysfunction. All patients were divided into 3 groups: G1 had both structural and functional abnormalities, G2 – had normal structure but phasic dysfunction and G3 – had normal LA parameters.

**Results:** The groups were similar in terms of age, body mass index, brachial blood pressure (BP) and antihypertensive therapy. The highest HR was in G1 patients [75 vs 71 and 70 bpm in G2 and G3 respectively, p=0,03]. Significant changes observed in timing to reflected wave (Tr), that was shortest in G1 group (p=0,02). Alx-HR75 had the highest range in G1 group [33 vs 25 and 22% in G2 and G3 respectively, p=0,02]. There was no difference in central BP and PWVcf between three groups. LAVI had significant (p < 0,05) inverse correlations with Tr (r=-0,22) and direct correlations with Alx-HR75 (r=0,16). Both LAEF and LA exp inx had equal negative relations with HR (r=-0,31), brachial and central DBP (r=-0,25 and r=-0,23 respectively) and PTIsystole (r=-0,22). Significant positive relations were observed between phasic function parameters and ejection duration, subendocardial viability ratio (SEVR) and Alx-HR75 (r=0,24 for all cases).

**Conclusion:** LA remodeling is associated with higher HR and Alx-HR75 and shorter Tr in AF patients with DHF. LAVI correlated with Alx-HR75 and Tr, while LA function had a relation with HR, brachial and central DBP, ejection duration, SEVR and PTIsystole.

## P275

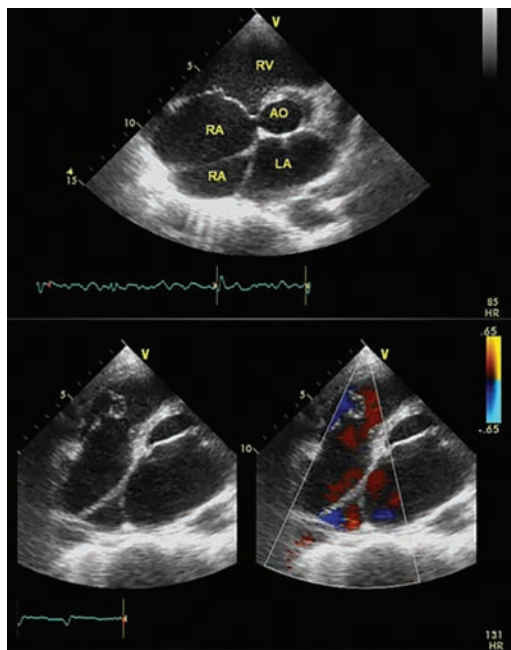
**Conservative approach for patient in acute heart failure with cor triatriatum dexter and atrial fibrillation : a rare case report**S M Satyadharma Michael Winata<sup>1</sup><sup>1</sup>Budhi Asih General Hospital, Cardiovascular Medicine, Jakarta, Indonesia

**Introduction:** Cor triatriatum dexter (CTD) is a very rare congenital cardiac anomaly in which right atrium (RA) is divided into 2 chambers by a membrane. This congenital abnormality is commonly associated with other right-sided cardiac abnormalities. In this report, we describe a patient presenting with acute heart failure precipitated by atrial fibrillation (AF) which was caused by CTD.

**Clinical summary:** A 33-year-old man was admitted to emergency room with acute-onset dyspnea and chest pain. He was presented with jugular vein distension with respiratory rate 36 / minute and 96% percutaneous oxygen saturation in air. Auscultation of the chest revealed bilateral fine crepitations on lung bases. Other physical examination results were between normal limit. A 12-lead electrocardiogram (ECG) showed irregular rhythm consistent with atrial fibrillation with a ventricular rate of 80, no ST segment or T wave changes. Chest X-ray showed cardiomegaly. An initial transthoracic echocardiogram showed a membrane partitioned the right atrium into two chambers consisted with CTD. The left ventricular function was normal and no abnormalities detected on the cardiac valve with no turbulent flow detected using the Doppler method. Medical treatment using intravenous diuretics, anticoagulation treatment and beta-blocker showed a significant improvement in patient's condition. The patient was discharged with beta-blocker and anticoagulation treatment. Outpatient clinic follow-up showed a good result with no complications detected, even though the ECG still showed atrial fibrillation. The patient refused to have further evaluation and management of his heart rhythm.

**Discussion:** Clinical manifestation in patients with CTD are variable from asymptomatic and often detected incidentally during echocardiography or surgery to correct other cardiac abnormalities. This condition can lead to trapped catheters, supraventricular arrhythmias (such as AF), or embolisms. CTD can be diagnosed by echocardiography and magnetic resonance imaging (MRI). Symptomatic patient with significant obstruction should have a surgical resection. In this patient, beta blocker and anticoagulant given with short course of parenteral diuretic eliminated the symptoms and shared a good results of the follow-up without any complication detected. Although we found that the AF associated with CTD had a tendency to be persistent or permanent, our further evaluation and treatment could not be done because of patient preferences.

**Conclusion:** Although CTD is extremely rare, it can be presented in a young patient with right-sided heart failure. It can be easily corrected by surgical excision of the membrane if indicated. Eventhough excision of an abnormal membranous septum could eliminate AF, our patient outcome for months was still good with beta blocker and anticoagulation treatment.



Transthoracic echocardiogram showing CTD

## P276

**Impact of atrial fibrillation patterns in patients with acute decompensated heart failure**J B Augusto<sup>1</sup>; M Borges Santos<sup>1</sup>; D Roque<sup>1</sup>; M Silva<sup>1</sup>; J Castro<sup>2</sup>; J Sala<sup>1</sup>; A Faustino<sup>1</sup>; M Branco<sup>1</sup>; F Frade<sup>1</sup>; C Morais<sup>1</sup><sup>1</sup>Hospital Prof Fernando da Fonseca EPE, Amadora, Portugal; <sup>2</sup>Hospital de Cascais, Cascais, Portugal

**Background:** Atrial fibrillation (AF) is a frequent comorbidity in patients with heart failure (HF) with an associated increase in mortality.

**Purpose:** We aimed to evaluate the prognostic value of different patterns of AF (paroxysmal vs non-paroxysmal) in patients with acute decompensated heart failure (ADHF).

**Methods:** 2181 consecutive patients with AF who were evaluated in our Emergency Department (ED) in a 12 month period were included retrospectively in our study. Among them, 423 patients were admitted for in-hospital management. All patients underwent routine clinical and laboratory exams. We evaluated medical charts in order to identify patients with ADHF. Non-paroxysmal AF included both persistent and permanent AF (defined according to the European Heart Rhythm Association). Patients were evaluated 30 days after discharge to assess the incidence of stroke.

**Results:** 101 patients were admitted with both AF and ADHF (mean age of 77.2 ± 9.6 years, 40.6% males). There were no differences in age (p = 0.664), admission heart rate (p = 0.318), nor in left ventricle ejection fraction (p = 0.229) between paroxysmal and non-paroxysmal AF. A non-paroxysmal pattern was associated with higher hospital admissions for ADHF (28.9% vs 19.7%; odds ratio, OR=1.65, 95% confidence interval, 95% CI 1.05-2.59, p = 0.03). In patients with ADHF, non-paroxysmal AF was more frequently associated with longer length of hospital stay (mean ± standard deviation, 2.4 ± 0.1 vs. 1.9 ± 0.1 days, p = 0.046) and higher HAS-BLED score (3.6 ± 1.1 vs. 2.8 ± 1.1 p < 0.001). Urgent pharmacological cardioversion was also less successful in patients with non-paroxysmal AF (7.1% vs 24.4%, OR=4.21, 95% CI 1.24-14.29, p = 0.023). There was no difference in CHA2DS2-VASc score between paroxysmal AF and non-paroxysmal AF (p = 0.961), nor in stroke rates 30 days after discharge (p = 0.782), despite patients with non-paroxysmal AF being more frequently under oral anticoagulation (55.4% vs 31.1%, p = 0.017). In-hospital death rates were also similar between both subgroups (p = 0.533).

**Conclusion:** In patients with AF, the risk of admission due to ADHF was higher among non-paroxysmal AF. These results suggest that maintenance of sinus rhythm may decrease the rate of admissions and the length of hospital stay for ADHF.

## P277

**CHA2DS2-VASc scores and HAS-BLED score in patients with paroxysmal atrial fibrillation treated in the intensive internal care unit**D Danijela Vranes<sup>1</sup>; B Dzudovic<sup>1</sup>; L Torbica<sup>1</sup>; N Ratkovic<sup>1</sup>; A Ristic<sup>1</sup>; V Milic<sup>1</sup>; S Obradovic<sup>1</sup><sup>1</sup>Military Medical Academy of Belgrade, Clinic of Emergency Medicine, Belgrade, Serbia

**Background:** Atrial fibrillation (AF) is the most common heart rhythm disorder that can be found associated with many acute diseases and carries an increased risk of ischemic stroke and systemic thromboembolic complications. Incidence of paroxysmal AF in patients admitted in the intensive care unit because of non cardiac reasons and risk of thromboembolic and bleeding complications in these patients is not studied well. Method. This is prospective study which included 1700 consecutive patients treated in the Clinic for Emergency and Internal Medicine of Military Medical Academy during 12 months (June 2014 – June 2015) and 200 (34%) patients had electrocardiographic evidence of AF. Thromboembolic and bleeding risk stratification was evaluated with CHA2DS2-VASc and HAS-BLED scores respectively.

**Results:** Among 200 patients with electrocardiographic evidence of AF 87 (43.1%) had paroxysmal AF, and the remaining 113 patients (56.9%) had permanent or persistent AF [92 (45.5%) or 21(10.4%), respectively]. CHA2DS2-VASc score 0 or-1 was found in 13 patients (14.8%), and CHA2DS2-VASc score ≥2 was detected in 74 (85.2%) patients. HAS-BLED skor 0-2 had 33 (37,9%) patients, and HAS-BLED ≥3 had 54 (62,1%) patients. In our group of patients with paroxysmal AF, 54 (62.1%) had an increased risk for thromboembolic complications and bleeding (CHA2DS2-VASc≥2 and HAS-BLED≥3, respectively), 25 (28.7%) patients had an increased risk for thromboembolic complications and low bleeding risk and 8 (9.2%) patients had a low risk for thromboembolic complications and low bleeding risk.

**Conclusion:** In patients with paroxysmal AF treated in the intensive care unit high proportion of patients have both high thromboembolic and bleeding risk.

## P278

**Prevalence and incidence of atrial fibrillation in heart failure patients with either reduced or normal left ventricular ejection fraction**

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**Background:** Heart failure (HF) and atrial fibrillation (AF) are both associated with increased morbidity and mortality. We aimed to determinate the prevalence and incidence of AF in patients with HF.

**Methods:** HF was defined by the presence of symptoms or signs of HF supported by objective evidence of cardiac dysfunction: either a left ventricular ejection fraction (LVEF)  $\leq 40\%$  (or worse than, or equal to, mild to moderate left ventricular systolic dysfunction (LVSD)) on echocardiography (HFref); or LVEF  $> 40\%$  and raised plasma concentration of amino-terminal pro-B type natriuretic peptide (NT-proBNP  $> 220$  pg/ml; HFnEF).

**Results:** Of 3570 patients with HF, 1164 were in AF at baseline (33%), with a greater prevalence among patients with HFnEF compared to HFref (40% vs 26%, respectively,  $p < 0.001$ ). Compared to patients with HF in sinus rhythm (SR), those in AF were older, had more severe symptoms, and higher NT-proBNP, worse kidney function and more often received loop diuretics, despite their higher LVEF. Of those in SR, 1372 patients had HFref and 1034 had HFnEF, the incidence of AF at one year was 2.8% in each group ( $p = 0.73$ ). Increasing age, male sex, history of paroxysmal AF and increasing NT-proBNP were independent predictors of incident AF during a median follow-up of 1574 (IQR: 749-2821) days; the predictors were similar for each cardiac phenotype.

**Conclusions:** The prevalence of AF is high, especially in patients with HFnEF but its incidence is modest. This may be explained by a high concurrent onset of HF and AF. Greater age, a prior history of AF and increasing NT-proBNP, a marker of congestion, but not LVEF predict the risk of developing AF in patients with HF.

## P279

**Atrial fibrillation, cognitive impairment, frailty and disability in older heart failure patients.**

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**Background:** Aim of the study was to prospectively assess the relation between atrial fibrillation (AF), cognitive impairment (CI), frailty and disability in older patients with chronic heart failure (HF).

**Methods:** 331 patients aged  $> 70$  years (mean  $78 \pm 6$ ; range 70-93; 43% women) in stable conditions and optimized therapy were enrolled in 7 HF cardiology clinics. CI was defined by a corrected Mini Mental State Examination score  $< 24$ . Gait speed was used as marker of frailty and measured on a 4 meters distance at usual pace (figure 1).

**Results:** 98 patients (30%) were on AF at enrolment and 20 (6%) had a history of paroxysmal/persistent AF. At multivariable analyses, AF emerged as independently related to CI (OR 1.909 [1.072-3.397];  $p = 0.028$ ), as well as to reduced gait speed (OR 4.366 [2.104-9.060];  $p < 0.001$ ). Furthermore, AF was significantly associated to disability in either basic or instrumental activities of daily living. During a 1-year follow-up, 80 patients died (24.2%), 125 (37.8%) had at least one hospital readmission due to HF and 147 (44.4%) had a non HF-related admission. There was no significant association between baseline AF and 1-year mortality (19.4% vs 18.4%,  $p = 0.188$ ) as well as between AF and HF readmissions (36.7% vs 38.2%;  $p = 0.451$ ) and non-HF related admissions (43.8% vs 46.8%  $p = 0.649$ ).

**Conclusions:** Among patients with chronic HF, those with AF present a high prevalence of frailty, CI and disability. The hypothetical mechanisms by which AF and HF may affect these conditions are multiple and further studies are warranted. However, screening for these variables in clinical practice is simple and inexpensive and may allow better strategies for intervention in this high risk population.

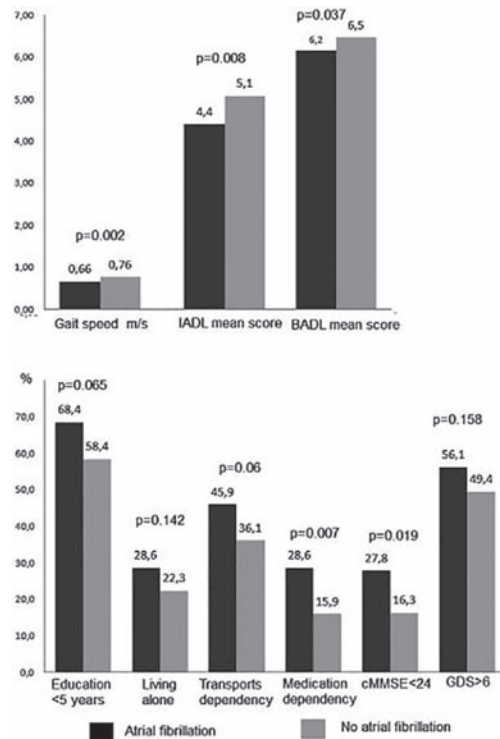


Figure 1

## P280

**Major bleeding among rivaroxaban users with nonvalvular atrial fibrillation and heart failure**

This study is funded by Janssen Scientific Affairs, LLC, and Bayer Healthcare. WF Peacock<sup>1</sup>; S Sally Tamayo<sup>2</sup>; Z Yuan<sup>3</sup>; NM Sicignano<sup>4</sup>; K Hopf<sup>4</sup>; M Patel<sup>5</sup>  
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**Background:** Predictors and outcomes of major bleeding (MB) in heart failure (HF) patients treated with anticoagulants for nonvalvular atrial fibrillation (NVAf) are poorly described.

**Purpose:** Our purpose was to describe the incidence of MB and evaluate outcomes in HF patients receiving rivaroxaban for NVAf.

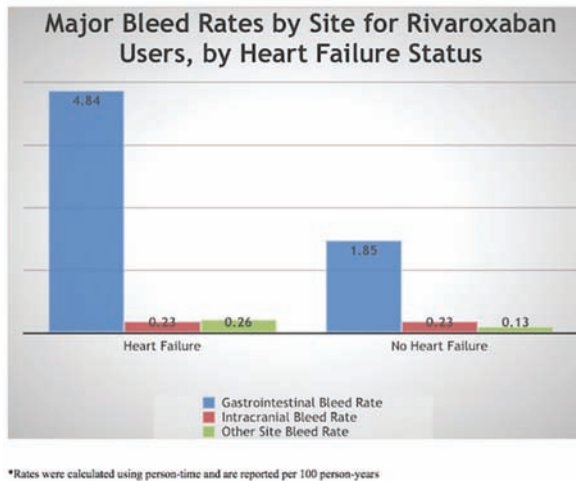
**Methods:** As part of an FDA post-marketing safety requirement, we queried nearly 10 million electronic medical records (EMRs) from the United States Department of Defense healthcare system, from January 1, 2013 to June 30, 2015, to identify MB-related hospitalizations among rivaroxaban users with NVAf. A validated case-finding algorithm was used for detection of MB, and the presence of HF was determined by evaluation of diagnosis codes in the EMRs. Incidence, outcomes, demographics and comorbidities associated with MB were stratified by HF status.

**Results:** Of 44,793 NVAf patients on rivaroxaban, 20.7% had HF. Major bleeding rates were higher with HF than without, 5.33 (95% CI 4.88-5.82) versus 2.21 (95% CI 2.06-2.37) per 100 person-years. Of MB patients, mean (SD) age was similar for those with and without HF, 78.8 (7.4) versus 78.7(8.1) years, respectively. Of MB patients, those with HF had more hypertension (90.0 versus 85.8%), coronary artery disease (62.5 versus 44.7%), diabetes (45.3 versus 31.2%), prior ischemic stroke (9.2 versus 6.5%) and higher mean (SD) CHA2DS2-VASc scores [5.4 (1.4) versus 4.1(1.4)], than those without HF. Fatal outcomes associated with MB were higher with HF versus no HF, 0.12 (95% CI 0.07-0.22) versus 0.08 (95% CI 0.06-0.12) per 100 person-years, respectively.

**Conclusion:** In a post-marketing study of 44,793 rivaroxaban users with nonvalvular AF, those with HF had more comorbidities and experienced higher rates of MB and fatal outcomes.



Figure 1. Major Bleed Rates by Site for Rivaroxaban Users, by Heart Failure Status



CARDIOMYOPATHY

**P281**  
Myocardial gene expression and cardiac remodeling in patients with myocarditis

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**Introduction:** Myocardial gene expression analysis has attracted attention as potential diagnostic tool for a differential diagnosis of heart failure.

**Purpose:** The aim of the study was to estimate the possible association between myocardial gene expression profile and the clinical data in patients with biopsy-proven lymphocytic myocarditis.

**Methods:** We analyzed 11 endomyocardial biopsies (EMBs) from patients with myocarditis and 6 heart transplantation autopsy samples. Individual normalized levels of heart-specific IgG autoantibodies (AAB) were quantified by ELISA. Circulating CD4+CD25bright+FOXP3+ cells were studied by flow cytometry. Thirty candidate genes were selected for the study. mRNA content was examined by quantitative PCR after reverse transcription (RT-qPCR).

**Results:** Expression of 10 candidate genes (NF-κB, IL2, NOTCH3, GLIPR, TMOD3, SEC24A, FCER1G, ITGB2, SIGLEC1, ADCY7) out of 30 studied was altered in EMBs from patients with myocarditis. Left heart dilatation was associated with down-regulated ITGB2 and SIGLEC1 gene expression. HLA expression was also associated with down-regulated NOTCH3 TMOD3 gene expression. Circulating FoxP3+ T-reg cells were correlated with up-regulated NF-κB and down-regulated IL2 gene expression. We identify the relationship between the gene expression and AAB profile.

**Conclusion:** Preliminary results suggest that the gene expression profile can predict the cardiac remodeling and outcome for patients with myocarditis.

Clinical and Morphologic Characteristics

	Patients of myocarditis
Age, yrs	39,2 ± 13,5
Male, n (%)	7 (64)
HF onset, n (%)	8 (73)
ACEI+BB	100%
LA, mm	49,9 ± 7,1
LVEDD,mm	60,1 ± 8,5
EF LV, %	39,1 ± 13,7
NT-proBNP, pg/ml	624 (113;2023)
CD3+cells	14,8 ± 6,5
Virus genome, %	36%
CD4+CD25bright+FOXP3+ cells	57(25;73)*106

ACEI- angiotensin-converting enzyme inhibitor ; BB - beta-blocker; LVEDD - left ventricular end diastolic diameter; EF LV - left ventricular ejection fraction.

**P282**

Endomyocardial miR-133a levels correlate with immunohistological markers of inflammation, improved LV function and clinical outcome in patients with inflammatory cardiomyopathy

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**Aims:** Inflammatory heart disease represents an important cause of chronic dilated cardiomyopathy. Predicting the clinical course of patients with inflammatory cardiomyopathy (iCMP) is difficult and the prognostic value of current biological markers remains controversial. We tested whether expression of selected microRNAs (miRNAs) in endomyocardial biopsies (EMB) is related to left ventricular (LV) functional recovery and clinical events during follow-up in patients with iCMP.

**Methods and Results:** EMB were obtained from patients with histologically proven iCMP (n = 76) and non-inflammatory dilated cardiomyopathy (n = 22). Based on literature search, we predefined a set of 6 miRNAs implicated in inflammation (miR-155, miR146b), heart failure (miR-21, miR-133a), endothelial cell (miR-126) and skeletal muscle function (miR-206). miRNA expression in EMB was quantified by RT-PCR. Expression of miR-155 and miR-133a was markedly upregulated in EMB from patients with iCMP as compared to patients with non-inflammatory dilated cardiomyopathy, irrespective of viral or non-viral etiology. Levels of miR-133a (R = 0.73, P < 0.01) and miR-155 (R = 0.63, P < 0.01) significantly correlated with the inflammatory cell count on EMB from patients with iCMP. Patients with iCMP and preserved LV function at study entry demonstrated higher endomyocardial expression of miR-133a than patients with reduced LV function. Also, higher expression levels of miR-133a were associated with recovery of LV function during a mean follow-up of 3.1 years. Importantly, in a Kaplan-Meier estimate, patients with iCMP and miR-133a levels in the upper tertile showed longer survival free of death, malignant arrhythmias and hospitalizations for heart failure.

**Conclusion:** The present study demonstrates that in a predefined set of miRNAs, relevant to cardiovascular pathology, endomyocardial miR-133a levels correlate with macrophage infiltration, improved LV function and clinical outcome in a comparatively large cohort of patients with histologically proven iCMP. miR-133a may serve as a potential novel biomarker and therapeutic target in human iCMP.

**P283**

Takotsubo cardiomyopathy with spontaneous left ventricular wall thickening

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**Purpose:** It is well known the functional disruption after takotsubo cardiomyopathy (TC) recovers within 1 or 2 weeks. Recently, we reported a case of TC with spontaneous left ventricular wall thickening (LVWT) after recovery of cardiac function. Therefore, we tried to elucidate the frequency and clinical characteristics of LVWT in TC patients.

**Methods:** We retrospectively investigated 65 patients with TC who were admitted to our hospital between 2004 and 2014.

**Results:** Six patients emerged LVWT, which were detected by echocardiography during 2 to 4 weeks after the onset of TC. In total, 31 patients underwent echocardiography during this period. Interestingly, all cases of LVWT occurred after the impaired contraction improved, and they persisted for several months. Comparing LVWT group (6 patients, 19.4%) with non-LVWT group (25 patients, 80.6%), the number of leads showing negative T wave in 12-lead electrocardiogram (9.3 ± 1.2 vs 6.0 ± 3.7, p = 0.01) and E/E' ratio on echocardiography (15.5 ± 4.5 vs 10.1 ± 3.0, p = 0.013) at the onset of TC significantly correlate to following LVWT.

**Conclusion:** The prevalence of LVWT is higher than previously reported. It is possible 12-lead electrocardiogram and echocardiography help to foresee LVWT. Although the mechanism of LVWT is still unknown, sequential cardiac magnetic resonance imaging obtained from two patients suggests edematous change.

**P284**

The relation between subclinical left ventricular systolic dysfunction in type II egyptian diabetic patients and grade of diabetic retinopathy by 2D Global longitudinal strain.

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**Background:** Alterations in cardiac structure and function occur in type 2 diabetes independently of coronary artery disease or hypertension, so it might be important to diagnose diabetic cardiomyopathy in the early stages to prevent development of heart failure in the future. Retinopathy is one of the micro vascular complications of

diabetic mellitus (DM). In some studies, it has been proposed that diabetic retinopathy might be associated with LV diastolic dysfunction and development of heart failure.

**Aim of study:** To evaluate left ventricular (LV) systolic function in Egyptian type II diabetic patients using two-dimensional (2D) global longitudinal strain and to study its relation to the grade of diabetic retinopathy.

**Patients and methods:** A total of 30 patients with type II (DM) enrolled after exclusion of ischemic heart disease by (negative Dobutamine stress echo), valvular heart disease, congenital and other related co-morbidities were included. In our study, Patients were classified according to diabetic retinopathy grade in to Group A: 22 patients with non proliferative diabetic retinopathy and Group B: 8 patients with proliferative diabetic retinopathy. All patients underwent conventional 2D echocardiography and longitudinal peak strain was calculated in apical long-axis, Apical four-chamber, and Apical two-chamber views, and values of the three views were averaged ( global longitudinal peak strain (GLPS)). Results for both groups were statistically analysed by SPSS).

**Results:-** All patients had preserved LV ejection fraction (LV-EF  $\geq 50$ ) by Conventional 2D Echo parameters. Both groups non proliferative and proliferative diabetic retinopathy had lower average GLPS mean =  $-17.7 \pm 2.4$ . There was no statistically significant difference on comparing the GLPS average ( $18.1 \pm 2.1$  vs.  $16.6 \pm 2.6$ ,  $p = 0.06$ ) in two groups.

**Conclusion:** The global longitudinal strain can be a useful novel technique in the determination of subclinical LV systolic dysfunction in egyptian diabetic patients. Diabetic patients have lower longitudinal myocardial mechanics. In our study, There was no significant association between diabetic retinopathy grade and sub clinical LV systolic dysfunction.

Average Global longitudinal peak strain

	Group A n(22)	Group B n(8)	p value		
mean	SD	Mean	SD		
GLPS Average	-18.1	2.1	-16.6	2.9	0.06

there is non significant difference in average GLPS between the 2 groups.

## P285

### Is there a Marfan cardiomyopathy?

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**Purpose:** Marfan syndrome (MFS) is the commonest inherited connective tissue disease, with an estimated prevalence of 1 in 5000 individuals. It occurs due to a mutation encoding fibrillin-1, essential to the structure of the extracellular matrix. The main system affected is the cardiovascular, namely the aorta. It has recently been proposed the existence of a primary cardiomyopathy in MFS patients (pts) with biventricular enlargement and dysfunction. The aim of this work was to evaluate the existence of a cardiomyopathy related to MFS in our population of MFS pts using echocardiography and cardiovascular magnetic resonance (CMR).

**Methods:** We enrolled 19 consecutive MFS pts, according to 2010 Ghent criteria, from 2011 to 2015, who underwent CMR for evaluation of the aorta and the heart. Echocardiography was also performed. Aorta was measured at different levels and left and right ventricular (LV and RV) volumes, ejection fraction (EF) and LV mass were evaluated as well as was the presence of late gadolinium enhancement. Echocardiographic parameters included dimensions of aorta segments accessible through this exam, left atrial (LA) dimensions, valvular evaluation and also LVEF. Data is presented as percentages and the relationship between variables is expressed by Pearson correlation test. A p value less than 0.05 was considered statistically significant.

**Results:** The majority of pts were male ( $n = 14$ , 73.7%) and all were on ARB II therapy. Four pts have already been submitted to aortic root replacement but as there were no differences in population characteristics, global results are presented. Aortic regurgitation was present in 26.3% of pts. Mitral valve prolapse was found in 42.1% and mitral regurgitation in 36.5%. LA dilation was observed in 36.5%, mainly graded as mild (26.3%). Concerning CMR evaluation, 21.1% of pts had reduced LVEF, 42.1% of pts had increased LV end-diastolic (LVED) and 68.4% had increased end-systolic (LVES) volumes. RVEF was normal in all pts, with increased RVED volume in 31.6% and increased RVES volume in 57.9%. Hypertabeculation matching criteria for myocardial non-compaction was found in 10.5%. Late gadolinium enhancement was present in 26.3% of pts, being the subepicardial pattern the most common form. Even though all pts had normal LV indexed mass values, a significant correlation was found between LV indexed mass and LVED volume ( $r=0,713$ ,  $p=0,001$ ) and also between LV indexed mass and LA dimensions ( $r=0,528$ ,  $p=0,036$ ).

**Conclusion:** These results support the existence of a primary cardiomyopathy at least in a subgroup of MFS pts. Biventricular enlargement and LV dysfunction found are usually mild. However, the impact of these changes in outcome of these pts is not fully understood. Indeed, further studies are needed to assess potential causes and

the natural history of this condition and also to help to support potential treatment decisions in these pts.

## P286

### Markers of takotsubo cardiomyopathy in clinical practice

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**Background:** Takotsubo cardiomyopathy (TTC) mimics acute coronary syndrome and is most often characterized by chest pain, ST segment elevation, cardiac enzymes increase and left ventricular dysfunction. It is important to distinguish ST elevation myocardial infarction (STEMI) and TTC at early stage. The symptoms are similar but the treatment and prognosis are completely different. The aim of the analysis was to find a simple marker that can differentiate patients (pts) with TTC from STEMI.

**Methods:** The analysis included 66 consecutive female pts diagnosed with TTC and 66 consecutive female pts with STEMI. In all pts we performed Echo examination during the first 24h of hospitalization. We measured level of biomarkers of heart failure and myocardial necrosis in order to correlate with the results of echocardiography. All pts had coronary angiography performed.

**Results:** The ejection fraction (EF) was lower in pts with TTC. Pts with TTC had higher NT-proBNP concentration. Pts with STEMI had higher concentration of Tnl and CKMB mass. The greatest differences between the two groups were observed when analyzing NT-proBNP and Tnl ratio. Pts with TTC had almost 30 times higher NT-proBNP/Tnl ratio that pts with STEMI. NT-proBNP and CK MBmass as well as NT-proBNP and EF ratio was also higher in TTC than STEMI.

**Conclusion:** Tnl, CK MB mass and NTproBNP concentration is performed routinely in all pts admitted to the hospital with chest pain. By correlating with EF which can be quickly calculated by echocardiography we can distinguish TTC from STEMI at early stage. High NT-proBNP/Tnl, NT-proBNP/CK MBmass and NT-proBNP/EF ratio suggest TTC rather than STEMI.

Results in TTC and STEMI group

	TTC	STEMI	p value
Tnl (ng/ml)	2,1	19	<0,05
CK MBmass (ng/ml)	9,5	73,3	<0,05
NT-proBNP (pg/ml)	4702	2138	<0,05
EF (%)	41	50	<0,05
NT-proBNP/Tnl	2235,2	81,6	<0,05
NT-proBNP/CK MBmass	678,2	27,5	<0,05
NT-proBNP/EF	110,4	39,4	<0,05

## P287

### Clinical heterogeneity of left ventricular non-compaction patients

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**Introduction:** Left ventricular noncompaction (LVNC), is a still misunderstood cardiomyopathy, although increasingly recognized. Its etiology is not definitely established and its natural history is largely unknown. The clinical presentation is very heterogeneous and the best therapeutic strategies have yet to be determined.

**Purpose:** We aimed to describe clinical characteristics and outcomes in adult patients with isolated LVNC followed at our referral center.

**Methods:** We retrospectively analyzed the medical records of patients followed in a tertiary care center with the diagnosis of LVNC, confirmed by CMR (3-T scanner, Siemens, Erlangen, Germany), interpreted by two experienced investigators (Radiologist/Cardiologist). Clinical data and echocardiographic, resting and 24 h-ECG parameters were collected.

**Results:** Thirty patients, mean age  $50 \pm 15$  years, 20 (67%) men, were included. Clinical presentation was heart failure in 8 (27%) patients, chest pain in 5 (17%), including 2 acute coronary syndromes, 5 (17%) patients had an arrhythmic event, with one episode of ventricular tachycardia (VT), 3 (10%) patients presented a syncopal episode and 9 (30%) were asymptomatic. Thromboembolic complications were documented in 4 (13%) patients. Neuromuscular disease was present in 4 (13%) patients and Fabry disease, disorder of fatty acid oxidation and systemic lupus were present in another 3. Nine patients (30%) had family history of cardiomyopathy (with 2 cases of familial forms of LVNC) and 5 (17%) had family history of sudden cardiac death. MYH7 gene mutations were present in 2 patients. Six (20%) of them had implanted an ICD, one a CRT device, one a CRT-D and another a conventional pacemaker. Mean LVEDV was  $120 \pm 34$  mL/m<sup>2</sup> and LVEF was  $41 \pm 15\%$ , with 11 (37%) patients presenting severe systolic dysfunction. Ventricular wall

thickness was within normal limits or slightly increased, except in 2 patients (22mm and 24mm). Apical segments of lateral wall and apex were the most frequently affected segments (in 80% and 53% of patients, respectively). Late gadolinium enhancement was presented in half. ECG was altered in 24 (80%) patients, the most common alteration being left bundle branch block (in 10 patients). Holter monitoring (available in 23) revealed no episodes of nonsustained VT or atrioventricular conduction disturbances. Of the 10 patients who underwent coronary angiography, only 3 had coronary artery disease.

**Conclusions:** Beyond the controversy around LVNC classification and morpho-functional development, our work illustrates the diversity of clinical scenarios where LVNC can be diagnosed and the requirement of a multidisciplinary approach in the diagnostic workup.

## P288

### Differential impact of statin treatment on clinical outcomes between patients with or without ischemic cardiomyopathy

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**Background:** Generally, statin treatment in heart failure is not recommended for reduction of mortality and rehospitalization rate according to recent American College of Cardiology / American Heart Association (ACC/AHA) guideline for heart failure (HF). We aimed to investigate whether statin is beneficial in patient with ischemic cardiomyopathy (ICMP) and old myocardial infarction (OMI).

**Methods:** Between November 2005 and August 2013, a total of 2,853 patients (64.7 ± 12.2 years, 2,133 men) with left ventricular (LV) dysfunction after acute myocardial infarction (AMI) enrolled in a nationwide AMI registry. Patients were divided into two groups (ICMP Group: LV dysfunction with LV dilation, OMI Group: LV dysfunction without LV dilation). LV dysfunction was defined as ejection fraction (EF) of less than 50% and LV dilation was defined as LV end diastolic dimension index (LVEDDI) of more than 32 mm/m<sup>2</sup>. LVEDDI was defined as LVEDD divided by body surface area. Primary endpoint was composite of major adverse cardiac event (MACE). MACE was comprised of death, stroke, myocardial infarction, stent thrombosis, target lesion revascularization, and target vessel revascularization.

**Results:** There were no differences in baseline characteristics between the two groups except older age in ICMP group (69.9 ± 11.7 vs. 64.0 ± 12.1, p < 0.0001). Also medical histories such as hypertension, diabetes, and smoking showed no significant differences, except more frequent smoking history in OMI group (62.5% vs. 53.6%, p = 0.002). In ICMP group, statin treatment showed no difference in composite MACE (13.6% vs. 15.5%, p = 0.652). In OMI group, however, statin was still effective in reduction of MACE (6.4% vs. 8.9%, p = 0.040).

**Conclusion:** Statin treatment in ischemic HF patients was effective before progression to ICMP.

## P289

### Factors associated to the occurrence of the burn out stage in patients with left ventricular noncompaction

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**Background:** Left ventricular noncompaction (LVNC) is a cardiomyopathy characterized by variable prognosis, that may evolve to LV dilation and dysfunction, known as burn out stage.

**AIM:** To determine the prevalence and factors associated to the development of the burn out stage in LVNC.

**Methods:** Retrospective multicenter study including all patients diagnosed with LVNC in 10 hospital centers. We evaluated clinical and genetic data, ECG, echocardiographic and cardiac MR (CMR) data. Mean follow up 3.4 years. Burn out stage was defined as the presence of LV ejection fraction (EF) below 50%. Statistical analysis was performed to find the factors associated to the development of the burn out stage (SPSS 20.0).

**Results:** The study included 86 patients with LVNC, 57% males, with mean age 51 ± 19 years. Clinical presentation was predominantly heart failure (30,2%), followed by dysrhythmia (15,1%) and embolic events (EE) (8,1%). The burn out stage was detected in 42% of patients (n=36).

The patients on burn out stage were older (58 ± 17 vs. 47 ± 18; p = 0.006), but no differences were found regarding gender (p = 0.187) or family history of LVNC

(p=1.000).

Clinical presentation in patients on burn out stage was more frequently heart failure (50% vs. 16%; p = 0.002) and less frequently an incidental finding (22% vs. 74%; p < 0.001). No differences were found regarding the frequency of dysrhythmias (19% vs. 12%; p = 0.518) or EE (14% vs. 4%; p = 0.210) on clinical presentation.

Symptoms tended to be more frequent in patients on burn out stage (75% vs. 52%; p = 0.052), with emphasis on dyspnea (61% vs. 20%; p < 0.001), unlike palpitations (28% vs. 32%; p = 0.855) or syncope (0% vs. 4%; p = 0.625).

Patients on burn out presented more frequently atrial fibrillation (AF) (20% vs. 4%; p = 0.045) and left bundle branch block (LBBB) (23% vs. 0%; p = 0.002). No differences were found regarding the occurrence of ventricular tachycardia (VT) on Holter monitoring.

On echocardiography, patients on burn out stage had lower values of EF (35 ± 11 vs. 62 ± 7%, p < 0.001), mitral S' at septal (6.4 ± 1.8 vs. 8.2 ± 1.9cm/s; p = 0.054) and lateral sites (6.3 ± 2.1 vs. 9.3 ± 2.8cm/s; p = 0.027) and mitral E' at septal site (6.1 ± 1.6 vs. 9.5 ± 3.6, p = 0.014). However, they had higher LV diameter (61 ± 9 vs. 52 ± 6%; p < 0.001) and higher prevalence of mitral disease (56% vs. 14%; p < 0.001).

On CMR, patients on burn out stage presented higher prevalence of late enhancement (41% vs. 5%, p = 0.002) and lower EF (33 ± 12 vs. 57 ± 9%; p < 0.001).

The burn out stage was not associated to higher risk of mortality (p = 0.391), EE (p = 0.704) or dysrhythmias (p = 0.118).

**Conclusion:** In this multicenter study, the burn out stage was detected in 42% of patients with LVNC. Factors such as age, heart failure on clinical presentation, the presence of symptoms and namely dyspnea, AF and LBBB, values of mitral S' and E', the presence of mitral disease and late enhancement on CMR were associated to development of the burn out stage in patients with LVNC.

## P290

### Prevalence of myocardial infarction with normal coronary artery in patients with multiple sclerosis. a new type of diastolic heart failure

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**Introduction:** Myocardial infarction with Normal Coronary Artery (MINCA) is a rare clinical entity. It's incidence in general population varies between 1% and 8.5%. Although several mechanisms have been proposed, the exact mechanism is unknown. Recently, patients with Multiple Sclerosis (MS) were reported with MINCA as a complication of autonomic nervous system dysfunction. Aim of our study was the prevalence of MINCA in MS and its possible association with ANS dysfunction.

**Methods:** A retrospective analysis of 183 hospitalized patients with MS (86 males) was performed and divided in two groups according to the presence of MINCA (group A) or not (Group B). Clinical profile of patients, predisposing factors for coronary artery disease, namely arterial hypertension (BP), diabetes mellitus (DM), hyperlipidemia (HLP), smoking (SM) and thyroid disease (TD) and the different treatment modalities were noted. Group A patients were also tested for Ewing's Test namely: (1) resting heart rate (HR), (2) HR variation in response to deep breathing, (3) HR response to standing, and (4) postural changes in systolic and diastolic blood pressure (SBP and DBP) namely orthostatic tolerance, inspiration-expiration test, the handgrip and the Valsalva Test implying sympathetic and/or parasympathetic abnormalities.

**Results:** Eleven patients were identified as MINCA (6%). The clinical profile of the patients MINCA patients had similar age (48.55 ± 8.2 y.o vs 44.52 ± 11.3 y.o (p=NS) and disease severity (EDSS scoring was 2.75 ± 1.6 vs 3.8 ± 1.9, p=NS) while the disease duration was significantly lower in Group A compared to Group B (4.25 ± 3.97 vs 10.26 ± 7.22, p = 0.001). MINCA's group had more predisposing factors than Group B (p < 0.05) while similar was the presence of thyroid disease in both groups. The Ewing Tests were abnormal in all patients of MINCA group. Discussion: The prevalence of MINCA in MS is 6% and seems to be correlated with the ANS dysfunction. This dysfunction might be either due to the presence of the predisposing factors or/and due to the lesions of MS and can.

## P291

### 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 10 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 was defined as a cut-off point 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 192 patients with TC. Full recovery of LV function was observed in 45% of patients at discharge. A mean follow up of  $45 \pm 32$  months was performed. Complete recovery of LV function during hospitalization was not associated with a lower incidence of death (3.5% vs 2.7%,  $p = 0.764$ ) or stroke / TIA (1.2% vs 4.0%,  $p = 0.249$ ) or lower recurrence of TC (3.5 % vs 4.0%,  $p = 0.864$ ) in the follow-up. In the 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 present a faster recovery of LV function do not have a better medium term prognosis. However, the low rate of complications in the follow-up may have limited the study results.

## P292

### The features of clinical course and echocardiographic parameters in patients with senile amyloidosis

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**Introduction:** To date, senile amyloidosis is difficult to diagnose.

**Purpose:** To establish the occurrence of senile amyloidosis in the structure of left ventricular hypertrophy (LVH) of various origins in elderly patients, and explore the echocardiographic parameters of hypertrophic phenotype and the clinical course of the disease. **Methods:** In the study were included 196 symptomatic patients (age:  $\geq 60$  years) with a wall thickness of the left ventricle  $\geq 15$  mm of various origins (ESC Guideline on diagnosis and management of Hypertrophic Cardiomyopathy, 2014). The standard clinical - laboratory and instrumental methods of diagnosis sarcomeric and nonsarcomeric hypertrophic cardiomyopathy (HCM) were applied.

**Results:** In accordance with the classification of the World Health Organization, patients with senile amyloidosis (71 patients, 80% women, 20% men) were divided by age into 3 groups: group 1 - elderly age (60-74 years) - 17%, group 2 - senile age (75 - 89 years) - 21%, group 3 - long-living persons ( $\geq 90$  years) - 62%. 83% of patients with senile amyloidosis from all age groups (in accordance with clinical cases and conclusions of outpatients cards of died patients) had a cardiovascular form of amyloidosis, characterized by congestive heart failure (II-IV NYHA). In 17% of patients (all patients in the group of long-living persons) were revealed amyloid deposits (on the results of post-mortem diagnosis), and these patients didn't have a clinical manifestations of the disease in their life. In 7% cases were found a combination of two forms of amyloidosis: AL- and senile amyloidosis. According to echocardiography in patients with senile amyloidosis were indicated moderate left ventricular hypertrophy, less expressed than in patients with sarcomeric HCM in the elderly (IVSd  $16.4 \pm 3.48$  mm, LVPWd  $15.71 \pm 3.28$  mm and IVSd  $19.57 \pm 4.26$  mm, LVPWd  $13.02 \pm 3.02$  mm, respectively,  $p < 0.001$ ). 20% of patients with senile amyloidosis had a wall thickness of the left ventricle less than 15 mm, but the LVMI were above the normal values (LVMI  $152.13 \pm 77.62$  gr/m<sup>2</sup>).

**Conclusions:** Senile amyloidosis was detected at the age of 75 years and older in the most cases, mainly in women, and was characterized by cardiovascular forms of the disease. Patients with asymptomatic senile amyloidosis were identified. Patients with senile amyloidosis and AL-amyloidosis didn't have significant differences in echocardiographic parameters.

## P293

### Profile of cytokines th1, th2 and th17 in patients with chronic chagas disease and systemic arterial hypertension

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**Background:** Chronic Chagas disease is a major health problem in Latin America, and has become globalized because international immigration. The disease is caused by the protozoan *Trypanosoma cruzi*. Chronic cardiomyopathy is the leading clinical manifestation of the disease. In areas where the disease is endemic, about 30% of patients with chronic Chagas disease have concomitant Systemic Arterial Hypertension (ChD-SAH). In the context of Chagas disease, the study of inflammation elicited by *T. cruzi* is very important for better understanding the pathophysiology of the disease. In addition, the study of parasite immune response capable of causing heart damage could provide insights into new therapeutic strategies. Little

is known about plasma cytokine profile in patients with ChD-SAH.

**Purpose:** Accordingly, this study was undertaken to determine the profile of cytokines plasma levels in patients with this condition.

**Methods:** Eleven patients with chronic Chagas disease diagnosed by a positive serology (G1 group), 9 patients with ChD-SAH (Group 2), and 28 healthy controls (Group 3) matched by age and sex were studied. The cytokine concentration of TH1 (IL-12, INF-Gamma), TH2 (IL-13, IL-5, and IL-10), and TH17 (IL-17, IL-23) was determined by ELISA (expressed as medians and equivalent units pg/mL plasma). The Kruskal-Wallis Test was used for statistical analyses.

**Results:** Median plasma levels of IL-12 in the G1 group was 250, in the G2 group 300, and in G3 group 70 ( $p < 0.001$ ). Median INF-Gamma was 140 in the G1 group, 180 in the G2 group, and 70 in the G3 group ( $p < 0.001$ ). Median plasma levels of IL-13 was 150 in the G1 group, 180 in the G2 group, and 50 in the G3 group ( $p < 0.001$ ), whereas median plasma levels of IL-5 was 140 in the G1 group, 190 in the G2 group, and 50 in the G3 group ( $p < 0.001$ ). Median plasma levels of IL-10 was 220, 250, and 180 in the G1 group, G2 group, and G3 group, respectively ( $p < 0.001$ ). Median plasma levels of IL-17 was 140 in the G1 group, 180 in the G2 group, and 70 in the G3 group ( $p < 0.001$ ), whilst median plasma levels IL-23 was 110 in the G1 group, 230 in the G2 group, and 80 in the G3 group ( $p < 0.001$ ). Interestingly, plasma cytokine activities in Chagas disease patients were increased in the G2 group in comparison with G1 group ( $p < 0.05$  for each comparison).

**Conclusion:** We have shown for the first time that patients with ChD-SAH have more activation of TH1 and TH2 cytokines pattern, modulated by TH17 pattern, than that seen in patients with isolated chronic Chagas disease. Such alterations could lead to more severe amplification of vascular inflammation, activation of other inflammatory mediators, and cell recruitment in patients with this condition.

## P294

### Race differences in timing of presentation in 1137 peripartum cardiomyopathy patients compared with 2.1 million delivering mothers without peripartum cardiomyopathy

University of Colorado Center for Women's Health Research Seed Grant  
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**Background:** Peripartum cardiomyopathy (PPCM) is a rare and life-threatening complication of pregnancy that is more common in patients of African ancestry (AA) than other racial groups. Some risk factors for PPCM have been identified, but race differences in patients presenting at or before delivery (antepartum) vs. those presenting postpartum are unknown.

**Purpose:** To characterize race differences in characteristics of PPCM patients presenting antepartum vs. postpartum.

**Methods:** Administrative records for all hospitals in the state of Florida from 2004-2013 were obtained. Patients hospitalized for delivery were identified (ICD-9 code V27.x). Hospital readmissions following delivery were identified using unique patient identifiers. All hospital records reporting PPCM were identified (ICD-9 code 674.5x). Antepartum presentation was defined as presence of PPCM during hospitalisation for delivery. Postpartum presentation was defined as hospitalization with PPCM within 5 months of hospitalisation for a delivery where PPCM was not reported. Patient characteristics were stratified by white, AA, and Hispanic race.

**Results:** In total, 2,142,363 delivering mothers were identified including 510 antepartum PPCM patients and 627 postpartum PPCM patients. AA patients had the highest rate of PPCM (1/1000 deliveries) followed by white (4/10,000 deliveries) and Hispanics (2/10,000 deliveries). AA patients more frequently presented post-partum (322/513, 63%) compared to 233/436 (53%) white patients and 41/124 (33%) Hispanic patient ( $p < 0.001$ ). Most (83%) postpartum PPCM patients presented within 30 days of delivery, and AA patients made up 78/108 (72%) of those presenting > 30 days of PPCM. Diabetes mellitus, hypertension, tobacco use, chronic obstructive pulmonary disease/asthma, multiple gestations, anaemia, mood disorders, obesity, and Caesarean section were associated with PPCM in all races. Of these, anaemia, obesity, and diabetes mellitus were stronger predictors of postpartum presentation in AA patients, chronic obstructive pulmonary disease and asthma were stronger predictors of postpartum presentation in Hispanic patients, and mood disorders and tobacco use were stronger predictors in white patients.

**Conclusions:** Important race differences exist in risk factors and timing of presentation in PPCM. These differences may reflect different race-based interactions between acquired and genetic predispositions to PPCM.

## P295

### Prevalence of left ventricular systolic dysfunction in a portuguese population of left ventricular non-compaction cardiomyopathy - A multicentre 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: The aim of this work is 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 86 patients with LVNC, 57% males, with mean age  $51 \pm 19$  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 12% of the patients and non-sustained ventricular tachycardia in 22% of the cases. Family history of LVNC was identified in 8% of cases. Diagnosis of LVNC was established by echocardiogram in 80% of patients: Chin criteria at 31%, Stollberger criteria at 78% and Jenni criteria at 96%. In this Portuguese population of patients with LVNC, the prevalence of patients with LV systolic dysfunction is 50%. The average LV ejection fraction was 48% and 42% patients had EF <50%. Mitral regurgitation was detected in 15% of cases. Delayed gadolinium enhancement on cardiac MRI was found in 20% of patients. Cardiac death occurred in 4.7% of cases (mean follow-up of 48 months). **Conclusions:** In this Portuguese population of patients with LVNC, the prevalence of LV systolic dysfunction is 42%, 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.

## P296

### Post-myocarditic dilated cardiomyopathy: characterization and long-term prognosis

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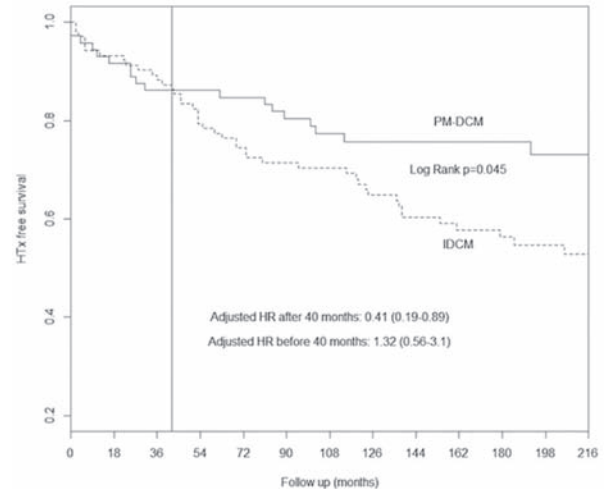
**Background:** Dilated cardiomyopathy (DCM) is the final common pathway of different pathogenetic processes and presents a significant prognostic heterogeneity, possibly related to its etiological variety. The characterization and long-term prognosis of post-myocarditic dilated cardiomyopathy (PM-DCM) remain unknown.

**Objective:** This study assesses the clinical-instrumental evolution and long-term prognosis of a large cohort of patients with PM-DCM.

**Methods:** We analyzed 175 DCM patients consecutively enrolled from 1993 to 2008 with endomyocardial biopsy (EMB) data available. PM-DCM was defined in presence of borderline myocarditis at EMB or persistent left ventricular dysfunction 1 year after diagnosis of active myocarditis at EMB. Other patients were defined as affected by idiopathic dilated cardiomyopathy (IDCM). Analysis of follow-up evaluations was performed at 24, 60 and 120 months.

**Results:** We found 72 PM-DCM out of 175 enrolled patients (41%). Compared to IDCM, PM-DCM patients were more frequently females and less frequently presented a familial history of DCM. No other baseline significant differences were found. During the long-term follow-up (median 154, 1st-3rd interquartile range 78-220 months) PM-DCM patients showed a trend towards slower disease progression. Globally, 18 (25%) PM-DCM patients vs 49 (48%) IDCM patients experienced death/Heart Transplantation (HTx) (p: 0.045). The prognostic advantage for PM-DCM patients became significant beyond 40 months of follow-up. At multivariable time-dependent Cox analysis, PM-DCM was confirmed to have a global independent protective role (HR = 0.53, 95% CI 0.28-0.97, p = 0.04).

**Conclusions:** PM-DCM is characterized by better long-term prognosis compared to IDCM. An exhaustive etiological characterization appears relevant in the prognostic assessment of DCM.



HTx-free survival in PM-DCM vs IDCM.

## P297

### Predictors of ventricular tachyarrhythmias in patients with dilated cardiomyopathy

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Purpose of this study is to investigate the markers of myocardial electric instability: microvolt T-wave alternations (mTWA), heart rate turbulence (HRT) and QT dispersion (QTd) in patients with dilated cardiomyopathy (DCM) with ventricular tachyarrhythmic (VTA) events.

**Methods:** the study enrolled and followed up  $38,1 \pm 12,6$  months 160 pts with DCM (78% male, aged  $47,2 \pm 11,7$  years, LVEF  $28,7 \pm 10,1\%$ ; NYHA class  $3,0 \pm 0,3$ ). We analyzed age, gender, NYHA, 6-MWT, peak VO<sub>2</sub>, EchoCG, Holter ECG (PVEct, sVT, nsVT, VF), QRS width, device telemonitoring and ECG (Intecard-7) assessment HRT, mTWA, QTd. For multivariate regression model as the primary endpoint had been taken VTA (nsVT/sVT without syncope) and the secondary end points were SCD, successful resuscitation, sVT with syncope, discharges of CRT-D/ICD.

**Results:** By multivariate regression analysis for primary end point ( $F = 7,1$ ;  $R^2 = 0,99$ ;  $p = 0,000$ ) as independent predictors of VTA are defined: PVEct ( $p = 0,00004$ ), LV systolic dimension ( $p = 0,0003$ ), QRS width ( $p = 0,0006$ ), LV End Diastolic Volume ( $p = 0,002$ ), 6-MWT ( $p = 0,002$ ) and LBBB ( $p = 0,01$ ). For secondary end points by multivariate analysis ( $F = 5,7$ ;  $R^2 = 0,77$ ;  $p = 0,0022$ ) were revealed independent predictors of fatal VTA as positive mTWA test ( $= 0,0033$ ) and pathological HRTs parameter ( $p = 0,043$ ).

**Conclusions:** Positive mTWA test and pathological HRTs were identified as independent predictors of life-threatening VTA. The use of these markers for screening stratification of DCM pts allows to select of potential candidates for preventive ICD therapy.

## P298

### Genotype-phenotype correlations: association between mutation status and left ventricular reverse remodeling in idiopathic dilated cardiomyopathy

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**Backgrounds:** Next-generation sequencing (NGS) increases diagnostic yield of genetic testing in Dilated Cardiomyopathy (DCM), but genotype-phenotype correlations have been poorly investigated, and the association between mutated genotype and therapeutic response remains unknown.

**Purpose:** To explore the genetic landscape of a highly selected DCM cohort and to assess genotype based clinical characterization, including the possible association with left ventricular reverse remodeling (LVRR). **Methods:** We performed commercially available NGS panels targeting 103-149 cardiomyopathy associated genes in 152 DCM patients from the Heart Muscle Disease Registry of Trieste. According to NGS results, patients were grouped in different "clusters" with functionally homogeneous genetic background. LVRR was defined by a LV ejection fraction (LVEF)

increase  $\geq 10$  points (or LVEF  $\geq 50\%$  for baseline LVEF  $\geq 45$  and  $45$  and  $\leq 49\%$ ) associated to a reduction in indexed LV end-diastolic diameter (LVEDDi)  $\geq 10\%$  (or a LVEDDi  $\leq 33$  mm/m<sup>2</sup>), at a mean follow-up of 24 months.

**Results:** A disease-related mutation was identified in 127 patients (84%); 28 (18%) TTN, 7 (5%) Lamin A/C, 24 (16%) Structural Cytoskeleton-Z Disk genes; 17 (11%) Desmosomal genes; 7 (5%) MYBPC3; 18 (12%) Motor Sarcomeric genes and 26 (17%) Other genes. Baseline clinical features were similar between different subgroups. A significant relationship was found between gene clusters subgroups and LVRR, with a low observed LVRR rate in Structural Cytoskeleton-Z Disk genes mutation carriers (10%,  $p < 0.05$  Vs all the subgroups).

**Conclusions:** NGS provides a powerful diagnostic tool for genetic characterization of DCM. A genetic "clusters" classification, based on functional similarities in different genes, might be helpful in the clinical management of genetically determined DCM. In our population, structural Cytoskeleton-Z Disk genes mutations were associated with a low therapeutic response.

## P299

### Natural history and prognostic factors in dilated cardiomyopathy

PTDC/BIM-MEC/0650/2012

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**Background:** Dilated cardiomyopathy is a heart muscle disease that affects 1:2500 adults and is characterized by ventricular dilation and impairment of systolic function. The main clinical features are heart failure, arrhythmias and sudden cardiac death. However, clinical course varies greatly between different patients and also among members of the same family, in case of familial forms.

**Purpose:** We aimed to determine the natural history of idiopathic (iDCM) and familial dilated cardiomyopathy (fDCM), and to identify predictors of poor outcome.

**Methods:** We studied patients with fDCM (defined as the presence of  $\geq 1$  family member with DCM or a first-degree relative with unexplained sudden death  $< 35$  year) irrespective of age and patients  $< 50$  years with iDCM. Patients underwent extensive clinical evaluation, ECG, 24h-Holter, echocardiogram and molecular analysis (including search of mutations in LMNA/C gene). For follow-up, assessment of vital status, heart transplantation and cardiac-related hospitalizations were registered.

**Results:** We included 92 patients, 51 (57%) male, with mean age at diagnosis  $37 \pm 14$  years, mean left ventricular ejection fraction  $33 \pm 12\%$  and left ventricular end-diastolic diameter  $64 \pm 9$  mm. Forty-eight (52%) patients presented criteria of fDCM and 47 (55%) were in NYHA class I. After a mean follow-up of  $20 \pm 9$  months (range 2-73), 12 (13%) patients experienced adverse events. Five patients were subjected to heart transplantation and 2 have died. Two patients experienced aborted cardiac arrest/appropriated ICD shock and 9 were hospitalized from cardiac causes (4 from heart failure, 3 with ventricular arrhythmia, one because of atrial fibrillation and another patient due to embolic acute coronary syndrome). For identification of prognostic predictors we used logistic regression analysis (the model included all variables associated with adverse event at a significance level of  $p < 0.10$ ). Presence of edemas (OR 46.9; 95%CI 3.5-629.2;  $p = 0.004$ ), previous pacemaker implantation (OR 16.1; 95%CI 2.1-121.1;  $p = 0.007$ ) and previous hospitalization from arrhythmic cause (OR 10.1; 95% CI 1.9-55.1;  $p = 0.007$ ) were independent predictors of adverse events.

**Conclusions:** In our study, 13% patients experienced a dismal outcome. Edemas, pacemaker (not biventricular) implantation and arrhythmia-related hospitalization were associated with worse outcome. These findings may help to identify patients at higher risk, whom might benefit from a more aggressive clinical vigilance and timely interventions.

## P300

### Retrospective assessment of immunosuppressive agents in virus-negative inflammatory cardiomyopathy: a long-term survival analysis.

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**Background/Purpose:** The ESC defines virus-negative inflammatory cardiomyopathy (infi-CMP) as a cardiomyopathy with  $\geq 14$  infiltrating inflammatory cells per mm<sup>2</sup> without viral presence in endomyocardial biopsy (EMB). This study assesses

the -till now yet unknown- impact of immunosuppressive agents in infi-CMP on long-term transplantation free survival.

**Methods:** Within an international cardiomyopathy registry, a total of 209 DCM patients who fulfilled the ESC criteria for virus-negative infi-CMP were included between 2008 and 2015. Ninety-nine patients did not, and 110 did receive additional immunosuppressive therapy. One on one propensity score matching using age, gender, duration of symptoms, NYHA class, hypothyroidism, and diastolic blood pressure corrects for possible selection bias, resulting in 90 untreated and 90 treated patients. Primary outcome was assessed using heart transplantation-free survival at 10 years.

**Results:** Baseline characteristics, including optimal standard heart failure (HF) medical treatment, did not differ between untreated and treated patients. During a mean follow-up time of 31 (15 - 47) months, a total of 14 (8%) patients reached the primary endpoint, including 13 (7%) deaths and 1 (0.5%) HTx. Additional immunosuppressive therapy resulted in an improved HTx-free survival as compared to conventional HF therapy alone (Log-rank  $p = 0.036$ ; Figure 1). Echocardiographic LVEF significantly improved in both groups at a mean follow-up of 1 year compared to baseline (LVEF baseline vs. follow-up:  $33 \pm 14$  to  $40 \pm 14$  in the standard HF therapy group,  $p < 0.001$ ; and  $31 \pm 11$  to  $44 \pm 12$  in the group who additionally receive immunosuppressive therapy,  $p < 0.001$ ). Of note, patients with additional immunosuppression had a significantly higher absolute increase in LVEF after 12 months, as compared to those not receiving immunosuppression (5% [-1,5 - 15] vs 10% [1,3 - 22];  $p = 0.028$ ).

**Conclusion:** This retrospective study illustrates that immunosuppression on top of HF medication improves long-term outcome in patients with virus-negative infi-CMP. This conclusion triggers further prospective trials.

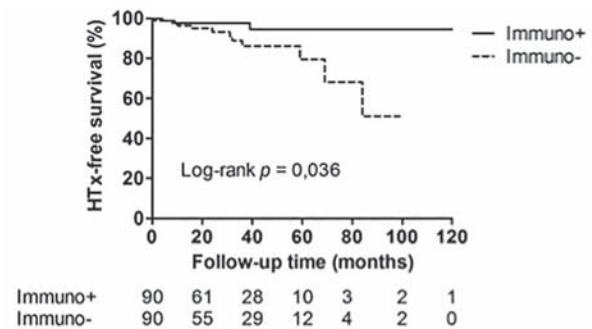


Figure 1: Htx-free survival

## P301

### A new predictor of outcome in non-infiltrative dilated cardiomyopathy: the presence of low voltage qrs in both limb and chest leads

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**Introduction:** Low voltage on the surface electrocardiogram (ECG) is defined as QRS voltage less than 5 mm in all limb leads and less than 10 mm in all precordial leads. There can be little question that, in many instances, low voltage complexes (LQRSV) are a result of severe myocardial disease. Infiltrative cardiomyopathies may lead to LQRSV involving both the limb and the precordial leads. As far as we are aware, the literature contains no study of the clinical significance of an ECG with LQRSV in all leads on the prognosis in patients with no-infiltrative dilated cardiomyopathy and heart failure.

**Aim:** The purpose of this study was to examine the association between QRS voltage and survival in patients with no-infiltrative dilated cardiomyopathy and heart failure.

**Methods:** We performed a retrospective analysis to examine the association between LQRSV in all limb and precordial leads and mortality in a study population included 362 patients with no-infiltrative dilated cardiomyopathy and heart failure. All the patients underwent Coronary Angiography, Magnetic Resonance Imaging and in some cases Myocardial Biopsy for establishing diagnosis. Two groups, on the basis of voltage QRS ( $< 5$ mm in limb leads and  $< 10$ mm in chest leads) were identified. All the patients were on sinus rhythm. The groups were compared with respect to total mortality and sudden death. Subgroups were also stratified by age , sex, left bundle branch block ,ejection fraction (EF)  $< 30\%$  and  $> \text{or} = 30\%$  to  $40\%$ , and the NYHA Heart Failure Class.

**Results:** The LQRSV was associated with a significant increase in mortality (51.2.3% vs 35.0%,  $P = .0001$ ) and sudden death (28.9% vs 18.4%,  $P = .0004$ ). Left bundle branch block was associated with worse survival ( $P = .004$ ) but not sudden death. In patients with an EF  $< 30\%$ , LQRSV continued to be associated with a significant increase in mortality (53.6% vs 34.6%,  $P = .001$ ) and sudden death (29.8% vs 19.8%,



$P = .002$ ). After adjustment for baseline variables, independent predictors of mortality were found to be LQRSV ( $P = .0029$ , risk ratio 1.48) depressed EF ( $P = .0001$ , risk ratio 0.965) and age  $< 49$  years ( $p = 0.03$ , risk ratio 1.53). In those with an EF of 30% to 40%, LQRSV was associated with a significant increase in mortality (41.8% vs 22.9%,  $P = .0034$ ) but not in sudden death (12.9% vs 11.0%,  $P = 0.625$ ). The sex and the NYHA Class were not predictive of mortality.

**Conclusion:** The low QRS complexes voltage in both limb and chest leads is an independent predictor of both increased total mortality and sudden death in patients with no-infiltrative dilated cardiomyopathy and heart failure.

### P302

#### Linear and cubic measurement of left atrial size are equally predictors of atrial fibrillation development in patients with hypertrophic cardiomyopathy.

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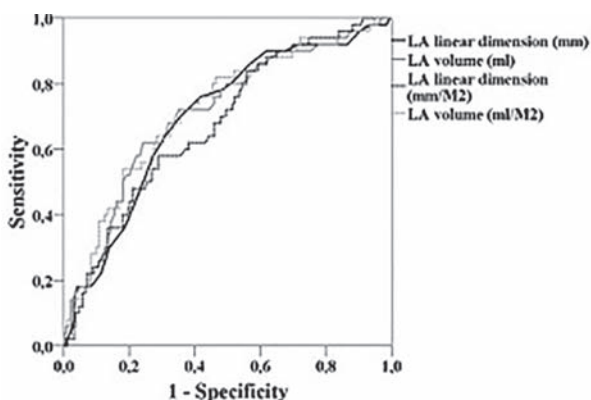
**Introduction:** Left atrial (LA) enlargement evaluated by echocardiography is a very strong predictor of cardiovascular (CV) outcomes such as atrial fibrillation (AF), stroke, congestive heart failure, and CV death in multiple clinical settings. Recently, in patients with hypertrophic cardiomyopathy (HCM), the measure of LA diameter has been taken into account for sudden death risk stratification in the European Society of Cardiology guidelines and for cardio-embolic risk assessment. Nevertheless, the measure of LA diameter disappeared in the last chamber quantification, and in the European Association for Cardiovascular Imaging recommendations for HCM multimodality imaging.

**Purpose:** To clarify the contradictory data between medical literature and current recommendations for LA size assessment, we investigated the role of LA size measured by different methods (linear and cubic ones) in predicting AF development in a group of patients with HCM.

**Methods:** 248 HCM patients (age  $42 \pm 16$  years, 65% men), without history of AF, were enrolled. LA size was assessed by linear dimension from parasternal 2D images and by volume from 4 chambers view. Data obtained from both methods were considered as continuous variables, both absolute and indexed for body surface area, and categorized to identify LA dilation.

**Results:** During a follow-up of  $8.1 \pm 5.8$  years, 50 patients (20%) developed a first episode of AF. At univariate Cox regression analysis age, NYHA functional class, significant left ventricular outflow tract obstruction and mitral regurgitation, and each of the LA size measures, were associated with AF development. Cox multivariate analysis was constructed by using significant variables at univariate analysis, and, because of their collinearity, using in turn LA variables. LA size, in each of the method evaluated, was the only predictor of AF development ( $p < 0.0001$ ), whereas the other variables were no more predictors of AF development. Furthermore, ROC curve analysis demonstrated that there were no differences between the linear or cubic assessment of LA size, neither their absolute or indexed measures, in the power of predicting AF development (Figure).

**Conclusions:** This study confirmed that LA size, irrespective of the way it is measured and categorized as dilated, is a strong predictor of AF development in HCM patients. Furthermore, for the first time, we confronted different methods to assess LA size demonstrating that LA diameter is still a valid echocardiographic measure in the prediction of AF even in small group of patients, encouraging its evaluation in the specific field of HCM.



ROC curve analysis. LA=left atrial

### P303

#### Impact of gender on heart failure development in nonobstructive hypertrophic cardiomyopathy

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**Background:** Little is known about the impact of gender difference on heart failure (HF) development in non-obstructive hypertrophic cardiomyopathy (HCM).

**Purpose:** We evaluated the association with gender and HF presentation in the patients with non-obstructive HCM and investigated clinical and echocardiographic parameters according to gender.

**Methods:** We studied 146 consecutive patients with non-obstructive HCM (age= $63 \pm 13$  years, male:female=98:48). Clinical parameters and conventional echocardiographic measurements including tissue Doppler measurements were evaluated and compared according to gender. Additionally, left ventricular (LV) deformation was assessed with global longitudinal strain utilizing 2D speckle tracking software.

**Results:** Of the 146 patients, 43 patients (30%) were presented with HF and female patients were more frequently had HF (52% vs. 18% in male patients,  $p < 0.001$ ). Females were older and had increased indexed left atrial (LA) volume and the ratio of early diastolic mitral inflow to early annular velocity (E/Em) than males ( $71 \pm 9$  years vs.  $60 \pm 14$  years for age,  $p < 0.001$ ;  $53.5 \pm 24.1$  mL/m<sup>2</sup> vs.  $42.3 \pm 17.1$  mL/m<sup>2</sup>,  $p = 0.005$  for indexed LA volume;  $18.0 \pm 6.6$  vs.  $13.1 \pm 5.1$ ,  $p < 0.001$  for E/Em). Whereas LV mass and LV ejection fraction were comparable between men and women, global longitudinal strain was significantly more decreased in female patients ( $141.2 \pm 32.6$  g/m<sup>2</sup> vs.  $137.1 \pm 30.2$  g/m<sup>2</sup>,  $p = 0.46$  for indexed LV mass;  $63.0 \pm 5.2$  % vs.  $64.2 \pm 5.4$  % for LV ejection fraction,  $p = 0.21$ ;  $9.5 \pm 1.5$  % vs.  $12.1 \pm 3.1$  % for global longitudinal strain). Even after adjusting for clinical factors, female was independently associated with HF ( $p < 0.001$ ).

**Conclusion:** In patients with non-obstructive HCM, female patients were presented with HF more frequently. LA volume, E/Em and LV mechanics were different between the genders, suggesting these might contribute to greater susceptibility to HF in women with HCM.

### P304

#### Association of NT-proBNP level with disturbance of microcirculation and intracardiac hemodynamic parameters in hypertrophic cardiomyopathy patients with heart failure with preserved ejection fraction

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**Purpose:** to assess the association between NT-proBNP level, parameters of intracardiac hemodynamic and disturbance of microcirculation in hypertrophic cardiomyopathy (HCM) patients with heart failure with preserved ejection fraction (HF/pEF).

**Methods:** 40 patients (21 men, 19 women) with HF/pEF included in the study. 47,5% (n = 19) of patients had a progressive course (PC) of the disease and 52,5% (n = 21) - stable course (SC). All patients were investigated according standard cardiac algorithm. We estimated NT-proBNP level, assessed endothelial function of large vessels (phase shear (PS, ms) and microcirculation (occlusion index (IO) by video-capillaroscopy. Remodeling of large vessels (stiffness index (SI, in/s), arteriols (index of refraction (RI)) and skin capillaries (capillary densities (CD, cap/mm<sup>2</sup>), maximal capillary densities (CD max, cap/mm<sup>2</sup>) were evaluated.

**Results:** Patients with PC of HCM are characterized by maximal left atrium (LA) size and atrio-ventricular ratio (AVR) (AVR = 1,205; LA=4,9 cm). Elevation of NT-proBNP level ( $> = 42,56 + 5,21$  ( $< 0,001$ )) is associated with unfavorable prognosis of HCM. Enlargement of LA size is associated with increase of NT-proBNP level ( $r = 0,3629$ ,  $p = 0,04$ ) and capillary remodeling (RI  $33,14 + -21$ ;  $r = 0,849$ ;  $p = 0,0002$ ). A positive correlation between NT-proBNP and RI ( $r = 0,563$ ;  $p = 0,09$ ) was revealed. Elevation of CD max were associated with increase of NT-proBNP level ( $r = 0,613$ ;  $p = 0,0596$ ) and it might occur due to compensatory reaction.

**Conclusion:** 1. The association between NT-proBNP level, parameters of microcirculation (RI and CD max) and intracardiac hemodynamic parameters (LA size) was revealed in patients with HCM. 2. It was found that RI is correlated with LA size and NT-proBNP level. 3. It was determined that CD max associated with increase of NT-proBNP level. 4. This interactions are common for patients with progressive course of HCM.

### P305

#### Sudden cardiac death in hypertrophic cardiomyopathy: can perfusion defects improve risk stratification?

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**Introduction:** Sudden cardiac death (SCD) continues to be the most devastating complication of hypertrophic cardiomyopathy (HCM). However risk stratification in these patients (pts) is still a challenge. Our aim was to investigate the value of

perfusion abnormalities as an additional predictor of SCD, in these populations.

**Methods:** We studied 28 HCM ambulatory patients, in our hospital. All of them performed, after a transthoracic echocardiogram, cardiac magnetic resonance (CMR) with late gadolinium enhancement (LGE) for fibrosis analysis and Tc-99m tetrofosmin single-photon emission computed tomography (SPECT) for perfusion defects evaluation. SCD risk was calculated by current guidelines. All statistics analyses were performed using SPSS 20.0 version.

**Results:** The mean age of our population was  $56 \pm 16$  years and 71% were male. The majority of pts were in NYHA class I (48%) or II (48%) and had septal HCM (58%). By 2014 guidelines, we found (89%) without ICD indication, fewer pts with a class IIa recommendation for ICD (8%) and 4% of pts had a class IIb indication. The mean of HCM SCD risk was  $2.4 \pm 1.5\%$ . LGE was present in 23% pts, SPECT perfusion fixed defects in 25% and reversible defects in 7%. There was no correlation between LGE-CMR and SPECT perfusion fixed ( $p=0.727$ ) or reversible defects ( $p=0.453$ ). HCM SCD risk by current guidelines did not correlate with the presence of LGE-CMR ( $p=0.372$ ) or SPECT perfusion reversible defects ( $p=0.224$ ). However HCM SCD risk correlate with the presence of fixed defects ( $p=0.028$ ).

**Conclusion:** These results support the existence of perfusion defects in HCM pts involving distinct mechanisms. Fixed abnormalities can be related to areas of microvascular disruption or perfusion mismatch and do not necessarily translate into fibrosis. Our data suggest that imaging perfusion modalities, like SPECT, can improve risk stratification in this population.

## CO-MORBIDITIES

### P306

#### Recording of clinical characteristics of hospitalized patients due to heart failure and comparison between age groups with emphasis to the elderly

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**Purpose:** Large proportion of pts with HF are elderly, who have a large number of comorbidities. The purpose of study was recording and comparison of characteristics among hospitalized elderly and nonelderly HF pts.

**Methods:** HF hospitalized pts in cardiac dept from Jan 2014 until Dec 2015 recorded. 712 patients included ( $76.15 \pm 8.86$  43-95 years). Recorded data: demographic, cardiological and general history, signs and symptoms, ECG and echo findings. Pts grouped to subgroup A1 of 485 pts above 70 - 68.11%- and A2 227 pts below 69 years and subgroup B1 of 297 pts above 80 - 41.7%- and B2 of 415 pts below 79 years. Results in table

**Conclusions:** elderly and elderly over 80s with HF less often are men, more rarely have PCI history and ventricular arrhythmias, adhere less dietary-exercise and have more often preserved EF, anemia, CKD, dementia, AF, rheumatological disorders, pleural effusions and NYHA III - IV than younger pts.

Elderly with HF less often suffer depression and comply better with therapy than younger pts. Moreover elderly over 80s more often have infection as decompensation, have more often history of stroke and endocrine disorders.

Table

	$\alpha 1$ (%)	$\alpha 2$ (%)	p	B1 (%)	B2 (%)	p
Male	52.7	66.5	0.000	46.8	64.6	0.000
Preserved EF	37.3	11.0	0.000	37.4	23.8	0.000
Infection as decompensation	27.8	22.0	ns	36.0	17.6	0.000
Non-compliance to therapy as decompensation	52.9	77.9	0.000	62.2	58.7	ns
Less adherence dietary exercise recommendations	48.0	22.0	0.000	46.8	35.1	0.01
CKD	42.2	33.0	0.003	53.2	29.4	0.000
$\alpha$ nemia	80.6	55.5	0.000	89.8	52.7	0.000
Rheumatological disorders	9.4	2.6	0.001	15.5	6.0	0.000
Dementia	36.0	5.7	0.000	60.9	11.5	0.000
Depression	11.3	33.0	0.000	15.5	17.6	ns
Endocrine disorders	23.0	27.5	ns	37.4	16.8	0.008
Stroke	4.9	2.2	ns	8.4	2.6	0.000
AF	60.8	33.0	0.000	68.6	40.9	0.000
History of PCI	9.4	28.1	0.000	8.8	23.1	0.000
NYHA III-IV	56.8	33.3	0.000	76.7	29.4	0.000
Pleural effusion	51.9	22.2	0.000	76.6	17.6	0.000
Ventricular arrhythmias	19.2	33.3	0.002	7.8	35.3	0.000

Comparison between subgroup A1-A2 and between B1-B2

### P307

#### Azilsartan medoxomil improves central and brachial 24-h ambulatory blood pressure control in diabetic hypertensive patients

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**Aim:** Ambulatory monitoring of central blood pressure (BP) and arterial stiffness is a new technique for evaluation of antihypertensive drugs efficacy. The aim of the study was to assess changes in ambulatory brachial and central BP and Alx after AM 40 mg adjunction to treatment regimen in hypertensive type 2 diabetic patients. Methods. AM 40 mg was given as substitution drug to ACEI to 20 hypertensive patients (8 male, age  $58 \pm 10$  years) with clinic BP>140/90 mmHg, 24-h BP>130/80 mmHg and/or daytime BP>135/85 mmHg previously treated with an ACEI and a second drug from another class. ABPM was done with BPLab VASOTENS ("OOO Petr Telegin", Nizhniy Novgorod, Russia). Brachial and aortic BP changes as well as changes in 24-h, day- and nighttime Alx were evaluated.  $p < 0,05$  was considered significant.

**Results:** Significant ( $p < 0,05$  vs baseline) decrease in 24-h, day- and nighttime BP after 4 weeks of Azilsartani medoxomil adjunction was observed: for brachial SBP, respectively, from  $150 \pm 10$  to  $134 \pm 8$ , from  $150 \pm 10$  to  $134 \pm 10$ , from  $148 \pm 15$  to  $132 \pm 12$  mmHg, for brachial pulse pressure (PP) from  $54 \pm 10$  to  $48 \pm 9$ , from  $54 \pm 8$  to  $46 \pm 8$ , from  $56 \pm 10$  to  $48 \pm 7$  mmHg. For aortic SBP corresponding changes were from  $139 \pm 10$  to  $126 \pm 9$ , from  $140 \pm 10$  to  $126 \pm 8$ , from  $138 \pm 12$  to  $128 \pm 10$  mmHg, for aortic PP, respectively,  $46 \pm 6$  to  $38 \pm 5$ , from  $44 \pm 6$  to  $36 \pm 8$ , from  $46 \pm 7$  to  $38 \pm 6$  mmHg. Alx@HR75 bpm decreased at daytime from  $28,3 \pm 12,6$  to  $21,7 \pm 10,1$ %, at night-time from  $32,2 \pm 10$  to  $26 \pm 9$ %. Increase in PP amplification was observed also and was more evident in nighttime: baseline difference between brachial and aortic PP was  $10,0 \pm 3,2$  for daytime,  $10,0 \pm 3,2$  mmHg for nighttime, after azilsartan medoxomil treatment  $10,7 \pm 2,6$  and  $10,2 \pm 2,8$  mmHg, respectively ( $p < 0,05$ ).

**Conclusion:** zilsartan medoxomil decreases significantly either brachial or aortic SBP and PP, as well decreases aortic PP augmentation. In hypertensive diabetic patient PP amplification was similar at day- and nighttime before and after treatment meaning proportional decrease of brachial and central SBP and PP.

### P308

#### Clinical implications of coronary artery disease after transcatheter aortic valve implantation in patients with severe aortic stenosis.

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**Background:** coronary artery disease (CAD) influence negatively prognosis of patients undergoing surgical aortic valve replacement and revascularization is generally recommended at the time of surgery. Implications of CAD in the setting of transcatheter aortic valve implantation (TAVI) are not known. The aim of this study was to determine the prevalence and impact having coronary artery disease in patients undergoing percutaneous valve implantation.

**Methods:** Between April 2008 and December, 2015 500 patients with severe symptomatic aortic stenosis were treated with high surgical risk, percutaneous aortic CoreValve prosthesis. All patients underwent coronary angiography prior.

**Results:** A total of 215 p (43%) had coronary disease. In 157 patients (31.4%) were performed PCI, 36 patients (7.2%) had CABG and 9 both techniques. Revascularization was complete in 65.3%. Patients with CAD were characterized by increased ventricular dysfunction than patients without CAD (24.7% vs. 11.2%,  $p=0.001$ ) and predominantly male (53% vs. 31.9%,  $p < 0.001$ ). The occurrence of periprocedural myocardial infarction was 2.3%. After a mean follow-up of  $34 \pm 23$  months, the total mortality was similar in both groups (44.3% vs. 42.6%,  $p=0.739$ ) and there were lower mortality for patients with complete revascularization versus partial, 19.4% vs. 27.3%,  $p=0.210$  Mean left ventricular ejection fraction increased from  $57.7 \pm 15$  mmHg to  $61.5 \pm 13$  mmHg after TAVI and  $61.2 \pm 10$  mmHg at 1-year (p for post-TAVI trend 0.023).

**Conclusions:** The prevalence of coronary artery disease in patients undergoing TAVI is high, but it was not associated with any increase in overall death, due to the majority of patients had complete revascularization. However, TAVI did have a positive effect on left ventricular function over time.

### P309

#### Cerebrovascular and other concomitant diseases in female and male patients with heart failure-results from CRO-HF Registry

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**Introduction:** Co-morbidities in heart failure (HF) could vary in different populations. The aim of this trail was to analyse cerebrovascular and other concomitant disease

that contribute to HF development in female and male HF patients from CRO-HF Registry.

**Results:** A total of 2203 in-hospital HF patients from CRO-HF Registry were analyzed: 1028 (46.7%) females (f) and 1175 (53.3%) males (m); median age was 76 y. One third had acute HF. Preserved left ventricular systolic function (LVEF $\geq$ 50%) was recorded in 37.8% patients. Males had frequently reduced LVEF (m-70.7%, f-50.7%) and females-preserved LVEF (f-49.3%, m-29.3%,  $P < 0.001$ ).

History of hypertension was recorded in 67.5% patients (58.7% f, 52.7% m), coronary disease in 18.5%, myocardial infarction in 22.7%, diabetes mellitus (DM) in 34.3%, renal failure in 19.2%, COPD in 17.3%, dilated cardiomyopathy in 32.8% and cerebrovascular disease in 16.5% patients. Atrial fibrillation or undulation was noted in 53.7% patients. Overweight was 46.3% patients. History of transient ischemic attack (TIA) had 8.9% and stroke 7.6% patients. TIA had 54.4% males and 52.9% females; stroke had 45.6% males and 47.1% females ( $P = 0.807$ ).

Active smokers were 11.1% patients and former-15.6%. Males were frequently active smokers (m-14.8%, f-6.4%,  $P < 0.001$ ). No differences in smoking habit was detected in HF patients with diabetes, renal failure and stroke (9.4% were active smokers, 11.7%-former and 15.6% non-smokers,  $P = 0.141$ ). COPD had 30.6% active smokers and 13.9% non-smokers ( $P < 0.001$ ). COPD was frequently disease in males (m-19.7%, f-14.7%,  $P = 0.009$ ) as well as renal dysfunction (m-23%, f-14.8%,  $P < 0.001$ ). Diabetes had 36.1% males and 32.6% females. DM I had 8.5% males and 11.9% females,  $P = 0.144$ . DM II had 91.5% males and 88.1% females. The leading "triggers" of HF were: hypertension 55.5%, arrhythmia 51.3%, valvular disease 32.8%, acute coronary syndrom-ACS 19.7%, infections 19.6% and non-compliance 5.1%. ACS was important "trigger" in males (m-22.1%, f-17%,  $P = 0.010$ ) and hypertension in females (f-58.7%, m-52.7%,  $P = 0.009$ ). No significant gender differences was detected according to arrhythmia, valvular disease and infection.

Lower haemoglobin value was recorded in 51.9% patients, higher creatinine in 46.8%, ALT in 29.8%, cholesterol in 32.7%, tryglicerides in 31.9%, uric acid in 79.3% and hyperglycaemia in 99.8% patients. Females had higher values of ALT (f-33%, m-27%,  $P = 0.012$ ), cholesterol (f-36.8%, m-29.1%,  $P = 0.009$ ), tryglicerides (f-36.1%, m-28.3%,  $P = 0.014$ ), and uric acid (f-82.9%, m-76.4%,  $P = 0.007$ ). Males had lower haemoglobin levels (m-58%, f-44.8%,  $P < 0.001$ ). In-hospital mortality rate was 13.8%.

**Conclusion:** Hypertension was important "trigger" of HF in females and ACS in males. There were no significant differences in TIA or stroke condition. Nevertheless, the concomitant disease in female and male HF patients could be different and we should hard work on prevention.

### P310

#### Diabetes in recipients after heart transplantation

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**Purpose:** To estimate the impact and the frequency of development diabetes after heart transplantation (HT).

**Methods:** From 2010 to November 2015 we performed 62 HT (mean age 44,2 $\pm$ 14,6 yrs; BMI - 24,3 $\pm$ 4,7 kg/m<sup>2</sup>), 16% (n = 10) of them had family history of diabetes. Before HT 11% (n = 7) of recipients had diabetes mellitus (DM) (HbA1c - 6,5 $\pm$ 0,52%), 29% of them were only on a diet, 71% - on oral medications (biguanides). After HT all patients were treated by triple-drug therapy - steroids, calcineurin inhibitors (tacrolimus) and mycophenolate mofetil. The induction therapy were basiliximab (69%), thymoglobulin (31%). Since early postoperative period we did follow-up of the glucose level. Every 6 months the level of HbA1c in patients with diabetes was controlled.

**Results:** After HT 86% (n = 6) patients from DM group required insulin, during first yr HbA1c increased to 7,1 $\pm$ 1,4%. In 3 months after HT post-transplanted diabetes (PTD) was diagnosed in 37% (n = 23) recipients, 91% of them (n = 21) were treated by insulin, others - on oral medications. The level of HbA1c in PTD group was 6,2 $\pm$ 0,9%. The level of glucose got normal in 1,5-2 yrs after HT, that is why insulin therapy was cancelled (78%, n = 18), others recovered in 3-4 yrs after HT.

**Conclusion:** After HT glucose level needs to be under control in all recipients. PTD is full reversible without secondary end-organ disease.

### P311

#### Hyponatremia in heart failure: clinical correlations and prognosis

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**Introduction:** The association between heart failure and hyponatremia has a major impact on clinical evolution and prognosis of hospitalized patients. The purpose of

the study was to analyze the frequency of hyponatremia and outcomes in patients with chronic heart failure admitted in the Internal Medicine Clinic of a University Emergency Hospital, between 1st of January 2014 and 31st of August 2015 (1 year and 8 months).

**Methods:** A total of 402 hospitalized patients with chronic heart failure were included. The level of seric sodium was recorded at the day of admission, several times during hospitalization and at discharge. Patients were classified with normonatremia (sodium level  $> 135$  mEq/L on admission), corrected hyponatremia ( $\leq 135$  mEq/L on admission and increased to  $> 135$  mEq/L during hospitalization) and with persistent hyponatremia ( $\leq 135$  mEq/L on admission and throughout hospitalization). We retrospectively analyzed data from the hospital database record.

**Results:** Hyponatremia was encountered in 60 patients with chronic heart failure (14.92%). Persistent hyponatremia was present in 37 patients; in 23 patients the serum sodium was normalized at discharge. Hemoglobin level on admission was lower than normal in 10 patients (27%) with persistent hyponatremia, in comparison with patients with corrected hyponatremia, where anemia was less frequent (21%). The mean glomerular filtration rate was lower in patients with persistent hyponatremia (68.9  $\pm$  32 ml/min/1.73m<sup>2</sup>) compared to patients with normal sodium at discharge (79.8  $\pm$  29 ml/min/1.73m<sup>2</sup>). Patients with persistent hyponatremia had higher in-hospital mortality rates compared with normonatremic ones (18.91% vs 1.46%). Conclusions Hyponatremia is a frequent comorbidity in patients with chronic heart failure. Persistent hyponatremia is correlated with heart failure severity and is associated with higher mortality rates in hospitalized patients. Persistent hyponatremia is also associated with lower glomerular filtration rates and hemoglobin level in patients with chronic heart failure.

#### Characteristics of studied patients

Clinical characteristics and investigations results	Persistent hyponatremia n = 37	>Corrected hyponatremia n = 23	Normonatremia n = 342
Age, mean [years]	72 $\pm$ 13	73 $\pm$ 8	77 $\pm$ 9
Serum sodium on admission, mean [mEq/L]	132.4 $\pm$ 5.0	133.2 $\pm$ 3.4	137.9 $\pm$ 2.2
Serum sodium at discharge, mean [mEq/L]	132.3 $\pm$ 3.4	138.9 $\pm$ 2.1	138.6 $\pm$ 1.8
Systolic blood pressure, mean [mmHg]	158 $\pm$ 38	170 $\pm$ 41	151 $\pm$ 35
Anemia at admission [%]	n = 10 (27%)	n = 5 (21%)	n = 62 (18%)
Glomerular filtration rate, mean [ml/min/1.73m <sup>2</sup> ]	68.9 $\pm$ 32	79.8 $\pm$ 29	84.3 $\pm$ 24
Rate of death during hospitalization	18.91%	4.34%	1.46%

### P312

#### Prevalence and prognosis of different patterns of cardiohepatic syndrome in acute decompensated heart failure

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**Objective:** Over the last several years different mechanisms of cardiohepatic syndrome (CHS) in acute decompensated heart failure (ADHF) have been discussed. Hepatocellular liver function tests pattern predominated in left sided forward AHF, cholestatic pattern occurred mainly in bilateral and right sided AHF. The purpose of the study was to assess the prevalence and prognostic value of different patterns of CHS in patients with ADHF.

**Methods:** In 322 patients with ADHF (190 male, 69.5  $\pm$  10.7 years (M  $\pm$  SD), arterial hypertension 87%, myocardial infarction 56.5%, atrial fibrillation 65.5%, diabetes mellitus 41.6%, known chronic kidney disease 39.1%, chronic anaemia 29.2%, ejection fraction (EF) 37.6  $\pm$  12.6%, EF  $<$  35% 39.1%) alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (AP) and gamma-glutamyl transpeptidase (GGT) were measured on admission. LFTs were considered abnormal when levels exceeded local upper normal limit. Only ALT and/or AST increase was considered as hepatocellular CHS, only GGT and/or AP increase - as cholestatic CHS. The simultaneous increase of markers of cytotoxicity and cholestasis was considered as mixed CHS. Mann-Whitney test and multivariate logistic regression analysis were performed,  $p < 0.05$  was considered statistically significant.

**Results:** Abnormal LFTs occurred in 166 (51.6%) of patients. Increase of ALT and/or AST were detected in 68 (21.1%) patients (alone ALT/ alone AST/ both TA - in 35.3, 26.5, 38.2% respectively), increase of AP and/or GGT in 140 (43.4%) patients (alone AP/ alone GGT/ both of them - in 27.15, 35.7, 37.15% respectively). Hepatocellular, cholestatic and mixed pattern of CHS was detected in 8.1, 30.4 and 13.1% of patients with ADHF. In patients with CHS the prevalence of hepatocellular, cholestatic and mixed pattern was 15.7, 59, 25.3% respectively. Patients with mixed



CHS comparing with hepatocellular or cholestatic patterns had lower BMI ( $28.4 \pm 5.3$  vs  $30.2 \pm 7.6$  or  $31.4 \pm 5.6$  kg/m<sup>2</sup>,  $p < 0.05$ ), total protein ( $64 \pm 4.8$  vs  $64.7 \pm 6.7$  or  $68.9 \pm 7.3$  g/l,  $p < 0.01$ ), eGFR ( $47 \pm 17$  vs  $57 \pm 17$  or  $56 \pm 20$  ml/min/1.73 m<sup>2</sup>,  $p < 0.01$ ), higher heart rate ( $118 \pm 35$  vs  $91 \pm 17$  or  $101 \pm 30$  per min,  $p < 0.01$ ), Hb ( $137 \pm 20$  vs  $120 \pm 22$  or  $129 \pm 24$  g/l,  $p < 0.05$ ), serum creatinine ( $146 \pm 71$  vs  $117 \pm 39$  or  $117 \pm 34$   $\mu$ mol/l,  $p < 0.001$ ). Only mixed CHS was associated with negative prognosis. In patients with versus without mixed CHS the incidence of all-cause death in 6 months was 24.2 vs 12.1%,  $p < 0.05$ .

**Conclusions:** Abnormal LFTs occurred in 51.6% of patients with ADHF. In patients with CHS the prevalence of hepatocellular, cholestatic and mixed pattern was 15.7, 59, 25.3%. Patients with mixed compared with hepatocellular or cholestatic pattern of CHS had a worse prognosis.

### P313

#### Impact of malnutrition on long-term mortality in outpatients with chronic heart failure.

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**Introduction:** Malnutrition determined by the Mini Nutritional Assessment (MNA) test is an independent predictor of long-term mortality in acute HF patients. The sum of the MNA score distinguishes between patients with: adequate nutritional status, MNA  $\geq 24$ ; undernutrition, MNA  $< 17$ ; at risk for malnutrition, MNA between 17 and 23.5.

**Purpose:** The aims of this study were to evaluate the prevalence of undernutrition and risk of malnutrition determined by MNA test and their possible influence on long-term mortality in outpatients with chronic HF.

**Methods:** 258 patients with chronic HF from November 2011 to November 2015 were prospectively analysed. A global evaluation by the MNA test was performed. In addition, usual demographic, clinical, functional and treatment variables were collected. The association between nutritional status and long-term mortality was assessed with the use of Cox multivariate analysis.

**Results:** The mean age was  $74.7 \pm 10$  years, 45.7% were female and the most frequent aetiology was ischemic heart disease (36.8%). At the median follow-up time (23 months, interquartile range 12-30 months), the overall mortality was 25.8%. 12% of the patients were classified as malnourished and 40.7% were classified as at risk of malnutrition. The remaining 47.3% had an adequate nutritional status. The three groups were homogenous in aetiology of heart failure (ischemic aetiology: 38.7%, 35.2% and 37.7%, respectively,  $p = 0.38$ ). However, malnourished patients presented a poor functional class (NYHA III-IV 71%, 51.4% and 22.1%, respectively,  $p < 0.001$ ), were older than those at risk of malnutrition or wellnourished ( $78.4 \pm 7.9$ ,  $75.8 \pm 9.2$  and  $72.8 \pm 10.8$  years, respectively,  $p = 0.008$ ) and presented lower hemoglobin levels ( $12.1 \pm 1.7$ ,  $13.2 \pm 2$  and  $14 \pm 1.6$  g/dL, respectively,  $p < 0.001$ ) and higher levels of serum creatinine ( $1.6 \pm 1$ ,  $1.2 \pm 0.5$  and  $1.1 \pm 0.4$  mg/dL, respectively,  $p < 0.001$ ) and NTproBNP ( $6313 \pm 6237$ ,  $3693 \pm 4044$ ,  $2255 \pm 2124$  pg/mL, respectively,  $p < 0.001$ ). At 23 months of follow-up, all-cause mortality in patients with malnutrition was 67.3%, among patients at risk of malnutrition was 28.2%, while in patients with adequate nutritional status was 13.7% (Log-rank,  $p < 0.001$ ). When Cox multivariate analysis was performed, the state of malnutrition determined by the MNA test was an independent predictor of mortality (with respect to adequate nutritional status: Hazard ratio 3.31; 95% confidence interval, 1.5-7.3,  $p = 0.003$ ).

**Conclusion:** We have found that malnutrition defined by MNA test is an independent predictor of long-term mortality in outpatients with chronic HF.

### P314

#### Erectile dysfunction in patients with heart failure, a matter of ejection fraction?

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**Background and purpose:** Erectile dysfunction (ED) is a common problem among patients with coronary artery disease (CAD) and heart failure and it is often under-diagnosed and thus under treated. Our main objective was to determine if ventricular dysfunction was associated per se with this condition.

**Methods:** We analysed 250 patients, all of them male, who were referred to our cardiac rehabilitation centre and filled in a SHIM (sexual health inventory for men) questionnaire, in which a punctuation of 21 points or less implies ED. An echocardiogram and a treadmill exercise test were performed in order to determine their left ventricular ejection fraction (LVEF) and functional capacity (FC). Chi-square and t-student tests were used to analyze categorical and numerical variables, respectively.

**Results:** Mean age was 55.4 years, and patients had a high burden of cardiovascular risk factors (see table 1). 45.6% had a depressed LVEF (EF  $< 52\%$  according

to new guidelines). The prevalence of ED was 63.6%: 64.9% in the low EF group vs. 62.5% in the preserved EF group ( $p = 0.79$ ). Mean EF among patients with ED was 50.4% vs. 51.9% in the non-ED group ( $p = 0.31$ ). Thus we found no association between LVEF and the presence of ED, obtaining the same results even when analysing the subgroup of patients with LVEF  $< 30\%$ . Interestingly, there was an association between ED and a poor FC: a mean of 7.9 METs in comparison to 9.2 METs in the non-ED group ( $p < 0.001$ ). Advanced age and history of hypertension or diabetes were found to be predictors of ED. There was a good correlation between ED and the severity of CAD, with a prevalence of 46%, 60%, 64% and 72% if there was no CAD - single vessel - 2 - 3 or more vessels affected, respectively, although statistical significance was not achieved. Among patients with ED, only 30.8% received pharmacological treatment, 24.5% with sildenafil and 6.3% with vardenafil or tadalafil.

**Conclusions:** Prevalence of ED among patients with heart disease is high. Depressed LVEF does not correlate with the presence of ED.

Table 1: Patient characteristics

Patients characteristics (%)	Patients with ED	Patients without ED	p	Patients characteristics (%)	Patients with ED	Patients without ED	p
Age (years)	57	52.6	< 0.001	Nitrates	5.4	1.2	0.16
Hypertension	51.6	33	< 0.01	Beta blockers	92.6	97.7	0.14
Diabetes mellitus	28	12.2	< 0.01	Diuretics	9.5	3.5	0.12
Dyslipidemia	60.5	64.8	0.59	ACEI / ARA-II	75	69.8	0.45
Obesity	27.8	23.3	0.46	LVEF (mean)	50.4	51.9	0.31
Smoking	57	57.8	1	LVEF $< 30\%$	4.4	3.3	0.75
Sedentary lifestyle	59.5	53.8	0.43	Exercise capacity (METs)	7.9	9.2	< 0.001

### P315

#### Validity of an algorithm in implantable devices for the diagnosis of sleep-disordered breathing in heart failure

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**Purpose:** Sleep-disordered breathing (SDB) affects over half of patients with heart failure (HF). Both obstructive sleep apnoea (OSA) and central sleep apnoea (CSA) are associated with a poor prognosis and are under-diagnosed in the HF population. Current evidence demonstrates benefits for positive airway pressure therapy in those with OSA and HF, whilst optimal management of CSA is unclear. A novel pacemaker algorithm (ApneaScan, Boston Scientific, Marlborough, Ma.) has been developed to diagnose and quantify SDB. There are no published data on the accuracy of this algorithm compared with sleep polygraphy.

**Methods:** Patients with systolic heart failure and an ejection fraction  $< 40\%$ , not on nocturnal non-invasive ventilation and with compatible pacing or ICD devices underwent home sleep polygraphy (Embletta, Embla, Canada) at least 4 weeks following device implantation or box change, with concurrent download of ApneaScan data from the pacemaker. The data for the study night were compared with the download using correlation coefficients, Bland Altman plots and a receiver operating characteristic curve (ROC).

**Results:** 60 patients (mean  $\pm$  SD: age  $69.1 \pm 11.9$  years, male 71%, NYHA  $2.4 \pm 0.5$ , BNP  $496 \pm 466$  ng/l, EF  $29.3 \pm 9.4\%$ ) underwent home sleep polygraphy and pacemaker download. 10 patients (17%) had no recorded data from the algorithm. Mean apnoea-hypopnoea index by polygraphy (PG-AHI) was  $16.3 \pm 15.0$ /hour and by ApneaScan (AP-AHI)  $34.8 \pm 13.8$ /hour. The intraclass correlation coefficient (r) for all patients was 0.78 (0.61-0.88,  $p < 0.01$ ). ApneaScan was more accurate in those with OSA ( $r = 0.86$ , 0.53-0.95,  $p < 0.01$ ) than CSA ( $r = 0.74$ , 0.48-0.83,  $p < 0.01$ ). It was accurate in those with moderate to severe SDB (AHI  $> 15$ /h,  $r = 0.79$ , 0.42-0.92,  $p < 0.01$ ), but inaccurate in those with mild or no SDB (AHI  $\leq 15$ /h) ( $r = 0.22$ , -0.60-0.62,  $p = 0.25$ ). Correlation was closer in those with predominantly apnoeic events ( $r = 0.83$ , 0.37-0.955,  $p < 0.01$ ) compared with hypopnoeic events ( $r = 0.62$ , 0.27-0.81,  $p < 0.01$ ). On the ROC curve, the optimal ApneaScan cut-off for the

diagnosis of moderate to severe SDB was 30.5/hour, yielding a sensitivity of 89%, specificity 68%, positive predictive value 62% and negative predictive value 91%. The area under the ROC curve was 0.84.

**Conclusion:** ApneaScan over-estimates the severity of SDB compared with sleep polygraphy. At the cut-off of 30.5 events per hour, ApneaScan is a sensitive screening test for moderate to severe SDB with a high negative predictive value. The algorithm may be a useful means of screening for SDB in those with HF and an implanted device – particularly for those with apnoeic episodes; a value above 30.5/hour should be confirmed with a sleep study.

**P316**

**Sleep-disordered breathing is associated with impaired cardiac sympathetic innervation and incrementally predicts prognosis in heart failure patients**

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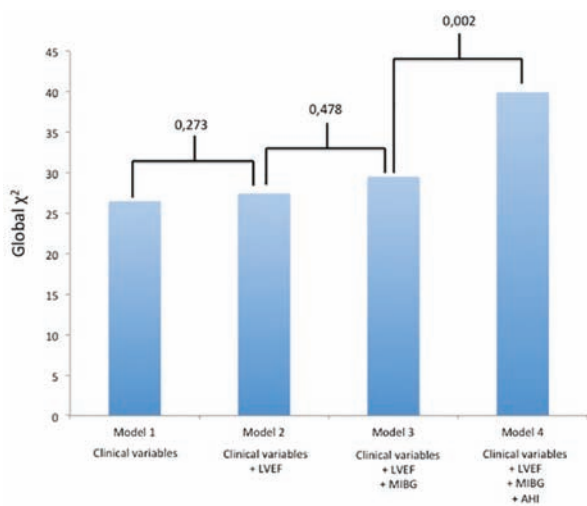
**Background:** Sleep-disordered breathing (SDB) is common in patients affected by heart failure (HF) and significantly impacts on disease progression and prognosis. Unfavorable effects of SDB in HF are mainly mediated by impaired sympathetic activity. However, few data are available on SDB and cardiac adrenergic impairment evaluated at myocardial level.

**Purpose:** Aim of the present study was to assess the relationship between SDB, cardiac sympathetic innervation assessed by 123I-MIBG imaging and prognosis in patients affected by HF with reduced left ventricular ejection fraction (LVEF).

**Methods:** Ninety-four patients (66.1±9.8 years) with moderate to severe HF (median LVEF 32% (IQR 7)) underwent nocturnal cardiorespiratory monitoring to assess presence and severity of SDB by Apnea/Hypopnea Index (AHI), and 123I-MIBG imaging to calculate heart-to-mediastinum (H/M) ratios and 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 H/M (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). Patients with AHI above the median showed higher event rates and worse survival compared to patients with AHI below the median (35% vs. 9%; p=0.003). Similarly, event rates of the study endpoint significantly differed in patients with normal (≥1.60) or abnormal late H/M (<1.60) (11% vs. 29%; p=0.039). 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. Comparison of global  $\chi^2$  scores of four different hazard models showed an incremental prognostic value of AHI over the combination of clinical variables, LVEF and MIBG.

**Conclusions:** Patients with systolic HF and SDB show more impaired cardiac adrenergic innervation assessed by 123I-MIBG imaging, and more adverse prognosis compared to HF patients without SDB.



**P317**

**Unpublished association between iron deficiency and left heart filling pressure in patients diagnosed of chronic heart failure and reduced ejection fraction**

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**Introduction:** There is an increasing interest among cardiologists in iron deficiency of patients with chronic heart failure, because it is known that its therapy with intravenous carboxymaltose improves these patients' well-being. However, it is unknown its correlation with echocardiographic variables.

**Purpose:** We want to show the prevalence of iron deficiency in chronic heart failure and depressed ejection fraction (EF) and its correlation with echocardiographic variables. We define absolute ferropenia as ferritin <100 ug/dl, relative ferropenia as ferritin <300 ug/dl + transferrin saturation <20%, anemia as hemoglobin <13 gr/(l men) and <12 gr/l (women)

**Methods:** This is a prospective study, including 50 consecutive patients attended at our heart failure clinic and diagnosed of chronic heart failure with EF depressed (EF=<0.4). Aetiologies: 22 dilated cardiomyopathy, 19 ischemic cardiomyopathy and 18 other aetiologies. General features: 39 men, average age 72 years (CI 95% 70-75,2 years) and 4,74 years elapsed from the diagnosis (CI 95% 3,43-6,04 years). These patients were attended from October 2014 until June 2015 and had a compensated heart failure (without any hospital admission in the last 3 months). Our patients had many cardiovascular risk factors (40% arterial hypertension, 54% dyslipemia, 28% diabetes mellitus and 14% were smokers). 72% were in NYHA II functional class and 64% had chronic kidney disease (Glomerular filtration-MDRD- <60 cc/min/m2). 66% received optimum therapy (betablockers, diuretics, ACE inhibitors/ ARB, aldosterone antagonists and digoxin -this one only with atrial fibrillation. Only 20% diagnosed of ferropenia received iron therapy (oral or intravenous).

**Statistical analysis:** correlation tests (Pearson's test, contingency and ANOVA tables) and ROC curves.

**Results:** The prevalence of iron deficiency in our patients was 38% (10 patients had absolute ferropenia and 9 relative iron deficiency), 8% had ferropenic anaemia and 14% other aetiologies anaemia. Statistical analysis shows a significant correlation between iron deficiency and E/e' (p=0,003) and the ROC curve that E/e'>=13 had a significant correlation with ferropenia (Sensibility 74%, Specificity 64%, Positive Predictive Value 76% and Negative Predictive Value 60%). Patients with E/e'>=15 had a systolic pulmonary arterial pressure =>33 mm Hg (Sensibility 65,5%, Specificity 71,4%, Positive Predictive Value 76% and Negative Predictive Value 60%).

**Conclusions:** 1- The prevalence of iron deficiency in our patients diagnosed of chronic heart failure with EF depressed is very high and scarcely treated. 2-Our patients has many cardiovascular factors and cardiorenal syndrome. 3-This study shows an unpublished and relevant correlation between ferropenia and left ventricular filling pressure probably related to a higher stimulation of renin-angiotensin-aldosterone and sympathetic nervous system

**P318**

**Chronic heart failure in diabetic patients with low extremity artery disease with/without anemia**

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**Background:** Prevalence of anemia in patients with chronic heart failure (CHF) and low ventricle ejection fraction (LVEF) range widely from 4% to 61% (median 18%). The aim of this study was to evaluate influence of anemia in diabetic patients with low extremity artery disease (LEAD) undergoing partial foot amputation

**Methods:** We evaluated 240 consecutive symptomatic patients (45-65 years old, 98 female and 142 male) with type 2 diabetes, CHF, LEAD and without history of coronary intervention or myocardial infarction, renal insufficiency undergoing partial foot amputation during January-May 2014. Physical and instrumental examination, laboratory tests were performed prior operation and in dynamics.

**Results:** Clinical coronary artery disease (CAD), atherosclerotic lesions of coronary and lower extremity arteries were similar to every patients (no clinically significant/obstructive stenosis). 120/240 patients had hemoglobin (Hb)>120 g/L, other half of patients had Hb <100 g/L. CHF Class I (NYHA) more often observed in patients without anemia 52(43.3%) vs. 12(10%). Class II detected in 38 patients (31.7%) without anemia vs. 50 (41.7%) with decreased Hb level. We found 2fold increase in prevalence of CHF Class III and IV in patients with anemia (p=0.0003). All patients in study received insulin therapy. We detected more increased HbA1c in anemic patients (p=0001). Brain natriuretic peptide was significantly elevated in the group with low Hb (p=0.001). LVEF was below 55% in 103 anemic patients (85.8%) vs. 41 (34.2%) with Hb >120 g/L; p=000.1 (Table).

**Conclusion:** Symptomatic diabetic patients with CAD, LEAD, undergoing partial foot amputation had more severe CHF in the group with anemia which characterized in increase heart failure NYHA Class, brain natriuretic peptide, decrease LVEF.

Parameters of symptomatic diabetic patie			
Parameters	Without anemia n = 120	With anemia, n = 120	P value
Hemoglobin, g/L	128.0 ± 6.0	82.5 ± 11.5	0.0001
Heart rate, beats/minute	82.4 ± 11.2	115.5 ± 12.9	0.0001
Systolic/diastolic blood pressure, (mmHg)	145.7 ± 55.4/ 90.4 ± 10.3	144.2 ± 58.5/ 91.9 ± 8.6	-
Left ventricle ejection fraction, %	55.2 ± 5.3	51.3 ± 4.7	0.0001
Glycosylated hemoglobin HbA1c, %	9.4 ± 1.7	11.1 ± 1.9	0.0001
Fasting plasma glucose, mmol/l	7.4 ± 3.6	7.1 ± 3.5	-
2h plasma glucose, mmol/l	10.2 ± 3.8	9.8 ± 3.4	-
Brain natriuretic peptide, ng/ml	257.7 ± 84.5	391.2 ± 98.1	0.0001
Blood urea, mmol/l	6.1 ± 2.9	6.7 ± 2.1	-
Blood creatinine, mmol/l	88.4 ± 18.5	92.7 ± 14.5	-

### P319

#### Use of two-dimensional "2D" stain imaging for early detection of iron overload cardiomyopathy in polytransfused patients.

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**Background:** Iron overload cardiomyopathy in polytransfused patients is characterized by a restrictive cardiomyopathy with early diastolic dysfunction and a late systolic dysfunction. The aim of this study is to determine the value of the two-dimensional "2D" stain imaging in the early detection and screening of iron overload cardiomyopathy.

**Methods:** This is a case-control study comparing eleven polytransfused patients followed at the hematology department and twenty apparently healthy patients randomly selected. All patients underwent conventional transthoracic echocardiography with an analysis of myocardial deformation "speckle-tracking" or two-dimensional "2D" stain imaging in the cardiology department of the same hospital.

**Results:** Our patients mean age was 58.4 years (19, 80) with a sex ratio of 1.75. Diseases treated in the long-term by transfusions were myelodysplastic syndrome in 8 cases, thalassemia major in 2 cases and myelofibrosis in one case. All patients received more than 20 red blood cells units. The majority of patients were asymptomatic (10/11). Mean left ventricular ejection fraction was 59.9%. The S wave in the lateral mitral annulus was 9.7 ± 2.1 cm/s. Diastolic function was preserved in 10 patients. The global longitudinal strain was -18.5 % ± 3.2 with a significant difference from the control group (-20.8% ± 2.05), p = 0.02. There is a significant correlation between the number of red blood cells units received and the global longitudinal strain (p = 0.019).

**Conclusion:** The two-dimensional "2D" stain imaging is a new non invasive technique that can better assess the real state of left ventricular function. In our study we found a significant decrease in global longitudinal strain in polytransfused patients compared to controls. Our results confirm the value of this new technique in the early detection of iron overload cardiomyopathy.

### P320

#### Iron deficiency and risk of early readmission after an admission for acute heart failure.

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**Introduction:** Early rehospitalizations after an episode of acute heart failure (AHF) remains excessively high and its prediction remains a challenge. Iron deficiency (ID) is a frequent finding in AHF but prognostic implications remains unclear.

**Purpose:** We sought to evaluate the association between ID and risk of 30-day readmission in a cohort of patients discharged for AHF

**Methods:** Serum ferritin and transferrin saturation (TSAT) were measure before discharge in 626 consecutive patients with AHF in a single teaching center. ID was defined as serum ferritin <100 µg/l (absolute ID) and as ferritin 100-299 µg/L with a TSAT <20% (functional ID). Cox regression adapted for competing event was used to determine the association between ID-related parameters and risk of 30-day readmission.

**Results:** Mean age was 75.6 ± 10.4, 48% were females and 52.1% showed left ventricular ejection fraction >50%. ID was identified in 463 patients (74%): 302 (48.2%) absolute ID and 161 (25.7%) functional ID. At 30-day after discharge, 20 (3.2%) patients died and 103 (16.5%) were readmitted. Patients with absolute ID showed an increase of rate of readmission compared to those with functional ID and no ID (19.9%, 13% and 13.5%, respectively, p = 0.005). In multivariate setting, absolute ID remained associated to higher risk of readmission (HR = 1.72; CI 95%: 1.13-2.60, p = 0.011). Compared to patients without ID, functional IF was not related to the risk of readmission (HR = 0.87; CI 95%: 0.46-1.62, p = 0.652)

**Conclusion:** In patients with AHF, absolute ID, but not functional ID, was associated to an increased risk of early readmission.

### 60108

#### Unpublished association between iron deficiency and left heart filling pressure in patients diagnosed of chronic heart failure

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**Introduction:** There is an increasing interest among cardiologists in iron deficiency of patients with chronic heart failure, because it is known that its therapy with intravenous carboxymaltose improves these patients' well-being. However, it is unknown its correlation with echocardiographic variables.

**Purpose:** We want to show the prevalence of iron deficiency in patients diagnosed of chronic heart failure and its correlation with echocardiographic variables.

**Methods:** This is a prospective study, including consecutive 50 patients attended at our heart failure clinic and diagnosed of chronic dysfunction (EF < 40%) with whatever aetiology (22 dilated cardiomyopathy, 19 ischemic cardiomyopathy and 18 other etiologies). General features: 39 men, average age 72 years (IC 95% 70-75.2 years) and 4,74 years elapsed from the diagnosis (IC 95% 3,43-6,04 years). These patients were attended from October 2014 until June 2015 and had a compensated heart failure (without any hospital admission in the last 3 months). The ECG show 16 LBB and the patients had 26 devices implanted (16 TCR and 10 ICD). Our patients had many cardiovascular risk factors (40% arterial hypertension, 54% dyslipemia, 28% diabetes mellitus and 14% were smokers). Most of them were in functional class II NYHA and 64% had chronic kidney disease (GF < 60 cc/m2). 86% of the whole patients received optimum therapy (beta-blockers, diuretics, ACE inhibitors and aldosterone antagonists and digoxin if atrial fibrillation was present) and only 20% iron therapy (oral or intravenous).

**Statistical analysis:** correlation tests (Pearson's test, contingency tables and ANOVA tables) and ROC curves

**Results:** the prevalence of iron deficiency in our patients was 38%, 8% had ferropenic anaemia and 14% other aetiologies anaemia. Statistical analysis showed a significant correlation between iron deficiency and E/e' (p = 0,003) and ROC curve that E/e' > 13 had a significant relationship with ferropenia (Sensitivity. 74%, Specificity, 64%, Positive Predictive Value 76% and Negative Predictive Value 60%). Patients with E/e' had a pulmonary arterial pressure > 40 mm Hg.

**Conclusions:** 1- The prevalence of iron deficiency was very high in our patients and scarcely treated. 2- Our patients had many cardiovascular factors and cardiorenal syndrome. 3- This study shows and unpublished and relevant relationship between ferropenia and left ventricular pressure, probably related to a higher stimulation of renin-angiotensin-aldosterone and sympathetic nervous systems.

### P321

#### Assessment of myocardial iron in heart failure before and after correction of functional iron deficiency by intravenous iron therapy with ferric carboxymaltose using cardiac magnetic resonance imaging

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**Background:** Chronic heart failure (CHF) is characterized by inflammation-related functional iron deficiency (ID). Its correction by intravenous iron has been shown to improve functional status independently of anaemia in CHF. However, the mechanism of improvement is not clear. As iron may play a key intracellular role in cardiac myocytes within mitochondria and in myoglobin, we hypothesize that myocardial iron content (IC) may change after intravenous iron application.

**Methods:** We prospectively quantified myocardial IC in 24 patients with systolic CHF (LVEF ≤ 40%) using cardiac T2\* magnetic resonance imaging (MRI). T2\* imaging was accomplished using 1,5-T scanner and multiecho gradient-echo sequence. Functional ID was diagnosed in 12 patients with ferritin < 100 µg/L or between 100 and 299 µg/L, if the transferrin saturation (TS) was < 20%, and a hemoglobin of 95 to 135 g/L. IC of heart, small and large intestines, spleen, liver, skeletal muscle and brain before and 12 weeks after intravenous iron therapy (IIT) using ferric carboxymaltose was assessed.



**Results:** Patients with functional ID had a lower ferritin and haemoglobin compared to patients with normal iron availability ( $67 \pm 17 \mu\text{g/L}$  vs.  $196 \pm 26 \mu\text{g/L}$  and  $123 \pm 11 \text{ g/L}$  vs.  $142 \pm 11 \text{ g/L}$ , all  $p = 0.0004$ ). In patients with functional iron deficit, TS correlated with low myocardial IC of the left ventricle (LV) indicating myocardial ID ( $r = 0.69$ ,  $p < 0.02$ ). Contrastingly, in patients with normal iron availability, there was no correlation of transferrin saturation with myocardial IC ( $r = 0.32$ ,  $p = 0.3$ ). After IIT, TS, ferritin and hemoglobin increased indicating therapeutic response ( $19.9 \pm 1.3$  vs.  $28.4 \pm 1.4\%$ ,  $90 \pm 15$  vs.  $321 \pm 36 \mu\text{g/L}$ ,  $124 \pm 2$  vs.  $134 \pm 3 \text{ g/L}$ , all  $p < 0.0004$ ). Peak VO<sub>2</sub> increased after iron application ( $18.2 \pm 1.3$  vs.  $20.9 \pm 1.3\%$ ,  $p = 0.05$ ). IC of spleen and liver increased as expressed by a shortened T<sub>2</sub>\* value by 40.2 and 18.2%, respectively, representing augmented storage of iron ( $78.3 \pm 7.2$  vs.  $46.8 \pm 7.8 \text{ ms}$   $p < 0.002$ ;  $33.5 \pm 1.7$  vs.  $27.4 \pm 2.5 \text{ ms}$ ,  $p < 0.02$ ). Myocardial IC of the left ventricle increased as expressed by a shortened T<sub>2</sub>\* value by 28.7% ( $54.3 \pm 6.3$  vs.  $38.7 \pm 3.1 \text{ ms}$ ,  $p = 0.05$ ). IC of the bone marrow and small intestine increased, too. However, this did not reach significance ( $9.8 \pm 0.4$  vs.  $13.7 \pm 2.6 \text{ ms}$   $p = 0.14$ ,  $34.3 \pm 6.5$  vs.  $25.3 \pm 4.3 \text{ ms}$ ,  $p = 0.19$ ). Contrastingly, IC of large intestine, brain and skeletal muscle remained unchanged ( $15.7 \pm 3.2$  vs.  $13.6 \pm 3.3 \text{ ms}$ ,  $p = 0.6$ ;  $81.0 \pm 1.8$  vs.  $82.9 \pm 2.9 \text{ ms}$ ,  $p = 0.5$  and  $31.8 \pm 2.6$  vs.  $30.3 \pm 0.4 \text{ ms}$ ,  $p = 0.6$ ). While IC in skeletal muscle of the limbs correlated with hemoglobin after IIT ( $r = 0.60$ ,  $p < 0.04$ ), increased myocardial IC did not correlate with hemoglobin level suggestive of implementation of iron into the myocardium independently of implementation into hemoglobin ( $r = 0.18$ ,  $p = 0.6$ ).

**Conclusions:** Myocardial IC increased after IIT using ferric carboxymaltose. IC in skeletal muscle remained unchanged. Increase in myocardial IC may contribute to clinical benefit of intravenous iron therapy.

### P322

#### Iron status in patients with heart failure with reduced ejection fraction with ischaemic versus non-ischaemic aetiology.

Supported by the National Science Centre (Poland) grant allocated on the basis of the decision number DEC-2014/13/B/NZ5/03146  
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**Background:** There are 2 major factors significantly contributing to the complex pathophysiology of heart failure (HF), namely impaired haemodynamics due to left ventricular dysfunction (a failure of mechanical pump) and in case of existing coronary artery disease (CAD) - myocardial ischaemia. It remains unknown if and how these 2 factors affect iron status in patients with heart failure with reduced ejection fraction (HFREF).

**Methods:** We prospectively analysed data of 732 stable patients with HFREF (confirmed CAD: 71%, mean age:  $58 \pm 11$  years, New York Heart Association [NYHA] Class III/IV: 44%, mean LVEF [left ventricular ejection fraction]:  $28 \pm 8\%$ ). ID was defined as serum ferritin  $< 100 \mu\text{g/L}$ , or serum ferritin  $100\text{--}299 \mu\text{g/L}$  with transferrin saturation (TSAT)  $< 20\%$ . Additionally, we also measured serum hepcidin and soluble transferrin receptor (sTfR) as circulating biomarkers of iron status.

**Results:** Patients with CAD as compared with those without CAD (nCAD) had a more prevalent ID (borderline) (37% vs. 31%,  $p = 0.08$ ), and also lower ferritin (165 (89-258) vs. 205 (117-325)  $\mu\text{g/L}$ ,  $p < 0.01$ ), lower hepcidin (52 (27-108) vs. 82 (45-170) ng/mL,  $p < 0.001$ ), lower haemoglobin ( $13.8 \pm 1.5$  vs.  $14.4 \pm 1.6 \text{ g/dL}$ ,  $p < 0.001$ ), and lower GFR (73 (58-90) vs. 83 (66-97) mL/min/1.73m<sup>2</sup>,  $p < 0.001$ ) without any differences in sTfR, TSAT and hs CRP (all  $p > 0.2$ ).

Both in CAD and nCAD groups, sTfR was higher in patients with markedly reduced LVEF: for those with LVEF 40-45%, 30-39%, 20-29% and  $< 20\%$  - in the CAD group 1.23 (1.06-1.79), 1.21 (0.97-1.66), 1.24 (1.00-1.64) and 1.69 (1.16-2.49) ng/mL ( $p < 0.01$ ) and in nCAD group 1.15 (0.97-1.41), 1.16 (0.91-1.60), 1.17 (0.95-1.52), and 1.50 (0.98-2.05) ( $p = 0.11$ ). Also, in both patients with CAD and nCAD, plasma NT-proBNP correlated positively with sTfR (respectively for CAD and nCAD -  $r = 0.29$ ,  $p < 0.001$  and  $r = 0.38$ ,  $p < 0.01$ ) and negatively with Tsat ( $r = -0.25$ ,  $p < 0.01$  and  $r = -0.33$ ,  $p < 0.01$ ).

Along with the decreasing LVEF, there was a tendency for a higher prevalence of ID defined based on serum ferritin and Tsat, but only in a nCAD group (LVEF  $< 20\%$  vs. 40-45%: 44% vs 22%,  $p = 0.08$ ). Serum ferritin was higher in nCAD as compared to CAD patients, but did not differ across LVEF groups in both aetiology subgroups ( $p > 0.2$ ). Serum hepcidin was higher in nCAD as compared to CAD patients, and among nCAD patients there was a tendency for even higher hepcidin in patients with lower LVEF ( $r = -0.21$ ,  $p = 0.07$ ). Neither in CAD nor in nCAD, ferritin and hepcidin correlated with hsCRP (both  $p > 0.2$ ).

**Conclusions:** Iron status differs in patients with HFREF depending on HF aetiology and LVEF value. Patients with ischaemic HFREF have markedly reduced iron stores

reflected by low ferritin and hepcidin. Regardless of aetiology, the magnitude of intracellular iron depletion (high sTfR) is the greatest among those with severely impaired LV systolic function and augmented neurohormonal activation without any association with inflammatory process.

### P323

#### Cardiorenal relations in patients with septic conditions

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**Purpose:** To study the features of type 5 cardiorenal syndrome in patients with sepsis and infective endocarditis (IE).

**Material and methods:** 25 patients with IE (Duke 2015; group 1) and 28 patients with sepsis (group 2) were included. Median age in group 1 was 65 [62-74], in group 2 - 62 [34-75] years. We evaluated the anamnesis, echocardiogram, renal function (GFR, proteinuria, microscopic hematuria, serum cystatin C, urinary Kim-1), heart failure (NYHA) rates, NT-proBNP values, acute kidney injury (AKI; KDIGO 2012) and mortality rates.

**Results:** Sex and age distribution did not differ between two groups. Condition severity in groups with IE and with sepsis were comparable. NYHA FC III/IV heart failure were more common in group 1 than in group 2 [21 (84%) vs. 13 (47%),  $p < 0.05$ ], that was confirmed by higher levels of NT-proBNP [5500 (3200-9200) pg/ml vs. 5200 (1900-8800) pg/ml,  $p > 0.05$ ]. Kidney injury occurred equally often in both groups [21 (84%) and 24 (86%),  $p > 0.05$ ]. However, AKI was observed more frequently in patients with IE than in patients with sepsis [14 (56%) vs. 13 (47%),  $p < 0.05$ ]. Proteinuria were also more common in group 1 [14 (56.0%) vs. 6 (21.4%),  $p < 0.05$ ].

Values of serum cystatin C were higher in patients with IE [2.01 (1.76-2.66) mg/ml vs. 1.72 (1.29-2.37) mg/ml,  $p = 0.13$ ], but urinary Kim-1 levels were slightly higher in patients with sepsis [1.68 (1.63-1.75) ng/ml vs. 1.60 (1.51-1.77) ng/ml,  $p = 0.29$ ].

Mortality rates were similar in both groups [7 (28.0%) and 6 (21.4%),  $p > 0.05$ ].

**Conclusion:** Patients with IE showed more severe heart failure, higher levels of NT-proBNP and more severe kidney injury presented by higher incidence of AKI and proteinuria compared with group of sepsis. Mortality rates did not differ between two groups.

### P324

#### Circadian blood pressure profile in patients with ischemic chronic heart failure with renal dysfunction

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The role of ambulatory blood pressure monitoring not been studied in patients with chronic heart failure, the prevalence of which is constantly growing, and there are practically no data on the nature of the daily profile of arterial pressure in chronic heart failure associated with renal dysfunction.

**Purpose:** The aim of the study was to investigate the characteristics of ambulatory blood pressure monitoring in patients with ischemic chronic heart failure (CHF) depending on renal function. Methods. The study involved 106 patients with ischemic CHF (90 men), mean age  $56.2 \pm 8.8$  years. In 35 (33.1%) patients were diagnosed II functional class (FC) CHF, in 71 (66.9%) - III FC. 24-hours ambulatory blood pressure monitoring (ABPM) was performed with the use of CardioTens. Variation row glomerular filtration rate (GFR) was divided into quartiles. A comparative analysis was conducted between CHF patients with  $\text{GFR} < 70.1 \text{ mL/min/1.73 m}^2$  (lower quartile) and  $> 86.5 \text{ mL/min/1.73 m}^2$  (upper quartile).

**Results:** Decreasing GFR in patients with ischemic CHF was associated with a more senior age ( $p < 0.0001$ ), FC of heart failure ( $p = 0.02$ ), more common history of hypertension ( $p = 0.04$ ), lower ejection fraction ( $p = 0.02$ ). Office arterial hypertension was found in 14 (13.2%) patients, ABPM established hypertension in 23 (21.7%) for SBP and 19 (17.9%) patients for DBP. Arterial hypotension was detected in 5 (4.7%) for SBP and in 11 (10.4%) patients for DBP. Increased variability for SBP in 44 (41.5%) and for DBP in 14 (13.2%) patients were revealed. Insufficient degree of nocturnal decline (non-dipper) SBP was observed in 43 (40.6%), DBP - in 32 (30.2%) patients. Excessive nocturnal decline (over-dipper) SBP detected in 6 (5.6%), DBP - in 29 (27.4%) patients. Raising a night (night-picker) SBP was observed in 12 (11.3%), DBP - 5 (4.7%) patients. In CHF patients with  $\text{GFR} \leq 70.1 \text{ mL/min/1.73 m}^2$ , compared with a group  $\text{eGFR} \geq 86.5 \text{ mL/min/1.73 m}^2$  revealed a lower average daily standard deviation for DBP ( $p = 0.02$ ), the daily index DBP ( $p = 0.05$ ) and the standard deviation of daytime DBP ( $p = 0.05$ ) and night ( $p = 0.03$ ) time. Multivariate regression analysis showed that eGFR is associated with age, FC CHF, ejection fraction, daily index for SBP and DBP ( $R^2 = 0.45$ ;  $p = 0.0001$ ).

**Conclusion:** ABPM in patients with ischemic CHF can significantly increase detectability hypo-hypertension, certain deviation daily index, variability BP. Level GFR correlated with age, functional class and the degree of blood pressure reduction at night.

**P325****Validated-internally kidney protection program (vkpp) scoring system as a predictor of worsening renal function among hospitalized acute decompensated heart failure patients**V Vebiona Surangayudha<sup>1</sup>; P Yamin<sup>1</sup>; N Hersunarti<sup>1</sup>; D Tobing<sup>1</sup>; R Soerarro<sup>1</sup>; B Siswanto<sup>1</sup><sup>1</sup>National Cardiovascular Center Harapan Kita, Department of Cardiology and Vascular Medicine, Jakarta, Indonesia**Background:** Worsening renal function (WRF) is associated with worse outcomes among patients who are hospitalized with acute decompensated heart failure (ADHF). Clinical characteristics at admission may help identify patients at increased risk of WRF.**Purpose:** The aim of this study was to create in admission scoring system to simplify identification patients at risk of WRF in ADHF setting. Methods. A retrospective data of 614 patients admitted with ADHF was analyzed. By the definition WRF occurred when serum Creatinin increased at anytime during hospitalization by  $\geq 0.3$  mg/dL or by  $\geq 25\%$  from admission.**Results:** Worsening renal function developed in near 26% patients. The independent predictors of WRF analyzed with backward selection logistic regression were: age > 75 years old ( $p < 0.0001$ ), female ( $p = 0.034$ ); history of hypertension ( $p = 0.001$ ); anemia ( $p = 0.005$ ); and in admission serum Creatinin ( $p = 0.013$ ). A scoring system was generated from this final model. An internal validation with bootstrap method showed good optimism (0.01088808).**Conclusion:** A new scoring system could predict in-hospital worsening renal function among patients hospitalized with acute decompensated heart failure.**P326****Short-term rosuvastatin therapy reduced risk of contrast-induced acute kidney injury in patients with delayed percutaneous coronary intervention**A Anna Gaskina<sup>1</sup>; S Villevalde<sup>1</sup>; Z Kobalava<sup>1</sup><sup>1</sup>Peoples Friendship University of Russia (PFUR), Moscow, Russian Federation**Introduction:** Contrast-induced acute kidney injury (CI-AKI) is a common complication of intra-arterial administration of iodinated radiographic contrast medium that may prolong hospitalization, increase costs, short- and long-term morbidity and mortality. Despite the obvious progress in modern interventional cardiology and angiology the question of effective prevention of CI-AKI remains relevant. We performed a single-centre prospective study to determine the effect of addition of rosuvastatin to routine preventive measures on the incidence of CI-AKI in patients with non-ST-elevation acute coronary syndrome (NSTEMI-ACS) and delayed percutaneous coronary intervention (PCI).**Methods:** 84 patients with NSTEMI-ACS scheduled to early invasive strategy were randomised by the method of blind envelopes were randomized to receive rosuvastatin 40 mg followed by 20 mg/day (intervention group,  $n = 42$ ) or routine atorvastatin 20-40 mg/day (control group,  $n = 42$ ). patients in intervention group continued treatment with rosuvastatin 20 mg/day at discharge. All patients received routine prevention - intravenous hydration with 0.9% sodium chloride for 12 h both before and after PCI, 1 ml/kg/h. Non-ionic low osmolar contrast agent iodaxol (Omnipaque 350) was used. We use transradial access for PCI in 98% of patients. Both groups were comparable in age ( $63 \pm 13$  and  $66 \pm 12$  years), comorbidity (hypertension 91 and 94%, chronic kidney disease 12 and 14%, diabetes mellitus 21 and 18%) and therapy. 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:** The incidence of CI-AKI in intervention group was significantly lower than in the control group (4,8 and 19%,  $p < 0.05$ ). Clinical follow-up at 6-month was completed for all 84 patients. Patients who developed CI-AKI presented a significantly higher rate of 6-month rehospitalizations for cardiovascular disease (70 and 47%,  $p < 0.05$ ) than patients without CI-AKI. The 6-month cardiovascular rehospitalizations was significantly lower in the statin than in the control group (31 and 52%,  $p < 0.05$ ). Patients in the statin group presented a significantly lower rate of persistent renal damage (24 and 45%,  $p < 0.05$ ) than patients in the control group.**Conclusion:** Short-term rosuvastatin therapy significantly reduced the risk of CI-AKI in patients with NSTEMI-ACS and delayed PCI and improved short-term clinical outcome.**P327****Incidence and outcomes of contrast-induced acute kidney injury in patients with elective percutaneous intervention**A Anna Gaskina<sup>1</sup>; S Villevalde<sup>1</sup>; A Milto<sup>1</sup>; Z Kobalava<sup>1</sup><sup>1</sup>Peoples Friendship University of Russia (PFUR), Moscow, Russian Federation**Aims:** Contrast-induced acute kidney injury (CI-AKI) is one of the most common complications after percutaneous coronary intervention (PCI) using intravascular radiocontrast media. CI-AKI has been associated with high in-hospital mortality and

poor long-term survival. The aim of the study was to evaluate the incidence, risk factors and outcomes of CI-AKI in patients with elective PCI.

**Methods:** 150 patients with stable angina pectoris (SAP) and elective PCI (102 male,  $61.3 \pm 11.2$  years ( $M \pm SD$ ), arterial hypertension 88%, previous MI 56%, diabetes mellitus 25%, known chronic kidney disease (CKD) 33%, anemia 17%, heart failure 67%, left ventricular ejection fraction  $42 \pm 16\%$ ) were examined. CI-AKI was defined using 2012 KDIGO Guidelines. Isoosmolar contrast media iodixanol (Visipaque-320) or low-osmolar contrast media iohexol (Omnipaque-350) were used. Transradial access for PCI was used in 98% of patients. Mann-Whitney test and multivariate logistic regression analysis were performed.  $P < 0.05$  was considered statistically significant.**Results:** 21 (14%) patients developed CI-AKI. Stages 1 and 2 of CI-AKI were found in 92 and 8% of cases accordingly. Main independent predictors of CI-AKI were contrast media volume (CV)/eGFR  $\geq 4.35$  (odds ratio (OR) 20.2; 95% confidence interval (CI) 3.4-120.8;  $p < 0.01$ ), CKD (OR 17.4; 95% CI 3.8-79.8;  $p < 0.05$ ), Mehran risk score  $> 10$  (OR 14.7; 95% CI 1.2-66.6;  $p < 0.0001$ ), CV  $> 350$  ml (OR 8.7; 95% CI 1.4-21.5;  $p < 0.05$ ), age  $\geq 74.5$  years (OR 6.9; 95% CI 1.4-34.1;  $p < 0.01$ ), baseline eGFR  $\leq 61$  ml/min/1.73 m<sup>2</sup> (OR 6.5; 95% CI 1.6-26.0;  $p < 0.01$ ), baseline serum creatinine (SCr)  $\geq 96$   $\mu$ mol/l (OR 5.5; 95% CI 1.4-21.5;  $p < 0.05$ ), anemia (OR 3.0; 95% CI 1.1-8.4;  $p < 0.05$ ). Patients with versus without CI-AKI had higher risk of 6 months rehospitalizations (59 vs 33%,  $\chi^2 = 8.53$ ,  $p < 0.05$ ).**Conclusions:** CI-AKI in patients with SAP and elective PCI developed in 14% of cases, predominantly stage 1. Main independent predictors of CI-AKI were factors related to the contrast media (CV/eGFR, CV) and factors related to the patient (CKD, Mehran risk score  $> 10$ , age  $\geq 74.5$  years, baseline eGFR  $\leq 61$  ml/min/1.73 m<sup>2</sup>, baseline SCr  $\geq 96$   $\mu$ mol/l, anemia). CI-AKI had negative impact on of 6 months rehospitalizations.**P328****Hemodynamic predictors of plasma NGAL concentrations and its response to intervention**

Supported, in part, by an operating grant from the Canadian Institute for Health Research (RN136292 - 260133)

L Goldraich<sup>1</sup>; DZI Cherney<sup>2</sup>; J D Parker<sup>3</sup><sup>1</sup>University of Toronto, Toronto, Canada; <sup>2</sup>University Health Network, Toronto, Canada; <sup>3</sup>Mount Sinai and University Health Network Hospitals, Medicine, Toronto, Canada**Background:** Neutrophil gelatinase-associated lipocalin (NGAL) has been reported as an indicator of acute renal injury and as an indicator of prognosis in patients with congestive heart failure (CHF).**Purpose:** We explored the relationship between plasma NGAL, invasive hemodynamics and measures of renal function in patients with and without CHF. We also examined the impact of an acute hemodynamic intervention (dobutamine and nitroprusside) on NGAL concentrations.**Methods:** We measured plasma NGAL concentrations and carried out right heart catheterization as well as arterial hemodynamic assessments in 29 patients with preserved left ventricular (LV) function and normal hemodynamics (the no CHF group) and 46 patients with reduced LV systolic function (EF  $< 40\%$ ) and a history of CHF (CHF group). We also made direct measures of GFR (inulin) and renal plasma flow (RPF; para-amino hippurate). Univariate and multivariate (stepwise) linear regression were used to explore the relationships between hemodynamics, renal function parameters and NGAL concentrations. After baseline measures were obtained, all subjects received an intravenous infusion of either dobutamine or nitroprusside with repeat measures of hemodynamics, renal function and NGAL concentrations**Results:** Plasma NGAL concentrations were elevated in the CHF vs. the no CHF group ( $202 \pm 109$  versus  $119 \pm 42$  ng/ml;  $P < 0.001$ ). In the no CHF group, in both the univariate and multivariate analysis, the only significant independent predictor of baseline plasma NGAL was RPF. In those with CHF, only right atrial mean pressure made an independent contribution to the multivariate model predicting NGAL. Right atrial mean pressure had a positive relationship with NGAL, with higher right atrial pressures associated with higher values of NGAL. In both groups, the administration of dobutamine and nitroprusside was associated with a highly significant decrease in plasma NGAL (table).**Conclusions:** These data reveal that plasma concentrations of NGAL are dependent on baseline hemodynamic status in patients with CHF with an independent positive correlation with right atrial pressure in that population. We also demonstrate that common hemodynamic interventions cause highly significant reductions in plasma NGAL concentrations in both patients with and without CHF. These findings have importance to our understanding of the utility of NGAL as a biomarker used in the assessment of acute renal injury and patient prognosis.

Table. NGAL pre and post intervention

	control	dobutamine	control	nitroprusside
Plasma NGAL non-CHF (ng/ml)	124 $\pm$ 45	87 $\pm$ 37*	108 $\pm$ 32	49 $\pm$ 30*
Plasma NGAL CHF (ng/ml)	206 $\pm$ 88	148 $\pm$ 73*	199 $\pm$ 120	128 $\pm$ 75*

\*  $P < 0.01$  vs control

## P329

**Demographic and clinical outcomes of patients admitted for acute decompensated heart failure (adhf) with worsening renal function(wrf) in a district general hospital in malaysia**WEIJYUNG Patrick Tiau<sup>1</sup>; ADRIAN Mark<sup>1</sup>; CM Ang<sup>1</sup>; SX Foo<sup>1</sup>; S Shahrani<sup>1</sup>; A Zainal<sup>1</sup>; R Yusoff<sup>1</sup>; R Abdullah<sup>1</sup><sup>1</sup>Hospital Sultan Haji Ahmad Shah, Medical Department, Temerloh, Malaysia

**Backgrounds:** Worsening renal function (WRF) is known to increase adverse clinical outcome in patients admitted with acute decompensation of heart failure (ADHF). We looked at admissions of ADHF, its etiologies and causes of admission, incidence of worsening renal function; its factors and outcomes in a district general hospital in Malaysia for 2014. Method and

**Results:** Worsening renal function is defined as increase in serum creatinine by at least 0.3mg/dL (26.5 mmol/L) or at least 25% increased from baseline. We looked into factors associated with worsening renal function and the clinical outcome of patients admitted for ADHF with worsening renal function. There were 197 patient admissions with ADHF during the year 2014 that accounted for 4.9% of total medical admissions in Hospital Sultan Haji Ahmad Shah, Malaysia. Fifty percent were males with a median age of 65 years (range 12-90). Median length of stay was 5 days (range 2-20). Seventy-seven percent had hypertension (n = 153), 50% had diabetes (n = 99), 42% had ischemic heart disease (n = 83), 17% had chronic kidney disease (n = 34). The precipitating factors for ADHF hospitalization was acute coronary syndrome (48.7%), followed by non-compliance (41.1%), uncontrolled hypertension (33.5%), infections (21.4%) and other causes 1.5%. Thirty percent (n = 60) of patients had worsening renal function. Use of inotrope (OR:3.09 P = 0.034) and concomitant in-hospital infection (OR:5.0 P = 0.023) were the only significant factors associated with worsening renal failure. Patient admitted with ADHF and developed WRF had higher in-hospital mortality (OR: 2.93 P = 0.009). However, this did not significantly affect 30-day and 180-day readmission rates (OR 2.3 P = 0.07 and OR: 0.8 P = 0.54) respectively.

**Conclusion:** Worsening renal function in ADHF is common in our cohort. This is associated with significant in-hospital mortality and a trend towards increase 30-day readmission in our study.

## P330

**In patients with CHF creatinine-based measures of GFR in response to acute intervention are directionally opposite to those obtained with inulin and cystatin-c**

Canadian Institute for Health Research (RN136292 – 260133)

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**Background:** Creatinine-based estimates of GFR are used to track changes in renal function over time. However, little is known about their ability to follow changes that occur in response to short-term therapeutic interventions.

**Purpose:** We explored the relationship between plasma cystatin-c (cys-c), invasive hemodynamics as well as direct measures of renal function in patients with chronic CHF. We measured the effect of dobutamine and nitroprusside on measures of GFR based on creatinine, cys-c and inulin.

**Methods:** We measured plasma cys-c and invasive hemodynamics in 46 patients with reduced LV systolic function (EF <40%) and a history of CHF. We calculated GFR based on creatinine (modified diet in renal disease (MDRD) and the chronic kidney disease epidemiology [CKD-epicreat] formulae), cys-c (CKD-epi cys-c formula) and inulin clearance. Univariate and multivariate (stepwise) linear regression was used to explore the relationships between hemodynamics, inulin-based GFR and plasma cys-c concentrations. All subjects received an intravenous infusion of either dobutamine (n = 16) or nitroprusside (n = 30) and repeat measures of hemodynamics, renal function, creatinine and cys-c concentrations were obtained.

**Results:** The multivariate regression analysis revealed that the only significant independent predictor of both plasma creatinine and cys-c was GFR measured by inulin. The administration of dobutamine and nitroprusside caused small, but significant increases in plasma creatinine (dobutamine 88 ± 31 vs. 92 ± 31 μmol/litre; nitroprusside 85 ± 40 vs 88 ± 38 μmol/litre, P < 0.01 for both). By contrast both dobutamine and nitroprusside caused significant reductions in cys-c (dobutamine 1.62 ± 0.62 vs. 1.43 ± 0.58 mg/L; nitroprusside 1.39 ± 0.54 vs 1.23 ± 0.48 mg/L, P < 0.001 for both). Based on these changes there was a decrease in GFR when measured using creatinine-based estimates. In contrast GFR increased when estimated with cystatin-c and measured with inulin (table).

**Conclusions:** These findings serve to demonstrate that changes in creatinine-based estimates of GFR can be very misleading as compared to estimates obtained with cys-c or measurements made using inulin.

Table, GFR responses to intervention

	control	dobutamine	control	nitroprusside
GFR (MDRD), mls/min	94 ± 34	88 ± 30*	101 ± 36	96 ± 34*
GFR (CKD-EPI) creat, mls/min	85 ± 24	82 ± 24	86 ± 25	84 ± 25*
GFR (CKD-EPI cyst-c, mls/min	49 ± 22	58 ± 26*	60 ± 26	69 ± 28*
GFR (inulin), mls/min	88 ± 19	107 ± 28*	93 ± 27	110 ± 34†

MDRD, modified diet in renal disease; CKD-EPI, chronic kidney disease epidemiology; creat, creatinine, cys-c, cystatin-c; \* P &lt; 0.05 vs control, †P = 0.06 vs control

## P331

**The role of urinary NGAL in acute heart failure**

Project is supported by Slovak Society of Cardiology research grant.

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**Purpose:** The aim was to evaluate differences in the levels of urinary NGAL and serum NT-proBNP in patients with acute heart failure (AHF) in relation to the loop diuretic treatment and development of acute kidney injury.

**Methods:** We analysed 60 patients admitted to coronary care unit with AHF. Urine samples were collected immediately at admission and after 24 hours. The samples were stored at -72°C and examined by enzyme-linked immunosorbent assay (Bioporto, Denmark). Acute kidney injury was defined according to KDIGO and patients were divided into groups without AKI (AKI-, n = 49) and with AKI (AKI+, n = 11).

**Results:** Sixty patients with median age 67 (IQR 61-79) and gender distribution 40/20 (M/F) were enrolled. Patients in the AKI+ group had significantly higher median admission u-NGAL levels compared with the AKI- patients (87 vs. 18.2 ng/ml; p = 0.003), also after 24 hours (163.7 vs. 34.5 ng/ml; p = 0.0004). Urinary NGAL/urine-creatinine ratio was higher in the AKI+ group compared with AKI- (at admission: 31.2 vs. 2.5; p = 0.03 and after 24 hours: 18.2 vs. 3.1; p = 0.002). Significant increase in serum creatinine was recorded in the AKI+ group after 24 hours (117.6 vs. 94.5 μmol/l, p = 0.02). Urinary NGAL positively correlated with s-NTproBNP (r = 0.39, p = 0.003). The average initial parenteral dose of furosemide was higher in the AKI+ compared with AKI- (85.9 vs. 32.4 mg, p = 0.002) and correlated with u-NGAL at admission (r = 0.39, p = 0.006) and after 24 hours (r = 0.38, p = 0.01).

**Conclusions:** Patients with the development of AKI had significantly higher u-NGAL concentrations at admission and after 24 hours correlated with increasing serum creatinine, admission NTproBNP and initial parenteral dose of furosemide.

## P332

**Cancer treatment-related left ventricular dysfunction: retrospective evaluation of a small group of patient treated with ivabradine**M Matteo Sarocchi<sup>1</sup>; V Sicbaldi<sup>1</sup>; E Arboscello<sup>2</sup>; A Bellodi<sup>1</sup>; P Ghione<sup>1</sup>; FGualandri<sup>2</sup>; C Bighini<sup>2</sup>; R Murialdo<sup>2</sup>; C Brunelli<sup>1</sup>; P Spallarossa<sup>1</sup><sup>1</sup>University of Genoa, Genoa, Italy; <sup>2</sup>San Martino Hospital, Genoa, Italy

Heart failure patients with cancer treatment related left ventricular dysfunction (CTR-LVD) often require a first-line treatment with inhibitors of angiotensin-converting enzyme (ACEi) or angiotensin receptor blockers (ARB) and β-blockers. Unfortunately, several cancer patients are susceptible to hypotension, fatigue and dizziness, limiting the use of these drugs.

**AIM OF THE STUDY** is to evaluate the efficacy and safety of the addition of Ivabradine to an optimized treatment of CTR-LVD.

**Methods:** We retrospectively analysed patients attending our cardio-oncologic ambulatory, with CTR-LVD defined as a drop in left ventricular ejection fraction (EF) to less than 50%, who received Ivabradine with a follow up of at least 3 months.

**Results:** We identified 30 patients with a mean age was 53 ± 16 y and prevalence of female sex (23/30). The most represented cancer diagnoses were breast cancer, acute leukaemia and non-Hodgkin lymphoma. No patient had less than 9,0 g/dl of haemoglobin. 27 patients had received a typically cardio-toxic anticancer treatment such as Trastuzumab, Anthracyclines or haematopoietic stem-cell transplant (HSCT); in 4 patients other chemotherapies were involved. 18 patients were symptomatic for typical dyspnoea, while 12 reported only atypical symptoms (fatigue, palpitation on exertion). Concomitant medications included a β-blocker and/or an ACEi or ARB in 17 patients; clinical reasons (hypotension, fatigue, renal function) had precluded any other introduction or further titration of these drugs. After a variable follow up (mean: 5,3 months), echocardiographic EF improved from 45,1(%) ± 6,4 to 52,0 ± 6,4 (p < 0,001), and NYHA class improved in 11/30 patients, from a mean of 1,8 ± 0,8 to 1,4 ± 0,6 (p < 0,01). Patients with palpitation or fatigue generally reported symptom amelioration. Heart rate was reduced from 84(bpm) ± 17 to 68 ± 10. Mean systolic and diastolic blood pressure slightly increased from 100(mmHg)



$\pm 17$  to  $117 \pm 22$  and from  $71 \pm 13$  to  $75 \pm 12$  respectively (both not significant). EF improvement was significant in any group of anticancer treatment (Trastuzumab, Anthracyclines, HSCT). In addition, EF and NYHA class improvement was similar in patients who completed the programmed anticancer treatment and in those who did not, stopping or changing the treatment. The starting dose of Ivabradine was  $7.0(\text{mg}/\text{die}) \pm 2.5$  and it had been titrated up to  $8.1 \pm 3.1$  during follow up. No patient had severe bradycardia or serious adverse events, two patients experienced transient phosphenes.

**Conclusions:** we found that a moderate dose of Ivabradine could be safe, effective and well tolerated in patient with CTx-LVD on top of the maximal tolerated treatment with  $\beta$ -blockers and ACEi/ARB. Such an integrated intervention improved EF, NYHA class and fatigue. Limitation is the heterogeneity of cancer treatments and the concomitant cardioactive therapy.

### P333

#### Echocardiographic indicators of left and right ventricular diastolic dysfunction in cancer patients complaining of an excessive fatigue

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**Introduction:** Fatigue is one of the most frequent symptoms reported by patients with neoplastic diseases and often results in specialist consultations and diagnostic tests. It may indicate a cardiac dysfunction, either as an independent co-morbidity, or as a complication of the anticancer therapy. Recently, an increasing number of diastolic dysfunction (DD) in patients with cancer is reported and it is said to precede systolic dysfunction (SD).

**Aims:** The purposes of the study were selection and validation of the optimal scale to assess fatigue, as well as distinguishing a set of parameters for the echocardiography assessment that correlate with the extent of fatigue.

**Methods:** 52 subsequent patients (6 males, 46 females), white, with a history of cancer (breast 71.3%, colon 11.5%, lung and mediastinum 7.7%, others 9.5%), referred to a cardiologist due to an excessive fatigue, were analysed for clinical data and a further three steps evaluation was performed. 1. Fatigue scales (FS) suitable for cancer patients (Fatigue Severity Scale – FSS, Cancer Fatigue Scale – CFS, Piper Fatigue Scale-12 – PFS-12) were implemented after their validation in polish; 2. Echocardiography (Echo) with tissue Doppler imaging (DTI) was performed - the mitral inflow velocity ratio (E/A), the septal and lateral mitral annular velocities and their ratio (Sep. and Lat. e'/a'), tricuspid annular velocities and their ratio (RV e'/a') were obtained; 3. A six-minute walking test (6MWT) with an assessment of the reference distance according to Enright's regression equation was performed. The Kaiser-Mayer-Olkin (KMO) test and alpha-Cronbach's internal consistency test were used for scales validation. The obtained results were analysed using Pearson's correlation coefficient, Shapiro-Wilk test, t-test, Mann-Whitney U test and Kruskal-Wallis test.

**Results:** All implemented scales showed a high level of adequacy in the selection of the sample with KMO>0.7 and a very high internal consistency (the FSS 0.946, the CFS 0.836 and the PFS-12 0.967). In 17 patients (32.7%), DD of the left ventricle and a tendency towards DD of the right ventricle was observed. It correlated with the level of fatigue ( $P < 0.05$ ): E/A -0.37, -0.36 and -0.35 for CFS, PFS-12 and FSS respectively; Sep. e'/a' and Lat. e'/a' -0.39 and -0.38 respectively for CFS physical subscale (-0.31 and -0.29 for total CFS); RV e'/a' -0.28 both for PFS-12 and FSS and -0.27 for CFS physical. The physical fatigue was confirmed in the 6MWT, where 53.8% of patients did not reach the reference distance. No significant statistical influence of the comorbidities or the anticancer treatment was shown as correlated with the results of FS, 6MWT and Echo.

**Conclusions:** FSS, CFS and PFS-12 scales are an optimal tool for assessment of fatigue in cancer patients. In Echo the E/A, septal, lateral and tricuspid e'/a' are the main indicators of a DD presence or possible occurrence in cancer patients with an excessive fatigue.

### P334

#### Wasting is not an independent risk factor of mortality in chronic heart failure patients with type 2 diabetes mellitus

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Body wasting is an independent risk factor of mortality in chronic heart failure (HF). Type 2 diabetes mellitus (DM) modifies the prognostic value of body mass index in HF, as among diabetic HF patients obesity paradox does not exist.

The purpose of the study was to analyze the prognostic value of body wasting in diabetic patients with HF with reduced ejection fraction (HFrEF).

Patients with stable HFrEF (without any clinical signs of congestion) treated in the heart failure outpatient clinic were included into the study. The body wasting was defined as at least 7.5% body mass reduction during HF (since the "dry" body

mass before first symptoms of HF). The probability of 1-year survival was compared between the groups with or without body wasting using log-rank test. The multiple Cox hazard model adjusted for age, sex, body-mass index, NYHA class, estimated GFR, left ventricular EF, peak oxygen consumption (peak VO<sub>2</sub>), NT-proBNP levels, HF etiology and HF duration was performed. The forward regression model was applied for 1-year follow-up mortality.

**Results:** Among 877 patients with HFrEF, 271 (30.9%) with DM were included into the analyses: age  $55.6 \pm 7.7$ ; 13.3% of them were women; BMI  $27.9 \pm 4.7$ ; LVEF  $23.8 \pm 5.8$ ; NT-proBNP  $2552 \pm 3051$  pg/ml; NYHA class III or IV: 67.5% and mean weight change  $-7.43 \pm 12.2$  %.

The median of HF duration (and body wasting) was 40.2 [IQR 40.8] months.

There were no differences between the probability of survival between the two groups with or without body wasting – 80.7% vs 83.3%, log-rank  $p = 0.56$ . In multivariate Cox model only peakVO<sub>2</sub> (HR 0.86 (0.79-0.94),  $p = 0.0006$ ) and LVEF (0.73 (0.53-0.99),  $p = 0.04$  for 5% LVEF increase) were independent predictors of 1-year survival. Body wasting  $\geq 7.5\%$  during HF was not included into the model ( $p > 0.2$ ).

**Conclusion:** Among patients with HFrEF and type 2 diabetes mellitus, body wasting was not an independent predictor of mortality in 1-year follow up.

### P335

#### Effect of trimetazidine on exercise capacity and muscle strength in patients with HFrEF

Ricerca corrente Italian Ministry of Health

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Patients with heart failure and reduced ejection fraction (HFrEF) have reduced exercise capacity in part related to a progressive loss of muscle strength. Trimetazidine (TMZ) has been shown to improve left ventricular function and exercise capacity in patients with HFrEF and to improve muscle performance in cachexia. We performed a randomised double blinded study to assess the effect of TMZ on exercise capacity and muscle strength in patients with HFrEF patients with >5% weight loss in the previous 6 months receiving optimised therapy and undergoing a cardiac rehabilitation programme.

Thirty-two patients were randomly allocated to receive TMZ 20 mg three times/day or matching placebo for 12 weeks. Compared to baseline, the distance walked on the 6-min walking test significantly improved in the TMZ group (28% vs 12%  $p < 0.01$ ), as did peak VO<sub>2</sub> ( $+3.6 \pm 1.6$  vs  $-0.4 \pm 1.3$  mL/kg/min,  $p < 0.05$ ). A significant decrease in the slope VE/VCO<sub>2</sub> and an increase in peak workload were observed in the TMZ group but not in the placebo group.

Maximal voluntary contraction of the quadriceps increased significantly with TMZ (34%) while remained unaltered in patients receiving placebo (-5%),  $p < 0.03$ . The isokinetic torque of the quadriceps improved with TMZ (+19 Nm) but not with placebo (+4 Nm),  $p < 0.03$ . Total work increased significantly with TMZ ( $14 \pm 7$  J) but not with placebo ( $2 \pm 5$  J),  $p < 0.03$ . The fatigue index significantly improved in patients randomised to TMZ ( $-41.1 \pm 9.1\%$ ) but not in those receiving placebo ( $-16.3 \pm 7.3\%$ ),  $p < 0.02$ . A significant correlation was found between change in muscle strength and change in exercise capacity.

In conclusion, TMZ improves muscle strength and performance in patients with HFrEF. The effect of TMZ on exercise performance appears to be related, at least in part, to the improvement in muscle function.

### P336

#### Breast cancer chemotherapy-induced cardiotoxicity; a 10-year observation.

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**Background:** Breast cancer is the leading cause of cancer in women. There has been significant progress in breast cancer therapeutics especially with the development of targeted therapy such as trastuzumab (Herceptin) resulting in remarkable improvements in cancer-free survival. However, with improving prognosis, there has also been an increasing incidence of chemotherapy-induced cardiotoxicity in this patient population. Contemporary guidelines mandate routine baseline and follow-up assessment of cardiac function prior to and following chemotherapy, however compliance to these recommendations is unknown.

**Purpose/Methods:** We aim to, firstly, determine the compliance to guideline recommendations and, secondly, the incidence of chemotherapy-induced cardiotoxicity among patients treated for breast cancer. We extracted data over a 10-year period (2003-2013) from a large regional cancer database in Scotland. This data was then linked to a health informatics database that tracks prescribing, investigational, morbidity and mortality data of patients across Scotland.

**Results:** A total of 1262 patients were given chemotherapy following a diagnosis of breast cancer. Mean age was 59.3 (+/- 11.1) years, there were 2 (0.2%) male

patients. 1039 (82.2%) patients received anthracycline monotherapy (MONO) while the rest were given combination therapy (COMBI) of anthracycline and trastuzumab. 683 (54.1%) patients had undergone baseline cardiac function assessment, all with normal left ventricular (LV) function. However, only 290 (23.0%) patients had follow-up assessments as per guideline recommendation. Of these 290 patients, 32 (11.0%) patients had incident LV dysfunction. 27 (84.3%) were on COMBI and the rest were on MONO.

**Conclusions:** Our observation demonstrates poor compliance to guideline-mandated surveillance of LV function in patients treated with chemotherapy. We also found a significant incidence of LV dysfunction early after initiation of chemotherapy, the vast majority of which were among patients on COMBI therapy. Prompt detection of LV dysfunction in this group is essential as trastuzumab-induced cardiotoxicity has been shown to be reversible, thereby underscoring the importance compliance to surveillance recommendations.

### VALVULAR HEART DISEASE (DIAGNOSIS, MANAGEMENT AND INTERVENTIONAL THERAPIES)

#### P337

##### Comparing one-year change in symptoms in operated versus non-operated patients with severe aortic valve stenosis

The National Union of Public Health in Norway

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**Introduction:** Assessment of symptoms plays a key role in patient evaluation. However, little is known about how symptoms change after aortic valve replacement (AVR), and how they evolve over time in non-operated patients with severe aortic stenosis (SAVS).

**Purpose:** To describe changes in prevalence of symptoms from inclusion to one year after AVR or refusal of intervention in patients with SAVS. **Method:** Of 480 patients with SAVS evaluated for AVR, 389 patients were operated (351 surgical, 38 trans catheter) (OP) and 91 were declined surgery (NON-OP). We collected data on symptoms at inclusion and follow-up using a self-reported questionnaire. We present paired analysis.

**Results:** Operated patients were younger than non-operated (mean 74 vs. 81 years) and a higher proportion were men (59 % vs. 48 %).

**Conclusion:** AVR reduces prevalence of symptoms in patients with SAVS. Patients declined for operation experience an increase in prevalence of dyspnoea, chest pain and dizziness, but a reduction in syncope during one year of observation. Our results advocate AVR in patients with SAVS.

Symptoms at inclusion and at one-year fo

	OP Inclusion	NON-OP Follow-up	p	Inclusion	Follow-up	p
Dyspnoea n (%)	n=282		<0,001	n=45		<0.001
Not the last two weeks	65 (22)	176 (60)		21 (47)	15 (33)	
Not daily	107(37)	75 (26)		7 (16)	10 (22)	
Daily	120 (41)	41 (14)		17 (38)	20 (44)	
Chest pain n (%)	n=282		<0,001	n=43		<0.001
Not the last two weeks	140 (49)	231 (80)		28 (65)	24 (56)	
Not daily	115 (40)	52 (18)		11 (26)	16 (37)	
Daily	33 (12)	5 (2)		4 (9)	3 (7)	
Dizziness n (%)	n =295		<0,001	n=45		0.006
Not the last two weeks	147 (50)	173 (59)		27 (60)	24 (53)	
Not daily	100 (34)	99 (34)		12 (27)	16 (36)	
Daily	48 (16)	23 (8)		6 (13)	5 (11)	
Syncope n (%)	n =297		<0,001	n=45		0.003
Not the last three months	275 (93)	279 (93)		36 (80)	41 (91)	
Not monthly	12 (4)	14 (5)		5 (11)	3 (7)	
Monthly	10 (3)	4 (1)		4 (9)	1 (2)	

#### P338

##### Utility of biomarkers in evaluating the success of percutaneous mitral commissurotomy in patients with severe rheumatismal mitral stenosis

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**Introduction:** Percutaneous mitral commissurotomy (PMC) is the gold standard technique for the management of severe rheumatismal mitral stenosis (MS). We investigated the utility of BNP, NT pro-BNP, MR pro-ANP, CD146 and sST2 in evaluating the success of the PMC procedure.

**Methods:** All 5 biomarkers were measured one day before and one day after the procedure in 43 patients presenting with severe MS (defined as mitral valve area (VA) by planimetry < 0.2cm<sup>2</sup>) and submitted to PMC in 2 large university hospitals in France (CHU Bichat; CHU Jean Minjot, Besancon). Patients were classified as procedural success (VA > 1.5cm<sup>2</sup> or increase in VA > 0.5cm<sup>2</sup>) or failure (VA < 1.5cm<sup>2</sup> or increase in VA < 0.5cm<sup>2</sup>) by echocardiography. The relative decrease in each biomarker between before and after the procedure was compared for each patient using the paired Student t test.

**Results:** In total, 43 patients were included (80% women, average 63.7 years), of whom 30 (70%) were judged to have a successful procedure by echocardiography; 11 (25%) were classed as procedural failure, and 2 (5%) had a major complication (1 mitral insufficiency requiring surgery, 1 tamponade). Among the 30 patients with procedural success, there was a significant decrease in MR pro-ANP (-40 ± 74, p=0.02) and CD146 (-43 ± 105, p=0.03). There was no significant decrease in these same biomarkers among patients classed as procedural failures. There was no significant decrease in BNP, NT pro-BNP or sST2 in patients with either successful or failed procedure.

**Conclusion:** There is a significant decrease in MR pro-ANP and CD146 after successful PMC. The difference is more pronounced in younger patients and in those in sinus rhythm. These two biomarkers could be of use in evaluating the immediate success of PMC.

#### P339

##### Determinants of one-year survival in infective endocarditis

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**Background and purpose:** Infective endocarditis (IE) is a serious condition associated with a significant mortality burden. Our aim was to identify determinants of long term survival in patients with infective endocarditis.

**Material and methods:** This study consisted in a retrospective cohort analyses of a registry base of 173 consecutive patients admitted in a tertiary hospital from July 2011 and July 2014, with the diagnosis of definite or possible IE.

**Results:** The mean follow up time was 12.7 months. During this period the all-cause death rate was 37.6%. From the demographic data studied, sex (males 70.1% vs females 30.6%, p = 0.008) and age (≥ 65 years-old: 51.1% vs <65 years-old: 75.9%, p = 0.001) were predictors of survival. At admission, a higher hemoglobin level and a lower natriuretic peptide value were significantly associated with one-year survival (p = 0.007). Community-acquired IE opposing to health-care associated IE (43.8% vs 73.3%, p < 0.001) was a predictor of survival. The microbiological agent did not have impact on outcome (p > 0.05). Appropriate antibiotics (67.6% vs 14.3%, p < 0.001) and surgical treatment (76.9% vs 40.6%, p < 0.001) during in-hospital stay were also determinants of survival. On the other hand, de novo heart failure and uncontrolled infection were associated with mortality. Independent predictors of one-year survival by multivariate logistic regression modelling were age under 65 years-old (OR 2.4, 95% CI 1.1-5.3, p = 0.025), community-acquired IE (OR 3.4, 95% CI 1.5-7.6, p = 0.003), absence of acute heart failure (OR 4.1, 95% IC 1.8-9.1, p = 0.001) and controlled infection (OR 3.0, 95% CI 1.3-6.5, p = 0.007), as well as surgical treatment (OR, 95% CI 2.0-9.9, p < 0.001).

**Conclusion:** The heterogeneity of this condition justifies the major role of a multimodal diagnostic and therapeutic approach. Therefore, identification of severity predictors is critical to select and reference complicated patients to Endocarditis Team Centres.

#### P340

##### Echocardiographic score, survival and event free-survival after mitral balloon valvuloplasty. follow-up of 25 years.

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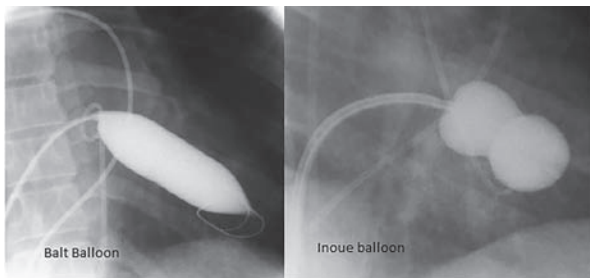
**Introduction:** Percutaneous mitral balloon valvotomy (PMBV) has become an accepted alternative for surgical commissurotomy for the treatment of mitral stenosis.

**Objectives:** To identify the independent predictors of death and combined events (death, new mitral balloon valvotomy, or mitral valve surgery) in long-term follow-up of patients undergoing PMBV.

**Methods:** From 1987 to 2013 a total of 312 patients were followed-up 54.0 ± 31.0 (1 to 126) months. The techniques were the single-balloon (84.4%), Inoue-balloon (13.8%), and double-balloon techniques (1.7%). The total group was divided in two: echocardiographic score > 8 and ≤ 8 points groups. Multivariate Cox regression analysis was performed to identify independent risk factors of long-term survival and event free survival.

**Results:** The mean age were 38.0 ± 12.6 years old (range, 13 to 83). Before the procedure, 84.42% patients had echo score ≤ 8, and 15.57% score > 8. Females comprised 85%, and 84% patients were in sinus rhythm. During follow-up, survival of the total group was 95.5%, echo score group ≤ 8 was 98.0% and echo score > 8 was 82.2% (p < 0.0001), whereas combined event-free survival was 83.4%, 86.1%, and 68.9%, respectively (p < 0.0001). In multivariate analysis, independent risk factors of death were pre procedure echo score > 8 and the presence of severe mitral valve regurgitation during the procedure. The predictors of combined events were a previous history of mitral valvular commissurotomy, atrial fibrillation, the presence of severe mitral valve regurgitation during the procedure and post procedure mitral valve area < 1.5 m<sup>2</sup>.

**Conclusion:** PMBV is an effective procedure. Survival was high, even higher in the group with lower echocardiographic scores. Over 2/3 of the patients were event-free at the end of follow-up. Independent predictors of survival were pre procedure echo score ≤ 8 and the absence of severe mitral valve regurgitation during the procedure.



### P341

#### Tricuspid annuloplasty: a ring or not?

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**Introduction:** Uncorrected tricuspid regurgitation (TR) has serious long-term morbidity and mortality. We reviewed our experience with DeVega tricuspid versus ring tricuspid annuloplasty for treatment of TR.

**Methods:** From 1999 to 2013, clinical and echocardiographic data of patients who underwent Tricuspid annuloplasty were recorded. Pre and postoperative transthoracic echocardiograms were assessed for severity of TR. Moderate or greater TR was considered significant. Development of recurrent TR was evaluated by COX analysis. TR and risk factors for recurrent regurgitation were identified and analysed by multivariable ordinal longitudinal methods.

**Results:** Ninety-one patients underwent tricuspid annuloplasty for TR as part of their cardiac surgical procedure. De-Vega annuloplasty was performed in 46 patients and ring annuloplasty in 45 patients. Preoperatively, all patients had moderate or greater TR with a median regurgitation of 3+. The mean follow-up time was around 3 years. At 3 years postoperatively, TR in patients treated by DeVega annuloplasty was significant in 30.4% of patients. In those undergoing ring annuloplasty, TR was significant in only 13.3%. There was a significant difference between the two groups (p = 0.04). Risk factors for recurrent TR included higher pre and postoperative pulmonary artery systolic pressure.

**Conclusion:** Ring annuloplasty had lower rate of recurrence TR compared with De Vega's suture repair.

### P342

#### The association between hs-CRP, hs-TnT and NT-proBNP, and all-cause mortality in operated versus non-operated patients with severe aortic stenosis.

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**Introduction:** A proper evaluation and risk stratification is important in patients with severe aortic stenosis (SAVS) as operation is associated with improved survival and quality of life, while refusal is associated with high mortality. We investigated whether use of high sensitivity C-reactive protein (hs-CRP), high sensitivity troponin T (hs-TnT) and N-terminal pro brain natriuretic peptide (NT-proBNP) and could be useful in risk stratification in patients with SAVS.

**Purpose:** To examine the prognostic value of hs-CRP, hs-TnT, and NT-proBNP levels in relation to all-cause mortality in patients with SAVS

**Method:** Of 480 patients with SAVS evaluated for AVR, 351 had surgical- and 38 transcatheter-AVR (OP), while 91 were declined operative treatment (NON-OP). On day of operation for OP and day of inclusion in the study for NON-OP, plasma levels of hs-CRP, hs-TnT and NT-proBNP were analyzed by enzyme immunoassay.

**Results:** During a median follow-up of 418 (103) days, 45 (9.4%) patients died. At inclusion, all patients had echocardiographic evidence of SAVS. The strongest conventional predictors of death were AVR (Hazard ratio, HR [95% CI] 0.29 [0.16-0.54] p < 0.001), diabetes (2.53 [1.29-4.96] p = 0.007), NYHA class (1.84 [1.19-2.84] p = 0.006) and LVEF (2.20 [1.11-4.36] p = 0.024). Analyzed separately and adjusting for these covariates in multivariable analysis revealed that hs-CRP (HR 1.38 [1.05-1.80] p = 0.021), NT-proBNP (HR 1.67 [1.16-2.41] p = 0.002) and hs-TnT (HR 1.30 [1.01-1.67] p = 0.042) were independently associated with death. However, NT-proBNP was the only biomarker that remained in the model when all three biomarkers were included in a stepwise approach. When analyzed separately, NT-proBNP gave similar prognostic information in patients who had AVR (HR 2.04 [1.30-3.22] p = 0.002) or not (HR 2.16 [1.30-3.59] p = 0.003) in univariate analysis. None of the 60 patients with all three biomarkers in the normal range (i.e. hs-CRP ≤ 2.0, hs-TnT ≤ 14 and NT-proBNP ≤ 35) died during follow up.

**Conclusion:** Results from this study show that for patients with SAVS, NT-proBNP is associated with all-cause mortality at 14 months in adjusted analysis. High sensitivity CRP or hs-TnT gave no additional prognostic information. This suggest that the level of NT-proBNP should be considered when deciding whether to operate or not in patients with SAVS.

### P343

#### Mitraclip percutaneous mitral valve repair, results in clinically-unstable heart failure patients

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Percutaneous edge-to-edge mitral valve (MV) repair with MitraClip System has become established as an alternative treatment in high surgical risk patients with severe mitral regurgitation (MR), presenting different heart failure (HF) stages. We performed the present study to report the outcomes of Mitraclip implantation in unstable HF patients with severe MR. Twelve HF patients were consecutively treated with Mitraclip (2013–2015) at a hospital without onsite cardiac surgery. Six procedures (50%) performed in clinically-unstable (NYHA IV) patients. Groups (unstable vs stable) were similar in gender and age: men represented 33.3% vs 50% (p = 0.55), with a median age of 63.5 (interquartile range IQR 56.25–71.50) vs 71 years old (IQR 62.5–76.75; p = 0.18). Unstable patients exhibited higher non-significant functional-ischemic MR (83.3% vs 66.7%, p = 0.51) and left ventricular (LV) severe dysfunction (50% vs 33.3%, p = 0.56). LV sizes were similar EDLVD 59 mm (IQR 52.5–67) vs 60 mm (IQR 55–66.5, p = 1). There was no differences regarding MR reduction measured by transesophageal echocardiography (≤ grade 2 MR: 66.7% vs 83.3%, p = 0.5), residual transmitral-gradient (2 mmHg, IQR 2–3.5, vs 3, IQR 2.5–3.5, p = 0.37) or > 1 clip implantation (33.3% vs 66.6%, p = 0.24). One stable patient was reoperated due to early partial-clip-detachment. Post-procedure hospital stay showed no significant difference: 11 days (IQR 7.5–50) vs 7.5 days (IQR 4.75–32.5, p = 0.41). 30-days post-procedure mortality were similar (16.7% vs 0%, p = 0.29) and 30-days NYHA functional class was 100% ≤ II in both groups. Median follow-up was 15.5 months (IQR 3–26) and 11 months (IQR 3–16.75) respectively. Finally, no significant differences were found in all causes death (50% vs 16.6%, p = 0.4), however it tends to be higher in unstable group. In conclusion, Percutaneous MV repair seems to be equally effective and safe in clinically stable and unstable patients, affording hospital discharge for acute-refractory HF patients with severe MR.



## P344

**Functional improvement analysis 1 year after per-cutaneous mitral valve repair**

The study was supported by Valtech Cardio

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**Aim:** The purpose of the study was to describe the changes in exercise tolerance (6MWT) after Cardio-band per-cutaneous mitral annuloplasty and the predictors of improvement.

**Methods:** Between February 2013 and October 2015, 49 patients with functional mitral regurgitation (MR) underwent transfemoral transseptal valve repair with Cardioband system of which 31 patients reached 1 year follow up. All patients had  $\geq$  moderate-severe functional MR at baseline and were considered high risk for surgery. Fourteen matched cases of 6 minute walk distance are available at one year follow up; 8 patients failed to perform the 6MWT at 1 year follow up or baseline, 5 patients died during the first year post procedure (unrelated to the Cardioband device) and 4 patients withdrew from the study.

**Results:** The six minute walking distance increased significantly from  $279 \pm 108$  at baseline, to  $351 \pm 151$  at one year post procedure ( $p < 0.001$ ). Improvement in walking distance was associated with improvement in MR ( $p = 0.04$ ), and stroke volume ( $p = 0.05$ ), but not necessarily with changes in LV size or function. One patient (7%) exhibited worsening and 5 patients (36%) showed no change of distance walked compared to 8 patients (57%) with improved exercise tolerance 1-year after Cardioband implantation. Patients with worsened distance had higher right atrial pressure ( $p = 0.04$ ), and less MR at baseline ( $p = 0.07$ ). Univariate analysis using all clinical, demographic and echo parameters identified only higher right atrial pressure ( $p = 0.03$ ), and less MR at baseline ( $p = 0.02$  for grade,  $p = 0.02$  for regurgitant volume), to be predictive of no improvement in 6-minute walk distance.

**Conclusion:** Most patients undergoing Cardioband per-cutaneous mitral repair show enhanced exercise capacity (assessed by the 6MWT), associated with improved MR and increased stroke volume, extending to at least 1-year after the procedure.

## P345

**Timing and mid-term outcomes for valve replacement in adult patients with pulmonary regurgitation following right ventricular outflow tract reparative surgery - Single center experience**

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**Purpose:** Surgical relief or right ventricular (RV) outflow tract obstruction in patients with tetralogy of Fallot (TOF) or similar physiology often results in pulmonary regurgitation (PR). The resultant chronic volume overload can lead to RV dilation, heart failure symptoms and arrhythmias, prompting pulmonary valve replacement (PVR). Our aim is to characterize the population and assess the mid term outcomes for bioprosthetic pulmonary valve replacement (PVR) in adult patients (P) with a previous corrective surgery resulting in PR.

**Methods and Results:** We retrospectively analysed 41 P ( $39.2 \pm 8.4$  years; 66% male) who underwent bioprosthetic PVR in our centre due to PR. All P had previous RV outflow tract (RVOT) reparative surgery, namely: TOF (33 P), pulmonary stenosis (6 P) and double outlet right ventricle (DORV) with pulmonary atresia (2 P). Mean age at corrective surgery was  $9.2 \pm 8.5$  years; 44% had previous palliative procedures. Within TOF patients, 85% had RVOT reconstructive surgery with transannular patch. Bioprosthetic PVR occurred at a mean age of  $36.4 \pm 8.7$  years with a mean interval between initial reparative surgery and PVR of  $27.2 \pm 5.9$  years. Indication for PVR were symptoms and signs attributable to RV volume overload and/or RV end diastolic volume index (RVEDVI)  $> 150 \text{ mL/m}^2$  on magnetic resonance imaging (MRI). Mean pre-operative MRI parameters for this population were: RVEDVI  $186 \pm 51 \text{ mL/m}^2$ , RV ejection fraction  $44 \pm 9\%$ , PR fraction  $51 \pm 11\%$ , left ventricular ejection fraction  $58 \pm 9\%$ . Bioprosthetic valve type used was CE Perimount Magna in 38 P and St Jude Epic in 3 P, with valve sizes implanted of 25mm ( $n = 33$ ) and 23mm ( $n = 8$ ). Half of the patients had concomitant procedures, mainly RVOT reconstruction or tricuspid valve annuloplasty. Mean cardiopulmonary bypass and aortic cross-clamp times were  $72 \pm 32$  and  $54 \pm 22$  minutes respectively. 15 P (36.5%) performed surgery under beating heart. Perioperative morbidity was low (significant bleeding in 1P, hemothorax in 1P and early RV dysfunction with ventricular arrhythmias in 1P). There was no early or late mortality. Mean post-PVR follow-up time was  $35 \pm 18$  months. Patients experienced significant NYHA functional class improvement (from  $2.05 \pm 0.50$  to  $1.22 \pm 0.42$ ,  $p < 0.001$ ).

Patients were regularly followed with transthoracic echocardiography and there were no signs of valve dysfunction during the follow-up time (maximum pulmonary systolic gradient  $20.9 \pm 9$  mmHg and regurgitation grading below moderate in all patients).

**Conclusions:** In this population of adult patients with pulmonary regurgitation, referral to PVR seems to be adequately timed, avoiding RV function deterioration and enabling functional improvement after surgery. Bioprosthetic valves in pulmonary position have low perioperative morbidity and show excellent mid-term outcomes.

## P346

**The improvement of right ventricular function following percutaneous mitral valve repair using MitraClip system: a two-dimensional speckle-tracking study**

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**Background:** Chronic mitral regurgitation (MR) often results in right ventricular (RV) dysfunction due to long-standing pressure and volume overload. Previous studies showed that concomitant tricuspid regurgitation (TR) and pulmonary hypertension in patients undergoing conventional surgery for mitral valve (MV) increases morbidity and mortality, especially in case of a poor right ventricle. It is widely known that percutaneous mitral valve repair (PMVR) improves left ventricular function, but to what extent this affects the right ventricle, remains the area of current research.

**Aims:** The main objective of present study was to investigate the role of preprocedural right ventricular dysfunction and pre-existing severe pulmonary hypertension assessed by means of two-dimensional echocardiography for patient clinical recovery following PMVR. Moreover, we tried to assess the potential for right ventricular remodeling after volume and pressure overload due to MR has been reversed.

**Methods:** 58 patients (52% women,  $76 \pm 6$  years) with moderate-to-severe mitral regurgitation (MR 2+) undergoing PMVR using the MitraClip system underwent transthoracic echocardiography at baseline and at six-month follow-up. Right heart echocardiographic parameters included RV diameter, RV systolic strain, TAPSE (tricuspid annular plane systolic excursion), tricuspid regurgitation grade and right atrial volume (RA Vol) whereas severe pulmonary hypertension was defined as systolic pulmonary arterial pressure (sPAP)  $> 60 \text{ mmHg}$ .

**Results:** MitraClip implantation resulted in significant improvement of RV systolic strain ( $-15.7 \pm 2.3\%$  vs.  $-19.1 \pm 2.9\%$ ,  $p < 0.001$ ), improved New York Heart Association (NYHA) class ( $3.0 \pm 0.5$  vs.  $2.3 \pm 0.7$ ,  $p < 0.05$ ), diminished RA volumes ( $46 \pm 10 \text{ ml}$  vs.  $38 \pm 10 \text{ ml}$ ,  $p < 0.001$ ) as well as reduced estimated pulmonary pressure (sPAP;  $52.5 \pm 11.5 \text{ mmHg}$  vs.  $42.5 \pm 14.1 \text{ mmHg}$ ,  $p < 0.05$ ). However, no change in TR grade was noted. In the subgroup of patients with pulmonary hypertension (PAH,  $n = 12$  patients) baseline RV systolic strain was lower, yet showed a tendency for improvement ( $-13.7 \pm 2.1\%$  vs.  $-16.1 \pm 2.7\%$ ,  $p < 0.001$ ), accompanied by reduced sPAP ( $68.1 \pm 7.5 \text{ mmHg}$  vs.  $55.7 \pm 7.2 \text{ mmHg}$ ,  $p < 0.05$ ). Most importantly, neither improvement in terms of NYHA class nor significant changes in any of the other RV parameters was observed in patients with severe PAH.

**Conclusions:** Our results confirm that percutaneous MV repair, in contrast to conventional MV surgery, does not negatively affect RV function. Due to the reduction in RV afterload, PMVR alleviates pressure overload thus leading to reduced RA volumes, improved RV contractility and ameliorated patient clinical status. In PAH patients, PMVR reduces sPAP and improves RV systolic function, but adversely affects NYHA functional class. Basing on our results, one might conclude that patients with pre-existing severe PAH exhibit little clinical benefit from the procedure.

## P347

**Effectiveness of transcatheter aortic valve implantation in patients with pure native aortic valve regurgitation**

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There are patients with severe aortic regurgitation and at high or extreme surgical risk for whom conventional surgical aortic valve replacement may be unsuitable and who might benefit from transcatheter-based therapy. The aim this study was to evaluate the use of Transcatheter Aortic Valve Implantation (TAVI) in patients with pure native aortic valve regurgitation and comparing them with patients with aortic stenosis.

**Methods:** From April 2008 to December 2015, the CoreValve prosthesis, was implanted in 13 (2.6%) consecutive high-risk surgical patients with symptomatic severe aortic regurgitation (AR) and in 487 patients with aortic stenosis (AS).

**Results:** The mean age was lower in AR  $71.3 \pm 19$  vs.  $79.3 \pm 6$  years,  $p = 0.001$  and logistic EuroSCORE was similar in both groups (AR vs. AS) and  $16.5 \pm 8\%$  vs.  $17.2 \pm 12$ ,  $p = 0.787$ . There were significant differences in measurement of annulus and ascending aortic size ( $24.2 \pm 1.8$  vs.  $22.1 \pm 1.8 \text{ mm}$ ,  $p = 0.001$  and  $34.1 \pm 4.4$

vs.  $31.6 \pm 4$  mm,  $p=0.034$ , respectively). Implantation of a TAVI was performed successfully in all patients with AR and the post-procedure aortic regurgitation grade was: absent in 30.8%, middle in 30.8%, moderate in 23.1% and moderate-severe in 15.4%. The NYHA functional class improved from  $3.2 \pm 0.6$  to  $1.6 \pm 0.5$  and remained stable at one year. The mortality at 30 days was 7.7% in patients with AR compared to 3.5% in patients with AS,  $p=0.422$  and there was no significant differences with late mortality (16.7% vs. 19.9%,  $p=0.780$ ) after a mean follow-up of  $34.3 \pm 23$  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 38.5% vs. 15.7% [OR=3.35 (95% CI 1.07-10.5),  $p=0.045$ ] and 8.3% vs. 47.4%, [OR=0.101 (95% CI 0.01-0.791)  $p=0.006$ ], respectively.

**Conclusions:** Treatment of high-risk patients with pure native aortic regurgitation using a self-expandable prosthesis is a safe and efficient option in long-term follow-up

## DEVICES / CRT / ICD

### P348

#### Comparison of transcatheter aortic valve implantation versus surgical aortic valve replacement and medical treatment: A systematic review and meta-analysis

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**Introduction:** Transcatheter aortic valve replacement (TAVI) is a promising therapy option for patients with severe aortic stenosis, multiple comorbidities and high risk for surgical aortic valve replacement (SAVR).

**Purpose:** To compare TAVI with SAVR and with medical therapy (MT) by meta-analysis.

**Methods:** A systematic review was conducted by two independent investigators. We carried out literature search using Medline (via PubMed), the Cochrane Library and Embase, and reference lists of identified primary studies. We included articles written in English, German, or Turkish that compared TAVI with other treatment options based on all cause-mortality, and which contained baseline characteristics of Gender, Age and EuroSCORE. Patients without aortic stenosis, healthy subjects and data with less than 30-days follow-up time were excluded. Relative Risk (RR) was calculated and graphically displayed in forest plots. We used  $I^2$  for heterogeneity and determined the source of it by metaregression. Funnel plots were investigated by Egger's regression test of asymmetry.

**Results:** 22 studies, existing of 19 observational studies and three randomized controlled trials, with a total of 6.539 patients were included. Compared with MT, TAVI showed a statistically significant benefit for all-cause mortality at 12 months (RR=0.68, 95% CI 0.49-0.95) and at 24 months (RR=0.75, 95% CI 0.44-1.27). TAVI versus SAVR, overall result on 12 months showed significant advantage for SAVR (RR=1.23, 95% CI 0.95-1.60). To be in contrast with that our subgroup analysis with two randomized controlled trials militated here a minimal better result for TAVI (RR=0.91, 95% CI 0.91-1.14). Long-term outcome between SAVR and TAVI at 2 years presented no significant difference (RR=1.09, 95% CI 1.01-1.17). Mean age showed a substantial influence on long-term survival (OR=7.375, 95% CI 0.78-69.43).

### P349

#### Outcome predictors in ICD patients with ischemic left-ventricular dysfunction

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**Background and objective:** Left ventricular (LV) dysfunction is a strong predictor of prognosis. Apart from the benefits of optimal medical therapy, the importance of implantable cardioverter-defibrillator (ICD) is undeniable. The goal of this study was to recognise prognostic indicators in patients with ischemic cardiomyopathy regarding appropriated therapy (defined as occurrence of ATP or shock triggered by ventricular arrhythmia at first event), hospital readmissions and mortality.

**Material and methods:** We performed a retrospective analysis of patients with LV systolic dysfunction who were submitted to ICD implantation from June 2012 to December 2014. Clinical data was collected and inserted in a registry base.

**Results:** From a total of 112 patients, 62 had a diagnosis of ischemic cardiomyopathy, the majority of those were male (93.5% vs 6.5%,  $p=0.008$ ) and older (mean age  $65.0 \pm 9.6$  vs  $61.1 \pm 10.8$  years,  $p=0.048$ ). At least one cardiovascular risk factor was present in 98.4% of these patients, being hypertension the most frequent (68.9%). Comparing the echocardiographic findings before implantation, there was no significant difference in the LV ejection fraction ( $26.4 \pm 9.5$  vs  $23.9 \pm 8$  %,  $p < 0.05$ ); however, the telediastolic LV diameter was significantly higher ( $66.4 \pm 11.1$  vs  $62.4 \pm 8.4$

mm,  $p=0.042$ ). In the group of patients with ischemic cardiomyopathy, 58.1% had ICD implanted for secondary prevention. The most common first event trigger was ventricular tachycardia (77.3%), and appropriated therapy was delivered in 30.6%. The only predictor of appropriated therapy at the first event was non-sustained ventricular tachycardia (OR 6.1, 95% CI 1.6-24.1,  $p=0.01$ ). During a mean follow up period of  $20.5 \pm 9.2$  months, 24 patients were readmitted to the hospital, 9 deaths occurred, and only 1 case of device-associated infective endocarditis was recorded. The occurrence of ICD shocks was a predictor of both hospital readmission and death.

**Conclusion:** ICD role in preventing sudden cardiac death (SCD) is well established in different groups of patients. Our study highlighted the occurrence of events like episodes of non-sustained ventricular tachycardia as predictors of appropriated therapy. These findings emphasize the importance of rhythm surveillance in patients with ischemic cardiomyopathy and LV systolic dysfunction in order to prevent SCD.

### P350

#### Effect of left ventricular assist device placement on preexisting implantable cardioverter-defibrillator leads

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**Purpose:** The left ventricular assist device (LVAD) is a therapy for patients with end-stage heart failure, many of whom have a preexisting implantable cardioverter-defibrillator (ICD). We investigated whether the implantation of a LVAD affects ICD function.

**Methods:** Patients implanted with a LVAD between December 2003 and April 2015 were studied. Right ventricular (RV), right atrial, and left ventricular lead impedance, sensing, and capture thresholds were recorded before and after LVAD placement and subsequent lead-related interventions were noted. Of the 35 patients receiving a LVAD, data were collected from 28 patients who had preexisting ICDs. Significant pre-post differences were noted for all RV lead parameters: sensing amplitude decreased from  $8.2 \pm 2.1$  to  $4.7 \pm 2.6$  millivolts ( $P < .001$ ); impedance decreased from  $479 \pm 118$  to  $418 \pm 94$  ohms ( $P=.008$ ); and threshold increased from  $4.3 \pm 6.7$  to  $11.0 \pm 16.8$  microjoules ( $P=.021$ ). As a result of alterations in lead parameters, 2 patients required lead revisions and all the patients required ICD testing every 6 months.

**Conclusion:** Differences in ICD lead function were observed after LVAD placement resulting in clinically significant interventions. These data suggest that ICD interrogation be performed post-LVAD placement and that patients be counseled for the potential need for lead revisions and ICD testing when consented for a LVAD

### P351

#### Non-invasive hemodynamic assessment in LVAD patients: validation of a bed-side echocardiographic approach.

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**Introduction:** Non-invasive hemodynamic evaluation of patients with LVAD represents a pivotal tool in order to optimize medical therapy and pump setting and to identify any malfunctions. However, no data exist about the accuracy and reliability of echocardiographic hemodynamic evaluation.

**Purpose:** Aim of the study was to validate a prespecified echocardiographic protocol for the estimation of invasive parameters.

**Methods:** In this pilot observational study we enrolled LVAD (HeartWare) patients who underwent right heart catheterization (RHC) according to clinical judgment. Within 1 hour before the procedure, transthoracic echocardiogram was performed by two independent operators blinded to hemodynamic data. According to an internal protocol, right atrial pressure (RAP) was estimated matching inferior cava vein diameter and collapsing with hepatic vein flow and right E/E', while left atrial pressure (LAP) combining RAP first with inter-atrial septum position (eLAP1) and then with mitral inflow pattern and Tissue Doppler variables (eLAP2). Results We enrolled 12 patients (age  $52.3 \pm 14.3$  years; 11 males; 8 with ischemic cardiomyopathy; all in sinus rhythm at the time of evaluation) between September and December 2015. At RHC mean systemic arterial pressure was  $83.6 \pm 8.1$  mmHg, mean cardiac index  $2.5 \pm 0.3$  l/min/m<sup>2</sup>, mean systolic pulmonary arterial pressure  $44.9 \pm 11.4$  mmHg, mean LAP  $20.6 \pm 8.1$  mmHg, mean RAP  $11.1 \pm 4.5$  mmHg. We found a strong correlation between estimated and invasive RAP ( $r=0.94$ ,  $r^2=0.88$ ,  $p < 0.001$ ) and LAP ( $r=0.96$ ,  $r^2=0.92$ ,  $p < 0.001$ ). The estimation of LAP was mildly improved by Doppler analysis ( $r=0.88$  vs.  $0.96$ ) as the evaluation with only RAP and inter-atrial septum position moderately underestimated LAP (eLAP1 vs. eLAP2,  $11.9 \pm 5.9$  vs  $17.2 \pm 5.6$  mmHg,  $p=0.08$ ).

**Conclusion:** In this pilot observational study we validated a simple bed-side non-invasive protocol for the estimation of RAP and LAP in LVAD patients.

**P352**

**The role of left ventricular assist device therapy for patients with end-stage heart failure - serbian experience**

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**Background:** Heart transplantation (HTx) is a realistic option for only a small number of end-stage heart failure (HF) patients. Due to organ donor shortage and a growing number of HTx ineligible patients, left ventricular assist device (LVAD) has become a more beneficial option.

**Purpose:** The goal of this study was to report our single-center experience concerning the treatment of patients with advanced HF with LVAD support.

**Methods:** Overall, 38 patients received long-term LVAD from 2013 to 2015; 7,9 % underwent HTx after a median duration of LVAD support of 13 months. The majority of subjects were male gender (94,7%). The most frequent etiology of the HF was ischemic cardiomyopathy (52,6%). Regarding the INTERMACS profile, the 52,6% of patients were profile 4, and 26,3% profile 2. The median follow up for consequent outcomes (overall survival and adverse events) was 7 (23) months.

**Results:** The mean age of patients was 50,24 ± 14,6. Median duration of LVAD support was 7 (23) months. The overall 30 day, 6-months and 1-year survival were 91,2%, 88,5% and 76,2%. Any kind of adverse events were present in 20 (52,6%). Serum creatinine, blood urea nitrogen, total bilirubin, infection and renal failure were associated with a significant decrease of overall survival rate in the Univariate Cox regression analysis (p<0,05), and renal failure was found to be an independent risk factor for the overall survival in multivariate Cox regression analysis (p=0,035).

**Conclusion:** LVAD is associated with acceptable mortality rate, similar to heart transplant. It represents an effective treatment option for patients with end-stage HF. Renal failure is common following LVAD implantation and is an independent risk factor for overall survival. The resolution of optimal timing of LVAD implantation will contribute in better survival rate.

**P353**

**Can a preoperative management checklist improve outcome after LVAD implantation?**

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**Background:** Left ventricle assist device (LVAD) is a reliable and effective treatment in selected patients with advanced heart failure. Adequate candidate preparation is mandatory.

**Purpose:** To evaluate the impact on short-term outcome of a checklist (CL)-guided pre-operative management of candidate patients to LVAD implantation.

**Methods:** Since July 2013 we conceived and implemented a pre-operative CL-guided approach for LVAD candidates (a brief version of CL is shown in Figure 1). The CL focuses on accurate evaluation of post-implantation thrombotic and hemorrhagic risk, research and treatment of silent infections, assessment and improvement of psychological and nutritional status, appraisal of arrhythmias impact on LVAD and right ventricular (RV) function, achievement of optimal hemodynamic (decongestion, LV download, reduction of end-organ damage, sildenafil for out-of-proportion pulmonary hypertension and pre-operative levosimendan). This overall evaluation is divided into 3 stages (once LVAD implantation is indicated, 7 days and 48 hours before LVAD implantation). We prospectively enrolled consecutive LVAD candidates who underwent CL-guided management and compared their short-term events (survival, stroke, bleeding, infections, RV failure) with patients implanted before CL implementation.

**Results:** We enrolled 25 patients in the CL-guided approach. 5 patients (20.8%) did not undergo LVAD implantation after the overall evaluation (3 for high bleeding risk, 1 for cancer, 1 for psychosocial issues). 20 patients underwent CL-guided LVAD implantation (all continuous-flow devices) were compared to 39 patients implanted before CL implementation. At 1 year after LVAD implantation, 19/20 CL-patients survived vs. 30/39 non-CL patients (HR 0.19, p=0.08), while stroke occurred in 4/20 CL patients vs. 7/39 non-CL patients (HR 0.68, p=0.58), bleeding 2/20 vs 7/39 (HR 0.5, p=0.18), infection in 7/20 vs. 19/39 (HR 0.41, p=0.04), RV failure in 4/20 vs. 3/39 (HR 1.82, p=0.42).

**Conclusion:** A CL-guided management of LVAD candidates improved both short term survival after LVAD implantation. This result may be driven by a more accurate selection of patients and a more comprehensive pre-operative management.

Brief LVAD preparation check list			
<i>(1 time when LVAD team gives indication to work up as LVAD)</i>			
✓ Infections			
Sub-items	Yes	No	
1. Creatinin	<input type="checkbox"/>	<input type="checkbox"/>	
2. Culture swabs	<input type="checkbox"/>	<input type="checkbox"/>	
3. Creatinin > 1.8 mg/dl	<input type="checkbox"/>	<input type="checkbox"/>	
4. CVC/PICC	<input type="checkbox"/>	<input type="checkbox"/>	
5. Depression	<input type="checkbox"/>	<input type="checkbox"/>	
Problems			
<input type="checkbox"/> renal wash (if Arterio)			
<input type="checkbox"/> renal wash (if Venous)			
<input type="checkbox"/> renal culture			
<input type="checkbox"/> captopril			
<input type="checkbox"/> cardiology tests			
<input type="checkbox"/> orthopneumography			
✓ Thrombotic profile	Yes	No	
1. History of stroke/TIA	<input type="checkbox"/>	<input type="checkbox"/>	
2. History of possibly likely HIT	<input type="checkbox"/>	<input type="checkbox"/>	
3. Thrombophilia screening	<input type="checkbox"/>	<input type="checkbox"/>	
4. Current anticoagp	<input type="checkbox"/>	<input type="checkbox"/>	
✓ Bleeding profile	Yes	No	
Sub-items			
1. Haemostasis > 31%	<input type="checkbox"/>	<input type="checkbox"/>	
2. Age > 65 years	<input type="checkbox"/>	<input type="checkbox"/>	
3. Previous bleeding	<input type="checkbox"/>	<input type="checkbox"/>	
4. Cholest	<input type="checkbox"/>	<input type="checkbox"/>	
5. Female gender	<input type="checkbox"/>	<input type="checkbox"/>	
6. Low body weight	<input type="checkbox"/>	<input type="checkbox"/>	
7. Syncope falls with head trauma	<input type="checkbox"/>	<input type="checkbox"/>	
✓ Physiotherapy	Yes	No	
✓ Psychological evaluation	<input type="checkbox"/>	<input type="checkbox"/>	
✓ Nutrition profile			
1. Total cholesterol	<input type="checkbox"/>	<input type="checkbox"/>	
2. Pre-Albumin	<input type="checkbox"/>	<input type="checkbox"/>	
3. Albumin	<input type="checkbox"/>	<input type="checkbox"/>	
4. Mini Nutritional Assessment	<input type="checkbox"/>	<input type="checkbox"/>	
✓ Arrhythmic profile			
1. Preoperative atrial fibrillation	<input type="checkbox"/>	<input type="checkbox"/>	
2. Atrial Fibrile	<input type="checkbox"/>	<input type="checkbox"/>	
3. ICD/CRT shock	<input type="checkbox"/>	<input type="checkbox"/>	
<i>2 days before surgery:</i>			
✓ Sildenafil	Yes	No	
1. Transcatheter gradient < 12	<input type="checkbox"/>	<input type="checkbox"/>	
2. Pulmonary systemic gradient > 7	<input type="checkbox"/>	<input type="checkbox"/>	
✓ Neurocognitive test	<input type="checkbox"/>	<input type="checkbox"/>	
<i>48 hours before surgery:</i>			
✓ End-organ damage resolution	Yes	No	
1. Troponin < 1.2 ng/dl	<input type="checkbox"/>	<input type="checkbox"/>	
2. Ammonia < 130 µg/dl	<input type="checkbox"/>	<input type="checkbox"/>	
✓ RV focused Echocardiography			
1. tricuspid annulus < 42 mm	<input type="checkbox"/>	<input type="checkbox"/>	
2. tricuspid regurgitation < 3+4	<input type="checkbox"/>	<input type="checkbox"/>	
3. RVCFI > 60 mm/s/sq/m2	<input type="checkbox"/>	<input type="checkbox"/>	
4. sEAP < 11 mmHg	<input type="checkbox"/>	<input type="checkbox"/>	
✓ Targeted lung ultrasound			
1. Pleural effusion less than moderate	<input type="checkbox"/>	<input type="checkbox"/>	
2. B lines	<input type="checkbox"/>	<input type="checkbox"/>	
✓ Chest X-Ray	<input type="checkbox"/>	<input type="checkbox"/>	
✓ Pre-operative Levosimendan	<input type="checkbox"/>	<input type="checkbox"/>	

Brief LVAD Preparation Checklist

**P354**

**Veno-arterial ECMO in terminal cardiogenic shock; lactate role as prognostic factor**

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**Introduction:** terminal cardiogenic shock is characterized by severe hemodynamic instability with high mortality rate (>70-80%). In most critical patients, unresponsive to inotropic agents and intra-aortic balloon pump (IABP), extracorporeal membrane oxygenation (ECMO) is the only therapy available nowadays that gives a possibility to survive because it guarantees continuous organs perfusion waiting for cardiac function recovery, left ventricular assist device or transplantation.

**Purpose:** a) improve outcome in terminal cardiogenic shock; b) find prognostic factors.

**Methods:** from 1st January 2009 to 30th April 2015 we prospectively analyzed patients admitted for acute heart failure in cardiac intensive care unit who developed terminal cardiogenic shock which required veno-arterial ECMO.

**Results:** 52 patients affected by myocardial infarction (30%), ventricular malignant arrhythmias (29%), dilated cardiomyopathy (25%), myocarditis (12%), pulmonary embolism (4%). 72% male gender, median age 57. Duration of ECMO support: 10 ± 9 days. Outcome: 14 patients (27%) died during ECMO because of multi organ failure, sepsis and bleeding; recovery: 13 patients (25%); bridge to ventricular assist device as destination therapy: 15 patients (29%); bridge to heart transplantation: 10 patients (19%). 12/38 patients died during hospitalization after ECMO removal; 26/52 (50%) were discharged with one year overall survival of 88%.

About prognostic factors, applying binary logistic regression model we found that serum lactate's level was the most important one with a mean peak value equal to 3.1 mmol/L. Serum peak value over than 5.2 mmol/L during ECMO support predicted in ECMO mortality with an area under the curve (AUC) of 0.9236 and a p value < 0.001; combination between Sequential Organ Failure Assessment (SOFA) score and peak lactate's level during ECMO support over than 2.9 mmol/L predicted in hospital mortality with an AUC of 0.8426 and a p value of 0.003.

**Conclusions:** a) ECMO allowed us to reduce in hospital mortality with an optimal percentage of survival after discharge; b) in literature different scores have been proposed to predict cardiogenic shock mortality as SOFA, APACHE (Acute Physiology and Chronic Health Evaluation) and SAVE (Survival After Veno-arterial ECMO). Applying serial dosage of serum lactate in addition to these scores we obtained better results in predicting outcome.



## P355

**Early postoperative outcomes in patients undergoing heart transplantation with pulsatile ventricular assist device as bridge to transplantation**

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**Introduction:** Heart transplantation (HTx) has been the treatment of choice for patients with advanced heart failure for the last three decades. However, the scarcity of organ donors fails to meet the demands of an increasing waiting list. To alleviate this burden ventricular assist devices (VADs) have emerged for support as a bridge to transplantation (BTT) and destination therapy (DT). Patients with VADs who undergo HTx have operative conditions that differ from patients without VAD. Although they have better end-organ function and nutritional status, risks such as bleeding, infection and surgical times may be higher.

**Purpose:** To describe the immediate postoperative outcomes of patients who undergo HTx with pulsatile LVAD compared to those without VAD.

**Methods:** Patients with advanced heart failure who underwent HTx between 2009 and 2015 were retrospectively evaluated. Patient characteristics and perioperative variables up to the time of discharge were compared between patients who had received HTx with pulsatile VAD support and those without VAD.

**Results:** 16 patients underwent HTx with previous VAD implantation vs 53 without VAD during the study period. All 16 patients with VAD and 33 (62%) without VAD were male. Age at the time of HTx in patients with VAD was 45 years (+/- 12.6) and 52 (+/- 11.5) in patients without VAD. Mean duration of VAD support was 137 days (+/- 79). Cardiopulmonary bypass time was on average 133 (70-215) minutes in patients without VAD vs 196 (74-360) with VAD (p = 0.145); median ICU stay was 4 (1-90 days) days in patients without VAD and 3 (1-26) days with VAD (p = 0.024), initial intubation lasted a mean of 8.5 days (0.25-54) in patients with VAD vs 4 (0.25-62) days in patients without VAD (p = 0.5). Patients with VAD received a mean of 15 RBC units vs 6.7 units in those without VAD (p = 0.145), 5.9 platelets apheresis units vs 2.4 (p = 0.002) and 27 fresh frozen plasma vs 7.2 U (P = 0.001). Rate of infection identified by procalcitonin levels > 2 mcg/L were observed in 8 (66.7%) patients with VAD vs 21 (42%) without VAD (p = 0.197); 5 (9.4%) patients without VAD had stroke vs none of the patients with VAD (p = 0.58); cellular allograft rejection occurred in 3 (18.7%) patients with VAD and in 15 (28.3%) patients without VAD (p = 1.0). Three patients (18.7%) with VAD died in the immediate postoperative period vs 16 (28%) without VAD (p = 0.533).

**Conclusions:** Patients who undergo pulsatile VAD implantation as bridge for heart transplantation have similar outcomes during the early posttransplant period compared to patients without VAD, though they receive more blood products to reverse anticoagulation and have a slightly shorter ICU stay.

## P356

**Copeptin in heart failure, post left ventricular assist device and post heart transplantation**

Swedish Research Council, the Swedish Heart Lung Foundation and the Stockholm County Council

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**Background:** Heart failure (HF) is associated with pathological activation of arginine vasopressin, measured in plasma by the pre-hormone fragment copeptin.

**Purpose:** To test the hypothesized that copeptin is elevated and associated with worse prognosis in HF, and that left ventricular assist device (LVAD) therapy and heart transplantation (HTx) are associated with lower levels in copeptin.

**Methods:** We measured copeptin in groups of 49 patients with advanced HF, 13 patients one year post-LVAD and 22 patients one year post-HTx and correlated with clinical data and cardiac output. In HF we assessed the prognostic role of copeptin with Kaplan-Meier analysis and multivariate Cox regression.

**Results:** In HF, median (interquartile range) copeptin was 28 (18-45) pmol/L, after LVAD 16 (6-27) pmol/L, and after HTx 12 (5-20) pmol/L (p overall < 0.001). In HF, copeptin was an independent predictor of death, LVAD or HTx (hazard ratio for log copeptin, 3.28 [95% confidence interval: 1.66-6.50], p = 0.001). Conclusions Copeptin was elevated in and independently predicted prognosis in HF. Copeptin was progressively lower after LVAD and HTx. This suggests that improvement in cardiac output with LVAD and HTx may induce progressively reduced activation of vasopressin, which may be a marker for the beneficial effects of LVAD and HTx.

## P357

**Clinical experience in advanced HF patients implanted with an extra-aortic counterpulsation device (EACD)**

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**Background:** Despite optimal medical and device therapy, patients with NYHA Class III/ambulatory IV HF experience high rates of morbidity and mortality. Due to the progressive nature of the disease, patients remain symptomatic requiring hospitalization, transplantation or LVAD thereby placing a significant burden on hospital resource utilization. A novel approach is the use of a para-aortic counterpulsation device (EACD), consisting of an extra-vascular cuff implanted on the ascending aorta. EACD operates on principle of counterpulsation to enhance myocardial perfusion and reduce cardiac afterload, and previous results demonstrate these may potentially be mediated through neuromodulatory mechanisms.

**Methods:** Data reported were collected following a specified protocol from a European multi-center, post-market study designed to observe the clinical outcomes of heart failure patients treated with EACD.

**Results:** EACD system implant occurred in 15 patients. EACD significantly improved QOL, 6 min Walk Distance and LV ejection fraction (Table 1). A non-significant trend was observed in pulse pressure and end-systolic volume. No patients experienced stroke or sepsis. Infection rate was 13.3% (2/15) for the entire cohort. Treatment effects were assessed by repeated-measures statistics.

**Conclusions:** In this cohort of patients with advanced HF, EACD demonstrated improvements in quality of life, functional capacity and cardiac remodeling with a favorable safety profile. Changes observed in the end-systolic volume have been shown to correlate with improved outcomes from several large trials. The modular design and non-obligatory features of the device will facilitate future studies to assess the potential for weaning from therapy.

Table 1

Parameter	N	Baseline	Δ6 Months	Δ12 Months
NYHA Class	6	3 ± 0.17	-0.93 ± 0.18†	-.74 ± 0.2†
QOL (KCCQ score)	6	30 ± 5	+26 ± 7†	+12 ± 8
6 min Walk Distance (m)	12	237 ± 31	+79 ± 34*	+101 ± 41*
Pulse Pressure (mmHg)	9	39 ± 4	+7 ± 5	+9 ± 7
LV End-Systolic Volume (mL)	4	152 ± 18	-43 ± 21(p=.08)	-51 ± 25 (p=.08)
LV End-Diastolic Volume (mL)	4	198 ± 23	-30 ± 31	-30 ± 36
LV Ejection Fraction (%)	4	22 ± 3	+10 ± 4*	+20 ± 5†

Baseline: Mean ± SE; Changes: Mean ± SE; \*p < 0.05; †p < 0.01

## P358

**Right - left ventricular interdependence in patients supported by extracorporeal life support: an echocardiographic study**

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**Background:** Right - Left ventricular interdependence may occur in severe heart failure. This dependence (Dep+) can be defined as an abnormal decrease of the left ventricular dimensions in the presence of a right ventricular dilatation induced by an increased preload. In cardiogenic shock patients (pts) supported by Extracorporeal Life Support (ECLS), weaning tests (wt) with decrease of the pump output induce severe pre- and post-load manipulations during which some pts could appear as Dep+.

**Aims:** To detect the presence of Dep+ pts in a cohort of pts supported by ECLS and to assess its prognostic value, and its echographic correlates. Methods. 33 pts were assessed by echocardiography at D1 (The first day following ECLS implantation) and at DL (The last day before death, heart transplantation or weaning). Weaning success from VA-ECMO was defined as device removal and no further requirement for mechanical support because of recurring cardiogenic shock over the following 30 days. We recorded at each level of support during wt: Left and right ventricular

volumes, Aortic ITV, E mitral flow velocity, Tissue Doppler (Ea and Sa, lateral (L) and Septal (S)).

**Results:** At D1, 14 pts were Dep+ and 19 Dep-. At D1, the number of post-cardiotomy was similar in the 2 groups. During wt, Dep- pts increased left ventricular volume of 28ml (+/- 26) on D1 ( $p < 0.05$ ) and 31ml (+/-14) on DL whereas Dep+ pts decreased left ventricular volume of 13 ml (+/- 9) on D1 and 27 +/- 21ml on DL ( $p < 0.05$ ). On D1, Dep+ pts and Dep- pts had similar ventricular volumes and LVEF. On DL, Dep+ pts had lower LVEF 14% +/-12 vs 30 +/- 14 ( $p = 0.001$ ), lower longitudinal velocities: Sa S=4.4cm/s +/- 1.2 vs 5.5 +/- 1.4 ( $p = 0.017$ ) and lower Aortic ITV 6.3cm +/- 3 vs 11 +/- 5 ( $p = 0.03$ ). On DL, aortic ITV increased significantly during wt in case of Dep- ( $p = 0.04$ ). At DL, among Dep+ pts, 12 remained Dep+ and none was weaned. The 2/14 Dep+ pts which became Dep-, were weaned. Among the 19 pts who were initially Dep-, 14 remained Dep- and were weaned. 4 Dep- pts became Dep+ and were not weaned. X2 Dep vs weaning:  $p < 0.05$ .

**Conclusion:** Right - Left ventricular interdependence is frequent in cardiogenic shock patients assisted by ECLS. It seems to have a strong negative prognostic value which could be helpful to predict weaning from ECLS.

### P359

#### Patient engagement with a novel e-counselling program for heart failure predicts therapeutic change in self-care and quality of life outcomes

Canadian Institutes for Health Research; Peter Munk Cardiac Centre Innovation Fund

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**Background:** A major challenge for e-health programs for heart failure (HF) is to sustain patient engagement to improve therapeutic outcome. Our aim was to identify prototypical patterns of patient engagement with a multifunctional e-platform that proactively sent links over 16 weeks to connect patients with our e-counseling program. We evaluated the dose-response relationship between patient engagement and HF outcomes for self-care and quality of life. **Method:** We used a k-means partitioning algorithm to evaluate patient engagement (cumulative % e-pages accessed) over 16 weeks for 77 patients with NYHA HF Class I-III. Between- and within-cluster covariance was optimized using the Calinski and Harabatz criterion. Statistical differences between Clusters over time were assessed with spline models. Baseline differences between patient Clusters were examined for demographic and medical features, self-care (6-minute walk test, 6MWT; 4-day step count; Diet History Questionnaire, DHQ, for daily fruit and vegetable intake), stress (Perceived Stress Scale, PSS) and quality of life (Kansas City Cardiomyopathy Questionnaire, KCCQ). The independent dose-response relationship between patient engagement and self-care and quality of life was evaluated with multilinear regression.

**Results:** Four clusters of patient engagement were identified:  $p < 0.001$ . For Group 1 (Optimal Engagement,  $n = 24$ ), e-pages were accessed weekly, with engagement above 80% at week 16. In Group 2 (Suboptimal Engagement,  $n = 19$ ) access to e-pages was stable and above 50% at week 16. Group 3 (Disengagement,  $n = 14$ ) failed to respond to the proactive links to our e-platform, and less than 10% of e-pages were accessed at week 16. Group 4 (Habituation,  $n = 15$ ) decreased progressively in engagement with less than 20% of e-pages accessed at week 16. Groups did not differ by sex, age or NYHA Class. Weeks 3, 9 and 12 were critical time-points where trajectories for patient Clusters differed significantly ( $p < 0.01$  for each comparison). Cumulative % e-pages accessed over 16 weeks was independently associated with improved KCCQ ( $p = 0.01$ ; dose response,  $\beta = 12.6$ , 95%CI, 2, 22), 4-day step count ( $p = 0.03$ ), 6MWT ( $p = 0.01$ ), and PSS ( $p = 0.03$ ), but not DHQ fruit and vegetable intake ( $p = 0.7$ ).

**Conclusion:** Our findings indicate that it is feasible for HF e-counselling programs to (i) monitor patient engagement over time, (ii) identify critical time points in patient response, and (iii) specify the dose-response relationship for outcomes. This information can guide tailoring of program content or incentives to optimize outcomes.

### P360

#### Telemonitoring and teleconsultation in the management of patients with chronic heart failure or chronic obstructive pulmonary disease (progetto Telescopico)

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**Introduction:** A system of tele-monitoring, tele-consultation, and telecare for patients with chronic heart failure (CHF), which allows a continuous interaction between general practitioners (GPs) and hospital cardiologists in the urban area of Bari (Apulia, Italy) has been implemented.

**Methods:** The project aims to enroll 200 GPs' outpatients with at least one hospitalization for HF in the last year and a NYHA class II/III; all the patients will be followed for one year using an integrated protocol hospital-GP. The study network includes 6 groups of associated GPs and 5 hospitals. All patients will be evaluated at baseline by a cardiologist (blood pressure, ECG, echocardiogram, therapy, quality of life questionnaire), at one month by remote assessment with ECG, every three months by remote assessment and laboratory tests, and finally at 12 months.

The telemedicine system consists of central hospital stations and stations located at the GPs' office permanently interconnected through physical or virtual server (cloud). Direct video communication between multiple locations is also possible by microphone and integrated HD camera (video calls can also be made by mobile devices such as notebooks, smartphones, tablets).

Every GP's unit allows to perform a 5-lead ECG, to monitor vital signs (heart rate, blood pressure, oxygen saturation, respiratory rate (data can be viewed on the high resolution TFT display), to deliver oxygen therapy, or vacuum aspiration, to forward a request for assistance from the central control, to display graphics trends for at least 72 hours.

Central units allows the cardiologist to visualize in real-time waveforms and vital signs recorded by GP's units, to receive video-communications and alerts from any peripheral unit connected, to access clinical data, structured in the form of medical records, and to export data for further analysis and statistical evaluation.

**Results:** In 6 months 65 patients have been enrolled (41 males, mean age 70 years, 67% with ischemic heart disease, 19% with hypertensive cardiopathy, 14% with valvular heart disease; 65% with NYHA Class II, 45% with NYHA class III, 79% with preserved ejection fraction 21%. with systolic dysfunction, with one hospitalization in the previous year in 73% of cases, two in 21%, >3 in 6%.

ACE inhibitors were used in 36% of patients, spironolactone in 16%, beta-blockers in 50%, diuretics in 62%; 43% of patients had chronic obstructive pulmonary disease, 20% renal failure, 20% diabetes, 38% dyslipidemia, 12% were hypertensive. Complete follow-up at three months it is available for the first 20 patients; none of them was hospitalized.

**Conclusions:** The implementation of an integrated model of telemedicine applied to the follow-up of patients with CHF, strictly linking cardiologists, GP and patient, was feasible and reliable. In a preliminary evaluation, the number of hospitalizations seems extremely low; patient's satisfaction was excellent.

### P361

#### Implementation of telemonitoring with daily measurements of the pulmonary artery pressure (PAP) in advanced systolic heart failure: first experience with the PAP-sensor

Unrestricted research grant from St. Jude Medical

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Patients with advanced heart failure suffer from frequent hospitalizations. Non-invasive hemodynamic telemonitoring using daily measurement of pulmonary artery pressures (PAP) has been shown to reduce hospitalizations. We report on the first 13 patients, in whom a pulmonary pressure sensor was implanted in our Heart Failure Center.

**Methods:** Patients in NYHA class III with documented prior cardiac decompensation received the PAP-sensor via right heart catheterization.

**Results:** Implanted patients were  $69 \pm 8$  years old and suffered from systolic heart failure (LVEF  $26 \pm 9$  %, cardiac index  $2.1 \pm 0.5$ ). In a total of 2606 active telemonitoring days, there were 284 telephone calls to the patients with a modification of therapy. Through intensive telemonitoring-guided therapy adjustments (mean follow-up  $6.7 \pm 4.0$  months), PAP was significantly reduced in 8 of 13 patients (delta PAPsys  $-7 \pm 5$ , delta PAPmean  $-7 \pm 4$ , delta PAPd  $-6 \pm 2$ ,  $p < 0.05$ ). No patient died and there was one hospitalization for cardiac decompensation.

**Conclusion:** The implantation of the PAP-sensor is a safe procedure in severe heart failure patients. PA-pressure telemonitoring-guided therapy is associated with significant reductions in PA-pressure over time. Taking into account the high number of telemonitoring alert-triggered telephone contacts, a reimbursement within the respective health care systems is essential for implementation of hemodynamic telemonitoring.

### P362

#### Telemonitoring favours health-related quality of life in patients with chronic heart failure: a randomised controlled longitudinal study

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**Background:** Chronic heart failure (CHF) is one of the major threats to public health worldwide. CHF patients are often hospitalized and face adverse prognosis. Telemonitoring of CHF patients seems promising and adds great benefits in health-related quality of life (HRQoL).

**Purpose:** To investigate the effects of a telemonitoring intervention in CHF patients through wireless devices following training in their use by a nurse, on HRQoL after a one year follow-up period.

**Methods:** A case-control interventional longitudinal survey design was selected. Study population consisted of 60 CHF patients of NYHA class II-IV, at the outpatients Heart Failure Clinic of a tertiary University Hospital. Data were processed and analyzed with a software package from Quality Metric Inc and the Statistical Package for Social Sciences (SPSS) v.22. Following examination of data and according to findings, Pearson's r and Spearman's rs were used to examine variables' correlations, t-test and Mann-Whitney test were used to compare two independent groups, paired t-test and Wilcoxon Signed-Rank test were used to compare a group in two separate time points, ANOVA test and Kruskal-Wallis test were used to compare more than two independent groups.

**Results:** At baseline, there was no difference between the two groups with regard to MLHF and SF36v2 scores. At 12 months, control group's scores in MLHF questionnaire deteriorated while scores in intervention group improved. Control group's scores in SF36v2 deteriorated in 5 subscales (PF, RP, VT, SF, RE) and 2 dimensions (PCS, MCS) and improved in three (BP, GH, MH). Intervention group's scores in SF36v2 improved in all subscales and dimensions. Between the two groups there was a statistically significant difference favoring the intervention group in 5 subscales (PF; p = 0.030, BP; p = 0.048, GH; p = 0.029, SF; p = 0.036, MH; p = 0.014, 1-sided) and one dimension (PCS; p = 0.046, 1-sided).

**Conclusions:** The present study showed that telemonitoring of CHF patients can contribute towards improving HRQoL, after one year of use. The findings suggest that the addition of such a method in current practice may have a favorable effect and accentuates nurses' involvement in planning and materializing implementations to holistically and effectively manage this patient population.

### P363

#### Evaluation of the effect of cardiac resynchronization therapy on left ventricular function in patients with chronic heart failure

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**Background:** Heart failure (HF) is a complex clinical syndrome that results from any structural or functional impairment of ventricular filling or ejection of blood. Cardiac resynchronization therapy (CRT) is associated with significant clinical improvement in patients who have advanced heart failure and left bundle branch block (LBBB). Echocardiography plays an important role in the assessment and follow-up of heart failure patients treated with cardiac resynchronization therapy.

**Purpose:** The current study was done in order to evaluate the effect of cardiac resynchronization therapy on left ventricular systolic function using echocardiography and tissue Doppler imaging (TDI).

**Methods:** 30 patients who were considered candidates for CRT according to the current guidelines were included. Echocardiographic examination, TDI, quality of life and NYHA functional class were assessed in all patients. Echocardiographic examination included the measurement of end systolic and end diastolic dimensions, ejection fraction (EF) and degree of mitral regurg. TDI included the measurement of peak systolic velocity, time to peak systole, isovolumetric contraction time, isovolumetric relaxation time and the calculation of myocardial performance index in the interventricular septum, lateral wall, anterior wall and inferior wall as well as the basal septum of the right ventricular free wall.

**Results:** The study demonstrated that, there was statistical significant improvement after CRT regarding EF, stroke volume, end systolic diameter, degree of mitral regurg, isovolumetric relaxation time, myocardial performance index, septal to lateral delay and the interventricular mechanical delay. Moreover, there was statistically significant correlation between the baseline standard deviation of the time to peak systole in all segments and the improvement of EF and between the acute and chronic changes in the EF. Our study also showed significant improvement in the quality of life and NYHA functional class after CRT.

**Conclusions:** CRT is an effective procedure for treatment of moderate to severe heart failure. CRT improves left ventricular systolic function and quality of life in HF patients with left ventricular systolic dysfunction and LBBB. Acute effects of CRT on EF can predict long-term effects on the EF. Baseline systolic dyssynchrony can predict improvement of EF after CRT.

### P364

#### Mitral valve coaptation depth as an independent predictor of response to CRT

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**Purpose:** to assess echocardiographic predictors of response to CRT in patients with chronic heart failure (CHF).

**Materials and methods:** We performed retrospective analysis of 120 clinical cases of patients with CHF after CRT implantation. All patients were divided into 2 groups: responders and nonresponders. The main selection criteria were: heart failure, II-IV NYHA functional class, left ventricular ejection fraction <35%, LBBB with QRS duration > 120 ms. All echocardiographic parameters were assessed according to ASE guidelines. Statistical analysis was performed using Poisson regression.

**Results:** Both groups were similar in gender characteristics (=0,3), age (=0,6), presence of atrial fibrillation (0,008), volumetric characteristics of the heart, ejection fraction, severity of mitral regurgitation (p>0,05). Significant differences of mitral valve leaflet coaptation depths were revealed (p≤0,001). Poisson regression analysis showed that increase of coaptation depth is a significant risk factor that affects response to CRT OR = 0,2; CI [0,091; 0,52] (p≤0,001).

**Conclusions:** 1) Mitral valve leaflet coaptation depth in patients with mitral regurgitation is a significant predictor of response to CRT. 2) CRT implantation in patients with mitral valve leaflet coaptation depth more than 11 mm does not lead to mitral regurgitation regression. This cohort of patients needs prior surgical reconstruction.

### P365

#### The old dilemma revisited: which patient will more likely respond to cardiac resynchronisation therapy? Retrospective identification of the baseline factors influencing short and long term outcome.

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Cardiac resynchronization therapy (CRT) is a mainstay for patients (pts) with advanced heart failure, although in up to 30% of subjects mechanical dyssynchrony does not improve despite this intervention. Several studies have evaluated the baseline echocardiographic and clinical factors more likely to influence response to CRT. **Aims & Methods:** We aimed to assess the efficacy of CRT in a population of pts treated at our institution between 01/2008 and 12/2009. We retrospectively evaluated which baseline clinical characteristics of the pts were highly linked to 5-year outcome.

**Results:** 99 pts received CRT (6 females, mean age 69.3±8.1years). From an echocardiographic point of view (reduction in left ventricular end systolic volume ≥15%), 72 pts (72.7%) responded to treatment, whereas 27 pts (27.3%) did not. Twelve additional pts were clinically non-responder despite good echocardiographic results, since they experienced at least one of the followings: death or hospitalization for heart failure, episodic need for intravenous diuretic or inotropes, increased dosage of home diuretic, worsening of NYHA class, enduring wide QRS. Thus far, the total number of non responder was 39 (27+12), with 60 responder. At 5 years follow up, 19 pts had died: 11 non-responder (15.3%) and 8 responder (11.1%). Mortality was mainly cardiovascular (14 pts, 73.7%). Other causes of death were sepsis (1 patient), pneumonia (2 pts), and malignant tumours (2 pts). Ten pts showed significant clinical improvement, with a marked overall benefit in terms of end systolic volume (reduction greater than 30%), ejection fraction, NYHA class, and pharmacological therapy. They were considered super responder. At the covariate analysis, outcome was significantly (positively or negatively) linked to the age at the time of CRT implantation, baseline ejection fraction, disease aetiology, presence of atrial fibrillation (AF, p=0.019), degree of mitral regurgitation, preserved renal function (p=0.0006) and QRS duration. Thirteen pts among the non-responder (33.3%), were treated with intermittent infusions of levosimendan approximately every 3-4 weeks for a median of 2.3 years. Although levosimendan was initially used as destination therapy in all 13 pts, it ended up to be a bridge to heart transplant in two cases, and a bridge to left ventricular assist device for one patient. Two pts on periodic levosimendan infusions died of end stage heart failure, whereas the remaining 8 pts are still alive, ongoing monthly cycles of therapy with levosimendan.

**Conclusion:** Several factors, mainly the status of renal function and the presence of AF, should be properly weighted in the selection of pts eligible to CRT, as these factors are directly linked to the overall clinical outcome. Moreover, since mortality rate in non-responder is higher than in responder, further therapeutic strategies should be evaluated for non-responder, such as for example intermittent infusions of Levosimendan.

### P366

#### Multi-centre asian data on risk factors for non-response to cardiac resynchronisation therapy

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**Introduction:** Up to 30% of patients with heart failure do not respond to Cardiac-Resynchronisation-therapy (CRT). Guidelines specify clear inclusion



criteria for CRT, but little is written to predict non-response. We hypothesized that patients with left-ventricular ejection fraction (LVEF) < 20%, left-ventricular internal dimension in diastole (LVlDd) >7.5cm represent a late stage of heart failure that may not respond to CRT. Prior literature has been conflicting regarding response to CRT in those with very long QRS duration (>180ms).

**Objective** We sought to determine if patients with the above risk factors (EF < 20%, LVlDd>7.5 cm and QRS>180ms) we more likely to be clinical non-responders.

**Methodology** We retrospectively evaluated patients from 3 centres implanted with CRTD from 2006 to 2014 with the above characteristics. Clinical non-response was defined by no reduction in New York Heart Association (NYHA) class.

**Results:** Available data from 118 patients were analysed, of these 47.1% were clinical non-responders. Comparison of non-response rates between patients with and without the above risk factors are tabulated below.

**Conclusion:** There were no significant differences in terms of clinical response between those with or without dilated hearts>7.5cm or EF < 20%. However, our findings suggest that patients with a very wide QRS duration are more likely to respond to CRT in terms of functional class.

**Risk factors for non-response**

Risk factor	Yes (n = )	No (n = )	P value
LVEF < 20%	Yes (n = 40)	No (n = 78)	
Non-responder	19 (47.5%)	38 (48.7%)	0.90^
LVlDd > 7.5cm	Yes (n = 16)	No (n = 94)	
Non-responder	9 (56.2%)	43 (45.7%)	0.59*
QRS > 180ms	Yes (n = 15)	No (n = 90)	
Non-responder	3 (20.0%)	51 (56.7%)	0.01*
2 or more risk factors	Yes (n = 17)	No (n = 101)	
Non-responder	9 (52.9%)	48 (47.5%)	0.80*

\*Fischer's exact test ^Chi-square test

**P367**

**Factors affecting cardiac resynchronisation therapy and defibrillator (CRT- D) response in heart failure: a retrospective study.**

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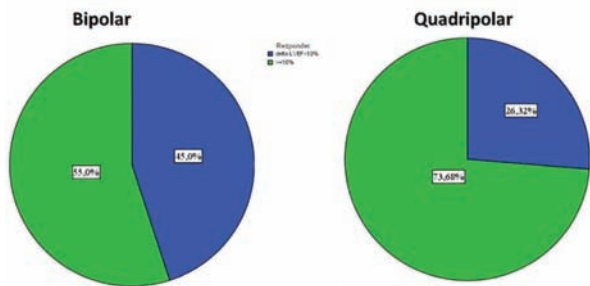
**Background:** Cardiac resynchronization therapy and defibrillator (CRT-D) has proven to be an effective treatment for patients affected by heart failure with left branch bundle block (LBBB) and severe contractile dysfunction, despite optimal medical therapy. Aim: Evaluate factors associated to better CRT-D response.

**Methods:** We have retrospectively evaluated seventy-eight patients (62 males and 16 females; mean age: 74.7 ± 10.5 years), affected by heart failure and already treated by CRT-D. We considered responder to a 10% increased in LVEF. All patients were assessed for ischemic heart disease, atrial fibrillation and chronic kidney disease (CKD). QRS reduction at implantation, left ventricular lead type (bipolar, quadripolar) and stimulation percentage were considered. Biochemical parameters, cardiovascular risk factors and treatments were evaluated.

**Results:** Patients were divided in two groups, responders and non-responders. Responder group was characterized by increased stimulation percentage, quadripolar lead implantation, greater QRS reduction. Severe CKD was associated to non-responder. No further difference was found.

**Conclusions:** This analysis shows the factor affecting better response to CRT-D are greater QRS reduction at implantation, left quadripolar lead and greater stimulation percentage, while severe CKD is a negative predictor for CRT-D response.

**Left ventricle lead & Responder**



Left catheter lead and CRT response

**Factors affecting CRT-D response**

	Total n =78	Responders n = 50	Non responders n = 28	P value
Hypertension n (%)	65 (83)	41 (82)	24 (86)	ns
Dyslipidemia n (%)	45 (58)	31 (62)	14 (50)	ns
Type 2 diabetes n (%)	37 (47)	24 (48)	26 (52)	ns
Ischemic heart disease n (%)	29 (37)	16 (32)	13 (46)	ns
Sever CKD (eGFR <30 ml/min/1.73m <sup>2</sup> ) n (%)	7 (92)	2 (4)	5 (18)	0,046
Atrial fibrillation n (%)	20 (26)	11 (22)	9 (32)	ns
ARBs n (%)	24 (31)	18 (36)	6 (21)	ns
ACE inhibitors n (%)	40 (51)	23 (46)	17 (61)	ns
Beta blockers n (%)	61 (78)	41 (82)	20 (71)	ns
Antimicrobialcorticoids n (%)	28 (36)	16 (32)	12 (43)	ns
QRS reduction (mm)	32 ± 25	40 ± 26	18 ± 15	<0,001
Ejection fraction change (%)	13 ± 12	21 ± 7	-0,07 ± 7,0	<0,001
Stimulation > 95% n (%)	63 (81)	44 (88)	19 (68)	0,030
Time from impantation (months)	32 ± 25	33 ± 26	29 ± 23	ns
Bipolar lead n(%)	40 (51)	22 (44)	18 (64)	0,086
Quadripolar lead n (%)	38 (49)	28 (56)	10 (36)	

**P368**

**Responders and quadripolar lead in cardiac resynchronization therapy - ResQ-CRT: prospective study on quadripolar pacing, preliminary results**

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**Introduction:** In CRT, left ventricle (LV) quadripolar leads offer the chance to overcome implant difficulties (phrenic nerve stimulation (PNS), unsatisfactory thresholds or pacing site) and potentially to reduce the need for reoperation, but few prospective data are available about effects on patient's response.

**Purpose:** This study aims to observe the evolution of CRT-D with quadripolar LV lead in terms of electrical parameters and patient's outcome, observing the differences between Responders and Non-Responders.

**Methods:** Were prospectively observed, in 15 Italian hospitals, 152 patients [Age(y) 69.4 ± 9; 76.3% Man; 42% Ischemic; 68% NYHA 3; LV EF(%) 27.6 ± 5.5] in which the CRT-D device was programmed with LV pacing from one distal dipole, when possible (142 distal, 93%). After 47(6M FU) and 1014(12M FU) months the patient clinical outcome is evaluated and the LV lead programming is recorded. Definition of Responder: improvement of HF Clinical Composite Index (CCI improved = no major clinical events and NYHA + health state improved) and at least one between improvement of EF more than 5 percentage points and 10% reduction of the LVESV, measured with echo.

**Results:** Were analyzed 117 "6M FUs"; 35 patients (30%) were classified as Non-Responder (NR), 8 (23% of NR) due to echo parameters not improved, while 12 patients (34% of NR) had echo improved but CCI not improved). It was noticed a mean increase in EF (+9 percentage points [95% C.I. 8-10], p < 0.001) from baseline in all patients; in NR patients the mean increase of EF was less than 5 percentage points (p < 0.001). Reduction of the LVESV from baseline was significant for all patients and in particular in Responder group (mean LVESV reduction = 27.7 %, n = 60, [95% C.I. 21.1-34.4], p < 0.001), but not in NR group. In 21 patients (60% of NR) the LV configuration was changed from distal to proximal dipoles, while it was not possible, for high threshold or PNS, in 5 patients (14%). Otherwise it was considered not clinically relevant.

Were also preliminarily analyzed 81 "12M FUs"; of 26 patients (32%), classified as NR at 6M FU, 15 of them had the LV configuration changed from distal to proximal dipoles at 6M FU, 8 (53%) of whom were classified as Responder at 12M FU. The other 11 NR patients, with no LV configuration change at 6M, became Responders at 12M only in 4 cases (2 of 8 LV distal; 2 of 3 LV proximal).

**Conclusion:** Data indicate a rate of NR with LV stimulation on distal dipoles as expected from previous studies. Follow-up data at 12 months, though preliminary, show potential benefit of quadripolar lead availability on this population.

## P369

**Middle-term stability of epicardial left ventricular electrodes for cardiac resynchronization therapy**

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**Introduction:** The standard for LV lead implantation is transvenous access via the coronary sinus. If unsuccessful, a possible alternative is to achieve stimulation of the left ventricle with an epicardial LV lead implantation.

**Goals**

The primary objectives were to determine medium-term electrical parameters of LV epicardial leads and to compare them with endocardially implanted electrodes, to compare the electrical performance and stability of epicardial leads from different manufacturers, and to determine whether epicardial lead stimulation parameters could be influenced by various clinical and demographic factors. Secondary objectives were to identify the main causes of transvenous LV lead implantation failures, to compare the clinical and echocardiographic resynchronization effect in both patient groups and to compare the safety of both approaches.

**Methods:** The study included consecutive patients undergoing implantation of a pacemaker with CRT function (CRT-P) or an implantable cardioverter-defibrillator with CRT function (CRT-D). The study group of cases was composed of patients with epicardial LV lead implantation, while the control group included patients with a completely transvenous system for CRT.

**Results:** 92 patients were included in each group (26 women, 66 men). LV pacing thresholds were significantly higher in the epi patient group at the 1 month, 1-year and 2-year follow-up compared to endocardially implanted LV leads (1.62 V vs. 1.06,  $p < 0.001$ , 1.57 V vs. 1.09 V,  $p < 0.001$ , and 1.54 V vs. 1.21 V,  $p < 0.010$ , respectively). Values of pacing thresholds of epi and endo LV leads at the 3-year follow-up were very similar, without a statistically significant difference due to counteracting trends in the pacing threshold curves (1.44 V vs. 1.25 V,  $p = 0.119$ ). Energy delivered by the device to achieve LV stimulation in the epi group of patients was significantly higher at all time points, which resulted in earlier battery depletion. Improvement of NYHA class by at least one grade occurred in 71.4% of patients in the epi group and in 68.1% of patients in the endocardial group. A positive echocardiographic response was comparable in both groups. A significantly higher one- and three-year total mortality was recorded in the epicardial group compared to the endo group (17.4% vs. 6% and 21.7% vs. 6.5%, respectively).

**Conclusion:** Epicardial leads are capable of effective LV stimulation over a medium-term period of three years. They have a higher pacing threshold, and lower pacing impedance in comparison with endocardial leads, which leads to a greater energy consumption per pacing impulse. Additionally, resynchronization effects in patients with LV epi electrodes is similar to patients with transvenously implanted LV leads, both in terms of clinical and echocardiographic response. However, overall mortality of patients with LV epicardial leads is higher compared to patients with endocardially implanted LV leads.

## HAEMODYNAMICS / CORONARY AND PERIPHERAL CIRCULATION

## P370

**Prognostic relevance of pulmonary haemodynamic response to exercise in patients with chronic left heart failure**

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**Background:** Exercise right heart catheterization (RHC) is emerging as a diagnostic tool in pulmonary hypertension (PH). However, the prognostic relevance of hemodynamic parameters derived from exercise RHC in heart failure with preserved ejection fraction (HFpEF) or heart failure with reduced ejection fraction (HFrEF) with or without the presence of resting pulmonary hypertension (HFpEF-PH or HFrEF-PH) is unknown. We hypothesized that exercise hemodynamics with assessment of pressure/flow slopes are of prognostic and clinical relevance.

**Methods:** We conducted an analysis of 305 patients enrolled in the Kerckhoff Clinic prospective heart failure registry. Patients with established diagnosis of HFrEF or HFpEF who were assessed by means of exercise RHC were included. A total of 130 of all patients (43%) had no resting PH, 175 (57%) had resting PH with mean pulmonary artery pressure (mPAP)  $> 24$  mmHg and mean PA wedge pressure (PAWP)  $> 15$  mmHg. The primary outcome was transplant-free survival; 21 patients were lost to follow-up. Factors shown to be of prognostic relevance in univariate Cox

regression analysis were entered into the multivariate model. Receiver operating characteristic (ROC) analyses were performed, while cut-offs were determined using the Youden Index.

**Results:** A total of 305 patients (124 female (40.7%), mean age  $69.1 \pm 12.3$  years) with a diagnosis of HFpEF ( $n = 138$ ; 45.2%) or HFrEF ( $n = 167$ ; 54.8%) were included. In all patients, resting diastolic PAP (dPAP) and maximum cardiac output during exercise (CO max) were independently associated with a favorable outcome (dPAP: hazard ratio (HR) 0.82; 95% CI [0.71-0.94],  $p = 0.006$ ; CO max: HR 0.26; 95% CI [0.12-0.58],  $p = 0.001$ , cutoff 5.3 l/min). The increase of PAWP was not an independent predictor of outcome in our cohort. In patients with HFpEF diastolic PAP/CO slope (slope =  $\Delta$ pressure /  $\Delta$ CO) was an independent predictor of a favorable outcome (HR 0.57; 95% CI [0.34-0.96],  $p = 0.035$ ). In HFrEF patients, resting systolic PAP, dPAP, PAWP, and the exercise parameters mPAP/CO slope, resting PAP/CO slope, dPAP/CO slope, and the absolute increase in mPAP were independently associated with a favorable outcome. Moreover, HFrEF patients with a mPAP/CO slope  $< 7.4$  mmHg/l/min had a significantly better 5-year survival (Kaplan-Meier-Analysis: 69% versus 44.7%; log rank  $p = 0.02$ ).

**Conclusions:** In the current study, we demonstrated the prognostic relevance of exercise haemodynamics in HFrEF and HFpEF patients independent of the presence of resting pulmonary hypertension. The maximum achieved CO during exercise seems to be of major relevance in all heart failure patients. In addition, exercise pressures and pressure/flow slopes are of prognostic significance in specific heart failure subgroups.

## P371

**Exercise hemodynamics in relation to cardiac amyloid deposit burden**

Health Research Fund of Central Denmark Region and the Danish Heart Association

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**Aims:** The present study aimed to characterize alterations in hemodynamics and oxygen consumption during exercise in patients with various cardiac amyloid (CA) deposits degrees.

**Methods:** Sixteen cardiac amyloid deposit patients underwent 11C-PIB positron emission tomography (PET) and 11C-acetate PET in order to quantify the burden of cardiac amyloid deposits. The patients were subjected to a symptom-limited, semi-supine exercise test with simultaneous right heart catheterization (RHC) and oxygen consumption assessment. Based on PET results, patients were divided into three groups: A: Genetically disposed ATTR-CA patients (PET negative) ( $n = 5$ ); B: ATTR-CA patients (PET positive) ( $n = 4$ ); and C: Wild type or AL amyloid patients ( $n = 7$ ). We considered pulmonary capillary wedge pressure (PCWP)  $> 15$  mmHg at rest and  $> 25$  mmHg during stress abnormal. The data are preliminary as we expect to include ten more patients.

**Results:** At rest, only a tendency towards increased LV and RV filling pressure was noted in CA patients (RAPrest: Group A:  $5 \pm 3$  mmHg, group B:  $5 \pm 3$  mmHg, group C:  $8 \pm 5$  mmHg,  $p = 0.23$ ; PCWPrest: Group A:  $9 \pm 4$  mmHg, group B:  $12 \pm 7$  mmHg, group C:  $17 \pm 5$  mmHg,  $p = 0.06$ ). With exercise a pronounced increase in LV and RV filling pressure was noted (RAPpeak: group A:  $5 \pm 3$  mmHg, group B:  $11 \pm 2$  mmHg, group C:  $18 \pm 11$  mmHg,  $p < 0.05$ ; PCWPpeak: group A:  $17 \pm 4$  mmHg, group B:  $30 \pm 4$  mmHg, group C:  $32 \pm 5$  mmHg). All patients in group B and C had exercise PCWP  $> 25$  mmHg. Interestingly, pulmonary vascular resistance (PVR) was significantly higher in CA positive patients (PVR: Group A:  $1.6 \pm 1.0$  wood units, group B:  $1.3 \pm 0.3$  wood units, group C:  $3.5 \pm 1.6$  wood units) and pulmonary arterial compliance significantly lower, especially at peak exercise (PACpeak: group A:  $9 \pm 2$  mmHg/l group B:  $4 \pm 1$  mmHg/l, group C:  $2 \pm 0$  mmHg/l,  $p < 0.0001$ ).

At rest, cardiac index was significantly reduced in CA patients ( $p < 0.05$ ) whereas oxygen consumption was not. In contrast, peak exercise cardiac index and oxygen consumption was significantly reduced in CA patients (CIpeak: group A:  $9.6 \pm 0.4$  l/min/m<sup>2</sup>, group B:  $6.5 \pm 1.3$  l/min/m<sup>2</sup>, group C:  $3.3 \pm 1.3$  l/min/m<sup>2</sup>,  $p < 0.0001$ ; V02 peak: group A:  $2380 \pm 806$  ml/min, group B:  $1690 \pm 543$  ml/min, group C:  $998 \pm 416$  ml/min,  $p < 0.01$ ).

**Conclusions:** Cardiac amyloid deposits are strongly associated with exercise induced elevated left and right ventricular filling pressure and reduced systolic capacity. Furthermore, CA patients have increased PVR and severely reduced PAC, which may contribute to the reduced exercise capacity in these patients.

## P372

**Absolute cerebral oximetry in different types of syncope during head-up tilt test in adults**

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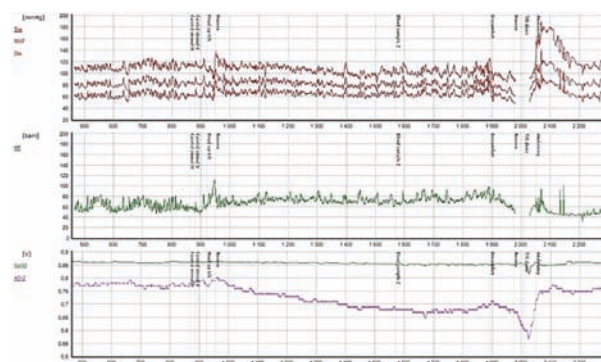
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**Background:** Absolute cerebral oximetry is a non-invasive technology, able to measure cerebral oxygen saturation (SctO<sub>2</sub>). We applied near-infra-red-spectroscopy (NIRS) to monitor SctO<sub>2</sub> during head-up tilt test (HUT) in patients investigated for unexplained syncope.

**Methods:** Thirty-two patients (mean-age 50 years; 34% male) were examined with NIRS during HUT (Italian protocol). Beat-to-beat blood pressure (BP), ECG, peripheral oxygen saturation (SpO<sub>2</sub>) and SctO<sub>2</sub> were continuously recorded using a non-invasive beat-to-beat monitor and an absolute cerebral oximetry monitor. The monitors were synchronized.

**Results:** HUT was diagnostic in 29 patients. Of these, 9 (31%) were diagnosed with orthostatic hypotension (OH) (classical OH; n=5, delayed; n=4), 23 (79%) with vasovagal syncope (VVS) (nitroglycerine (NTG) induced; n=14, spontaneous; n=9), 1 (3%) with postural tachycardia syndrome (POTS), and 2 (7%) with orthostatic intolerance (OI). Three (10%) participants were diagnosed with the combination of delayed OH and spontaneous VVS and one (3%) individual with classical OH and spontaneous VVS. During syncope, a significant decrease in absolute SctO<sub>2</sub> from  $72 \pm 5\%$  right frontal and  $71 \pm 4\%$  left frontal at baseline to  $57 \pm 6\%$  right frontal and  $54 \pm 6\%$  left frontal at the time of loss of consciousness (LOC) ( $p < 0.0001$ ) was observed. SpO<sub>2</sub> remained at a constant level during HUT, both at baseline ( $96 \pm 3\%$ ) and at the time of LOC ( $96 \pm 2\%$ ).

**Conclusions:** We observed a significant decrease in SctO<sub>2</sub> in patients with all types of syncope. SpO<sub>2</sub> remained stable. Patients experienced syncope at SctO<sub>2</sub> below 60% and mean arterial pressure (MAP) below 60mmHg. Positive results during HUT were predicted by a progressive SctO<sub>2</sub> decrease independently of haemodynamic parameters in patients with spontaneous VVS.



Cerebral desaturation in VVS during HUT

### P373

#### Uncovering the timeline of cardiogenic shock

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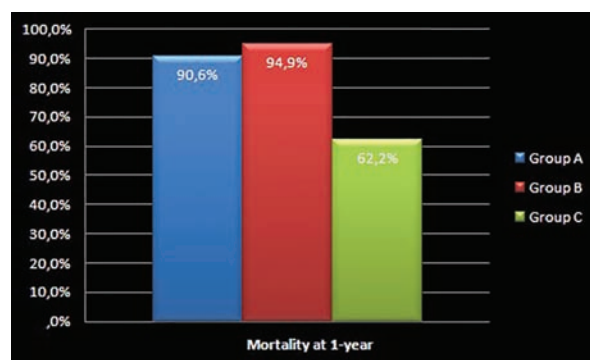
**Introduction:** Cardiogenic shock (CS) remains the leading cause of mortality in patients hospitalized with acute myocardial infarction (AMI). Significant therapeutic advances have emerged throughout the last decades improving the outcomes of these patients.

**Purpose:** Review the evolution of cardiogenic shock, after an acute coronary syndrome (ACS), throughout the past 3 decades.

**Methods:** Single-center registry of 137 patients, admitted for ACS, which developed cardiogenic shock in the first 72 hours. They were divided into 3 groups: between the years of 1989-1994 (Group A: n=53; 62.3% men); between 1999-2004 (Group B: n=39; 46.2% men); and between 2009-2014 (Group C: n=45; 66.7% men). The groups were compared regarding their baseline characteristics, therapeutic procedures and prognosis during in-hospital stay and at 1-year follow-up.

**Results:** Group A had lower age [median/years (A=69 vs B=71.5 vs C=75)]. They had more history of smoking habits (A=50.9% vs B=20.5% vs C=15.6%,  $p < 0.001$ ), angina (A=49.1% vs B=23.1% vs C=6.7%,  $p < 0.001$ ) and acute myocardial infarction (A=26.4% vs B=12.8% vs C=8.9%,  $p < 0.048$ ). No differences were found regarding arterial hypertension, Diabetes Mellitus, dyslipidemia or family history of cardiovascular disease. Group C was less submitted to thrombolysis (A=30.2% vs B=15.4% vs C=2.2%;  $p < 0.001$ ), performed more PCI (A=18.9% vs B=43.6% vs C=88.9%;  $p < 0.01$ ) and was more medicated with aspirin (A=45.3% vs B=53.8% vs C=97.8%,  $p < 0.001$ ). Intra-aortic balloon pump was introduced later, being used only in Group C (17; 38%). No differences in ischaemic arrhythmias. Group C had a lower mortality rate during in-hospital stay (A=84.9% vs B=92.3% vs C=55.6%;  $p < 0.001$ ) and at 1-year follow-up (A=90.6% vs B=94.9% vs C=62.2%;  $p < 0.001$ ).

**Conclusion:** Medical advances have permitted a different management of patients with cardiogenic shock, leading to an increase in survival. Unfortunately, the mortality rate is still high.



### P374

#### Natural history of vessel remodeling in heart transplant recipients - an IVUS substudy with long term follow up

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**Background:** There is limited long-term data on vessel remodeling after heart transplantation (Tx).

**Methods:** We compared baseline vs follow-up IVUS evaluation of the LAD in 60 consecutive heart Tx recipients. Proximal LAD segments were matched among time points, a  $\geq 20$ mm long segment was analyzed every 1mm, and results were normalized for analysis length and reported as mm<sup>3</sup>/mm. Excluding 6 pts with a history of rejection, we divided Tx recipients into an Early group (n=36, last IVUS <5 yrs post-Tx) vs a Late group (n=18, last IVUS >5 yrs post-Tx).

**Results:** In the Early group vessel area ( $16.0 \pm 4.6$ mm<sup>3</sup>/mm vs  $15.8 \pm 4.3$ mm<sup>3</sup>/mm,  $p=0.7$ ) and lumen area ( $11.7 \pm 3.6$ mm<sup>3</sup>/mm vs  $11.1 \pm 4.0$ mm<sup>3</sup>/mm,  $p=0.21$ ) did not change between the 2 time points, although plaque area increased ( $4.3 \pm 2.2$ mm<sup>3</sup>/mm vs  $4.7 \pm 2.3$ mm<sup>3</sup>/mm,  $p=0.04$ ); the change in lumen area ( $-0.4 \pm 1.4$ mm<sup>3</sup>/mm/yr) was well correlated to the change in vessel area ( $-0.2 \pm 1.3$ mm<sup>3</sup>/mm/yr) ( $r=0.91$ ,  $p < 0.01$ ), but not to the change in plaque area ( $0.2 \pm 0.6$  mm<sup>3</sup>/mm/yr) ( $p=0.07$ ). In the Late group vessel area ( $15.5 \pm 4.4$ mm<sup>3</sup>/mm vs  $15.2 \pm 3.4$ mm<sup>3</sup>/mm,  $p=0.6$ ), lumen area ( $11.7 \pm 4.0$ mm<sup>3</sup>/mm vs  $11.2 \pm 2.9$ mm<sup>3</sup>/mm,  $p=0.4$ ), and plaque area ( $3.8 \pm 1.2$ mm<sup>3</sup>/mm vs  $4.0 \pm 1.6$ mm<sup>3</sup>/mm,  $p=0.4$ ) did not change; again, the change in lumen area ( $-0.3 \pm 0.1$ mm<sup>3</sup>/mm/yr) was well correlated to the change in vessel area ( $-0.3 \pm 1.1$  mm<sup>3</sup>/mm/yr) ( $r=0.98$ ,  $p < 0.01$ ), but not to the change in plaque area ( $0.0 \pm 0.3$ mm<sup>3</sup>/mm/yr) ( $p=0.12$ ).

**Conclusion:** In the absence of rejection, lumen area is preserved for a long period after heart Tx due to vessel remodeling despite plaque progression that was noted within 5yrs post-Tx.

### P375

#### Inferior vena cava diameter predicts renal function and outcomes in patients with heart failure.

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**Background:** Renal dysfunction in patients with heart failure (HF) has traditionally been attributed to poor cardiac output. There is currently a growing body of evidence to suggest that renal venous congestion (VC) plays a more important role than hypo-perfusion. However, a vast majority of them have been invasive studies measuring pulmonary artery and central venous pressures as markers of venous congestion. We, therefore, aimed to determine if VC as determined by inferior vena cava (IVC) dilatation using echocardiography was associated with worsening renal function, HF hospitalisation and all-cause mortality. **Methods:** We designed a population-based, longitudinal cohort study of 1034 unselected (acute/chronic) HF patients. All patients were symptomatic and required the use of loop diuretic therapy. VC was defined as IVC diameter  $> 2.1$  cm as determined by echocardiography performed nearest to the time of recruitment into study. Renal function was determined by estimated glomerular filtration rate (eGFR) using the abbreviated MDRD equation. Logistic regression models were used to examine the association between VC and eGFR. Cox proportional hazard models were applied to examine the influence of VC on all-cause mortality and CHF hospitalisations.



**Results:** Logistic regression models showed that those with severe renal impairment (eGFR<30) were more likely to have VC compared to those with an eGFR > 60 (Odds Ratio=7.7; 95% CI(1.6-10.5), p=0.012). Multivariate analysis showed that those with VC had significantly worse survival than those without VC after adjusting for age, sex, eGFR and furosemide daily dose (hazard ratio [HR]: 1.15-1.96; p=0.002). There was also a nonsignificant trend towards shorter time to first hospitalisation for HF in the VC group compared to those without VC (hazard ratio [HR]: 1.22, 95% CI:0.96-1.56; p=0.103).

**Conclusions:** VC as determined by dilated IVC on echocardiography is associated with worsening renal function in an unselected group of HF patients. This readily available and non-invasive test can also be used to predict HF hospitalisation and all-cause death in this patient group.

### P376

#### Congenital arterio-venous and arterio-systemic coronary artery fistulae - prevalence and clinical significance in patients undergoing coronary intervention

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**Background:** Congenital coronary artery anomalies have been reported in up to 1.3% of patients undergoing cardiac catheterization. Most frequent are abnormalities of coronary origin and distribution. Coronary artery fistulae are rare (0.2%), more than 90% being arterio-venous. Arterio-systemic fistulae so far have been described only sporadically.

This study aimed to assess the prevalence and clinical significance of coronary artery fistulae in patients undergoing coronary angiography.

**Methods:** Over an 8-year period, 11842 patients underwent coronary angiography with or without coronary intervention. Patients with a coronary artery anomaly prospectively identified by 2 independent observers were included in a data base.

**Results:** Among 11842 patients undergoing cardiac catheterization, 202 with a coronary anomaly were identified (1.7%). An abnormal origin of a coronary artery was seen in 123 patients (1%). Coronary artery fistulae were diagnosed in 78 patients (0.7%), 55 female, 23 male, mean age 66 years (range 39-88).

Arterio-venous fistulae were present in 15/78 patients (19%), connecting LAD with pulmonary artery (n=12) or right ventricle (n=1), RCA with right ventricle (n=1) and CX with pulmonary artery (n=1). The shunt size was negligible and the arterio-venous fistulae were coincidental findings without clinical relevance in all patients.

Arterio-systemic fistulae with multiple small fistulous channels draining into the left ventricle (LV) were present in 63/78 patients (81%). Origin of the fistulous communication was LAD (n=24), LAD and CX (n=19), LAD and RCA (n=12), CX (n=2), and all major vessels (n=6). Associated cardiac lesions were present in 35/78 patients (significant CAD: n=28, valve disease: n=6, apical hypertrophic cardiomyopathy: n=1). 22 patients with isolated arterio-systemic fistulae complained of anginal chest pain and showed ECG changes in the anterior leads attributable to ischemia due to a coronary steal mechanism. Intracoronary injection of nitroglycerine resulted in increased shunting into the LV. In 1 patient with anterior myocardial infarction and an occluded LAD, attempted LAD recanalization resulted in enlargement of a small fistulous arterio-systemic channel with significant shunting from the LAD into the LV. Subsequently, the dilated fistulous channel closed spontaneously.

**Conclusion:** In contrast to previous reports, diffuse arterio-systemic coronary artery fistulae draining into the LV are more common than arterio-venous fistulae. Chest pain and ECG changes are typical clinical findings. Nitrate therapy may aggravate the coronary steal phenomenon.

### P377

#### Primary percutaneous coronary intervention in diabetic patients with acute myocardial infarction

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**Introduction:** Some studies showed that diabetic patients (D) group (DG) had a worse outcome when compared to nondiabetic (ND) patients group (NDG), after primary percutaneous coronary intervention (PCI).

**Objective:** The objectives were to compare mortality and major coronary events (MACE) at 30 days and 1 year of DG and NDG submitted to primary PCI and to study whether another conditions were related to worst outcome of patients in 30 days or one year.

**Methods:** Prospective study with 450 consecutive patients submitted to PCI from 01/01/2001 to 12/31/2006 (121 D and 329 ND) with ST-segment elevation acute myocardial infarction (AMI) in the first 12 hours of symptoms presentation treated with balloon catheter or bare metal stent and without cardiogenic shock. We used in statistical analysis: Student t test, chi-square test, Fischer exact test, and multivariate analysis: logistic regression and Cox analysis.

**Results:** DG and NDG had similar age (63.1 ± 10.0 and 62.3 ± 11.7 years, p=0.443),

male gender (63.6% and 69.9%, p=0.205) and multivascular disease (66.1% and 60.8%, p=0.301). The diabetic group had more dyslipidemia (65.3% x 51.7%, p=0.009) and severe left ventricular dysfunction (15.7% x 8.2%, p=0.019). The stent implantation rate was (83.5% and 81.1%, p=0.863) and glycoprotein (GP) IIb/IIIa inhibitors utilization (79.3% and 82.2%, p=0.831) were similar. The mortality at 30 days (2.5% and 2.7%, p=1.000) and at 1 year (5.0% and 6.7%, p=0.650) and MACE at 30 days (4.1% and 6.4%, p=0.496) and at 1 year (19.4% and 15.4%, p=0.3492) were similar. The absence of TIMI III flow after the procedure (procedure failure) was the only independent hospital mortality (30 days) predictor (P<0.001, OR=8,045, CI95 2,327-27,816). Procedure failure (p=0.023, HR=3,364, CI95 1,182-9,578) and age ≥ 65 years (P=0.035, HR=3,391, CI95 1,091-10,543) were independent predictors of mortality at 1 year. The multivessel coronary disease (p=0.023, OR=4,218, CI95 1,223-14,545 and procedure failure (P<0.028, OR 3.155, CI95 1,132-8,799) were independent predictors of MACE at 30 days and multivessel coronary disease was independent of MACE at 1 year (p=0.034, HR=1.854, CI95 1.048-3.280).

**Conclusion:** The diabetic patients submitted to primary PCI had mortality rate and MACE similar to none diabetic patients at 30 days and 1 year. The absence of TIMI III flow were predictor of mortality at 30 days and 1 year and age ≥ 65 years at 1 year. Independent predictors of MACE at 30 days were multivessel coronary disease and absence of TIMI III flow (procedure failure) and at 1 year was multivessel coronary disease.

### P378

#### Management of ST-elevation myocardial infarction according to European guidelines in a university hospital in Tunisia: Results of RESCAS registry

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**Background:** Early reperfusion therapy has proven benefit in reducing mortality in patients with ST-segment elevation myocardial infarction (STEMI). Expert guideline committees have defined recommendations to improve the management of patients with STEMI and decrease their mortality rates. Our Registry of ST-Segment-Elevation Myocardial Infarction (STEMI) was designed to assess the situation in our city regarding the clinical profile, diagnostic and therapeutic management and medium-term prognosis, as well as to evaluate compliance with contemporary clinical guidelines.

**Methods:** RESCAS registry was a 1-year, single-centre, prospective, multidisciplinary study, conducted between september 2012 and August 2013 in our hospital, including 215 consecutive patients with STEMI of less than 24 hours duration. Data were recorded during the emergency phase and after admission to cardiology. Baseline characteristics, treatments, in-hospital and mid-term outcomes were analyzed.

**Results:** Seventy-seven per cent of patients were men; the mean age was 62 years. The most prevalent risk factor was smoking, followed by diabetes. Killip class greater or equal to 2 was observed in 24% of cases. 87% received reperfusion treatment; twenty-nine (13%) patients underwent thrombolysis and one hundred fifty-nine (74%) had percutaneous coronary intervention (PCI). Among patients undergoing primary percutaneous coronary intervention, first medical contact (FMC) to treatment 135 min, symptoms to treatment 300 min. FMC to PCI delay was less than 120 min in 68% of patients residents in Sfax city, while only 39% of patients residents in the delegations within 40 km of the hospital and 12.5% of patients in the delegations of more than 40 km are supported within the 2 hours following the ESC guidelines (p<0.001). The only factor independently associated with guideline compliance was place of first medical contact. The radial access was used in 83% of patients. Thrombectomy with the use of a manual aspiration catheter was performed in 78 patients (49,5%). In-hospital mortality was 9,3% in all patients, and it was highest in the group of patients without reperfusion therapy (14,8%). Follow-up after a median of 9,3 months was obtained for 185 patients (94,8%). Overall 6-months mortality rate was 12,6%. The cumulative incidence of myocardial infarction, stent thrombosis and target-lesion revascularization was 7%, 4,12% and 8,8% at overall follow.

**Conclusion:** In contemporary community practice, achievement of quality performance measures in patients presenting with ST-segment-elevation myocardial infarction was high, regardless of time of presentation. Most of our patients presenting with STEMI undergo reperfusion therapy with percutaneous coronary intervention. However an important number of patients did not receive revascularization within the recommended time frame. Efforts should be made to improve the estimation of delay before reperfusion therapy.

### P379

#### Endothelium dysfunction as pathogenetic factor of labile arterial hypertension at children with vegetative nervous system disturbances

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**Purpose:** It was to investigate the role of the endothelial dysfunction at labile hypertension pathogenesis at children with vegetative nervous system pathology. Methods. It was examined 314 children with vegetative dysfunction and 190 healthy children (10-16 years) – control group in Grodno region (Belarus) by clinical, spectrophotometric, agregatometric and statistic methods. The endothelium function with reactive hyperemia method was investigated.

**Results:** At patients with vegetative nervous system pathology and the severe degree of the risk factors influences the increasing of blood pressure and aggravating the clinical manifestations with decreasing the endothelium-dependent vasodilation, nitrite and nitrate (the metabolites of nitric oxide), the values of antioxidants (retinol and tocoferol) in the plasma of blood and activation of the platelets aggregation was noted. These changes were absent at children with vegetative dystonia and at all children of control group with mild and moderate degree of risk factors influences.

**Conclusions:** The endothelium dysfunction is the important factor of the arterial hypertension at the children with vegetative nervous system disturbances. Action of risk factors in the children organism with disturbances of the nervous system (hereditary, active or passive smoking, hypodynamia, atherogenic diet, stress) induces oxidative processes activation and endothelium dysfunction development.

**P380**

**Primary percutaneous coronary intervention in women with acute myocardial infarction**

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**Background:** Coronary heart disease is the leading cause of mortality and morbidity. A higher mortality risk for women with acute ST-elevation myocardial infarction has been a common finding in the past, even after acute percutaneous transluminal coronary angioplasty (PTCA). Prior studies have reported worse results after PTCA in women than in men. However, recent data suggest that this difference is less marked.

**Objective:** To determine gender-related differences and risk factors for death and major events, both in-hospital and at six-month follow-up, of patients that have been admitted within the first twelve hours of ST-segment elevation acute myocardial infarction (AMI) and primary PTCA in order to set out whether there are gender differences in a real-world contemporary treatment and outcome.

**Methods:** For two consecutive years, 199 consecutive patients were enrolled in the study, with ST-segment elevation AMI and primary PTCA without cardiogenic shock. The immediate outcome, in-hospital and six-month follow-up were studied. Multivariate Cox analysis were performed to identify independent predictors of death and major events.

**Results:** Clinical characteristics were similar in both groups, except that women were older than men (67.04 +/- 11.53 x 59.70 +/- 10.88, p < 0.0001). In-hospital mortality was higher among women (9.1% x 1.5%, p = 0.0171), as was the incidence of major events (12.1% x 3.0%, p = 0.0026). The difference in mortality rates remained the same at six months (12.1% x 1.5%, p = 0.0026). The independent predictors of death in multivariate analysis: were: female gender and age > 80 years old. Independent predictors of major events and/or angina were: multivessel disease and severe ventricular dysfunction.

**Conclusion:** After ST-segment elevation AMI and primary PTCA, the independent predictors of mortality throughout the follow-up were female gender and age > 80 years, in both in-hospital and six months follow-up.

Events after primary PTCA x Gender

	WOMEN	MEN	P
AGE	67.04 ± 11.53	59.70 ± 10.88	P < 0.0001
IN-HOSPITAL MORTALITY	9.1%	1.5%	P = 0.0171
MAJOR EVENTS	12.1%	3.0%	P = 0.0026
MORTALITY AT SIX MONTHS	12.1%	1.5%	P = 0.0026

**METABOLISM / DIABETES MELLITUS / OBESITY**

**P381**

**Lipid profile in acute coronary syndrome: does age matter?**

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**Introduction:** Several studies suggest the presence of a link between atherogenesis and hyperlipidemia. This fact plays a central role in the pathogenesis of acute coronary syndromes (ACS).

**Objective:** To compare the lipid profile of young and older patients admitted with a diagnosis of acute coronary syndrome.

**Methods:** Retrospective study of patients admitted for ACS. Clinical and laboratory parameters were evaluated, including total cholesterol (TC), HDL cholesterol (HDL), LDL cholesterol (LDL) and triglycerides (TG). The following ratios were calculated: TC/HDL, LDL/HDL and TG/HDL. Parameters in mg/dL. The patients were divided into 2 groups: group A (GA) with < 55 years vs group B (GB) with ≥ 55 years.

**Results:** Total sample of 1168 patients, 70.1% male, mean age 69 ± 12 years. The younger group accounts for 15.8% of the population. The sample had an average of CT of 176 ± 55 mg/dL, LDL of 111 ± 45 mg/dL, HDL of 40 ± 12 mg/dl and Triglycerides of 137 ± 102 mg/dL. The following average ratios were attained: TC/HDL 4.6 ± 1.9, LDL/HDL 2.9 ± 1.4 and TG/HDL 3.8 ± 3.5.

**Conclusion:** In this population, there was a consistently worse lipid profile in young patients with ACS. This data validate the role of dyslipidemia in the pathogenesis of coronary heart disease, contributing to an early and accelerated atherosclerosis process. This reinforces the importance of adopting a healthy lifestyle and therapeutic compliance in primary and secondary prevention of cardiovascular events.

	GA with <55 years	GB with ≥55 years	
Total cholesterol	199 ± 44	170 ± 56	p < 0.001
LDL cholesterol	128 ± 37	107 ± 46	p < 0.001
HDL cholesterol	39 ± 10	40 ± 12	p = 0.307
Triglycerides	195 ± 189	125 ± 66	p < 0.001
TC/HDL	5.3 ± 1.5	6.8 ± 2.0	p < 0.001
LDL/HDL	3.4 ± 1.1	2.8 ± 1.4	p < 0.001
TG/HDL	5.6 ± 6.3	3.5 ± 2.5	p < 0.001

Lipid profile differences based on age

**P383**

**Effect of glycaemic status on left ventricular diastolic function detected by pulsed tissue doppler imaging in type 2 diabetes patients**

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**Background:** Diabetes mellitus is considering an important independent factor in developing diastolic dysfunction. Diastolic dysfunction comprises about 30 to 50% of all patients hospitalized for heart failure. The aim of this study was to determine the effect of glycaemic status on left ventricular diastolic function by pulsed tissue Doppler imaging in type 2 diabetic patients

**Methods:** our study included (100) subjects, 20 normal healthy subjects, 80 known to be Diabetic patients presented in our diabetic outpatient clinic and echocardiographic unit at Al-Hussein University Hospital between November 2010 and June 2011. The patient were classified according glycaemic status in to three groups: Group (A) Normal healthy control subjects. Group (B) well controlled diabetes HbA1C less than 7, Group (C) uncontrolled diabetes HbA1C more than 7.

**Results:** There was no statistically significant difference between the three groups as regard LV EDD, LVESD, LV EF% and LVFS%. There was statistically significant difference between the three groups as regard LA dimension mean E wave mean of A wave mean of E/A ratio diameter mean of DT mean of IVRT mean of Em wave mean of E/Em degree of diastolic dysfunction. There was statistically significant difference in patient have LV diastolic dysfunction between the three groups as regard E wave, A wave, DT, and IVRT. but there was no statistical difference between patient have diastolic dysfunction as regard mean of Em. There was negative correlation between HbA1c level and E wave, E/A, Em and positive correlation with LA dimension, A wave, IVRT, DT and E/Em.

**Conclusion:** The Glycemic status is well correlated with severity of diastolic dysfunction in asymptomatic type 2 diabetic patients. Tissue Doppler imaging has been shown to be more sensitive and more independent from various confounders, such as preload for assessment of diastolic function in asymptomatic type 2 diabetic patients and its results are significant correlated with glycemic state.

**P384**

**Diabetes in cardiac rehabilitation programs: how does it influence outcomes in patients with systolic dysfunction?**

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**Background and objectives:** Cardiac rehabilitation programs (CPR) have shown to be specially beneficial for patients (P) with low ejection fraction (EF) and they allow to improve diabetes (D.) control. We compared characteristics and functional

improvement in this particular subgroup according to the diabetes status.

**Methods:** Data were collected retrospectively of 509 P. with low EF (defined as EF<51%) referred to a CRP between May 2006 and October 2014 (97,4% after an acute coronary syndrome). They were categorized as diabetic whether they had previous history of D. or fulfill the criteria for the diagnosis of D. during the program. EF was determined using the Simpson method before starting the CRP and at the end of it; and functional capacity was evaluated with a treadmill exercise test (METs). Chi-square and t-student tests were used to analyze categorical and numerical variables, respectively.

**Results:** 88,6% were male with a mean age of 57,78 years. 124 P. (24,6%) had been diagnosed of D. and had a significantly higher prevalence of other cardiovascular risk factors. In P. with D., the mean EF was significantly lower (36,99% vs 38,91%, p=0,036) and severe systolic dysfunction was more frequent too (21% (43 P.) vs 11,3% (26 P.), p=0,007). Exercise capacity, which was significantly lower in diabetics before starting the CRP (5,98 vs 8,38 METs, p=0,01), improved in both groups with non-significant differences between them (6,64 vs 5,78 METs increase, p=0,66). The same results were obtained when evaluating the EF (9,27% vs 11,71% improvement, p=0,19), although systolic dysfunction continued to be more frequent in diabetics at the end of the CRP (49 P. (65,3%) vs 130 P. (53,9%), p=0,08). In fact, we observed in this subgroup a non-significant trend toward a worse metabolic profile when comparing them with P. with D. and normal EF, as it is summarized in table 1. **Conclusion:** The presence of D. is related to worse outcomes in cardiac patients. Cardiac rehabilitation has a key role in improving lifestyle and risk factor control of diabetic patients, in order to improve their cardiovascular outcomes.

Table 1

	Systolic dysfunction	Normal EF	Level of significance
HbA1c	9,64%	6,70%	p=0,34 (NS)
Glucose	134,09 mg/dL	130,80 mg/dL	p=0,75 (NS)
LDL	72,64 mg/dL	67,46 mg/dL	p=0,46 (NS)
Triglycerides	119,83 mg/dL	116,75 mg/dL	p=0,83 (NS)
BMI	27,69 Kg/m <sup>2</sup>	27,33 Kg/m <sup>2</sup>	p=0,85 (NS)

Metabolic control depending on the EF at the end of the CRP in diabetics with previous systolic dysfunction

### P385

#### Heart failure following acute st-elevation myocardial infarction: prognostic role of hyperglycemia, cardiotrophin-1 and galectin-3 plasma levels

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**Background:** Hyperglycemia on admission in patients with acute coronary syndromes (ACS) is common, and is considered as a powerful predictor of survival and increased risk of adverse cardiovascular events. Cardiotrophin-1 (CT-1) is a factor enhancing cardiomyocyte survival and protection in response to biomechanical stress, and a key regulator of glucose and lipid metabolism. It has been shown that galectin-3 (Gal-3) deficiency exacerbates hyperglycemia. There are still many gaps in our understanding of the association between elevated glucose levels and myocardial remodeling in acute ST-elevation myocardial infarction (STEMI).

**Purpose of the study** was to assess the significance of changes in CT-1 and Gal-3 levels over time in patients with STEMI and hyperglycemia on admission.

**Methods.** 60 male patients with STEMI without prior detected impaired glucose tolerance aged 39...60 were included in prospective open local study. The plasma concentrations of CT-1 and Gal-3 were determined using commercially available immunoassay kits on admission and on 7th day. Patients were followed-up for duration of hospital stay, cardiovascular rehospitalization, cardiovascular death and heart failure signs and symptoms (shortness of breath, ankle swelling, weight gain>2 kg within 3 days).

**Results:** Hyperglycemia>7.1 mmol/L at baseline was in 16.7% patients included in the study. In patients with hyperglycemia on admission CT-1 baseline level was higher (260.6 (229.6; 277.9) pg/mL vs 226.2 (220.2; 253.1) pg/mL, p=0.035). There were no differences in Gal-3 level at baseline in patients with and without hyperglycemia (17.5 (15.4; 22.2) ng/mL vs 21.9 (14.6; 30.7), p=0.222). In 86.6% of patients, changes in CT-1 and Gal-3 levels over time were of same direction: CT-1 increase between baseline and 7th day was associated with augmentation in Gal-3, and vice versa. In patients whose CT-1 level increased, left ventricular myocardial mass index was significantly higher than in patients with the opposite dynamics of CT-1 (84 (73; 98) vs 97 (92; 104) g/m<sup>2</sup>, p=0.023) independent of blood glucose level at admittance. In studied patients CT-1 at admittance correlated with blood glucose level (Spearman R=0.42, p<0.05). 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)). Using a multivariate binary logistic model, CT-1 decrease by>10% between

baseline and 7th day (HR 1.8, CI: 1.1-3.2, p=0.031) predicted death or heart failure onset within 6 month independent of age, serum creatinine, blood pressure and Killip class. The logistic model combining the CT-1, Gal-3 and blood glucose level yielded an AUC of 0.86 (p<0.05).

**Conclusion:** Hyperglycemia on admission, high levels of cardiotrophin-1 and galectin-3 with subsequent decrease are more informative at predicting cardiovascular death or heart failure than either marker alone in patients with acute ST-elevation myocardial infarction.

### P386

#### Nutritional indices, weight change, and mortality in heart failure: the nutrition Day survey analysis

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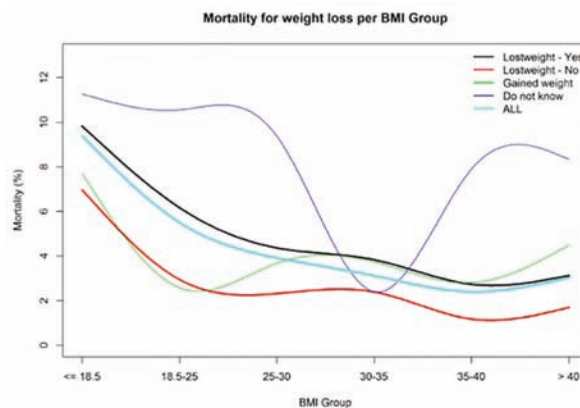
**Background:** Nutritional status and body weight trajectory are associated with outcome in patients with heart failure. To what extent this applies to hospitalized patients and whether there is association with appetite and nutritional intake during acute event is largely unknown.

**Purpose:** This analysis aimed to investigate relations between nutritional status, weight changes, nutritional intake, and all-cause mortality in patients with heart failure.

**Methods.** The NutritionDay survey is an ongoing multinational registry that collects comprehensive data about nutritional indices and in-hospital outcome. Body mass index (BMI), body weight changes within last 3 months, nutritional intake during last week and on the survey day were recorded; investigators reported about all-cause in-hospital mortality.

**Results:** We identified 10763 patients with HF (75±14 years, 51% men) with an average BMI of 27±7 kg/m<sup>2</sup>. Overall, 6% had BMI <18.5 and were classified as malnourished. Weight loss within last 3 months was self-reported by 48% of patients (most often 4-5kg - 7%). During last week, 30% reported to eat less than half of what they normally eat; on survey day, 50% ate half or less of their lunch/dinner. Lowest mortality risk was observed for patients with BMI 35-40 kg/m<sup>2</sup> while malnourished patients had 4 times higher risk of death. Relative risk for mortality increased with decreased food intake on survey day or during week prior to survey day (p<0.001 for both). Weight loss in last 3 months was associated with increased mortality, irrespective of BMI (Figure).

**Conclusions:** Malnutrition, weight loss and poor food intake are common in hospitalized patients with HF and are associated with in-hospital mortality.



### P387

#### Diabetes in chronic heart failure patients: the road to hell is sweet

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**Introduction:** Diabetes mellitus increases the risk of heart failure in patients with cardiovascular diseases. The purpose of the study was to analyze the characteristics of patients with chronic heart failure and diabetes, hospitalized in the Internal Medicine clinic of a University Clinical Emergency Hospital, as compared with those without diabetes.

**Methods:** The study included 80 patients with chronic heart failure, consecutively admitted in 2015. We have retrospectively and comparatively analyzed the characteristics of patients with heart failure and diabetes (group 1) versus patients without diabetes (group 2), using Analyse-it software.

**Results:** The distribution by sex in the group of study: 53.9% men, 46.1% women. The mean age of the whole group was 71.1 ± 11.6 years. 31.1% of the 180 patients had type 2 diabetes (41% on insulin). The distribution of comorbidities in diabetic patients was: 80.4% arterial hypertension, 47.7% coronary heart disease, 43.5% atrial fibrillation, 42.9% dyslipidemia, 35.2% chronic kidney disease, 34.1% anemia, 34.1% obesity, 23.3% pulmonary hypertension, 20.9% depression, 14% peripheral arterial disease, 35.7% mitral stenosis, 10.7% aortic stenosis. The frequency of chronic kidney disease was statistically significant higher in patients from group 1 (p 0.017), as well as arterial hypertension (80.4% in group 1 vs 62.5% in group 2, p 0.046). Obesity: 34.08% in group 1 vs 26.4% in group 2, p 0.46. Anemia: 34% in group 1 versus 12.7% in group 2, p = 0.007. Less patients from group 1 had atrial fibrillation (statistically significant). There was a significant difference in the frequency of coronary heart disease (47.7% in group 1 vs 29% in group 2, p 0.04). Dyslipidemia: 42.9% in diabetics and 32.5% in nondiabetics, p 0.2. In conclusion, almost 1/3 of admitted patients with chronic heart failure had type 2 diabetes. Conclusions Chronic heart failure patients with diabetes had a higher frequency of arterial hypertension, chronic kidney disease, obesity, coronary heart disease, mitral stenosis and anemia compared with patients without diabetes.

**P388**

**Blood glucose levels increase significantly across higher NYHA functional class categories in patients with chronic heart failure: results from TREAT HF**

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**Purpose:** Dysglycaemia and diabetes have been shown to be common in patients with heart failure (HF) and associated with worse prognosis. NYHA functional class has also been known to be a strong marker of poor prognosis. TREAT HF (Turkish Research Team-HF) data were analyzed for the assessment of any relationship between fasting blood glucose levels and NYHA functional class in patients with HF and reduced ejection fraction (HFrEF).

**Methods:** TREAT HF is a network which undertakes multicenter, national, observational studies designed to evaluate HF patient's clinical characteristics and current treatment modalities. 887 patients with the diagnosis of HFrEF and > 18 years of age who had fasting blood glucose measurement were included in this analysis. Out of 887 patients, 109 patients (12.2%) were in NYHA class I, 399 patients (44.9%) in NYHA class II, 337 patients (37.9%) in NYHA class III and 42 patients (4.7%) in NYHA class IV. Patients with recent acute coronary syndromes, severe hepatic or renal dysfunction, severe chronic obstructive pulmonary disease, severe anemia, cancer, hyper-/hypothyroidism and pregnant women were excluded from the study.

**Results:** Mean blood glucose level was 135 ± 68 mg/dL in study population, 123.2 ± 53 mg/dL in those with NYHA class I, 131.2 ± 66 mg/dL in those with NYHA class II, 140.8 ± 71 mg/dL in those with NYHA class III and 156.4 ± 77 mg/dL in those with NYHA class IV and overall, mean blood glucose levels were found to gradually and significantly increase across NYHA functional class categories (p = 0.01). Hyperglycaemia defined as blood glucose level > 126 mg/dL was found in 32 patients (29.4%) in those with NYHA class I, 128 patients (32.1%) in those with NYHA class II, 138 (40.9%) in those with NYHA class III and 25 patients (59.5%) in those with NYHA class IV and overall, the rate of hyperglycaemia was also found to gradually and significantly increase across NYHA functional class categories (p < 0.001).

**Conclusions:** These results suggest that there is a close relationship between NYHA functional class and fasting blood glucose levels or hyperglycaemia in patients with HFrEF as the blood glucose level increases significantly across higher NYHA functional class categories.

**DISEASE MANAGEMENT PROGRAMMES**

**P389**

**Experience in a cardiac rehabilitation unit with heart failure patients.**

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**Introduction:** More and more patients (p.) with heart failure (HF) or left ventricular systolic dysfunction (LVSD) are being referred to cardiac rehabilitation units. This is

a challenge because their particular characteristics compel us to adapt the type of training as well as the objectives of the program.

**Methods:** We received 206 p. (89.8% men) with severe LVSD (LVEF ≤35%, 17.5% of all p.), 92% of them with coronary disease. We performed a comprehensive program combining educational talks with supervised exercise sessions 3 days a week during 6-8 weeks, including an individualized medical consultation. We analysed the risk profile of the p., as well as the results obtained during the program with t-Student test.

**Results:** There was a high burden of risk factors: 52.9% had hypertension, 28.6% diabetes, 53.4% dyslipidemia, 55.6% were smokers and 25.5% former smokers, 25.9% obese and 55.1% had a sedentary lifestyle. In addition, they had a high rate of cardiac and non-cardiac co-morbidities. Medical treatment was optimized with 94% receiving beta blockers, 89% ACE inhibitors or ARA-II, 78% aldosterone antagonists and 15% ivabradine, 28% were on diuretic treatment and 92% on ASA and statins. During the program, there was a significant improvement in metabolic profile, as seen in table 1. Weight loss (>5% of basal weight) occurred in 15% of overweight p. Moreover, smoking cessation was achieved in 77% of patients at 3 months. Mean functional capacity (FC) improved from 6.1 METs at the beginning of the program up to 9.7 METs at the end of it. Only 4.5% of p. presented a poor FC (≤5 METs) when finishing the program, in contrast with a 43.2% in the basal ergometry. Regarding LVEF, there was a >10% improvement in 81% of p.: mean LVEF went from 29.5% to 42% at the end of the program, although we have to keep in mind that revascularization after STEMI had been performed in 68% of them. An ICD (implantable cardioverter defibrillator) was implanted in 22% of the p. Throughout the program, the rate of inappropriate shocks or shocks during exercise was 0%. Abandon rate was 12%.

**Conclusions:** Patients with LVSD and HF benefit from a structured cardiac rehabilitation program, with improvement both in metabolic risk profile through lifestyle correction and in FC by means of adapted exercise training.

Table 1.

Metabolic parameters	Basal	End of program	p	Other parameters	Basal	End of program	p
LDL (% <70 mg/dl)	104 ± 37	75 ± 28	< 0.001	Body mass index	27.9 ± 4.9	27.3 ± 4.3	< 0.001
HDL (mg/dl)	36 ± 10	37 ± 10	0.54	Waist circumference	100.3 ± 12	98.4 ± 11	< 0.001
TG (mg/dl)	143 ± 84	112 ± 52	< 0.001	METs	6.1	9.7	< 0.001
HbA1c (%)	6.3 ± 1.7	6 ± 1	0.047	FEV1	29.5 %	42 %	< 0.001

**P390**

**Day-care heart failure unit - a missing link in the management of refractory heart failure**

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**Background:** Heart failure (HF) is an increasing medical and economic burden worldwide. Despite the progress in cardiology, the prevalence of HF is increasing and the outcome remains poor. In advanced HF 1-year mortality as well as 1-year rehospitalization rates may exceed 50%. The comprehensive medical day care unit may be a clue of novel HF management. Day-care unit may possibly fill a gap between hospital and outpatient HF treatment.

**Purpose:** The purpose of the study was to assess the safety and clinical usefulness of day-care HF unit (DCHFU) among patients with refractory HF.

**Methods:** The study is a prospective analysis of consecutive patients and visits in DCHFU. The unit is a part of the tertiary cardiology hospital with possibility of cardiac surgery, heart transplantation and mechanical circulatory support. Patients with refractory HF fulfilling followed criteria were included into the study: NYHA class II-IV, at least two HF hospitalizations during preceding 12 months. Moreover, all possible methods of interventional treatment should be utilized – optimal revascularization, valvular correction and/or ablation performed, as well as ICD/CRT-D implanted if applicable. Optimally decongested patients qualified either for optimal medical therapy or heart transplantation were recruited during hospitalization. DCHFU is a hospital ward equipped with cardiac monitors, infusion pumps and other tools necessary to intravenous drug administration (diuretics, dobutamin). Furthermore, educational and dietetic activities, as well as diagnostic procedures and

ICD/CRT interrogations might be performed. Intervals between visits were individually arranged and two kinds of visits were scheduled depending on patients' clinical status - diagnostic (physical examination, body weight measurement, laboratory test, echocardiography etc.) and therapeutic (diagnostic + drug administration). The clinical parameters, procedures, events and the outcomes were monitored.

**Results:** During the initial 3 months of the project, 24 patients (age:  $60.9 \pm 13.5$  years; 12.5% of them were women; NYHA class  $2.88 \pm 0.79$ ; LVEF  $21.1 \pm 9.3$ ; NT-proBNP  $4130 \pm 1922$  pg/ml) were enrolled into the program. Out of first 140 visits, 100 (71.4%) had therapeutic

**Purpose:** Loop diuretics were administered during 92 (65.7%), low-dose dobutamine ( $<3.0$   $\mu\text{g}/\text{kg}/\text{min}$  infusion) - 70 (50%) and kalium - 27 (19.3%) visits. Moreover there were 3 (2.1%) pleurocenteses. There were no adverse events during the visits in DCHFU. In the course of the median 66 [64] days of observation, five (3.6%) patients were hospitalized, two (1.5%) patients died due to exacerbation of HF and four (2.9%) underwent heart transplantation.

#### Conclusion:

The day-care HF unit seems to be safe and useful option for refractory heart failure management.

### P391

#### Multidisciplinary telehealth program for patients affected by chronic heart failure and chronic obstructive pulmonary disease.

This work was financially supported by the Italian Ministry of Health -CCM 2011; project n. 14)

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**Background:** Chronic heart failure (CHF) and chronic obstructive pulmonary disease (COPD) frequently coexist, significantly reducing quality of life (QoL) and increasing morbidity and mortality. For either single disease, a multidisciplinary disease-management approach supported by telecommunications technologies offers the best outcome in terms of prolonged survival and reduced hospital readmission.

**Purpose:** The aim of study was to investigate the feasibility and efficacy of an integrated medical/nursing intervention plus rehabilitation program running at home versus conventional care in patients with coexisting CHF/COPD.

**Methods:** Patients, after inpatient rehabilitation, were randomly assigned to Treatment group (TG) or Control group (CG), followed for 4 months at home, then assessed at 4 and 6 months. The TG followed a telesurveillance (phone-contacts by nurse and telemonitoring of cardio-respiratory parameters) and telerehabilitation program ( $\geq 3$  sessions/week of mini-ergometer, calisthenic exercises and twice weekly pedometer-driven walking, plus phone-contacts by physiotherapist). Telephone follow-up served to verify compliance to therapy, maintain exercise motivation, educate for early recognition of signs/symptoms, and verify the skills acquired. At baseline and 4 and 6 months, the exercise capacity by the 6-min walk test (WT), dyspnoea and fatigue at rest (Borg scale), Physical Activity by a Scale for the Elderly (PASE), and QoL by Minnesota Living with Heart Failure Questionnaire (MLHFQ) and COPD assessment Test (CAT) were assessed. Serious clinical events were recorded and analysed as days free from hospitalization and death during 6 months of study.

**Results:** We enrolled 56 patients for group. 11 patients in the TG were lost to follow up (20%) as did 21 patients (37.5%) of the CG ( $p=0.036$ ). After 4 months TG improved significantly respect to CG in the change ( $\Delta$ ) of exercise capacity ( $\Delta\text{WT}$   $60 \pm 133$  in TG vs  $-15 \pm 82$  in CG,  $p=0.004$ ), dyspnoea ( $\Delta\text{Borg}$   $-0.4 \pm 1.2$  in TG vs  $0.7 \pm 1.4$  in CG,  $p=0.0001$ ), muscular fatigue ( $\Delta\text{Borg}$   $-0.5 \pm 1.5$  in TG vs  $0.8 \pm 1.4$  in CG,  $p=0.0000$ ), physical activity ( $\Delta\text{PASE}$   $18 \pm 65$  in TG vs  $-21 \pm 47$  in CG,  $p=0.0015$ ) and QoL ( $\Delta\text{MLHFQ}$   $-10.5 \pm 12.7$  in TG vs  $-0.44 \pm 14.5$  in CG,  $p=0.0007$  and  $\Delta\text{CAT}$   $-5.3 \pm 5.6$  in TG vs  $-1.6 \pm 6.4$  in CG,  $p=0.0000$ ). After farther 2 months, the TG had maintained significantly improvement in the exercise capacity ( $p=0.004$ ) and dyspnoea ( $p=0.0266$ ). The free days of events were significantly higher in the TG ( $p=0.0374$ ).

**Conclusions:** Our multidisciplinary telehealth program showed that this approach is feasible and effective in the management of such complex, frail patients with very high risk of exacerbation.

### P392

#### The impact of a comprehensive acute heart failure service on clinical outcomes

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**Background:** Acute heart failure (AHF) is a frequent cause of admission to hospital and is associated with a high mortality rate. Recent ESC guidelines recommend a multidisciplinary team approach to improve outcomes. In 2014 we introduced an acute HF outreach service to our medical wards led by a HF specialist nurse and HF consultant. This included proactively seeking patients with AHF on medical wards, education programmes for staff and daily review. We also implemented a novel initiative to improve care for patients approaching end of life.

**Purpose:** To describe the impact of the specialist HF outreach service on mortality, length of stay and 30-day readmission on medical wards.

**Methods:** We performed a retrospective analysis of data from all patients admitted to a medical ward (excluding cardiology) in our institution with a diagnosis of AHF during a 12 month period before and after the service was introduced. Patients were included if AHF had contributed to their admission. We assessed 30-day readmission rates, length of stay and mortality rates. We documented the number of discussions about prognosis and end of life care.

**Results:** (Table 1) Mean age of the AHF patients was 81 years in both periods. Following introduction of the outreach service 116 additional AHF patients were seen; there was a significant reduction in mean length of stay by 2.3 bed days per patient and a 4% decrease in 30 day readmissions. In contrast, there was a (non-significant) increase in mortality (possibly due to failure of the UK flu programme in 2014/15). Prior to the outreach programme, few AHF patients were being identified prospectively as nearing end of life on discharge. After introduction of a comprehensive treatment programme including education and linking with palliative care services, this was significantly increased with 116 discussions about prognosis and patients' end of life wishes documented prior to discharge.

**Conclusions:** Introduction of a specialist AHF outreach service from cardiology to medical wards resulted in a significant reduction in length of stay and 30-day readmission rates. The old age of many of these patients and high mortality of AHF emphasise the need for difficult discussions with patients about prognosis and planning of appropriate end of life care on discharge.

Table 1

	Pre	Post	p value
number of patients	623	739	
30 day re-admission rate (% , n)	17.3% (108)	13.3% (98)	0.04
30 day mortality rate (% , n)	15.1% (94)	18.5% (137)	0.1
mean length of stay (days)	13.5	11.2	0.01

Clinical impact of the AHF multidisciplinary team

### P393

#### Distribution and organization of heart failure outpatient clinics in Italy: preliminary data from the national working group survey

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**Background:** The role of traditional Heart Failure (HF) outpatient clinics (HFOC) in evolving health systems is challenged by the advocated shift from tertiary-based care to community-based outpatient services for the management of chronic conditions. To fulfil the claim to enhanced quality of care HFOC should relocate across the spectrum of HF population care and network to ensure that ambulatory HF patients are followed-up by the most appropriate health care providers in the right setting.

**Purpose:** To describe the national distribution and characteristics of HFOC offer and to investigate whether a reciprocal referral system exists between centres with different capabilities as preliminary step to the establishment of a national HF network based on specific regional features.

**Methods:** We used data from the last cardiology units census carried out by our national scientific society to identify departments that declared an HFOC offer in 2010. We e-mailed a 18-item questionnaire to investigate HFOC characteristics in terms of facilities, equipment, staffing and patient volume and established connections for upstream and downstream patient referral.

**Results:** Out of 432 cardiology units, 268 (62%) answered the questionnaire and 251 declared they have a dedicated HFOC. Most HFOC (233, 93%) have a Cardiology inpatient unit. Only 17% HFOC are located outside the hospital. Two-hundred-two HFOC (80%) are staffed by dedicated physicians and 163 (65%) by dedicated nurses. Approximately two-thirds of HFOC (164, 65%) are located in centres with a CCU, catheterization and electrophysiology labs and cardiac surgery and 14% (36) have heart transplantation and/or mechanical circulatory support program. A formal system for upstream patient referral exists in 72% of centres without advanced facilities.

**Conclusion:** The survey highlights that formal upstream referral, although available in most national centres, needs to be further strengthened. Conversely, there is ample room to improve HFOC networking with community care services.

**P394**

**The Italian heart failure care network guidance document**

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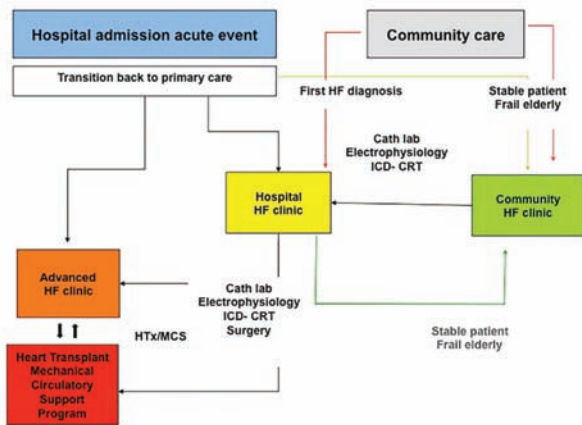
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**Background:** Changing demographics and an increasing burden of multiple chronic comorbidities in Western countries dictate refocusing of heart failure (HF) services from acute in-hospital care to better support the long inter-critical out-of-hospital phases of HF. In ours, as well as in other countries, needs of the HF population are not adequately addressed by current HF outpatient services, as documented by differences in age, gender, comorbidities and recommended therapies between patients discharged for hospitalised HF and those followed-up at HF clinics.

**Purpose:** Our national Working Group on Heart Failure has drafted a guidance document for the organisation of a national HF care network. Aims of the document are to describe tasks and requirements of the different health system points of contact for HF patients, and to define how diagnosis, management and care processes should be documented and shared among health care professionals.

**Methods and Results:** The document classifies HF clinics in 3 groups: 1) Community HF clinics, devoted to management of stable patients in strict liaison with primary care, periodic re-evaluation of emerging clinical needs and prompt treatment of impending destabilizations, 2) Hospital HF clinics, that target both new onset and chronic HF patients for diagnostic assessment, treatment planning and early post-discharge follow-up. They act as main referral for medicine units and community clinics, 3) Advanced HF clinics, directed at patients with severe disease or persistent clinical instability, candidates to advanced treatment options such as Heart Transplant or Mechanical Circulatory Support. Those different types of HF clinics are integrated in a dedicated network for management of HF patients on a regional basis, according to geographic features. By sharing pre-defined protocols and communication systems, these HF networks integrate multi-professional providers to ensure continuity of care.

**Conclusion:** This guidance documents is expected to promote a more efficient organization of HF care, in particularly for elderly patients and in transition phases from acute to chronic HF, by networking outpatient cardiology offer and primary care.



**P395**

**Effect of extended follow up in a specialized heart failure clinic on health related quality of life: northstar quality of life substudy**

Roche Diagnostics  
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**Background:** The mortality rate for patients with heart failure (HF) and reduced left ventricular ejection fraction has been reduced and it has been suggested that physicians and researchers should pay more attention to quality of life in these patients. Health related quality of life might, therefore, be important clinical endpoint in future clinical trials. Purposes: In The NorthStar Quality of Life Substudy we evaluated the effect of extended follow up in aHF clinic on health related quality of life and the relationship between Minnesota Living with HF questionnaire (MLwHFQ) Score and risk of death and a re-admission.

**Methods:** Post hoc analyses on data from a randomized clinical trial. A total of 961 systolic HF patients educated in HF and on optimal medical therapy according to

European guidelines were randomized to either extended follow up in a HF clinic or follow up in Primary Care and followed for a period of 2.5 years (6 months- 4.5 years) and the effect of the intervention on MLwHFQ Score at follow up end was evaluated by paired a T-test. Patients were stratified according to MLwHFQ Score and the relationship to risk of readmission and death were evaluated by Cox Proportional Hazard Multivariate Models.

**Results:** The patients had an age of Mean age was 69±10 years, 75 % were males, 59 % had ischemic heart disease 90 % were NYHA II-III, LVEF 0.30±0.07, NT-proBNP 801 pg/ml (IQ range: 111- 6500 pg/ml) and MLwHFQ was 24 (IQ: 12-41). Extended follow up had no effect on health related quality of life (-1 versus 0 (P=0.573)). MLwHFQ Score was associated with an increased risk of time to death or a cardiovascular admission (Hazard Ratio (HR): 1.43 (1.10-1.85, P=0.007)), a HF admission (HR: 1.93 (1.25-2.97, P=0.003) and an over all admission (HR: 1.43 (1.15-1.77, P=0.001) in multivariate analyses adjusted for traditional confounders. Patients with a poor quality of life were more frequently admitted (58 % vs 45 %, P=0.01, had more admission days (10 vs 7, P=0.002) and had a higher number of admissions (1.6 vs 1.0, P=0.003).

**Conclusions:** Extended follow up in a HFC had no effect on health related quality of life. However, a poor MLwHFQ Score was associated with an increased risk of death and re-admission. Improving health related quality of life may reduce admission rates in HF and this endpoint should be further evaluated by new interventions.

**P396**

**Effect of successful treatment and non - pharmacological disease management program on severity of anxiety and depression symptoms in congestive heart failure patients.**

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**Background:** CHF is frequently associated with depression and anxiety. It is disputable that depressive symptoms may be reversible without specific therapy in parallel with improving of physical condition. Disease Management Programs (DMP), consisted of structured education and regular phone calls, have been shown significantly reduce risk of death and hospital readmission and in CHF patients.

**Objectives:** To evaluate - is it real connection between CHF symptoms reduction and improvement of depression and anxiety scores during CHF treatment plus DMP. **Materials and Methods:** We analyzed the data from 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-hospitalization and prognosis in patients (CHANCE)). DMP did not include any special psychological intervention. Patients' assessment of depression and anxiety were determined at baseline, on 24 and 48 weeks by Hospital Anxiety and Depression Scale (HADS). Clinical symptoms and functional capacity of the patients were assessed by 'Scale of Heart failure Optimizing Clinical Status (SHOCS)', routinely used in Russia and with 6 minute walk test (6MWT).

**Results:** HADS questionnaire was performed in 737 patients at baseline. Clinically relevant depression (HADS > 10) was found in 272 (37%) of patients (III-IV NYHA FC, 34,6% women, average age - 62,7 ± 10,9). Symptoms improved at 48 weeks in all patients (univariate ANOVA for HADS p < 0,000001). But in DMP group, number of patient with clinically relevant depression (HADS > 10) decreased by 19,7% more, compare with usual care group (p < 0,001). There were positive correlations between the average clinical improving of CHF symptoms, assessed by SHOCS, or increased 6MWT distance and depression and anxiety score reduction (HADS) in both groups at 48 weeks of treatment.

In pts, whose clinical symptoms of CHF have not improved or deteriorated (N = 120), that underwent DMP more likely significantly reduce depressive OR 2,54 [95% CI:1,094-5,9] p=0,02 and anxiety symptoms OR 2,82 [95% CI:1,21-6,56 p=0,0139], than patients in usual care group.

**Conclusions:** Depressive and anxiety symptoms in patients with CHF in the majority of cases are reversible and decreasing without specific therapy is in parallel with improving CHF symptoms. But non-pharmacologic DMP even without specific psychological support give additional benefit due positive impact on emotional wellbeing of CHF patients, even in unsuccessful treatment of CHF.

**HEART FAILURE IMAGING**

**P397**

**Right ventricular inflow tissue doppler time intervals in patients with left heart failure**

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The purpose of our research was to study the changes in right ventricular (RV) TDI parameters in patients with Heart Failure (HF). Material and

**Methods:** We studied 110 patients with II-IV NYHA functional class HF (I gr.) and 110 patients with Arterial Hypertension and Coronary Artery Disease but without HF. RV TDI was registered from lateral corner of tricuspid valve. In HF group 53 patients had systolic and 57 - diastolic HF. All patients were in sinus rhythm. We measured maximal systolic (S2), isometric contraction (S1), early diastolic (E) and late diastolic (A) velocities; ejection (RVET), Isovolumic Contraction (ICT) and Isovolumic Relaxation (IRT) time intervals, calculated RV Tissue TEI index as  $TEI_{RV} = (ICT + IRT) / RVET$ .

**Results:** The difference between patients with and without HF in TDI velocity parameters was not significant, but ICT ( $81.4 \pm 35.4$  msec. in I gr. versus  $69.4 \pm 17.2$  msec. in II gr.,  $p < 0.05$ ), IRT ( $75.0 \pm 30.2$  msec. in I gr. versus  $16.8 \pm 12.8$  msec. in II gr.,  $p < 0.001$ ) and  $TEI_{RV}$  ( $0.55 \pm 0.24$  in I gr. versus  $0.35 \pm 0.24$  msec. in II gr.,  $p < 0.001$ ) were significantly greater in patients with HF. 94 % of patients with HF and only in 7% of patients without it had IRT more than 35 msec. The Sensitivity of  $RVIRT > 35$  msec in diagnosis of HF was 0.94, specificity – 0.93. **Conclusion:** There are prominent changes in RV TDI Time Intervals in patients with left ventricular HF. The prolongation of IRT on RV TDI ( $> 35$  msec.) is sensitive EchoCG marker of HF.

### P398

#### Cardiovascular remodeling in patients with essential hypertension and concomitant type 2 diabetes depending on polymorphism of agtr1 gene

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In recent years the researchers have been paying much attention to study of genetic components of essential hypertension (EH) and type 2 diabetes (DM2) - one of the most common noninfectious diseases in the world. The aim of the study was to investigate the polymorphism of angiotensin II receptor type 1 gene (AGTR1) and its associations with cardiovascular remodeling in patients with EH and concomitant DM2. The main study group consisted of 320 patients, aged from 45 to 60 years old with EH stage II, grade 2, heart failure I-II functional classes in combination with DM2 moderate, subcompensated. The group of comparison consisted of 90 patients with EH without DM2. The control group consisted of 31 healthy individuals with no EH and DM2, as they were excluded on the basis of the complex clinical and instrumental examinations. It was established that more than half of patients with EH both as in presence and absence of DM2 had A/C and C/C genotypes of AGTR1 (61,6% and 57,8% respectively), which are regarded as unfavorable for the development of the cardiovascular pathology. As to the spectrum of these genotypes the main group and comparison group significantly differ from control group ( $p < 0,01$  and  $p < 0,05$  respectively). It was found that allele C was present in about a third of patients with EH (both in presence and absence of DM2 (33,1% and 31,1% respectively)), while in control group it was present significantly much less frequently (in 19,4% of patients,  $p < 0,05$ ). It was established that patients with A/C and C/C genotypes of AGTR1 had significantly higher blood pressure levels ( $p < 0,001$ ), sizes of left ventricle (LV) and myocardial mass index (MMI) LV ( $p < 0,01$ ), intima-media thickness (IMT) at lower degree of endothelium-dependent vasodilatation ( $p < 0,01$ ) than in A/A genotype. Thus, no significant difference in hemodynamic indices between homozygous genotype C/C and heterozygous genotype A/C was found. However in patients with EH without DM2 as well as in patients with comorbidity, polymorphism of AGTR1 was associated with the difference of blood pressure ( $p < 0,001$ ), severity of cardiac remodeling ( $p < 0,001$ ) and less vessel remodeling (significant difference only in IMT,  $p < 0,01$ ).

**Conclusions:** It was established that there is an association of A/C and C/C genotypes of AGTR1 gene with the development of comorbidity EH and DM2 in Ukrainian population. A/C and C/C genotypes of AGTR1 gene were characterized by significantly higher levels of blood pressure, more pronounced disorders of structural and functional parameters of the heart and vessels than A/A genotype.

### P399

#### Evaluation of left and right ventricular systolic and diastolic function with tissue doppler, strain echocardiography imaging and myocardial performans Ttei ) index

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**Introduction:** Manifest Cardiac Sarcoidosis is readily diagnosed in only 5% of the cases. Nonetheless in post-mortem series pathologic investigation reveals

cardiac involvement in about 20-30% of sarcoidosis patients. There is variation in the prevalence of Cardiac involvement among different ethnic populations with numbers reported up to 58%. Early diagnosis and treatment can reverse pathological findings in cases with cardiac involvement. We aimed to investigate the prevalence of sub-clinical cardiac involvement by strain echocardiography imaging and myocardial performance (Tei) index calculated from tissue doppler echocardiography in sarcoidosis patients with normal conventional echocardiographic findings.

**Methods and Materials:** The study population were enrolled in between June 2015-January 2016 from the outpatient clinics of Department of Internal Medicine at an University Hospital. Sarcoidosis group consists of 31 patients, including 16 males and 15 females. Control group consists of 30 healthy volunteers including 15 males and 15 females. Tissue doppler, strain echocardiography and myocardial performance index values were analysed and compared between the patient and control groups.

**Results:** Mean age of the patient group was  $41,32 \pm 7,56$  years. Age, sex, body-mass index (BMI), functional capacity, family history of cardiac disease and conventional echocardiographic findings except left atrial volume and left atrial area index values were similar between the groups. Global longitudinal strain, longitudinal strain rate, diastolic E and A strain rates were found to be lower in the patient group compared to the control group. ( $p < 0,05$ ) Radial strain values were found to be similar between the patient and the control groups. ( $p = 0,096$ ) While Left Ventricular MPI were found to be higher in patient group ( $p = 0,01$ ), Right ventricular MPI were found to be similar. (0,193) **Conclusion:** Cardiac involvement of Sarcoidosis could be recovered with early diagnosis and treatment. Strain echocardiography and myocardial performance index investigations can guide early diagnosis and can be effective and feasible instruments in clinical follow up.

### P400

#### What is the best method to measure the left atrium in hypertrophic cardiomyopathy

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**Introduction:** Left atrium (LA) enlargement in hypertrophic cardiomyopathy (HCM) is associated with an increased risk of arrhythmias, thromboembolism and heart failure (HF). However, it remains unclear what is the best method to measure the LA. Our purpose was to assess the LA dimension by one-dimensional (M mode or 2D) and with the volumetric method. We subsequently analyzed which was more reliable to predict a clinical outcome.

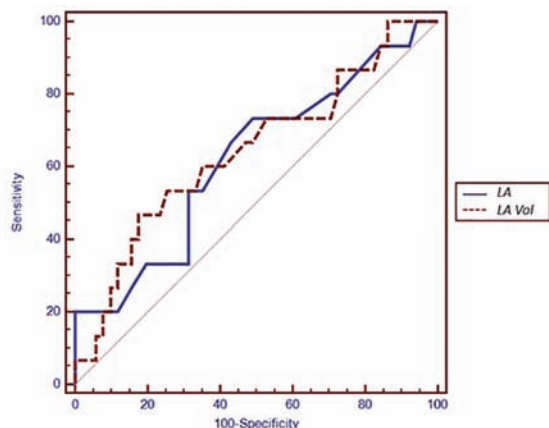
**Methods:** Retrospective study of 80 consecutive patients with HCM, all in sinus rhythm. We evaluated demographics, cardiovascular history, medication, laboratorial data, electrocardiogram and echocardiogram. We measured the LA with one-dimensional method (M or 2D mode) and with the volumetric method (modified Simpson). A clinical follow-up (combined) for mortality, HF hospitalization and sustained ventricular arrhythmia was performed (mean time of 18 months). The sample was divided into two groups: Group A (no event), N = 60; Group B (with events), N = 20.

**Results:** The mean age of the sample was  $58 \pm 18$  years with gender balance. 75% of patients had septal hypertrophy and 15% apical hypertrophy. Obstruction of the left ventricular outflow tract was present in 43,8% and about a quarter had an ICD. The mean LA diameter was  $4,3 \pm 0,8$  cm and the mean volume was  $87,7 \pm 34,5$  mL. The groups were homogeneous regarding the parameters described above. During follow up, patients with events (Group B), had a larger LA, either by one-dimensional ( $4,6 \pm 0,7$  vs.  $4,2 \pm 0,8$  cm;  $P = 0.035$ ) or by the volumetric assessment ( $103,0 \pm 45,7$  vs.  $82,7 \pm 29,8$  mL,  $P = 0.046$ ).

LA one-dimensional and the volumetric assessment had a similar accuracy to estimate the clinical outcome (area under curve one-dimensional: 0.62 vs. volumetric: 0.64, P for comparison = 0.72) – Figure 1.

Indexing to the body surface area did not improve both measurements discriminatory capacity.

**Conclusion:** According to our data, for HCM patients in sinus rhythm, LA volume was not superior to one-dimensional assessment to estimate a combined clinical outcome.



Area under curve comparison

**P401**

**Apical vs non-apical HCM: myocardial deformation assessment using 3D wall motion tracking**

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**Introduction:** Apical Hypertrophic cardiomyopathy (HCM) is a phenotypic variant of non-obstructive HCM, characterized by hypertrophy of apical segments, and is associated with a more favorable clinical outcome when compared with other types of HCM.

**Objective:** To evaluate the differences between patients with apical HCM and non-apical forms of HCM using three-dimensional echocardiography with 3D speckle-tracking (3DSTE).

**Methods:** Single-center study, including patients with HCM underwent assessment of atrial and ventricular strain by 3DSTE. Parameters of diastolic dysfunction were also assessed. Divided patients into 2 groups according to morphology: apical HCM and non-apical HCM. Statistical analysis was performed to assess differences among groups.

**Results:** 35 patients were included, mean age  $61.4 \pm 10.3$ ; 62.9% male. 10 patients (28.5%) had apical HCM. The mean left ventricular function by 3D volumetric evaluation was  $55.2 \pm 11.4\%$ . No statistically significant difference between the two groups was found ( $p = 0.26$ ). Myocardial deformation parameters of the left ventricular: there were no statistically significant differences in global longitudinal strain ( $-10.4 \pm 4.0$  vs.  $-10.3 \pm 2.9$ ;  $p = 0.93$ ), global circumferential strain ( $-24.9 \pm 9.4$  vs.  $-23.8 \pm 2.5$ ,  $p = 0.73$ ) global radial strain ( $28.9 \pm 12.7$  vs  $26.8 \pm 4.6$ ,  $p = 0.64$ ), area tracking ( $33.9 \pm 10.2$  vs  $30.4 \pm 4.4$ ,  $p = 0.19$ ) or twist ( $5.9 \pm 2.8$  vs  $5.5 \pm 3.7$ ,  $p = 0.73$ ). There were no statistically significant differences in the left atrial longitudinal strain ( $12.13 \pm 7.9$  vs  $13.8 \pm 7.4$ ,  $p = 0.81$ ), left atrial radial strain ( $13.9 \pm 9.4$  vs  $19.6 \pm 10.3$ ,  $p = 0.15$ ) or left atrial tracking area ( $32.5 \pm 21.9$  vs  $33.2 \pm 17.9$ ,  $p = 0.43$ ). The left atrial volume (systolic  $59.7 \pm 23.6$  vs  $54.6 \pm 14.7$  mL,  $p = 0.5$ ; diastolic  $88.2 \pm 26.8 \pm 14.9$  vs  $77.3$ ,  $p = 0.15$ ), left atrial ejection fraction ( $32.8 \pm 12.7$  vs  $29.9 \pm 9.1\%$   $p = 0.48$ ), ratio E / A ( $1.6 \pm 0.9$  vs  $1.7 \pm 1.2$ ;  $p = 0.95$ ), ratio E / E' ( $13.5 \pm 5.6$  vs  $11.5 \pm 4.8$ ,  $p = 0.32$ ) and E wave deceleration time ( $0:20 \pm 0.05$  vs.  $0:20 \pm 0.08$  msec,  $p = 0.87$ ) were not statistically different in both groups.

**Conclusions:** Although considered a more benign form of HCM, patients with apical morphology when compared with non-apical HCM patients showed no significant differences in the parameters of ventricular or atrial global deformation. Similarly, there were no significant differences in diastolic function parameters between the two groups.

**P402**

**Global longitudinal strain to identify patients with LVEF < 35% and LVEF < 30%**

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**Objectives:** Current pathophysiological understanding of the interrelation and similarities between strain and volumetric indices like LVEF is limited. For identifying patients with certain LVEF values, GLS has not played a role so far.

**Background:** Measurement of global longitudinal strain may prove useful in subdivision and risk stratification of patients with reduced ejection fraction. In patients

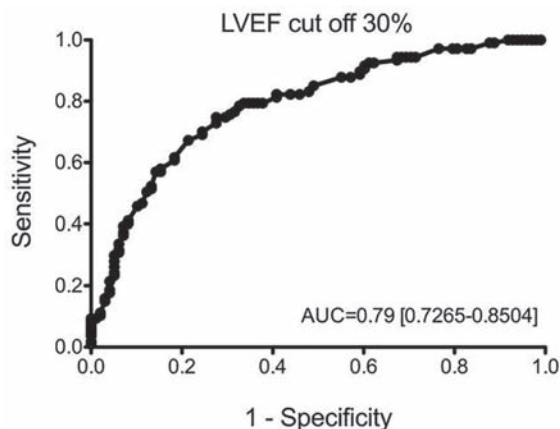
with heart failure a closer linkage and correlation between longitudinal strain values with LVEF may be at hand.

**Methods:** A total of 633 patients have been studied via conventional echocardiography and clinical characteristics have been documented. Subsequently echocardiographic images were reviewed by expert echocardiographers and 2D speckle tracking based strain analysis was performed.

**Results:** Myocardial tissue deformation is closely and meticulously linked with conventional parameters of systolic function. Correlation of conventional volumetric parameters such as LVEF with GLS was statistically highly significant ( $r = 0.90$ ,  $R^2 = 0.81$ ,  $p < 0.05$ ). For the subgroup of patients with LVEF 25-30% mean GLS was  $-6.48\%$  ( $\pm 0.12\%$  SEM), patients with LVEF 30-35% had a mean GLS of  $-7.88\%$  ( $\pm 0.13\%$  SEM). GLS values of  $-6.25\%$  to  $-6.71\%$  identified patients with LVEF 25-30% ( $n = 98$ ) with a 95% confidence interval. For patients with LVEF 30-35% ( $n = 107$ ) 95% confidence interval ranged from  $-7.63\%$  to  $-8.13\%$ . Further statistical correlation of GLS with LVEF allows objectifying the degree of left ventricular dysfunction: ROC analysis of the above mentioned GLS cut-off values proved GLS  $-7\%$  to be optimal in identifying LVEF  $< 30\%$  (AUC 0.79, Youden's Index 0.45) and GLS  $-9\%$  to identify LVEF  $< 35\%$  (AUC 0.86, Youden's Index 0.6) respectively. In a multivariate analysis parameters as age, sex, heart rate, arterial hypertension, body mass index, etc did not modify the relationship between GLS and LVEF significantly. **Conclusions:** GLS possesses excellent potential in stratifying patients with heart failure and reduced ejection fraction according to LVEF and thereby possibly help to identify candidates for ICD (GLS  $> -7\%$ ) and resynchronization therapy ( $> -9\%$ ).

LVEF and mean GLS 95% CI

LVEF (%)	n	GLS mean $\pm$ SEM (%)	GLS 95% CI	p
25-30	98	-6.48 $\pm$ 0.12	-0.12	< 0.05
30-35	107	-7.88 $\pm$ 0.13	-0.13	< 0.05
35-40	169	-10.12 $\pm$ 0.13	-0.13	< 0.05



Correlation GLS and LVEF 30%

**P403**

**Difference in prognostic impact of E to E prime ratio between decreased and preserved left ventricular function in patients with acute decompensated heart failure**

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**Background:** The ratio of early transmitral velocity to tissue Doppler mitral annular early diastolic velocity (E/E') is widely used for estimating pulmonary capillary wedge pressure, which can be one potent prognostic marker in patient with heart failure. Recent studies have shown that this estimation is quite inaccurate in patients with decreased left ventricular (LV) function. We aimed to investigate difference in prognostic impact of E/E' on long term prognosis between decreased and preserved left ventricular function in patients with acute decompensated heart failure (ADHF).

**Methods:** A total of 836 patients ( $66.2 \pm 14.7$  years-old, 442 men) who suffered acute decompensated heart failure between Jan. 2005 and June. 2015 were included. Composite of all-cause mortality and re-hospitalization for ADHF was recorded for 5-years follow-up. Results During follow-up ( $22.0 \pm 18.5$  months), 343 (41.0%) events were recorded. In overall patients, E/E' was an independent prognostic

marker for adverse events (hazard ratio [HR] 1.01 [1.00-1.03],  $p=0.023$ ) together with age, NYHA class, and serum creatinine. Kaplan-Meier analysis revealed that patients with high  $E/E'$  ( $E/E' > 15$ ) exhibited significantly worse prognosis (49.7% vs. 25.7%,  $p < 0.001$ ) compared to those with low  $E/E'$  ( $E/E' \leq 15$ ) in patients with preserved LV function (LV ejection fraction  $> 30\%$ ), whereas there is no significant difference in prognosis between high and low  $E/E'$  group (45.0% vs. 36.4%,  $p=0.144$ ) in patients with decreased LV function (LV ejection fraction  $\leq 30\%$ ). In crude analysis model,  $E/E'$  significantly predicted prognosis in patients with preserved LV function group (HR 1.05 [1.03-1.07],  $p < 0.001$ ), whereas  $E/E'$  could not (HR 1.00 [0.99-1.02],  $p=0.611$ ) ( $p$  for interaction  $< 0.001$ ). In adjusted model including age, sex, body mass index, heart rate, hypertension, diabetes, serum sodium, serum creatinine and inotropics use,  $E/E'$  still significantly predicted prognosis in patients with preserved LV function (HR 1.04 [1.02-1.06],  $p < 0.001$ ) and it could not in patients with decreased ejection fraction (HR 0.996 [0.98-1.01],  $p=0.634$ ). There was significant interaction in adjusted model ( $p$  for interaction  $= 0.011$ ).

**Conclusion:**  $E/E'$  significantly predicted long-term outcome in patients with heart failure of preserved LV function, whereas it could not in patients with decreased LV function in acute heart failure setting.

#### P404

##### Radial deformation of the left ventricular myocardium in patients with STEMI with different outcomes of revascularization as a stabilizing factor of systolic function of the heart

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**Objective:** to study alterations of different types of deformation parameters of the left ventricle (LV) for 3 months by a two-dimensional Strain (PAD) in patients with acute myocardial infarction (AMI) with segment ST elevation (STEMI) based on the results of revascularization by TIMI scale (0-4) and hemodynamic parameters.

**Methods:** The study included 49 patients (group 1) with STEMI ( $51.25 \pm 9.05$  years), confirmed by ECG, coronary angiography (CAG), the level of troponin I, CK-MB. Inclusion criteria were the absence of hemodynamically significant coronary artery stenosis in addition to the infarct-related, previous myocardial infarction and other cardiovascular diseases. Control group 2 consisted of 21 healthy volunteers, the average age -  $44.9 \pm 6.8$  years. Echocardiography was performed by ultrasound scanner My Lab 900 (Esaote, Italy) at 7 day and 3 months from the onset of the disease. With the software X-Strain the global longitudinal, circular and radial deformation (%) (Global Longitudinal Strain - GLS), (Global Circular Strain - GCS), (Global Radial Strain - GRS) have been determined. Among the traditional echocardiographic parameters the index of end-diastolic volume (EDV index) and ejection fraction (EF) has been analyzed.

**Results:** Group 1 were divided into 2 subgroups based on TIMI scale: group 1a included 34 patients (69%) with good angiographic result (TIMI 2-3), in 1b - 15 patients (31%) with unsatisfactory result (TIMI 0-1). Patients of group 1a and healthy persons had a comparable level of EF, respectively 66.0 (61.0; 70.0), and  $68.2 \pm 5.1\%$  (ns), in the group 1b values were decreased ( $50.3 \pm 12.2\%$ ) ( $p < 0.01$ ). Patients with TIMI 0-1 and 2-3 had no significant deterioration of the EF. In groups 1a and 1b GRS was initially reduced to a lesser degree than other types of deformation, respectively 8.7 ( $p < 0.05$ ) and 31% ( $p < 0.01$ ), GLS -11.4 ( $p < 0.05$ ) 50% ( $p < 0.01$ ), GCS - 16.5 and 62.5% ( $p < 0.05$ ). After 3 months, the most positive trend (10%) had GRS in patients with TIMI 0-1.

**Conclusion:** Damage of the middle layer of the myocardium is not accompanied by significant reduction of global radial Strain which characterized its function. In groups with different outcomes of revascularization after 3 months radial deformation has been increased to a greater extent in the group TIMI 0-1. Increased radial deformation contributes more to the left ventricular contractile function in patients with TIMI 0-1 and promotes long-term maintenance of the pumping function of the heart.

#### P405

##### New insights from 2D speckle-tracking echocardiography analysis in chronic heart failure.

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**Introduction:** B-type natriuretic peptide (BNP) is secreted from the heart primarily in response to stretch due to left ventricular (LV) overload. BNP plasma levels increase in heart failure (HF) according to augmented LV filling pressure and dysfunction of left atrium (LA). Speckle-tracking two-dimensional strain echocardiography (2DSE) analysis is considered a feasible and reproducible approach to quantify LA dynamics.

**Purpose:** Accordingly, the purpose of the present study was to correlate the LA intrinsic myocardial function using 2DSE analysis to BNP levels in patients with chronic systolic HF and to assess its prognostic value to develop new-onset atrial fibrillation (AF).

**Methods:** We prospectively studied 121 consecutive outpatients with chronic HF of ischemic or non ischemic etiology. Eligible patients were 18 to 85 years of age, with left ventricular ejection fraction (LVEF)  $< 40\%$  and sinus rhythm. Exclusion criteria were refractory atrial arrhythmias to medical therapy, pregnancy, primary valvular disease, mechanical valve prosthesis, recent myocardial infarction or coronary intervention, severe obstructive pulmonary disease or severe renal failure (creatinine clearance  $< 30$  ml/min). Simultaneously to BNP determination, peak atrial longitudinal strain (PALS) were measured in all enrolled subjects. PALS values were obtained by averaging all segments (global PALS), and by separately averaging segments measured in the 4-chamber and 2-chamber views.

**Results:** At linear regression analysis, Log\_BNP was directly correlated with age, NYHA class, LA volume and mitral effective regurgitant orifice area; inversely correlated to global PALS (Figure 1,  $R = -0.47$ ,  $p < 0.0001$ ), LA and LV ejection fraction (EF). According to the multivariate regression analysis, reduced global PALS independently correlates to BNP levels ( $\beta = -0.22$ ,  $p = 0.01$ ). During 3-year follow-up, AF occurred in 29 of 121 patients. Reduced global PALS had the highest accuracy to predict new-onset AF ( $p < 0.05$ ).

**Conclusions:** In chronic systolic HF-population, LA longitudinal deformation by 2DSE analysis independently correlates to BNP values reflecting LA dysfunction and predicts long-term new-onset AF.

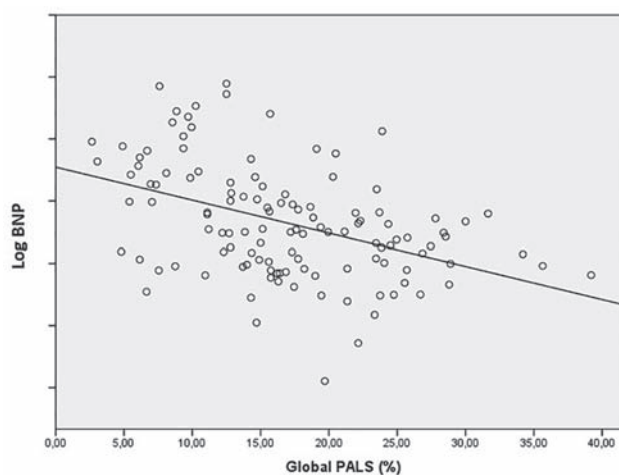


Figure 1

#### P406

##### Prognostic relevance of the pulmonary artery diameter in relation to the ascending aorta

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**Background:** The pulmonary artery (PA) diameter and its relation to the ascending aorta (PA:Ao ratio) by cardiovascular magnetic resonance (CMR) or computed tomography (CT) have been identified as non-invasive markers for pulmonary hypertension in heart and lung disease. However, the prognostic value of such measurements is largely unknown.

**Methods and Results:** 650 consecutive patients (47.2% female, mean age  $56.1 \pm 17.1$  years) referred to CMR were prospectively enrolled. Diameters of the great arteries were measured in axial black blood images. Based on previous results, a PA:Ao ratio  $\geq 1.0$  was chosen as cut-off for further analysis. The primary endpoint was defined as a composite of cardiovascular hospitalization and death. 131 (20.2%) patients presented with a PA:Ao ratio  $\geq 1.0$ . These patients were more frequently female ( $p = 0.010$ ), presented with more atrial fibrillation ( $p < 0.001$ ), more diabetes ( $p < 0.001$ ), worse renal function ( $p < 0.001$ ), higher NT-proBNP levels ( $p < 0.001$ ), larger left ( $p = 0.023$ ) and right ventricles (RV,  $p = 0.002$ ), and worse RV function ( $p < 0.001$ ). Patients were followed for  $17.8 \pm 12.9$  months, during which 110 (16.9%) experienced an event. Kaplan-Meier analysis revealed worse event-free survival rates in patients with a PA:Ao ratio  $\geq 1.0$  (log-rank,  $p < 0.001$ ). By multivariable Cox-regression analysis, a PA:Ao ratio  $\geq 1.0$  was independently associated with outcome, in addition to age, NT-proBNP serum levels, and RV size. **Conclusion:** The PA:Ao ratio is an easily measurable parameter by CMR and CT. A ratio  $\geq 1.0$  identifies patients at risk, most likely due to elevated pulmonary artery pressures. Based on these results, the PA:Ao ratio should routinely be assessed in CMR and CT scans.



## P407

**Myocardial remodelling and fibrosis in nonischaemic dilated cardiomyopathy: insights from cardiovascular magnetic resonance**

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**Background:** In nonischaemic dilated cardiomyopathy (DCM), myocardial fibrosis can be detected by cardiovascular magnetic resonance (CMR) as late gadolinium enhancement (LGE) and has been associated with worse prognosis.

**Purpose:** We investigated whether LGE is associated with left ventricular (LV) reverse remodelling in DCM.

**Methods:** Ninety-seven DCM patients (age  $56 \pm 14$  years, 62 male) with LV ejection fraction  $\leq 50\%$  were enrolled and underwent baseline CMR; patients with ischaemic, valvular, congenital heart disease, other cardiomyopathies or contraindications to CMR were excluded. After a median 29-month follow-up (interquartile range 16-46) 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. LGE was quantified on post-contrast CMR images as percentage of LV mass. LV reverse remodelling was defined as a decrease  $>10\%$  of LV end-systolic volume at follow-up.

**Results:** Mean LV ejection fraction was  $37 \pm 10\%$  at baseline,  $44 \pm 12\%$  at follow-up. LGE was present in 56 (58%) patients at baseline (median 6% of LV mass, interquartile range 3-11%), without significant differences at follow-up (median 7%, interquartile range 4-11%,  $p=NS$ ). Patients experiencing LV reverse remodelling during follow-up ( $n=53$ , 55%) presented a baseline worse LV ejection fraction ( $34 \pm 11\%$ ) than patients not experiencing LV reverse remodelling ( $41 \pm 8\%$ ,  $p < 0.01$ ), greater LV end-diastolic volume ( $125 \pm 38$  vs.  $112 \pm 26$  ml/m<sup>2</sup>,  $p=0.05$ ), worse right ventricular ejection fraction ( $54 \pm 13\%$  vs.  $59 \pm 10\%$ ,  $p=0.03$ ), but significantly less fibrosis (median 5% of LV mass, interquartile range 2-9% vs. median 9%, interquartile range 3-15%,  $p < 0.01$ ); no age or gender differences were observed ( $p=NS$ ). Multivariate regression analysis showed that LGE extent at baseline CMR was a negative predictor of LV reverse remodelling ( $p < 0.01$ ), even after correction for age, New York Heart Association class, LV volumes and systolic function.

**Conclusion:** In DCM patients, LGE extent was a negative independent predictor of LV reverse during follow-up, irrespective of the initial clinical status and the severity of ventricular dysfunction.

## P408

**Prognostic value of left ventricular dyssynchrony and diastolic dysfunction 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, left ventricular (LV) diastolic dysfunction adversely influences LV function and is therefore associated with a poor prognosis. The aim of this study was to assess prognostic value of quantitative measurement of left ventricular diastolic function of ECG gated SPECT MPI in Patients with CKD.

**Materials and Methods:** 112 (mean LVEF,  $58 \pm 15\%$ , mean estimated GFR  $42 \pm 17$  ml/min, QRS width  $109 \pm 21$  msec) with CKD underwent rest and exercise 99m Tc tetrofosmin SPECT examination.

PFR, 1/3FR, TPFF and Phase SD 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:** 26 cardiac events (2 cardiac death, 9 ACS, and 14 HF progression, 1 lethal arrhythmia) occurred during a follow-up period of  $30 \pm 16$  months. There is no difference between the both group for QRS width and eGFR. ( $110 \pm 23.9$  vs  $105 \pm 21.1$   $p=0.853$ ,  $40 \pm 18$  vs  $43 \pm 15$ ,  $p=0.622$ ). The patients with cardiac events were associated with significantly diastolic abnormality PFR ( $1.86 \pm 0.64$  vs  $2.4 \pm 0.69$ ).

The subgroup of 37 patients with ischemic group and cardiac events also had a significantly lower PFR ( $1.78 \pm 0.54$  vs  $2.37 \pm 0.62$ ,  $p=0.013$ ,  $1.92 \pm 0.71$  vs  $2.31 \pm 0.73$ ,  $p=0.110$ ), than did the ischemic and non cardiac events.

When the patients with diastolic dysfunction (PFR  $< 1.8$ ) were divided into the low ( $> 26$ ) and high (PhaseSD  $> 26$ ) groups, High Phase SD group significantly had more cardiac event (CI: 0.2050-3.3846,  $p=0.013$ ).

**Conclusion:** Our preliminary results indicate that diastolic abnormality using SPECT may provide prognostic information in patients with CKD.

## BIOMARKERS

## P409

**The significance of serial changes of high sensitivity cardiac troponin I in coronary vs. non-coronary disease**

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**Introduction:** The new high-sensitivity assays (hsTnI) have been developed to increase the clinical sensitivity for detection of myocardial injury. It has been found that elevated levels of hsTnI, above the upper limit of the reference interval (RI) (men  $< 34.2$  ng/L; women  $< 15.6$  ng/L), occur in coronary and non-coronary disease.

**Purpose:** The aim of this study was to determine the limit of quantification for hsTnI analyzer Abbott Architect i1000SR in Croatia and compare the concentration hsTnI in patients regarding the diagnosis and clinical condition.

**Methods:** Retrospective analysis included 98 patients: 38 with coronary heart disease (20 with angina pectoris and 18 with acute transmural myocardial infarct), and 60 with non-coronary disease for which an initial measurement and a control measurement of the hsTnI level was conducted. The hsTnI concentration was determined by chemiluminescent immunoassay the microparticles (CMIA, Abbott Architect i1000SR). Limit of Quantification determined according to the protocol NCCLS EP17.

**Results:** The maximum concentration of hsTnI was measured in patients with acute myocardial infarct (186135.0 ng/L), and in the group of non-coronary disease in patients with peripheral atherosclerotic disease (4823 ng/L). For the following diagnoses the obtained concentration levels, presented as median and range to each diagnosis (ng/L) for initial/control test were: acute transmural myocardial infarct: 270(19.5 to 4056)/904(36-186134); angina pectoris: 98(10-1478)/83(7-1363); For those with non-coronary disease: atrial fibrillation waveform: 20.2 (5 to 282)/22(4.5 to 272); peripheral atherosclerotic disease: 428(3.0-4823)/2082(3.3-4696); diabetes mellitus: 22 (1.3 to 73)/20(1.9-80); chronic renal disease: 119 (50-164)/84(26-163.0); hypertension: 12 (3.3-17)/14 (5-33). The limit of quantification was verified at the concentration of 4.71 ng/L with a CV% 8.41%. Central values (ng/L) patient samples were 1.72, 4.80, 4.82, 5.08, 6.44 and 8.56 with coefficients of variation (CV%) 23.04%, 8.59%, 8.22%, 9.88%, 8.33% and 5.76%. Median serum pool value was 4.71 ng / L with a CV% 8.41%.

**Conclusion:** The most common cause significantly elevated troponin I was acute coronary syndrome. The resulting CV of 8.41% meets the criterion for total error (CV  $< 10\%$ ) and is confirmed by laboratory quantitation limit of 4.7 ng / L. Quantification of very low concentrations hsTnI reflect subclinical ischaemia and increases the possibility of more frequent and earlier detection of acute coronary disease with mandatory monitoring the dynamics of change in relation to the initial value.

## P410

**HSP70-molecular marker of cardioprotection in ischemic heart disease patients in physical rehabilitation**

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**Objective:** assessment of cardioprotection effect formation by analyzing the relationship between HSP 70 level in ischemic heart disease (IHD) patients with documented ischemia and the value of myocardial ischemia index at the stage of physical rehabilitation.

**Material and methods:** The study included 65 IHD patients (men and women) aged 39 - 65 y.o. (mean age  $54.6 \pm 9.2$  y.o.) with incomplete myocardial revascularization according to the results of percutaneous coronary intervention (PCI). Patients were included in the first 10 days after PCI. All patients performed 10-days course of daily controlled physical exercise (CPE) (up to 80% of maximal threshold load power) under ECG control, assessment of ischemia index, blood pressure and heart rate, and analysis of laboratory markers of myocardial injury (myoglobin, troponin, CK-MB, BNP - using immunofluorescent analyser Biosite Triage Meter Pro, Germany, and measurement of stress protein HSP70 with the use of laboratory diagnostics. ELISA on immunofluorescent analyser Stat. Fax USA. Safety and effectiveness of CPE were proved by study methods.

**Results:** HSP70 analysis showed that in IHD patients before CPE HSP70 values varied depending on patients' clinical status and at first were determined firstly by the severity of ischemic manifestations (Spearman Rank Order Correlations (Data HSP70 and Ischemia Index.sta) MD pairwise deleted Marked correlations are significant at  $p < 0.05000$ . During diagnostics test stress-resistance was increased in all patients after CPE with 80% intensity from threshold load and it was accompanied by the elevated expression of inducible form of HSP70; this was documented by the significant decreasing of HSP70 level in systemic circulation. High correlation ( $r=0.88406$ ) was shown for HSP70 level and ischemic index interaction in IHD

patients with incomplete myocardial revascularization during physical rehabilitation with CPE based on ischemic preconditioning. At the same time the values of threshold ischemia were increased: maximum ST depression decreased, decreasing ECG leads with depression of ST > 1 mm Hg and time to initial ST recovery, elevation of peak Minpostexercise diagnostic stress-test. Increased induction of HSP70 proved elevation of physical activity threshold (stress-resistance) and cardioprotective effect on IHD patients; it was proved by HSP70 level in systemic circulation.

**Conclusion:** Activation of proper intracellular system targeted for protection of cardiomyocytes from ischemia in IHD patients during CPE took place. This can be proved by increasing induction and expression of inducible HSP70 and can be used as molecular marker of cardioprotective effect in IHD patients.

#### P411

##### **Galectin 3 and chagas cardiomyopathy: relationship of this myocardial fibrosis marker with myocardial deformation measured by speckle tracking in patients with chagas disease.**

COLCIENCIAS and RED CHAGAS COLOMBIA. BIOCHAGAS project, code 501453730398, CT 380-2011.

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**Purpose:** Global Longitudinal Strain (GLS) has emerged as a superior method to detect early systolic left ventricular dysfunction when compared to ejection fraction. Galectin-3 is a beta-galactoside-binding lectin released by cardiac activated macrophages, which has been extensively evaluated as a marker of inflammation and cardiac fibrosis, the latter contributing to ventricular remodeling and dysfunction. In patients with hypertrophic cardiomyopathy, galectin-3 has proven to be a good marker of myocardial dysfunction, however, the correlation between levels of galectin-3 and GLS in patients with chronic heart failure of chagas etiology has not been previously evaluated.

**Methods:** Analytical cross-sectional study. Patients older than 18 years with chagas disease were included. Those patients with uncontrolled hypertension, diabetes, history of coronary artery disease and valvular disease were excluded. The GLS was established by speckle tracking electrocardiography and blood levels of Galectin-3 were determined, both measures were taken the same day. A descriptive analysis was performed, the correlation between the GLS and Galectin-3 was evaluated by scatter plot and Spearman's rank correlation coefficient. Finally, a multiple linear regression analysis adjusted by sex and age was performed.

**Results:** A total of 100 patients were analyzed, 55% (55/100) were men; the mean age was 61 years (SD ± 12 years); the median and interquartile range of LVEF was 42% (Q1 = 27; Q3 = 56), of galectin-3 was 14 ng / mL (Q1 = 11; Q3 = 19); of GLS was -12.6% (Q1 = -17.8; Q3 = -7.2). A positive correlation between GLS and galectin-3 values ( $\rho = 0.370$ ,  $p = 0.000$ ) was established; on the other hand, galectin-3 and LVEF presented a negative correlation ( $\rho = -0.374$ ,  $p = 0.000$ ). In addition, an association between GLS and galectin-3 ( $\beta = 0.309$ ,  $p = 0.005$ ) and LVEF and galectin-3 ( $\beta = -0.872$ ,  $p = 0.000$ ) both adjusted by sex and age was established.

**Conclusions:** Galectin-3 is a powerful marker of endomyocardial fibrosis. Chagas cardiomyopathy is a disease with apical and postero-basal fibrosis determined by NMR studies. In patients with Chagas cardiomyopathy, galectin-3 showed a moderate negative correlation with LVEF and a moderate positive correlation with the GLS. A linear regression model adjusted for sex and age showed association between these variables, suggesting its clinical utility as a marker of myocardial dysfunction in this group of patients.

#### P412

##### **Serial changes and associated clinical variables of cardiac troponin release in patients with acute heart failure syndrome**

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**Purpose:** Cardiac troponin (cTn) elevation in acute heart failure syndrome (AHFS) has been well-established, and referred as a potent predictor of poor prognosis. However, less is known about serial changes in cTn during hospitalization and clinical variables associated with cTn increase. So, we evaluated serial changes and associated clinical variables of cTn release in AHFS.

**Methods:** This study enrolled 230 patients hospitalized with NYHA III-IV AHFS and LVEF <35% in whom an acute coronary syndrome was not suspected. Patients were treated with optimal pharmacologic therapy with oxygen, diuretics and intravenous vasodilators. Blood samples for cTnI measurements were obtained from all patients at admission and after HF therapy. The detectable level of cTnI for the assay used in this study was  $\geq 0.01$  ng/ml and the 99th percentile of cTnI concentration in normal healthy individuals was 0.07 ng/ml. So, cTnI was considered to be abnormal if cTnI was detected above this level.

**Results:** At admission, 196 patients (85.2%) had a detectable level of cTnI ( $\geq 0.01$

ng/ml) and 73 patients (31.7%) had an abnormal level of cTnI ( $>0.07$  ng/ml). A new cTnI increase was observed in 44 patients (28.2%) during hospital stay. Patients with cTnI  $>0.07$  ng/ml had higher resting heart rate (HR) (85 [72-97] vs 79 [69-89] bpm,  $p = 0.02$ ), lower LVEF (22 [20-28] vs 26 [21-31] %,  $p = 0.003$ ), higher NT-proBNP (7604 [3434-10763] vs 4154 [1463-7248] pg/ml,  $p = 0.001$ ), higher creatinine (Cr) (1.17 [0.96-1.41] vs 1.00 [0.87-1.30] mg/dl,  $p = 0.013$ ), higher blood urea nitrogen (BUN) (29 [21-39] vs 24 [19-33] mg/dl,  $p = 0.03$ ) and higher high sensitive C-reactive protein (hsCRP) levels (27.7 [12.7-64.5] vs 14.3 [5.1-25.8] mg/dl,  $p = 0.001$ ). Furthermore, a significant positive correlation was found between cTnI levels and NT-proBNP ( $p < 0.001$ ), Cr ( $p < 0.002$ ), BUN ( $p < 0.001$ ) and hsCRP levels ( $p < 0.002$ ).

**Conclusions:** This study suggests that majority of patients with AHFS have detectable or abnormal levels of cTnI at admission and considerable proportion of patients shows cTnI increase during hospital stay and cTnI release is associated with lower LVEF, higher resting HR, NT-proBNP, Cr, BUN and higher hsCRP levels.

#### P413

##### **Decreased miR-1 expression is associated with ventricular tachyarrhythmia in patients with post-myocardial infarction heart failure**

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**Purpose:** Some preclinical trials suggest that miR-1 dysregulation may induce ventricular tachyarrhythmias by alteration in expression and function of connexin 43 located in gap junctions. The impact of this muscle-specific molecule on the development of life-threatening arrhythmias in humans has not been evaluated so far. The aim of this study was to compare the expression of miR-1 in ischaemic heart failure (HF) patients with and without symptomatic ventricular tachycardia (VT).

**Methods:** 49 consecutive patients admitted to the Intensive Cardiac Care Unit due to HF exacerbation underwent the research. miR-1 expression was evaluated by qRT-PCR. The serum concentrations of gal-3 and NT-proBNP were determined with the use of available diagnostic tests. A history of symptomatic non-sustained or sustained VT confirmed in ECG or Holter ECG monitoring was collected. In addition, all patients underwent a transthoracic echocardiographic examination. Subjects with acute coronary syndrome in the past 30 days were excluded.

**Results:** There were 9 patients aged  $70.5 \pm 9.6$  yrs identified with symptomatic VT and 40 patients aged  $71.7 \pm 0.9$  yrs without such arrhythmias in a medical history. The groups did not differ in terms of age, NYHA class, HF etiology and NT-proBNP levels. No significant differences between the groups were found for left ventricle ejection fraction, left ventricle end diastolic diameter, left atrium and right ventricle diameter or inter-ventricular septum (IVS) and posterior wall thickness as well.

The expression of miR-1 was decreased in patients with symptomatic VT (0.284 (0.189-1.74) change fold vs. 0.346 (0.163-0.69) change fold,  $p < 0.05$ ). Noteworthy, there was a significant negative correlation between the IVS diameter and miR-1 expression ( $R_s = -0.815$ ,  $p < 0.05$ ) and positive correlation between the RVd and NT-pro-BNP concentration ( $R_s = 0.829$ ,  $p < 0.05$ ) in this group. There were no significant differences in miR-21 expression and galectin-3 concentration between HF patients with and without VT.

**Conclusions:** miR-1 downregulation might be associated with symptomatic VT in patients with post-myocardial infarction HF. Further prospective studies are necessary to confirm its role in the pathogenesis of arrhythmias.

#### P414

##### **Use of biomarkers in the prognostic stratification of elderly patients with chronic advanced heart failure**

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**Background:** – Biomarkers can be useful in the prognostic stratification of patients (pts) with chronic heart failure (CHF). Among them, Brain Natriuretic Peptide (BNP) prevalently indicates volume overload, while Galectin-3 (Gal-3) and Soluble ST2 (sST2) are linked to myocardial stretch and fibrosis.

**Methods:** We reviewed data from 82 pts (75 ± 9 years, 68% males) followed by our Outpatients' CHF clinic (Table 1). In this group, values of BNP, Gal-3 and sST2 were assessed at the first visit; moreover, both six- and 12-months outcomes were known. Biomarkers were analyzed using Triage BNP Test for BNP, VIDAS Gal-3 for Galectin-3, and Presage ST2 Assay for sST2. ROC curves were built to determine optimal sensitivity and specificity of each biomarker in predicting cardiovascular mortality at six- and 12-months' follow-up. The interval of significance was 95%.

**Results:** BNP and Gal-3 levels were affected by age, NYHA class, HF duration, body weight, renal function and treatment with ACE inhibitors or angiotensin-receptor

blockers. On the contrary, sST2 levels were not influenced by any of these variables. Biomarkers' levels were higher in pts who died at follow-up (8 pts at six months, i.e. 9.8%; 10 pts at 12 months, i.e. 12.2%). From the analysis of ROC curves, BNP  $\geq$  600 pg/ml, Gal-3  $\geq$  25.9 ng/ml and sST2  $\geq$  35 ng/ml predicted mortality at six and 12 months ( $p < 0.05$ ): AUC was 0.69 for BNP, 0.74 for Gal-3 and 0.89 for ST-2 (sensitivity 89%, specificity 100%). CONCLUSIONS – In this CHF population (older than those examined in the available literature), sST2 was the more reliable biomarker for the prediction of medium-term cardiovascular mortality. The cutoff value of 35 ng/ml accurately distinguished low risk patients, who might be safely followed up in community-based facilities, from high risk ones, who should be referred to more specialized centers.

Table 1

TABLE 1	
NYHA class	2.8 $\pm$ 0.9
Ischemic aetiology	65%
Left ventricular ejection fraction (EF %)	38 $\pm$ 10
Hypertension / diabetes / anaemia / GFR $\leq$ 60ml/min	70% / 30% / 43% / 68%
Atrial Fibrillation	34%
ICD / CRT	61%
ACEi - ARBs / beta blockers / aldosterone-blockers	71% / 83% / 51%

clinical characteristics of patients

#### P415

##### Test-retest-reliability of measurement of circulating endothelial and endothelial progenitor cells in peripheral blood in patients with heart failure, diabetic nephropathy and arterial hypertension

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**Background:** Endothelial damage is a crucial factor leading to heart failure (HF) and other cardiovascular diseases. Circulating endothelial cells (CEC) and endothelial progenitor cells (EPC) have been described as new non-invasive markers of endothelial damage. They are measurable in peripheral blood and their level correlates with other markers of endothelial function. Ability to quantify and observe changes in CEC and EPC levels reliably will open new doors in screening and supervision of treatment effects. However, uniform procedures to isolate and determine CEC/EPC numbers accurately still have to be established.

**Aim:** We carried out a test-retest-study by applying the same method of isolating and counting CEC/EPC levels at two time points and calculated the correlation between both visits.

**Methods:** Endo-CEC was a prospective observational trial in 100 patients (mean age 65  $\pm$  9.6, 69% male and 31% female) consisting of four different groups; 25 HF rEF patients (HF with reduced ejection fraction, LVEF < 45%), 25 HF pEF patients (HF with preserved ejection fraction, LVEF  $\geq$  45% and echocardiographic evidence of diastolic dysfunction), 24 patients with diabetic nephropathy and 26 patients with arterial hypertension. Blood samples were obtained at two separate visits (mean time interval 7  $\pm$  3). CEC and EPC were determined via flow cytometry and expressed both in CEC/EPC per ml and as a percentage of peripheral blood mononuclear cells (PMNC). Intraclass correlation (ICC) between both visits was assessed.

**Results:** When comparing CEC levels of visit one and two, neither of the groups showed a correlation (overall ICC, CEC/ml: 0.078; CEC/PMNC 0.191). In contrast, the ICC of EPC measurements was statistically significant in each group (overall ICC, EPC/ml: 0.904; EPC/PMNC: 0.811 with group-specific ICC, EPC/ml: HF rEF: 0.946; HF pEF: ICC = 0.685; DiabNeph: ICC = 0.946; Arterial Hypertension: ICC = 0.683).

**Conclusion:** Our analysis show that our method of flow cytometry is a reliable tool to assess EPC levels in cardiovascular patients but also suggest that the CEC measurement has to be enhanced by identifying disturbing factors and reasons for the invalid

**Results:** As understanding and estimating the occurrence of CEC and EPC promise high potential for further treatment and supervision of heart failure and endothelial dysfunction associated diseases, further research is warranted.

#### P416

##### Association of plasma fischer ratio with left ventricular function in patients with idiopathic dilated cardiomyopathy

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**Backgrounds:** Fischer ratio is the molar ratio of branched-chain AAs (BCAAs: leucine, valine, isoleucine) to aromatic AAs (phenylalanine, tyrosine) and is important for assessing liver metabolism, hepatic functional reserve and the severity of liver dysfunction. It is recently known that Fischer ratio are decreased in heart failure patients. Furthermore in the failing heart, BCAA suppresses cardioprotective autophagy, repair mitochondrial biogenetic regulation in the heart and reduced reactive oxygen species (ROS). However, the associations between its levels and cardiac function are remain unclear. To explore in vivo evidence for potential role of Fischer ratio in human failing heart, we measured plasma Fischer ratio 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 51 patients with DCM (M/F: 37/14, mean age: 62 years) and 35 patients with normal cardiac function (Control group) were enrolled. Subjects showing abnormal liver enzyme level or chronic hepatitis viral infection were excluded. Plasma Fischer ratio 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 Fischer ratio in DCM were comparable to those in control subjects with normal LV function. However Fischer ratio in severely reduced LV function (LVEF < 30%) (n = 21) were significantly lower than those of remainings (2.98  $\pm$  0.68 vs 3.32  $\pm$  0.43,  $p < 0.05$ ). Also plasma Fischer ratio showed a significant positive association with LVEF ( $r = 0.28$ ,  $p < 0.05$ ) and FS ( $R = 0.28$ ,  $P < 0.05$ ). Plasma Fischer ratio showed a significant negative association with LVDD ( $r = -0.37$ ,  $p < 0.05$ ) and LVDDs ( $R = -0.46$ ,  $P < 0.05$ ). Conclusions The plasma Fischer ratio could be a novel biomarkers of left ventricular dysfunction and the extent of heart failure in patients with DCM.

#### P417

##### The role of postoperative measurement of cystatin C and NGAL in early detection of acute kidney injury after heart transplantation

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**Background:** Acute kidney injury (AKI) following heart transplantation (HTx) is associated with dismal survival. During acute changes in the renal function, however, the serum creatinine level is not an accurate indicator. Early diagnosis of AKI may contribute to timely intervention aimed at improving outcome.

**Purpose:** We focused on serum cystatin C (S-cystatin C) and urinary Neutrophil gelatinase-associated lipocalin (U-NGAL). We aimed to identify the diagnostic and prognostic value of these biomarkers.

**Methods:** In the prospective study we evaluated 117 consecutive patients after HTx. Based on the AKI definition (KDIGO AKI Guidelines 2012) of the change in serum creatinine or diuresis, we have defined AKI as the serum creatinine increase by  $\geq 50\%$  during the first seven post-HTx days or a worsening of the renal function requiring renal replacement therapy during the first week post-HTx. S-cystatin C as a marker of glomerular filtration and U-NGAL as a marker of tubular damage were serially measured.

**Results:** Overall 30 patients (25.6%) experienced the criteria of AKI. Preoperative renal function, demographics and comorbidities were similar between AKI and non-AKI groups. S-cystatin C showed the earliest separation between AKI and non-AKI group, with a significant difference already 3 hours after HTx ( $p = 0.016$ ) and persisting on day 7 ( $p = 0.0048$ ) and day 10 ( $p = 0.0072$ ). The increase in S-cystatin C preceded the S-creatinine elevation by 4 days. In all HTx recipients, U-NGAL was elevated in the early postoperative period. However, an increase in U-NGAL level was significantly higher at day 3 ( $p = 0.003$ ) in the AKI group compared to the non-AKI group. In a multivariate analysis, S-cystatin C > 1.6 mg/L at 3 hours after HTx predicted AKI with OR 4.3 (95% CI: 1.6-11.5). We found that elevated S-cystatin C ( $\geq 2.54$  mg/L on day 7) could also predict one-year mortality after HTx ( $p < 0.0001$ ).

**Conclusion:** Our results show that early elevation of postoperative S-cystatin C improve the ability to detect AKI and may determine the one-year prognosis after HTx.

#### P418

##### Effects of a cardiac rehabilitation program on plasma cardiac biomarkers in patients with chronic heart failure

French Federation of Cardiology, HOMAGE, GREAT

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**Background:** Cardiac rehabilitation (CR) improves symptoms, exercise capacity and quality of life of chronic heart failure (CHF) patients. Its effects on new plasma biomarkers of prognostic importance are unknown.

**Objective:** The present study aimed to analyze the effects of a structured CR program on plasma cardiac biomarkers in a large population of patients with CHF and reduced left ventricular ejection fraction (LVEF).

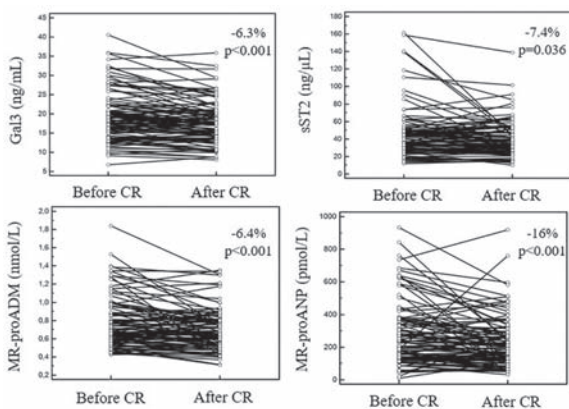
**Methods:** We enrolled 107 consecutive CHF patients with LVEF  $\leq$ 45% in an ambulatory CR program. Peak VO<sub>2</sub> and plasma levels of Galectin 3, MidRegional-proAdrenomedullin (MR-proADM), soluble Suppressor of Tumorigenicity 2 (sST2) and MidRegional-pro A-type natriuretic peptide (MR-proANP) were assessed at inclusion and at the end of CR. 24 unenrolled patients were managed with standard medical care and evaluated on a same period (no-CR group).

**Results:** Galectin 3, sST2, MR-proADM and MR-proANP plasma levels decreased after CR, with respective median reductions of 6.3% for Galectin 3 ( $p < 0.001$ ), 7.4% for sST2 ( $p = 0.036$ ), 6.4% for MR-proADM ( $p = 0.001$ ) and 16% for MR-proANP ( $p < 0.001$ ). MR-proADM negatively correlated with peak VO<sub>2</sub> (Rho = -0.529, CI [-0.654 to -0.375],  $p < 0.001$ ) and so were their relative variations along the course of CR (Rho = -0.357, CI [-0.518 to -0.172],  $p < 0.001$ ). No change occurred in terms of biomarkers in no-CR group. Plasma levels only decreased in patients who benefited the most from CR (peak VO<sub>2</sub> variation (Var(VO<sub>2</sub>))  $\geq$  14.5%, the median increase in the variation of peak VO<sub>2</sub>).

**Conclusions:** Plasma cardiac biomarkers such as Galectin 3, MR-proADM, sST2 and MR-proANP all decreased after CR in CHF patients suggesting an overall improvement in the neuro-hormonal profile. MR-proADM was well correlated with peak VO<sub>2</sub> and emerges as an interesting predictor of beneficial response to CR.

Biomarkers according to benefit of CR

Plasma levels	Before rehabilitation	After rehabilitation	p	
Galectin 3 (ng/mL)	Var(VO <sub>2</sub> ) $\geq$ 14.5%	19.0 [13.7;22.5]	16.9 [13.8;19.9]	< 0.001
	Var(VO <sub>2</sub> ) < 14.5%	17.3 [15.0;22]	17.7 [14.0;22.0]	0.057
MR-proADM (nmol/L)	Var(VO <sub>2</sub> ) $\geq$ 14.5%	0.7101 [0.5975;0.8887]	0.6369 [0.5299;0.7963]	< 0.001
	Var(VO <sub>2</sub> ) < 14.5%	0.6630 [0.5556;0.8317]	0.6878 [0.5431;0.8309]	0.928
MR-proANP (pmol/L)	Var(VO <sub>2</sub> ) $\geq$ 14.5%	262 [143;422]	176 [106;294]	< 0.001
	Var(VO <sub>2</sub> ) < 14.5%	202 [131;280]	202 [138;272]	0.502
sST2 (ng/ $\mu$ L)	Var(VO <sub>2</sub> ) $\geq$ 14.5%	36.0 [26.4;52.4]	31.0 [24.4;47.7]	0.001
	Var(VO <sub>2</sub> ) < 14.5%	37.1 [30.1;48.0]	37.3 [27.5;53.0]	0.682



#### P419

**Role of oxidized low-density lipoprotein in the development of adverse events in patients with Non-ST-elevation acute coronary syndrome**

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**Objective:** to examine the relationship of oxidative metabolism of lipoproteins markers with the development of adverse outcomes in Non-ST-Elevation Acute Coronary Syndromes (NSTE-ACS) during one year of follow-up.

**Materials and Methods:** A total of 159 patients with NSTE-ACS have been included in the study. The average age of patients was 61.0  $\pm$  9.19 years. Among the patients studied was 61.0% of men and 38.99% women. Determination of oxidized low-density lipoprotein (ox-LDL) and antibodies to ox-LDL serum in all patients was fulfilled by the 10th day of hospitalization. Follow-up was 12  $\pm$  4 months for the study group. All patients were divided into two groups: with a favorable (n = 123) and unfavorable (n = 35) outcomes [death from cardiovascular causes, unstable angina (UA), myocardial infarction (MI)].

**Results:** The ox-LDL level in serum was significantly higher in patients with unfavorable outcome. It was found that increased levels of ox-LDL more than 2.4 mg/kg/ml increases the risk of an unfavorable outcome for the year in patients with NSTE-ACS more than 10 times (OR = 10.4, 95% CI: 2.38-45.7;  $p < 0.0001$ ). The differences in the levels of antibodies to ox-LDL in the groups were not found.

**Conclusion:** The elevated levels of ox-LDL more than 2.4 mg/kg/ml in hospital period can be laboratory markers of adverse prognosis in patients with NSTE-ACS.

#### P420

**Red blood cell distribution width longitudinal changes in acute heart failure patients: a prospective study**

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**Background:** Red Blood Cell Distribution Width (RDW) is a simple parameter of the standard full blood count and a measure of heterogeneity in the size of circulating erythrocytes.

**Purpose:** The aim of this study was to investigate the clinical correlates, prognostic value and longitudinal changes of RDW in patients initially admitted for acute heart failure (AHF).

**Methods:** We conducted a prospective study of patients presented in the emergency department with AHF (denovo or acute decompensation of chronic HF) between January 2014 and July 2014. A clinical, ultrasound and hematological assessment was performed at admission, discharge, 4, 8 and 12 months after discharge and at every rehospitalization. Exclusion criteria were presence of cancer, sepsis, Hb <10g/dL and previous transfusions. The endpoint was death from any cause and/or rehospitalization for HF at 1 year. There were no missing values.

**Results:** 104 AHF patients (mean age, 73.5  $\pm$  12.0 years; male gender, 55.8%; mean LVEF, 38.9  $\pm$  14.7%) were enrolled in the study with 62.5% of them having reduced ejection fraction (HFrEF, i.e. LVEF < 40%). Admission RDW (mean value, 15.0%) showed significant correlation with Brain Natriuretic Peptide (Rho: 0.351,  $p < 0.001$ ), New York Heart Association class [ $p < 0.01$ , 95% CI (0.92-2.06)] and emerged as an independent prognostic marker regarding events at 1 year post discharge in the multivariate analysis, after adjustment for factors such as Hb and erythropoietin [adjusted OR: 1.67, 95% CI (1.18-2.38),  $p = 0.004$ ]. RDW longitudinal changes post discharge showed no significant difference in HFrEF versus HFpEF patients ( $p = 0.978$  adjusted for admission RDW) and in patients without events versus those with events ( $p = 0.349$  adjusted for admission RDW), although the latter had significantly higher mean RDW values at every time point ( $p < 0.001$ ). Patients on ACE-inhibitors (ACE-I) at admission had significantly lower mean RDW values compared to those who were not on ACE-I ( $p < 0.0001$ ). In addition, a statistically significant difference in the changes over time of the RDW was observed between patients who received ACE-I and those who didn't ( $p = 0.045$ ).

**Conclusions:** Admission RDW in AHF was found to be an independent prognostic marker for death or rehospitalization at 1 year after discharge. RDW longitudinal changes do not differ significantly among patients with or without events and in HFpEF versus HFrEF. The significantly lower RDW values in the population of AHF patients under ACE-I might be served as an insight to the pathophysiological mechanism of RDW change in HF, which remains unknown.

#### P421

**Association of putative biomarkers with polymorphisms of ACE1 and NOS3 in hypertension and heart failure**

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**Introduction:** EPO regulates many cellular functions and can be a biomarker for HF. Moreover Galectin-3 (an intercellular acute phase protein) is an emerging cardiac biomarker. The angiotensin I converting enzyme (ACE1) and endothelial nitric oxide (NOS3) polymorphisms have been associated with HF.

**Objective:** To assess the association of ACE1, NOS3 polymorphisms and cardiac biomarkers (Galectin-3 and EPO) in patients with HF.

**Material and Methods:** In patients with HF and preserved or decreased EF (EF<40%) were evaluated the genetic polymorphisms of ACE1 and NOS3 by PCR. There were also evaluated some possible cardiac biomarkers, NT-proBNP (pg/mL), Galectin-3 (ng/mL) and EPO (mIU/ml) determined by ELISA. The sample consisted in 162 patients with HF, aged 72.1 ± 12.5, 80 women (49.4%) and 82 men (50.6%). Statistical methods were the chi-square, Student's t-test, ANOVA and binary logistic regression, or its nonparametric equivalent. Statistical significance were considered for P < 0.05.

**Results:** NOS3 AA genotype was more frequent in patients with decreased EF (n = 6 (14.3%), P = 0.009), being the carriers of allele A with 3.64-fold at risk (OR = 3.68, 95% CI [1.57-8.63], P = 0.003). There weren't significant differences in the distribution of ACE1 genotypes according with EF (P>0.05). EPO levels were statistically significant lower in patients with EF<40% (median ± std.error, EF<40% (n=26): 6.2 ± 3.8mIU/ml vs. EF>40% (n=34): 14.8 ± 3.3mIU/ml, P = 0.025). The risk associated to carriers of allele A of NOS3 in patients with EF<40% was significantly greater, 3.64-fold to 10.73-fold, when adjusted for EPO levels (OR = 10.73, 95% CI [1.66-69.52], P = 0.013). The levels of Galectin-3 and NT-proBNP weren't associated with EF or NOS3 or ACE1 genotypes (P>0.05).

**Discussion and Conclusions:** Patients with lower levels of EPO and NOS3 allele A, were associated to lower EF, which may result in a physiologically effect of EPO on NOS3, reflecting the influence of hypoxia status in patients with HF.

#### P422

##### ST2 is an independent predictor of all-cause hospitalization in elderly patients.

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**Background:** NtproBNP is a known predictor of hospitalization. A new biomarker, suppression of tumorigenicity 2 (ST2) has been introduced as a marker for fibrosis and hypertrophy and may thus predict hospitalization. There is a lack of knowledge about the predictive value of ST2 in elderly primary health care (PHC) patients.

**Purpose:** To compare ST2 with NTproBNP as a predictor of time to first hospitalization in elderly patients with clinical symptoms of heart failure (HF).

**Methods:** Explorative analysis of a 10-year longitudinal study. Patients were recruited from one selected PHC in northern Sweden between 2000 and 2003 and comprised both registry patients and incident cases with suspected HF identified by the general practitioner (GP) at the PHC. All patients had clinical symptoms of HF and significant co morbidities. Blood samples were collected at baseline and stored frozen for future analysis. NTproBNP was analyzed with Roche Elecsys proBNP immunoassay. ST2 was analyzed with Critical Diagnostics Presage ST2 immunoassay. ST2 and NTproBNP were used as continuous variables in the analysis. Departments of medicine and surgery records were used to identify hospitalizations. The association between baseline characteristics and hospitalization at 10 years of follow up was analyzed with Cox regression analysis. Adjustments were made for significant variables from the univariate Cox regression analysis and from fixed factors as age, gender and smoking habits.

**Results:** We studied 159 patients (mean age 80 years, 66% women). During 10 years of follow up 128 (81%) patients had at least one hospitalization. In the univariate Cox regression analysis significant associations with time to first all-cause hospitalization were found for ST2 (hazard ratio [HR]: 1.04; 95% confidence interval [CI]: 1.02-1.05), age (HR: 1.04; CI:1.02-1.07), kidney dysfunction, defined as creatinine > 100µmol/L (HR: 2.56; CI:1.67-3.93), all HF (HR: 1.64; CI:1.12-2.42), NTproBNP (HR: 1.0002; CI:1.0001-1.0002), male gender (HR: 1.65; CI:1.13-2.40), underlying heart disease (HR: 2.04; CI:1.21-3.43), atrial fibrillation (HR: 2.24; CI:1.37-3.68). In the following multivariate analysis ST2 (HR:1.05; CI:1.03-1.08), age (HR: 1.04; CI:1.01-1.08), kidney dysfunction (HR: 2.26; CI:1.19-4.30), smoking habits (HR: 2.25; CI:1.23-4.10), underlying heart disease (HR: 4.29; CI:1.75-10.52) and NTproBNP

(HR: 1.0001; CI:1.0000-1.0002), were independently associated with time to first hospitalization at ten years of follow up.

**Conclusion:** ST2 was an independent prognostic marker of time to first all-cause hospitalisation in elderly PHC patients with clinical symptoms of HF. In these patients the clinical value of ST2 as an additive prognostic marker to NTproBNP needs to be further evaluated.

#### P423

##### Significance of copeptin concentration in acute decompensated heart failure patients long-term risk stratification

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**Background:** Copeptin concentration was strong predictors for of the adverse long-term prognosis in pts with ADHF.

**Purpose:** to evaluate the significance of copeptin concentration in risk stratification in patients (pts) with ADHF in one year follow-up period.

**Methods:** In our study were included 159 pts with ADHF III-IV FC NYHA. Blood samples to determine copeptin concentration were collected at the admission and at discharge from the hospital, and after 3, 6 and 12 months of follow-up. The primary end point was total cardiovascular events that included cardiovascular (CV) death and hospitalization due to HF.

**Results:** At admission all pts had elevated copeptin concentration: 41,56 ± 19,68 pmol/l. During the period of hospitalization mean copeptin concentration was decreased to 30,34 ± 15,51 pmol/l. During 1-year follow-up (mean 277 ± 115 days) 54 pts (33,96%) had CV events. At the admission copeptin concentration in low risk pts (without CV events) were significantly lower compared with high risk pts (with CV events): 35,79 ± 15,72 pmol/l versus 48,52 ± 21,71 pmol/l respectively, < 0,0001. The similar trend was observed and at discharge: 24,67 ± 11,79 vs 37,33 ± 16,75 respectively, p < 0,0001. At the discharge from the hospital copeptin concentration had the most predictive capacity relatively the primary end point during 1-year follow-up: AUC=0,745 (0,652-0,839), < 0,0001, sensitivity 83%, specificity 52,7% compared with copeptin concentration at the admission: AUC=0,682 (0,581-0,784), < 0,0001, sensitivity 66,7%, specificity 64,2%. Lack of copeptin concentration decrease below 23,9 pmol/l was associated with the highest risk of CV events (OR 5,597 (2,23-14,03), p < 0,0001). The copeptin concentration in pts with ADHF at the discharge was a predictor of adverse prognosis in the long-term follow-up (beta=0,626, p < 0,004).

**Conclusion:** The values of copeptin at the discharge from the hospital reflects the adverse long term prognosis in patients with ADHF.

#### P424

##### Detectable plasma levels of interleukin-9 are associated with impaired exercise capacity and poor survival in chronic heart failure.

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**Background:** Inflammation plays a pivotal role in Chronic Heart Failure (CHF) through increased expression of pro-inflammatory cytokines. Previous reports showed increased levels of Interleukin-9 (IL-9) in CHF and their negative association with left ventricular systolic function.

**Aim:** To test whether increased IL-9 levels are associated with impaired exercise capacity and poor outcome in CHF.

**Patients and methods:** Seventy-five CHF patients were enrolled and divided according to IL-9 levels. All patients underwent cardiopulmonary exercise test, echocardiography and were regularly followed-up for 59 ± 29 months.

**Results:** As shown in table 1, patients with detectable IL-9 showed impaired exercise capacity compared to patients with undetectable IL-9. Moreover, detectable IL-9 was associated with lower survival (figure 1). Cox-Univariate and multivariate analysis indicated that IL-9 was independently associated with all-cause mortality (HR = 2.36, 95% CI = 1.42–5.23, p: 0.01).

**Conclusions:** Detectable IL-9 plasma levels are associated with impaired exercise capacity and independently predict reduced survival in CHF patients.

Table 1

Variable	All Patients (n = 75)	Undetectable IL-9 (n = 40)	Detectable IL-9 (n = 35)	p value*						
Age-years	65.73	±	9.53	64.7	±	10.2	67.5	±	8.6	0.35
BMI-m <sup>2</sup> /Kg	27.48	±	3.86	27.9	±	3.4	27.1	±	4.2	0.28
Female sex (%)	15 (19.7%)	6 (17.1%)	9 (22.5%)	0.77						
T2DM prevalence (%)	23 (30.6%)	10 (28.6%)	13 (32.5%)	0.91						
ischemic etiology prevalence (%)	46 (60.5%)	21 (60%)	25 (62.5 %)	0.89						
NYHA class	2.34	±	0.68	2.1	±	0.6	2.5	±	0.7	0.04
NTproBNP (pg/ml)	2756	±	2920	2797	±	2491	2727	±	3269	0.91
GFR (ml/min)	79.9	±	19.9	78.1	±	19.5	81.4	±	20.4	0.51
Ejection Fraction (%)	32.74	±	4.31	32.4	±	4.7	33.1	±	4.1	0.49
Peak VO <sub>2</sub> (ml/Kg/min)	16.75	±	4.1	18.2	±	3.3	15.5	±	4.2	0.004
VE/VCO <sub>2</sub> slope	30.6	±	7.1	28.7	±	6.7	32.3	±	7.1	0.03
Peak Workload	91.1	±	26.9	100.9	±	25.5	82.6	±	24.5	0.003

Data shown as mean ± SD; \* = detectable vs. undetectable; T2DM = Type 2 Diabetes Mellitus; NYHA = New York Class Association; NTproBNP = N-terminal of the prohormone brain natriuretic peptide; GFR = glomerular filtration rate according to Cockcroft-Gault formula; VO<sub>2</sub> = oxygen consumption; VCO<sub>2</sub> = carbon dioxide production; VE = ventilation per min.

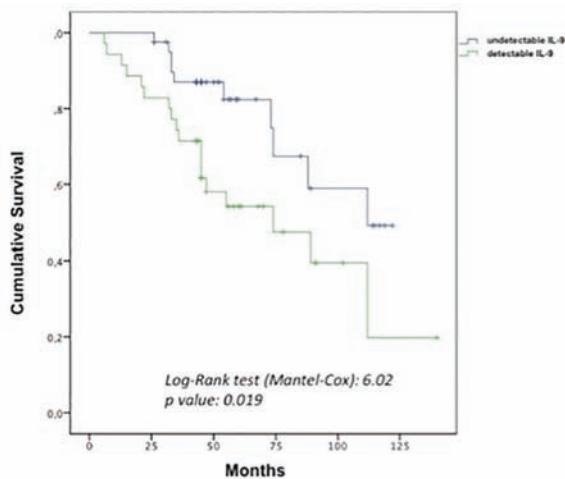


Figure 1

## P425

#### Galectin-3 as a predictor of heart failure and other complications at long-term follow-up after right ventricular myocardial infarction

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**Background:** Galectin-3 (Gal-3) is a mediator of cardiac fibrosis which has a prognostic value after acute coronary syndrome. The relationship between Gal-3 level, risk of heart failure (HF) and adverse cardiovascular events (ACVE) after posterior STEMI involving right ventricle (RV) is not studied.

**Purpose:** To evaluate the significance of Gal-3 as a predictor of ACVE and of HF at 30-month follow-up in patients with RV MI.

**Methods:** The study involved 155 patients with RV MI aged 64.11 ± 0.78 years. Gal-3 levels were determined in 6th month after RV MI by ELISA. Follow-up was 30 ± 2.5 month. Endpoints were: unstable angina (UA), recurrent MI (Re-MI), stroke, cardiovascular (CV) death and HF-hospitalizations.

**Results:** Study endpoints occurred in 65 (41.9%) patients: UA - 51 (32.9%), Re-MI - 16 (10.3%), stroke - 9 (5.8%), CV-death - 16 (10.3%), HF-hospitalization - 22 (14.2%). Median Gal-3 values at 6th month after RV MI (38.61 vs. 18.8 ng/ml; p < 0.0001) was higher in patients with study endpoints. Multivariable analysis revealed, that 6th month Gal-3 level was an independent risk factor for UA (p = 0.000028), CV-death (p = 0.00001), Re-MI (p = 0.002259) and stroke (p = 0.000514) at 30 month. Gal-3 level was also a predictor of HF-hospitalization (p = 0.0069) in 30-month follow-up after RV MI.

**Conclusion:** Gal-3 level at 6th month after RV MI could be useful as an additional

marker of progressive HF and as a predictor of adverse cardiovascular events during long-term follow-up.

#### Regression summary for Galectin-3

	Beta	B	The degree of influence	P
CV-death	0.43	15.65	14.1	0.00001
Unstable angina	0.34	9.77	12.5	0.000028
HF-hospitalization	0.76	6.98	8.6	0.0069
Stroke	0.24	12.39	7.9	0.000514
Re-MI	0.19	7.5	6.5	0.002259
Diabetes Mellitus	-0.17	-0.26	2.44	0.089
Arterial Hypertension	0.19	3.91	2.18	0.1453

## P426

#### High serum d-dimer and alfa- tumor necrosis factor predict worse prognosis in systolic heart failure regardless of etiology

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**Purpose:** Inflammation and thrombosis play an important role in systolic heart failure (SHF) pathophysiology. Among SHF patients, Chagas' cardiomyopathy has higher inflammatory and pro-thrombotic markers. We sought to evaluate the prognosis of a long term cohort of SHF patients according to pro-inflammatory and pro-thrombotic biomarkers at baseline.

**Methods:** Non-randomized prospective Cohort study. Inclusion criteria: Left ventricle ejection fraction <45% and onset of symptoms time > 1 month. Exclusion criteria: varfarin or heparin anticoagulation, mechanic heart valve prothesis, neoplasia, pregnancy. We divided these patients in two groups: G1 - Chagas' cardiomyopathy and G2 non-Chagas' cardiomyopathy. Alpha-Tumor Necrosis Factor - TNF and Interleukin 6 - IL6) and pro-thrombotic (Anti-thrombin factor - ATf, fibrinogen -Fb, von-Willebrand factor antigen -vWFA, D-dimer and thromboelastography parameters) were determined in both groups. Sample size calculated for 90% power. P value significative if <0,05. Fischer's exact test for categoric variables; non-paired T-student test for parametric continuous variables and Mann-Whitney test for non-parametric continuous variables. Spearman Test was used to correlate baseline variables. Covariance analysis was performed. Kaplan-Meier method for survival estimates. Log-rank test for comparison between groups.

**Results:** From January 2008 to April 2009, 287 patients were prospectively included. Mean follow-up time was 7.8 years. G1 patients were younger, had lower body mass index, lower blood pressure and LVEF, and higher BNP levels. Hypertension, diabetes, tobacco use and dislipidemia were less frequent in G1. Previous stroke was more prevalent in G1. Aspirin use was more prevalent in G2. TNF and IL6 levels were higher in G1. Among prothrombotic markers, D-dimer (p < 0,0001) vWF (p < 0,0001) and sP-selectin (p0,0262) levels were also higher in G1 than in G2.



On the other hand, fibrinogen was higher in G2 than in G1 ( $p=0,0424$ , as well as TEG parameters MA( $p=0,004$ ), G( $p=0,002$ ) and TG ( $p=0,001$ ), even though all of these were at the normal reference range in most patients in both groups. Only D-dimer and TNF differences persisted significant after covariance analysis. In G1 and G2, 5.6% and 6.8% were lost to follow-up, respectively. From these variables D-dimer and alpha-TNF positively correlated with each other ( $R=0,312$ ;  $p=0,0001$ ). D-dimer under the mean value of 230ng/mL predicted better transplante-free survival rates (58.3% vs 34.3%;  $\log\text{-rank}=0,0001$ ). Alpha-TNF D under the mean value of 17.9ng/mL predicted better transplante-free survival rates (56.3% vs 34.5%;  $\log\text{-rank}=0,0001$ ).

**Conclusions:** Inflammation markers measured by alpha-TNF was independently greater among Chagas' cardiomyopathy than non-Chagas' cardiomyopathy patients, as well as, pro-thrombotic status measured by D-dimer. These biomarkers were well correlated with each other and predicted prognosis in the long-term follow-up.

#### P427

##### Utility of bio-adrenomedullin (bio-ADM) and pro-enkephalin (pro-ENK) for the prediction of in-hospital mortality in patients with acute heart failure

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**Background:** Bio-Adrenomedullin (bio-ADM) and Pro-Enkephalin (pro-ENK) have already proved to be good predictors of short term mortality in patients with sepsis. No data are available so far on their predictive value for in-hospital mortality in patients with acute heart failure.

**Methods:** This was a prospective, observational trial conducted in intensive care unit. We enrolled patients admitted from the emergency department of Sant'Andrea hospital in Rome for acute heart failure. Clinical and laboratory data, bio-ADM and pro-ENK values were collected at arrival and patients were followed until hospital discharge.

**Results:** 209 patients with a final diagnosis of acute heart failure were recruited (44% male, mean age  $78.4 \pm 9.5$ ). Regarding patients' characteristics we found out that 49.7% had prior history of heart failure, 58% had reduced systolic function, 17% presented with pulmonary edema, and 21% developed acute kidney injury, defined as serum creatinine increase by 0.3 mg/dl within 48 hours after hospitalization. Using Pearson's analysis, a significant correlation was found between bio-ADM and inferior vena cava index ( $r=0.20$ ,  $p=0.003$ ), suggesting a potential role of bio-ADM in the detection of intravascular congestion, that is considered to be the main cause of re-hospitalization for acute heart failure patients. Moreover, admission pro-ENK significantly correlated with serum creatinine ( $r=0.56$ ,  $p < 0.0001$ ) and chronic kidney disease ( $r=0.31$ ,  $p < 0.0001$ ). This result seems to extend the already known role of pro-ENK for renal impairment identification to the heart failure condition. Finally, both analyzed biomarkers, bio-ADM and pro-ENK, proved their value in predicting in-hospital mortality in acute heart failure patients (bio-ADM: Area Under Curve = 0.65,  $p=0.047$ ; pro-ENK: Area Under Curve = 0.73,  $p=0.0011$ ).

**Conclusions:** bio-ADM and pro-ENK are suitable biomarkers for risk prediction of in-hospital mortality in patients hospitalized for acute heart failure. The pathophysiological mechanism of the two biomarkers for the prediction of in-hospital death for acute heart failure patients seems to be linked to intravascular congestion for bio-ADM and to renal dysfunction for pro-ENK.

#### P428

##### ST2 is an independent predictor of all-cause mortality in elderly patients.

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**Background:** NtproBNP is a known predictor of mortality. A new biomarker, suppression of tumorigenicity 2 (ST2) has been introduced as a marker for fibrosis and hypertrophy and may thus predict mortality. There is a lack of knowledge about the predictive value of ST2 in elderly primary health care (PHC) patients.

**Purpose:** To compare ST2 with NTproBNP as a predictor of mortality in elderly patients with clinical symptoms of heart failure (HF).

**Methods:** Explorative analysis of a longitudinal study. Patients were recruited from one selected primary health care in northern Sweden between 2000 and 2003 and comprised both registry patients and incident cases with suspected HF identified by the general practitioner (GP) at the PHC. All patients had clinical symptoms of HF and significant co morbidities. Blood samples were collected at baseline and stored frozen for future analysis. NTproBNP was analyzed with Roche Elecsys proBNP immunoassay. ST2 was analyzed with Critical Diagnostics Presage ST2 immunoassay. ST2 and NTproBNP were used as continuous variables in the analysis. The association between baseline characteristics and mortality at 10 years of follow up was analyzed with Cox regression analysis. For mortality data death certificate were used. Adjustments were made for significant variables from the univariate Cox regression analysis and from fixed factors as age, gender and smoking habits.

**Results:** We studied 159 patients (mean age 80 years, 66% women). During ten years of follow up 80 (50%) patients had died. In the univariate Cox regression analysis significant associations with all-cause mortality at 10 years of follow up were found for ST2 (hazard ratio [HR]: 1.03; 95% confidence interval [CI]: 1.01-1.05), age (HR: 1.09; CI:1.05-1.12), kidney dysfunction, defined as creatinine  $> 100\mu\text{mol/L}$  (HR: 2.31 ; CI:1.43-3.74), all HF (HR: 2.00; CI:1.20-3.31), NTproBNP (HR: 1.0001; CI:1.0001-1.0002). In the following multivariate analysis ST2 (HR: 1.03; CI:1.00-1.06), age (HR: 1.12; CI:1.06-1.18), kidney dysfunction (HR: 2.12; CI:1.08-4.17), smoking habits (HR: 4.27; CI:2.22-8.23) and NTproBNP (HR: 1.0001; CI:1.0000-1.0002) were independently associated with all-cause mortality at ten years of follow up. For cardiovascular mortality ST2 (HR: 1.03; CI:1.00-1.05) was significant associated in univariate analysis but not after adjustment for age. **Conclusion:** ST2 was an independent prognostic marker of all-cause mortality in elderly PHC patients with clinical symptoms of HF. In these patients the clinical value of ST2 as an additive prognostic marker to NTproBNP needs to be further evaluated.

#### P429

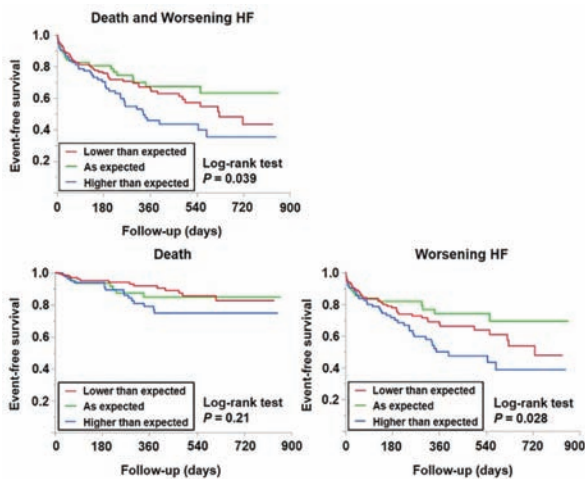
##### Impact of endogenous erythropoietin level on long-term clinical outcomes in patients with acute decompensated heart failure

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**Backgrounds:** Although previous reports suggest that an elevated endogenous erythropoietin (EPO) level is associated with worse clinical outcomes in chronic heart failure (HF) patients, the prognostic implication of EPO in patients with acute decompensated HF (ADHF) and underlying mechanisms of the high EPO level in severe HF patients who have poor prognosis remain unclear. Purpose; To investigate whether the high EPO level on decompensated phase of HF was associated worse clinical outcomes, and to explore the pathophysiological mechanisms of high EPO level in high-risk HF patients in a relatively large ADHF cohort.

**Methods and Results:** We examined 539 consecutive ADHF patients with EPO measurement on admission from our registry. During a median follow-up period of 329 days (IQR 110 - 541), higher EPO level on admission was independently associated with worse clinical outcomes (composite of death and worsening HF) (HR 1.25, 95%CI 1.06 - 1.48,  $P=0.008$ ) in multivariate Cox proportional hazards model. Hemoglobin level was the strongest determinant of EPO level ( $\beta = -0.30$ ,  $P < 0.001$ ), whereas estimated glomerular filtration rate (eGFR) was not significant ( $P=0.13$ ) in multivariate regression analysis. In anemic subgroup of 318 patients, higher EPO level than expected on the basis of their hemoglobin level was related to increased adverse events (Figure), and was an independent determinant of worse clinical outcomes (composite of death and worsening HF) (HR 1.63, 95%CI 1.05 - 2.49,  $P=0.028$ ) in multivariate Cox proportional hazards model. Moreover, estimated plasma volume excess rate was positively associated with EPO level ( $\beta = 0.15$ ,  $P=0.003$ ), and anemic patients with higher-than-expected EPO level tended to have higher estimated plasma volume excess rate, plasma lactate level and lower systemic oxygen saturation level with the preservation of reticulocyte-production potential than those with lower-than-expected EPO level ( $P < 0.001$ ). Conclusions; High EPO level predicts long-term worse clinical outcomes in ADHF patients, independent of anemia and impaired renal function. Anemia and hypoxia due to severe congestion may synergistically contribute to high EPO level in high-risk HF patients.



Expected EPO Level and Clinical Outcomes

#### P430

##### Relevance between tolvaptan and RAS activation in severe heart failure.

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**Background:** Since tolvaptan is a selective vasopressin receptor inhibitor, which belongs to the water diuretic drug, it may be the ideal diuretic for heart failure due to minimum activation of renin angiotensin system (RAS). Thus, we investigated the relevance between tolvaptan and RAS activation in the patients who had severe heart failure by pharmacologic mechanisms.

**Patients and methods:** Twelve patients who were hospitalized and had severe heart failure with NYHA III or IV, and they took 50mg of furosemide, had been registered for the present study from May, 2013 to September, 2014. The combination therapy with tolvaptan and low dose thiazide was commenced, and circulatory dynamics had been well observed for three months. Plasma renin activity (PRA), plasma renin concentration (PRC) and soluble prorenin receptor (s-PRR) were evaluated.

**Result:** All patients were discharged by three months. However, four of them were readmitted because of aggravation in heart failure. There were no significant differences in PRA/PRC of the patients in the vicinity of this study. However, four patients who were readmitted showed significantly higher s-PRR level than those of non-readmitted patients ( $141.8 \pm 2.9$  vs  $136.3 \pm 3.6$  ng/ml;  $p = 0.026$ ).

**Conclusion:** There may be no advantage in the tolvaptan therapy on the patients who had severe heart failure. However, the s-PRR concentration may be a predictive factor of aggravation in heart failure.

#### P431

##### Effects of beta-blocker therapy on hs-CRP levels in elderly patients with ischemic and non-ischemic heart failure: Results from the CIBIS-ELD trial

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**Background:** C reactive protein (CRP) is a biomarker indicating systemic inflammation. Elevated levels of this biomarker are associated with increased rates of cardiovascular disease, including chronic heart failure (HF). In the past years, high-sensitivity CRP assays were developed in order to measure lower levels of CRP, down to 0.3mg/l (hs-CRP). Up to now, beta blocker (BB) therapy in HF has been researched thoroughly, though still, very little is known about the effects of BB titration on hs-CRP levels in ischemic and non-ischemic HF patients. Also, little is known if this effect differs between selective vs. unselective BB.

**Purpose:** To explore the trajectories of hs-CRP before and after BB (carvedilol vs bisoprolol) titration in elderly HF patients depending on the type of BB used and the etiology of the disease (ischemic vs non-ischemic).

**Methods:** We measured plasma levels of hs-CRP and NT-proBNP in 520 HF patients  $\geq 65$  years ( $72.06 \pm 5.24$  y, 38% f, LVEF  $41.8 \pm 13.8\%$ ; ischemic  $n = 243$ ; non-ischemic  $n = 277$ ) of the CIBIS-ELD trial. In this trial, patients were randomized to bisoprolol vs. carvedilol and doses were up-titrated to the target or maximally tolerated dose. hs-CRP and NT-proBNP levels were assessed at baseline (BL) and after 12 weeks (FU).

**Results:** In patients with ischemic HF, hs-CRP levels decreased in the bisoprolol group (BL =  $0.60 \pm 0.94$  mg/dl,  $n = 166$ ; FU =  $0.43 \pm 0.694$  mg/dl,  $n = 131$ ;  $p = 0.010$ ), and were without a change in the carvedilol group (BL =  $0.60 \pm 1.69$  mg/dl,  $n = 181$ ; FU =  $0.57 \pm 0.982$  mg/dl,  $n = 136$ ;  $p = 0.731$ ). There was also no change of hs-CRP levels in non-ischemic HF patients in both groups (bisoprolol: BL =  $0.64 \pm 1.175$  mg/dl,  $n = 197$ ; FU =  $0.470 \pm 0.81$  mg/dl,  $n = 152$ ;  $p = 0.069$ ; carvedilol: BL =  $0.45 \pm 0.78$  mg/dl,  $n = 198$ ; FU =  $0.41 \pm 0.701$  mg/dl,  $n = 152$ ,  $p = 0.420$ ). Plasma levels of NT-proBNP decreased in ischemic patients treated with bisoprolol, (BL =  $1594 \pm 2146$  pg/ml,  $n = 169$ ; FU =  $1468 \pm 2110$  pg/ml,  $n = 133$ ,  $p = 0.04$ ), while changes in the carvedilol group were not significant (BL =  $1648 \pm 1991$  pg/ml,  $n = 188$ ; FU =  $1567 \pm 2119$  pg/ml,  $n = 135$ ,  $p = 0.556$ ). In the non-ischemic group NT-pro levels did not change significantly in the carvedilol group, while there was an increase in non-ischemic patients in the bisoprolol group (BL =  $1427 \pm 3113$  pg/ml,  $n = 208$ ; FU =  $1533 \pm 5385$  pg/ml,  $n = 166$ ,  $p = 0.017$ ).

**Conclusion:** Results indicate that bisoprolol might be associated with a decrease of hs-CRP and NT-proBNP levels only in ischemic HF patients, while in non-ischemic HF patients there was no change of hs-CRP and an increase of NT-proBNP levels. In carvedilol treated patients no significant changes was shown in neither group.

#### P432

##### Inflammatory biomarkers as predictors of acute decompensated heart failure in patients with atrial fibrillation

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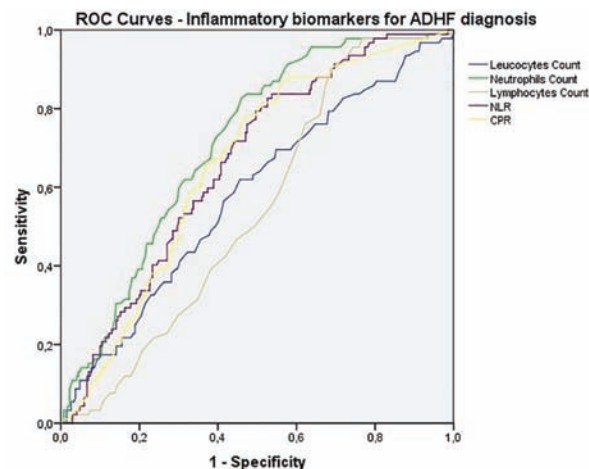
**Background:** Atrial fibrillation (AF) is a frequent comorbidity in patients with heart failure (HF). There is a well-documented relationship between inflammatory markers and both AF and HF.

**Purpose:** We aimed to evaluate the diagnostic value of wide used routine inflammatory blood markers in the prediction of hospital admissions due to acute decompensated heart failure (ADHF) in patients with AF.

**Methods:** 2181 consecutive patients with AF who were evaluated in our Emergency Department (ED) in a 12 month period were included retrospectively in our study. Among them, 423 patients were admitted for in-hospital management. All patients underwent routine clinical and laboratory exams. We also evaluated medical charts in order to identify patients with ADHF. Routine inflammatory biomarkers at hospital admission included: leucocytes, neutrophils and lymphocytes counts, and C-reactive protein (CPR). We also evaluated the diagnostic value of the neutrophil-to-lymphocyte ratio (NLR).

**Results:** 101 patients were admitted with both AF and ADHF (mean age of  $77.2 \pm 9.6$  years, 40.6% males). In receiver-operating characteristic (ROC) analyses (figure) neutrophils count performed better than other inflammatory markers in predicting ADHF (neutrophils count - c-index 0.711,  $p < 0.001$ ; NLR - c-index 0.662,  $p < 0.001$ ; CPR - c-index 0.658,  $p < 0.001$ ; Leucocytes count - c-index 0.581,  $p = 0.020$ ; Lymphocyte count - c-index 0.544,  $p = 0.208$ ). A neutrophils count  $> 4.85 \times 10^9/L$  had a sensitivity of 83.7% and specificity of 52.6% (negative predictive value = 76.5%, positive predictive value = 63.9%) in prediction of ADHF.

**Conclusion:** Neutrophils count is a routine blood test which can prove an easy and simple tool with modest performance to predict the risk of admission due to ADHF in patients with AF.



## P433

**The incidence of chronic heart failure in patients with STEMI during therapy with different doses of atorvastatin**V Valentin Oleinikov<sup>1</sup>; L Salyamova<sup>1</sup>; A Golubeva<sup>1</sup>; N Burko<sup>1</sup><sup>1</sup>Penza State University, Penza, Russian Federation

**Objective:** To assess the incidence of congestive heart failure in patients after acute myocardial infarction with ST segment elevation (STEMI) against the backdrop of 24 weeks of treatment with different doses of atorvastatin.

**Methods:** The study included 45 patients with STEMI, confirmed by ECG, troponin I, CK-MB and the results of coronary angiography with hemodynamically significant stenosis of one artery (the infarct-related artery). In the first 24-96 hours of the onset of the disease, patients were randomized into two groups. Patients of the control group (C) (n=23) received atorvastatin 20 mg/day. Patients of the main group (A) (n=22) received atorvastatin 80 mg/day. Compared subjects were matched by age, height, BMI, office BP. At baseline at 7-9 hours and after 24 weeks of drug therapy brain natriuretic peptide (BNP) was determined; in addition, patients filled the rating scale of clinical condition in CHF (SHOKS, 2000). 6-minute walk test was carried out after 3 and 6 months after acute myocardial infarction.

**Results:** The mean values of BNP at baseline in Group C were 102,9 (49,3; 139,9) pg/ml, in group A - 60,8 (22,6; 104,8) pg/mL, respectively, ( $p > 0,05$ ). After 24 weeks of treatment there was a significant decrease in BNP by 48% in patients receiving atorvastatin 20 mg (to 52,7 (15,8; 82,6) pg/ml,  $p < 0,05$ ) in patients treated with high doses of the drug - 55% (to 27 (21,4; 42,8) pg/ml,  $p < 0,05$ ). In the group C the baseline values of BNP, exceeded the threshold, were identified in 22% of cases (5 persons), at 24 weeks - 4% (1 person) ( $p > 0,05$ ); in the group A, respectively, in 36% (8 people) and 9% (2 people) ( $p < 0,05$ ). Analyses of SHOKS scale at 7-9 day from the onset of the disease in group C no signs of CHF have been found in 6 subjects (26%), 1st FC - in 17 persons (74%). After 24 weeks of follow-up, 0 point was determined in 6 patients (26%,  $p > 0,05$ ), 1st and 2nd FC of CHF - in 14 (61%,  $p > 0,05$ ) and 3 patients (13%  $p < 0,05$ ) respectively. In group A, initially 6 patients (27%) with no signs of heart failure have been found, 1st FC - in 16 patients (73%). On follow-up 0 point was reported in 7 patients (32%,  $p > 0,05$ ), 1st FC - in 15 subjects (68%,  $p > 0,05$ ). According to the analysis of the 6-minute walk test after 12 weeks of treatment in the group C - 0 FC was detected in 17% of cases (4 subjects), 1st FC - in 44% (10 people), 2nd FC - 39% (9 patients). Against the background of the 24-week treatment 0 FC was registered in 26% of cases (6 people), 1st FC - in 44% (10 people), 2nd FC - 30% (7 people) ( $p > 0,05$ ). In the group A at baseline: 0 FC - 36,4% (8 people), 1st FC - 45,4% (9 patients), 2nd FC - 18,2% (4 people), again, respectively, 36% (8 people), 59% (12 people), 5% (1 person) ( $p > 0,05$ ).

**Conclusions:** the results of clinical and laboratory examinations in patients with STEMI, against the background of the 24-week treatment with atorvastatin 80 mg have shown a less frequent development of symptoms of chronic heart failure.

## P434

**CoQ10 treatment of patients with CHF and effects of BNP level**O Oleg Medvedev<sup>1</sup>; OG Tokareva<sup>1</sup>; EA Gorodetskaya<sup>1</sup>; EI Kalenikova<sup>1</sup>; ZM Sizova<sup>2</sup><sup>1</sup>M.V. Lomonosov Moscow State University, Pharmacology, Moscow, Russian Federation; <sup>2</sup>I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation

**Background:** CoQ10 is a powerful antioxidant and is one of recommended for CHF treatment. Decreased level of myocardial CoQ10 is correlated with the severity of symptoms and the degree of left ventricular dysfunction. Brain natriuretic peptide (BNP) is a peptide, which has recently been used in the differential diagnosis and follow-up of patients with heart failure. It is well known that the severity of the disease also correlates with the plasma BNP levels.

**Purpose:** To evaluate the effects of long-term coenzyme Q10 treatment as part of standard therapy in patients with NYHA class II-III chronic heart failure on plasma BNP levels, left ventricular ejection fraction, and the 6-minute walk test.

**Materials and Methods:** 78 patients with NYHA class II-III chronic heart failure aged from 40 to 70 years with EF less than 45% were randomized in clinical trial. During the study period (24 weeks) participants received solubilized oral form of CoQ10 (90 mg/d) or placebo in addition to standard medical therapy. Left ventricular ejection fraction, 6-minute walk test, plasma brain natriuretic peptide (BNP) (fluorescent analyser with test strips) and CoQ10 levels (HPLC with electrochemical detection) were measured in all patients prior to and after six months treatment.

**Results:** In 37 patients from 78 the baseline level of BNP was below 100 pg/ml. 6 months administration of CoQ10 did not change BNP level, but in placebo group BNP level increased by 176% ( $=0,0092$ ). In group of 41 patients baseline level of BNP was above 100 pg/ml level. In this group administration of CoQ10 was followed by the decrease in BNP level by 6.8% ( $p = 0.02$ ) whereas in placebo group BNP level did not change.

**Conclusion:** 6 months administration of coenzyme Q10 prevents progression of congestive heart failure in patients with reduced contractility and baseline plasma BNP levels within normal ranges (less than 100 pg/ml) and leads to a significant

reduction of BNP levels in patients with initial BNP levels higher than 100 pg/ml, increase in left ventricular ejection fraction and improvement in exercise tolerance.

## P435

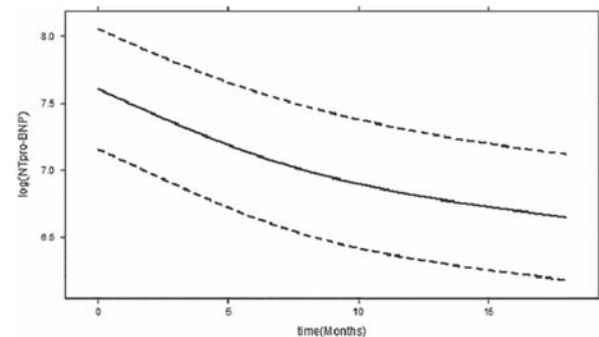
**Serial changes in N-terminal pro-brain natriuretic peptide in heart failure patients after surgical ventricular reconstruction: the biomarker plus study**S Serenella Castelvachio<sup>1</sup>; E Baryshnikova<sup>1</sup>; F Ambrogio<sup>2</sup>; B Girardi<sup>3</sup>; A Camporeale<sup>4</sup>; R Tramarin<sup>5</sup>; E Costa<sup>5</sup>; L Menicanti<sup>6</sup><sup>1</sup>IRCCS Policlinico San Donato, San Donato Milanese, Milan, Italy; <sup>2</sup>University of Milan, Department of Clinical Sciences and Community Health, milano, Italy; <sup>3</sup>IRCCS Policlinico San Donato, Department of Cardiac Rehabilitation, milano, Italy; <sup>4</sup>IRCCS Policlinico San Donato, Department of Multimodality Cardiac Imaging, milano, Italy; <sup>5</sup>IRCCS Policlinico San Donato, Service of Laboratory Medicine, milano, Italy; <sup>6</sup>IRCCS Policlinico San Donato, Department of Cardiac Surgery, Milan, Italy

**Background:** Plasma concentrations of natriuretic peptides have been shown to predict long-term morbidity and mortality in heart failure (HF) patients with left ventricular (LV) dysfunction, although most of data comes from medical trial including relatively young patients affected by HF of ischemic aetiology in a small percentage and the results are not uniform. Furthermore, it is still unclear if changes after cardiac surgery predict therapeutic effect on mortality or risk of hospitalization.

**Purpose:** To prospectively investigate the longitudinal profile of serial changes in N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels from baseline to different time-points at follow-up in ischemic HF patients undergoing Surgical Ventricular Reconstruction (SVR) and how changes in NT-proBNP affect the prognosis. Methods. Between January 2010 and June 2014, one hundred and forty-three patients (122 men,  $64 \pm 9$  years old) with previous myocardial infarction and LV remodeling referred to our Center for SVR had an assessment of NT-proBNP levels at baseline and at 6 months, 12 months and 18 months after surgery. The association between serial measurements of NTpro-BNP and the time to the composite event of all-cause death or first hospitalization was studied adjusting for gender, age and creatinin level at baseline. The analysis was performed using joint modeling of the serial measurements of NT-proBNP through mixed models together with Cox regression to analyze time to event data. The logarithm of the biomarker was used in the analysis.

**Results:** The estimated average level of the biomarker decreased by about 50% during the first year after the intervention. Serial measurements of NTpro-BNP were associated with the hazard of event with a parameter estimate of 1.09 (95% confidence interval [CI] 0.62 - 1.56). Therefore, considering the log transformation, a 1% increase in NTpro-BNP during follow-up was associated with 1.1% increase of the risk of the composite event (95% CI 0.6% - 1.6%).

**Conclusions:** Changes over time of NT-proBNP concentrations in ischemic HF patients undergoing Surgical Ventricular Reconstruction are associated with long-term prognosis. Serial changes (either in increasing or in decreasing) at different time points have resulted into a modulation of the risk of adverse events.



## P436

**The prevalence of elevated natriuretic peptide in a diabetic population without a history of heart failure**

Irish Heart Foundation

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**Purpose:** Patients with diabetes are at increased risk of several cardiovascular disorders including heart failure. The objective of this study is to determine the prevalence of elevated natriuretic peptide (NP) in a diabetic population, characterise diabetics with normal and elevated NP levels, and examine the association between



## Echocardiographic parameters

	NTproBNP < 125 (n = 17)	NTproBNP 125 - 250 (n = 33)	NTproBNP > 250 (n = 120)
Relative Wall thickness > 0.42	7 (41.2%)	13 (39.4%)	56 (47.1%)
E/e ratio > 13	2 (12.5%)	5 (20.0%)	28 (30.4%)
Lateral e velocity < 10	10 (62.5%)	26 (89.7%)	77 (75.5%)
LVEF > 50% 45 - 50% 35 - 45% < 35%	17 (100%) - - -	30 (90.9%) 1 (3.0%) 2 (6.1%) -	101 (84.2%) 8 (6.7%) 6 (5.0%) 5 (4.2%)
LAVI > 34	4 (23.5%)	3 (12.0%)	61 (64.2%)

NP and heart failure in this population to allow appropriate structuring of heart failure prevention services.

**Methods:** Patients enrolled in the HSE Midland Diabetes Structured Care Programme between May 2013 and Feb 2015 were included in this study. We measured the NP level of all participants and examined the characteristics of those with normal and elevated NP levels. We also determined the presence of heart failure in the elevated NP group using specific echocardiographic parameters.

**Results:** There were 611 patients with diabetes who had an NTproBNP level measured (58.6 % male, mean age 65.6 yrs). Two hundred and six patients (33.7%) had an NP level > 125 pg/ml. Those with an elevated NP (>125 pg/ml) had higher rates of atrial fibrillation (18% vs 0.74%), HTN (51.5% vs 32.1%) and hyperlipidaemia (35.9% vs 25.4%) compared with the normal NP group. The use of Angiotensin receptor blockers (27% vs 18.9%), loop diuretics (25.8% vs 3.9%) and B blockers (50% vs 16.8%) was higher in the elevated NP group. The rate of hypoglycaemic medication use between the two groups was higher in the normal NP group (63.2 vs 54.5%). Thiazolidinedione use was higher in the high NP group (7.9% vs 3.9%). The median HbA1C level was 47 (42 - 55) with no significant difference between the groups. Baseline echocardiography was performed in 170 patients. Twenty patients (11.7%) had LV systolic dysfunction (LVSD, EF <50%) and 68 (49.6%) had LV diastolic dysfunction (LVDD, LAVI > 34). An NP level > 250 pg/ml was most predictive of the presence of LV dysfunction (LVSD 16.9%, LVDD 64.2%)

**Conclusions:** Diabetic patients had a high prevalence of elevated NP. There was a high prevalence of LV dysfunction in those with elevated NP. Interval NP screening of this at risk population should be considered as part of the approach in reducing cardiovascular morbidity.

## DRUG THERAPY, OTHER

## P437

#### Laboratory aspirin resistance reversibility in coronary artery disease and chronic obstructive pulmonary disease patients after coronary stent implantation

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**Background:** Acetyl salicylic acid (ASA) resistance occurs most frequently in patients with comorbidities and is associated with poor prognosis. The purpose of this study was to evaluate the prevalence of aspirin resistance in a cohort of patients with CAD and COPD, who underwent coronary stent implantation, and whether it can be reversed using original enteric-coated aspirin.

**Methods:** Platelets function of 244 patients after PCI taking ASA 75 mg daily has been evaluated with VerifyNow. Patients found resistant by test (ARU > 550) were switched to original enteric-coated aspirin 100 mg. Platelets function was measured again after 24 h. Patients whose the resistance was reswitched to noncoated ASA 162 mg daily and their aggregation status was re-evaluated after 1 week of therapy.

**Results:** Prevalence of ASA resistance in our population was 15,9 % (39/244) with ARU from 554 to 793. In 37 out of 39 patients (95 %) aspirin resistance was reversed within 24 h from the change to original enteric-coated aspirin. 36 out of 37 patients (97 %) were found fully aspirin-sensitive after 1 month of oral therapy; two other patients were found with borderline value ARU=550 after 1 week of use noncoated ASA 162 mg daily. No adverse reactions were observed. Conclusion(s): A significant number of patients with CAD and COPD are resistant to ASA therapy 75 mg daily. A single dose of original enteric-coated acetylsalicylate 100 mg can reverse the platelet hyper-aggregability and laboratory aspirin resistance in large majority of patients.

## P438

#### Temporal trends in the use of digoxin in patients heart failure

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Digoxin is a recommended therapy for heart failure (HF) with reduced ejection fraction (HFrEF), but its use has recently casted doubts about its utility and safety. Furthermore, the use by specialist has been declining in the past decades. We conducted a retrospective analysis of 1216 patients admitted with HFrEF in a six year period and we assessed the temporal trends, and factors associated with digoxin use. Out of 1216 patients with HFrEF patients, 21.6% received digoxin at discharge. Digoxin prescription decreased by 3 fold in 6 years (P < 0.001). The trend was similar and significant across all age groups and sexes. Atrial fibrillation was associated with a greater probability of digoxin prescription at baseline (p < 0.001). Patients in AF had a 3.4 fold greater probability of being prescribed digoxin (OR 3.4, 95% CI 1.92-5.6). COPD was also associated with a greater probability of digoxin use (OR 1.71, 95% CI 1.12-2.08). In conclusion the use of digoxin is progressively decreasing in patients with HFrEF attending a tertiary hospital. Digoxin is mainly prescribed to patients with atrial fibrillation and COPD.

## P439

#### P2Y12 inhibitors in acute coronary syndrome: relation to hemorrhagic events in routine clinical practice

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**Introduction:** In the context of acute coronary syndromes (ACS), ticagrelor demonstrated to reduce cardiovascular death, myocardial infarction and stroke when compared to clopidogrel. These benefits did not seem to be associated with increasing rates of hemorrhagic events (HE) and, thus, ticagrelor has been introduced in routine practice. However, little is known about ticagrelor's safety in "real world" clinical practice, since available evidence comes mainly from clinical trials.

**Objective:** To assess the occurrence of major HE in ACS patients treated with ticagrelor or when the switch between both P2Y12 inhibitors (ticagrelor/clopidogrel) was required during hospitalisation, compared to clopidogrel.

**Methods:** This study is part of an ongoing prospective cohort study of ACS survivors consecutively recruited between August 2013 and December 2014, at the cardiology departments of two hospitals in Portugal. Data was collected through face-to-face interviews and medical records review. This evaluation comprised socio-demographic characteristics, clinical history and information during hospitalization. We evaluated 939 patients under dual antithrombotic therapy (aspirin and ticagrelor or clopidogrel) during hospitalization. Major HE were defined as a drop in hemoglobin (Hb) between 3 and 5 g/dL or over 5 g/dL, or intracranial hemorrhage (ICH). The association between the drug used and HE was estimated by logistic regression analysis, taking into account other demographic and clinical characteristics.

**Results:** The mean age was 64 years and 74.3% were male. Most patients (86.2%) were medicated with clopidogrel, 7% with ticagrelor and 6% switched between P2Y12 inhibitors (with another new loading dose) during hospitalization. The incidence of HE was 4.6%, with 2.9% having a drop of 3-5 g/dL in Hb, 1.2% a drop > 5 g/dL in Hb, and 0.5% considering ICH. There were no differences in HE in patients treated with clopidogrel, ticagrelor or who switched between the two drugs (4.6%, 6.4% and 1.9%, respectively, p=0.512).

**Conclusion:** Our results found that ticagrelor was safe in routine clinical practice, independently of patients' characteristics, and support the safety of P2Y12 inhibitors even when overlapping is required, with a new loading dose. However these interpretations need to be cautious, because the ticagrelor group is still small in our sample.

**P440****Hyper-Kalaemia as cause for discontinuation of RAASi in patients with heart failure**

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ACE inhibitors and Aldosterone antagonists (or mineralocorticoid receptor antagonists [MRAs]) are guideline-recommended therapy for patients with heart failure reduced left ventricular ejection fraction (HFrEF), and in postmyocardial infarction patients with HF.

Often the use of drugs acting on the renin angiotensin aldosterone system (RAASi) cannot be fully implemented because of the occurrence of hyperkalaemia.

Aim of the present study was to assess the occurrence of hyperkalaemia and the need for discontinuation of RAASi therapy because of high K levels in patients with chronic heart failure attending a tertiary health care centre over a period of 5 years. Amongst 968 patients with full available data 402 had to discontinue at least one RAASi because of hyperkalaemia. Hyperkalaemia was mild in 45% of patients discontinuing RAASi and moderate-severe in 55%.

Discontinuation of RAASi therapy was more frequent in patients with preserved or in those with severely impaired renal function while no correlation was found with NYHA class or LVEF.

In conclusion hyperkalaemia is a frequent occurrence in patients with heart failure, limits the implementation of life-saving medications. This may well translate into a negative prognostic effect.

**P441****Effects of ivabradine on coronary flow reserve and left ventricular diastolic function in patients without coronary artery stenosis**

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**Background:** Doppler-derived coronary flow reserve (CFR) can be impaired in both obstructive coronary artery disease (CAD) and coronary microvascular disease (CMD). Otherwise, CMD has been regarded as an important cause of left ventricular (LV) diastolic dysfunction. In different trials, ivabradine showed to improve CFR and diastolic function, but these effects were never correlated. The aim of our study was to assess the combined effect of ivabradine on CFR and LV diastolic function and the correlation between these two parameters. **Methods:** 86 patients (52 M, 34 F; mean age 64 ± 7 years) without obstructive CAD were enrolled in the study. After baseline data were collected, all patients underwent Doppler-derived CFR. Coronary flow was assessed in the left anterior descending coronary artery (LAD), and was identified as the color signal directed from the base to the apex of the left ventricle, containing the characteristic biphasic pulsed-Doppler flow signals. CFR were determined as the ratio of hyperemic, induced by intravenous dipyridamole administration, to baseline diastolic coronary flow velocity. Doppler echocardiography included pulsed tissue Doppler of the mitral annulus. The ratio of mitral velocity to early diastolic velocity of the mitral annulus (E/e') was used as a surrogate marker of diastolic function. Patients were randomly assigned to ivabradine or placebo for one month (after up-titration phase). Doppler echocardiography and CFR assessment were performed again at the end of treatment period.

**Results:** There were no significant differences in baseline characteristics between ivabradine and placebo group. CFR was successfully performed in all patients. Baseline CFR was not significantly different in both groups. After treatment, in ivabradine group CFR significantly increased (3.34 ± 0.41 vs. 2.24 ± 0.36 - p < 0.01) and E/e' significantly decreased (8.3 ± 1.8 vs. 10.4 ± 2.1 - p < 0.01). At baseline, a significant inverse association between CFR and E/e' was observed. After treatment, a weaker correlation was observed.

**Conclusions:** CFR is associated with LV filling pressure in patients without obstructive CAD, and ivabradine is able to improve both CFR and diastolic function. A weaker correlation after treatment, is probably due to a more complex effect of ivabradine, beyond the single parameters.

**P442****Analysis of changes of ECHO-cardiogram indices in patients with chronic heart failure during therapy with coenzyme Q10**

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**Aim:** To evaluate changes in echocardiogram (Echo-CG) indices in patients with chronic heart failure (CHF) in functional NYHA class II-III and a history of myocardial

infarction, who were treated with coenzyme Q10 in addition to standard therapy.

**Method:** 120 patients with class II-III CHF and a history of myocardial infarction were enrolled into the study. The patients were randomized into two groups: group I patients received optimal standard therapy and in addition coenzyme Q10 at a dose of 120 mg/day for 3 months; group II patients received optimal therapy only. Echo-CG was used for the evaluation of post infarction remodeling at the start of the study, at 3 months and at 12 months.

**Results:** Increase of the left ventricular end-diastolic volume index (iLVEDV) of more than 75 ml/m<sup>2</sup> was found in 24 (47.1 %) patients of group I and 26 (49.1 %) patients of group II. Significant differences were only found in group I patients (<0.05 for Wilcoxon criteria and Friedman criteria ANOVA). Thus, after 3 months of treatment patients in group I showed a decrease of iLVEDV with values of 65.67 (56.54; 77.94) ml/m<sup>2</sup> (<0.05), and only in 15 patients (29.4 %) this index was above 75 ml/m<sup>2</sup>. In group II patients, the iLVEDV showed no change compared to the initial test and measured 71.86 (58.55; 89.83) ml/m<sup>2</sup> (>0.05), and 24 of these patients (45.3 %) showed an iLVEDV level of more than 75 ml/m<sup>2</sup>. In group I patients the iLVESV initially was 24.87 (19.28; 35.43) ml/m<sup>2</sup>, but after 3 months of therapy it measured 22.12 (16.74; 30.98) ml/m<sup>2</sup> (<0.05). In group II, the initial measurement of iLVESV was 25.54 (18.00; 33.18) ml/m<sup>2</sup> and after 3 months there were no significant changes at 25.12 (17.38; 33.74) ml/m<sup>2</sup> (>0.05). Overall, the median indices of iLVESV did not exceed the reference ranges, however the higher quartile of iLVESV in group II over 3 months exceeded 31.0 ml/m<sup>2</sup>. Moreover, in 12 patients of group II the iLVESV was more than 35 ml/m<sup>2</sup>, indicating an unfavourable course of post infarction remodeling process. In group I patients the left ventricle ejection fraction (LVEF) was initially 60.00 (54.00; 67.00) %, and at 12 months 64.00 (56.00; 70.00) %. The LVEF in group II was initially 63.00 (56.00; 69.00) %, and at 12 months 62.00 (55.5; 68.5) %. The left atrium index (iLA) was initially 21.62 ± 2.17 ml/m<sup>2</sup> in group I patients, and outcome progression was 22.30 ± 2.22 ml/m<sup>2</sup>. In group II this was 21.80 ± 2.14 ml/m<sup>2</sup> and 23.29 ± 2.47 ml/m<sup>2</sup> correspondingly. The index of relative wall thickness in group I initially and at 3 months was 0.41(0.37; 0.46) and 0.42 (0.37; 0.48) correspondingly, but in group II patients this index practically did not change: 0.42 (0.34; 0.48) and 0.42 (0.35; 0.48).

**Summary:** The prescribing of coenzyme Q10 in addition to the standard group of medications used in the treatment of patients with class II-III CHF (after myocardial infarction resulted in improvement of echocardiogram indices.

**P443****Prognostic impact of polypharmacy drugs across heart failure phenotypes: an unmet need.**

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**Background:** Data on prognostic role of polypharmacological therapy in HF phenotype (HFrEF - LVEF <50% versus HFpEF-LVEF ≥ 50) are lacking.

**Objective:** To compare the prognostic role of polypharmacy across EF-HF phenotype.

**Methods:** All outpatients with HF and available LVEF enrolled consecutively from November 2009 to October 2013 in the community-based population. Clinical variables of study population were derived from the E-chart for outpatient collected in a regional data warehouse. Polypharmacological therapy was defined as sum of non HF related treatment per patients.

**Results:** A total of 2314 patients (mean age 78 ± 8, 57% men) were included. Of these 1373 (59 %) had HFpEF and 941 (41%) HFpEF. The high mean age, comorbidity rates (mean 3.2 ± 2.5; 54% patients with ≥ 3 non cardiac comorbidities) and numbers of drugs (6.1 ± 1.7) ran similarly between HF groups. 933 HF patients (42%) were treated with ACE/ARB and betablocker. At a follow-up of 28 ± 14 months, 472 (20%) patients died. Of these 225 (24%) had HFrEF, 247 (18%) had HFpEF. The increasing number of drugs per patient was associated with higher mortality rates (HR 1.3 [IC 1.2-1.6]; p = 0.001), all-cause hospitalization (HR 1.8 [IC 1.3-2.4]; p < 0.001), HF hospitalization (HR 1.7 [IC 1.3-1.9]; p < 0.001), and non cardiovascular Hospitalization (HF 1.7 [IC 1.3-2.3]; p < 0.001). This trend was revealed to have a similar prognostic impact among HF groups (interaction test analysis, p = 0.917). This adverse relationship remain unchanged in subgroups under optimal HF medical treatment. Finally, a multivariable model confirmed the polypharmacy therapy as independent predictor along with age, sex, non cardiac comorbidities, HF related treatment.

**Conclusion:** In an HF community-based population, predominantly elderly with high comorbidity burden, polypharmacy contributed significantly to high rates of mortality and morbidity irrespective of HF phenotypes and HF related medical treatment.

## P444

### Enoxaparin and fondaparinux better than unfractionated heparin improve endothelial function in patients with acute decompensated chronic heart failure

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**Objective:** to compare changing levels of endothelial dysfunction serum markers in patients with acute decompensated chronic heart failure (ADCHF), depending on a received anticoagulant.

**Materials and Methods:** The study included 60 ADCHF patients with sinus rhythm, mean age 69 ± 10 years, 35 women (58%), treated with standard ADCHF therapy. Patients with acute exacerbation of chronic diseases and active cancer were excluded from the study. All patients were randomized into 3 equal groups to prophylactic subcutaneous anticoagulants (fondaparinux, enoxaparin or UFH), using the envelope method. Serum levels of E-1,vWF:Ag, sICAM-1 and sVCAM-1 were measured before and after treatment with anticoagulants.

**Results:** Under standard treatment, including anticoagulants, all patients in three groups had decreased levels of serum endothelial dysfunction markers. Thus, in the heparin group vWF:Ag decreased from 1,70 ± 0,07 to 1,10 ± 0,02 IU/ml (=0,001), ET-1 – from 2,6 ± 1,8 to 1,9 ± 0,7 fmol/ml (=0,02), sVCAM-1 – from 1950 ± 193 to 1743 ± 174 ng/ml (=0,02) and sICAM-1 – from 441 ± 75 to 407 ± 57 ng/ml (=0,03). In the enoxaparin group vWF:Ag went down from 1,80 ± 0,08 to 1,00 ± 0,02 IU/ml (=0,001), ET-1 – from 3,05 ± 2,00 to 1,60 ± 0,80 fmol/ml (=0,003), sVCAM-1 – from 1997 ± 179 to 1604 ± 168 ng/ml (=0,003) and sICAM-1 – from 404 ± 85 to 358 ± 68 ng/ml (=0,003). In the fondaparinux group vWF:Ag decreased from 1,90 ± 0,06 to 1,00 ± 0,04 IU/ml, (=0,001), ET-1 – from 3,4 ± 2,1 to 1,5 ± 0,6 fmol/ml (=0,001), sVCAM-1 – from 2024 ± 186 to 1587 ± 170 ng/ml (=0,001) and sICAM-1 – from 492 ± 92 to 324 ± 64 ng/ml (=0,015). Being compatible in vWF:Ag delta rates, the groups were significantly different in delta ET-1 (-0,7 ± 1,0 vs -1,4 ± 1,1 and -1,9 ± 1,4 fmol/ml, respectively; =0,002), sVCAM-1 (-191 ± 27 vs -235 ± 12 and -506 ± 15 ng/ml, respectively; =0,01) and sICAM-1 (-34 ± 23 vs -46 ± 26 and -168 ± 27 ng/ml, =0,008). The most noticeable delta rates were seen in patients, treated with either fondaparinux or enoxaparin.

**Conclusion:** Standard ADCHF treatment, including anticoagulants (unfractionated heparin, enoxaparin and fondaparinux) improved endothelial dysfunction, by significantly decreasing ET-1, sVCAM-1 sICAM-1, especially in patients under enoxaparin or fondaparinux.

## P445

### Mortality in patients exposed to Digoxin: a meta-analysis

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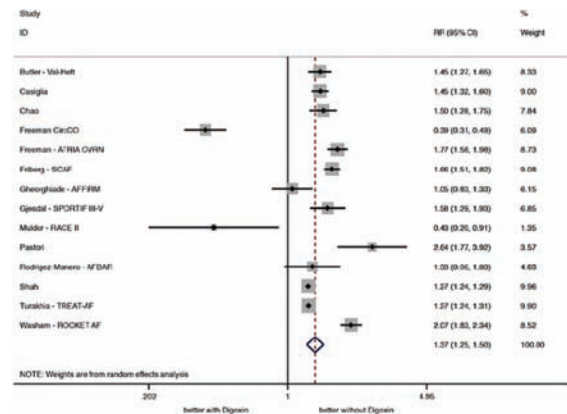
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**Background:** Digoxin is authorized in European Union for the reduction of ventricular rate in patients with atrial fibrillation (AF) and for the management of chronic heart failure (HF). However, the data from randomized clinical trials about the use of digoxin in AF patients with and without HF are limited and a long-term assessment of mortality in patients taking digoxin is missing.

**Purpose:** To perform a meta-analysis of clinical trials and non-interventional studies to assess the digoxin-related mortality in patients with AF, with or without HF. Methods. A comprehensive MEDLINE search of literature was performed using the following search terms ((atrial fibrillation AND digoxin) AND (mortality OR death)). The following selection criteria were applied: 1) types of studies: randomized controlled trials, open-label studies, observational studies; 2) target population: patients with AF in adults; 3) treatment: digoxin; 4) outcome: all-cause mortality or death. Meta-analysis was performed to assess the influence of treatment on pre-specified end points.

**Results:** 14 studies including 157,392 patients, 70,799 treated by digoxin and 86,593 not using the drug, were selected. Median follow-up of the analysis was 34 months, the median age of the population enrolled was 72 years and 38% were women. Digoxin use, as compared with no-digoxin use, was associated with a 37% increased risk of mortality (RR:1.369; 95% CI: 1.247 to 1.503; p < 0.001)

**Conclusions:** The results of the current meta-analysis suggest an increased mortality in AF patients with and without HF using digoxin.



## P446

### Efficacy of long-term ivabradine therapy on prognosis, right heart and left atrial parameters in patients with severe systolic chronic heart failure

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The aim of study was to assess efficacy of long-term ivabradine (I, up to 15 mg) therapy on prognosis, right ventricular (RV), right (RA) and left atrial (LA) functional parameters, BNP, NT-pro-BNP and high sensitivity CRP levels in pts with III-IV NYHA FC systolic CHF. Methods. 106 pts (age 57.4 ± 0.4) were randomly assigned to group A (n=53, non-receiving I) and group B (n=53, receiving I), in addition to ACE inhibitors, beta-blockers, digoxin and diuretics. 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) transtmitral filling, pulmonary artery ejection (PAET) times, BNP, NT-pro-BNP and CRP levels were assessed at baseline, 3, 6, 12, 24 and 36 months.

**Results:** 1-year mortality, hospitalization rate and mortality and hospitalization (%) were, respectively, 34, 54.7 and 88.7 and 20.8, 32.1 and 52.8 in groups A and B. 2- and 3-year mortality were 39.6 and 50.9 and 28.3 and 39.6 in groups A and B. Event-free analysis showed lower probability (RR reduction, %) of 1-, 2- and 3-year mortality at 38.8, 28.5 and 22.2, hospitalization at 41.3 and mortality and morbidity at 40.5, respectively, in group B compared to A. 1-year treatment with I increased (% from baseline) RA EF at 38.1, FAC at 33.3, TAPSE at 59.6, RA and LA FI at 120 and 113.6, FC at 50.8 and 36.3, PA ET at 11.7, PV S/D at 53.5, SC at 63.7, decreased HR at 21.6, Ar-A at 34.2, BNP at 44, NT-pro-BNP at 40.6 and CRP at 38.1 (p < 0.01). Reduction from baseline of BNP, NT-pro-BNP ≥ 50%, CRP ≥ 40% and HR ≥ 30% was associated with significant improvement of prognosis compared to decrease of BNP, NT-pro-BNP < 30%, CRP and HR < 20% (RR 0.35, 0.36, 0.32 and 0.33, p < 0.01). Similarly, decrease of Ar-A and increase of RV EF and FAC, RA and LA FC at ≥ 40%, FI ≥ 80%, PV SC at ≥ 50% was associated with significant improvement of prognosis compared to changes of Ar-A, RV EF and FAC and RA and LA FC < 20%, FI < 60% and PV SC < 30% (RR 0.36, 0.35, 0.34, 0.37, 0.39, 0.38, 0.35 and 0.34, p < 0.01), respectively.

**Conclusions:** 1) Decrease of BNP, NT-pro-BNP ≥ 50%, CRP and Ar-A ≥ 40%, HR ≥ 30% and increase of RA and LA FI ≥ 80%, FC, RV EF and FAC ≥ 40%, PVSC ≥ 50% identified pts with cardiac events reduction. 2) I use associated with lower mortality and morbidity due to significant improvement of right heart and LA functional parameters, neurohormonal and inflammation status and HR reduction.

## POPULATION STUDIES / EPIDEMIOLOGY

## P447

### Metolazone therapy in elderly heart failure patients - prognostic implications

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**Background:** Metolazone (MTZ), a thiazide-like diuretic is used together with loop diuretics in the management of refractory congestive heart failure.

**Aim:** The aim of this study was to identify the demographics of the patients over the age of 75 prescribed MTZ and to identify the 30 day and 1 year event rates in this



group.

**Method:** A retrospective analysis of data was taken of patients prescribed MTZ at Bradford Foundation Teaching Hospitals. The time period of prescription was from 1/1/14 to 31/12/14 and the 30 day and 1 year event rates in this group was studied.

**Results:** In the 12 month period, 50 patients were prescribed MTZ of which 37 (74%) patients were over the age of 75.

The mean age of patients receiving MTZ (over 75) was 86.2 years (standard deviation - 5.3) ranging from 76-95. The mean age of patients receiving MTZ (under 75) was 59.3 years (standard deviation - 13.4) ranging from 32-73.

In the elderly cohort, 15 (40.5%) patients had Atrial Fibrillation, 15 (40.5%) had Chronic Kidney Disease, 15 (40.5%) had Diabetes, 13 (35.1%) had Hypertension, 16 (43.2%) had known ischaemic heart disease, 3 (8.1%) had an ICD/Bi-vent in-situ and 2 (5.4%) had a previous/current malignancy. 28 patients (75.7%) were Caucasian, 7 (18.9%) were South-Asian and 2 (5.4%) were Afro-Caribbean.

In the elderly cohort, 16 patients (43.2%) had one or more readmission(s) within 12 months of which 8 patients (21.6%) were readmitted due to heart failure. 3 patients (8.1%) were readmitted within 30 days.

In the over 75 group, 9 patients (24.3%) died within their first 30 days from admission compared to no patient deaths in the under-75 group (Z-score is 1.96,  $p < 0.05$ ).

In the over 75 group, 23 patients (54%) who took MTZ died within 1 year compared to 5 (38.5%) patients in the under-75 group (Z-score is 1.47,  $p = 0.14$ ).

In the over 75 group, the average time to death was 121 days from the first dose of MTZ to the day of death.

**Conclusion:** 1. MTZ treatment is predominantly used in the elderly population in our local practice.

2. Patients over 75 prescribed MTZ have, in particular, a statistically significant higher 30 day mortality rate compared to the under 75 MTZ treated group.

3. MTZ prescription is associated with a high readmission and mortality rate at 1 year in the elderly.

4. Further study is advocated to investigate the safe prescribing of MTZ in the elderly population.

#### P448

##### The impact of gender, age, and education on depression among arab cardiovascular patients: findings from a middle-eastern study

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**Introduction:** Depression is associated with cardiovascular diseases. Early detection and intervention for depression among cardiovascular (CV) patients can reduce morbidity and mortality rates. Understanding how gender, age and educational level contributed as risk factors is necessary to adequately address the complex nature of depression as co-morbidity among Arab CV patients in the Middle East region.

**Objectives:** To evaluate the prevalence and severity of depression among Arab CV patients and to find ways to manage depression among male and female Arab CV patients.

**Methods:** A cross-sectional survey was conducted with 688 (69%) male and 312 (31%) females Arab CV patients admitted to 4 cardiology units at a hospital in the Middle East region. Inclusion criteria were  $\geq 20$  years of age, agreeing to participate in the study (98% response rate), and having final confirmation of acute cardiac conditions. Face-to-face interviews were conducted using structured survey questionnaires which included an Arabic demographic questionnaire and the Arabic version of the Beck Depression Inventory 2nd Edition (BDI-II). Descriptive and inferential statistics were performed using SPSS version 20.

**Results:** 80% of the patients had no depressive symptoms, 15% of the patients had Mild Mood Disturbance and 5% had symptoms of clinical depression. Almost twice as many females (29%) than males (16%) were found to suffer from Mild Mood Disturbance and Clinical Depression. Approximately half of both male and female patients who scored  $\geq 17$  on the BDI-II (suggesting symptoms of clinical depression) refused psychiatric assistance. Chi Square tests indicated that gender and age were significantly related to depression (all  $p < 0.001$ ). Educational level was not statistically significantly related to depression, however, its relationship clearly reflected an U-shaped relation (i.e. no linear pattern, but quadratic).

**Conclusion:** (1) Health care providers should be aware and integrate gender, and age differences approach into their clinical practice; (2) routine systematic screening for depression and mental health counseling available for all CV patients, especially for patients of working age groups and females; and (3) Public awareness and education about mental health are critical in order to reduce the stigma associated with accessing treatment for it.

#### P449

##### Prevalence and in-hospital mortality of heart failure patients in the emergency department

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**Background:** Heart failure is the most common cause for hospitalisation in Germany. It is associated with a reduced quality of life and a poor prognosis. The prevalence will increase due to demographic changes, the epidemiological transition with more chronic conditions instead of infectious diseases and improved medical care. However, analyses of routine data of patients treated in the Emergency Department (ED) with heart failure are sparse. Aim: Our aim is the analysis of prevalence and mortality of hospitalised patients with heart failure in comparison to all inpatients in the ED. Methods: Administrative data of 34,333 patients (thereof 13,536 inpatients) were available for two ED's at our university for the period between 15.02.2009 until 15.02.2010. Inpatients were included if they had a main hospital diagnosis of I11; I13 or I50 according to the International Classification of Disease, version 10 (ICD-10). Patients with a hypertensive heart disease without (congestive) heart failure (I11.90 and I11.91) were excluded. The statistical evaluation was performed with SPSS 22.

**Results:** In total, heart failure was diagnosed in 388 of 13,536 hospitalised patients (median age: 71 years; male: 59%), who were treated in the ED (thereof 40% with NYHA IV). The prevalence of heart failure increased with age ( $< 30$  years 0.3%;  $> 80$  years 4.2%). From the age of 60 years patients with heart failure are older than all hospitalised patients (83.5% vs. 65.8%). Patients with heart failure had a longer hospital stay (median: 7 days vs. 5 days) and a higher proportion of patients was treated in intensive medical care units (30.2% vs. 18.25%). Dyspnoea was the leading chief complaint of patients with heart failure at the initial contact in the ED (63.9%); 8% of all admitted patients with heart failure in the ED died in comparison to 4.7% of all hospitalised ED patients during hospital stay. Most of them were older than 80 years (38.7% vs. 30%).

**Conclusion:** In comparison to all hospitalised patients in the ED, patients with heart failure are characterised by a higher age, a need for more intensive medical care, an increased length of stay and higher mortality. They are a vulnerable group, who require a complex diagnostic work up and treatment. More than likely this group will increase continually. Due to this background, an early risk stratification by appropriate routinely available parameters seems to be most valuable and should be the aim of future studies in the setting of emergency and acute medicine.

#### P450

##### Short- and long-term mortality and heart failure hospital re-admissions among patients hospitalised for heart failure: a regional population-based investigation from Italy

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**Background:** In population-based studies on patients admitted for HF, 1-y mortality ranged from 22% and 40%, while all-cause readmissions was higher than 50%.

**Purpose:** Aim of the present study was to identify short-term (30d) and long-term (1y) prognostic factors for HF re-hospitalization or death in a unselected population in the northern-east Italy, with structured pathways for outpatient HF care post discharge.

**Methods:** Data were retrieved from the Cardiovascular Observatory of Trieste area. Different databases were linked: hospital records with discharge diagnosis, cardiological chart, laboratory tests, outpatient drug prescriptions. Individuals hospitalized for HF at least once during the period 2009-2014 were identified. HF diagnosis included ICD-9th codes for heart failure (428.x) and hypertensive heart failure (402.01, 402.11 and 402.91) according to National Outcome Evaluation Program (PNE) made by the National Agency of Regional Health-Care Services. "Worsening" HF (WHF) was classified on the base of at least one HF hospitalization in the 5 years preceding the index admission. Cumulative incidence probabilities of re-hospitalization were computed taking into account death as a competing risk; cause-specific regression was applied to find factors associated with death or re-hospitalization.

**Results:** 4935 HF admissions were recorded, and 4666 were discharged alive (94%). Median age was 82 yrs (IQR: 75-87), 46% males. 40% had a Charlson Index  $\geq 3$  (CH) and 16% were 'WHF'. Most severe cases (709, 15%) received a phone call from nurse-led HF clinic to verify clinical stability and therapy adherence within 7d and ambulatory or home cardiological evaluation within 30d post discharge. Cumulative incidence of 30d re-HF hospitalization was 4%, rising at 22% at 1y; death was respectively 3% at 30d and 24% at 1y. Predictors of re-HF hospitalization were at 30d lower values of CKD EPI ( $< 50$  ml/min, median), reduced LVEF ( $< 50\%$ ) and

beta-blockers therapy. At 1y advanced age, reduced LVEF, CH<sub>2</sub>≥3, 'WHF', prescribed CV therapy (aldosterone antagonists, ACE-I/sartans and diuretics) and a cardiologist visit within 30d were all associated with an higher risk. Regarding death, early events were associated with advanced age, CH<sub>2</sub>≥3, longer length of stay; CV therapy was instead protective. At 1 y these parameters were confirmed and were also significant male sex, reduced LVEF, higher BNP values, being hospitalized in a non-cardiology department and admission to home care services/intermediate care units within 30d after the index hospitalization.

**Conclusions:** Short- and long-term mortality and re-admissions for HF with structured pathways for outpatient care post hospital discharge is relatively low as compared with previous experience. Characterization of HF patients is very important in assisting clinicians in decision-making, targeting treatment and implementing clinical pathways for outpatients care in high-risk cases.

#### P451

##### The profile of Romanian hypertensive patients with heart failure

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**Background:** Heart failure is more and more a public health problem in Romania, with frequent hospitalization, high cost, low quality of life and decreased survival. Also the prevalence of hypertension in the general population is increasing.

**Purpose:** To analyze the clinical profile of hypertensive heart failure patients in a Romanian Hospital. **Methods:** There were enrolled a total of 187 patients admitted in the Cardiology Department of Rehabilitation Hospital, Cluj-Napoca, Romania, previously diagnosed with heart failure. The mean age was 70.70 ± 8.99 years, 54% of the patients were women. Heart failure was defined according to 2012 ESC criteria. All patients were evaluated for cardiovascular risk factors, NT-pro-BNP levels and by echocardiography.

**Results:** The average NT-pro-BNP was 2032.71 ± 2281.19 pg/ml, men presenting a tendency to higher levels compared to women: 2350.93 ± 2609.61 vs. 1759.04 ± 1927.1 pg/ml, p=0.08. 71.7% (n=134) of the patients enrolled in this study had arterial hypertension, with a significantly higher prevalence in female gender (78.2% vs. 64%, p=0.023). Both male and female hypertensive patients were older (71.85 ± 7.92 vs. 67.83 ± 10.78 years, p=0.006). There was no significant difference between heart failure patients with or without arterial hypertension regarding the presence of diabetes mellitus (17.9 vs. 24.5%, p=NS), obesity (8.5 vs. 7.5%, p=NS) or dyslipidemia (38.8 vs. 34%, p=NS). Hypertensive patients had a higher prevalence of heart failure with preserved ejection fraction than normotensive subjects: 73.9 vs. 47.2%, p=0.001. Hypertensive patients had a lower NT-pro-BNP mean value than patients without hypertension (1715.18 ± 1924.27 vs. 2829.53 ± 2865.16 pg/ml, p=0.002) irrespective of the gender: females -1565.04 ± 1679.92 vs. 2446.86 ± 2554.26 pg/ml, p=0.058; males-1928.11 ± 2224.51 vs. 3101.10 ± 3078.74 pg/ml, p=0.04. A significant negative correlation between NT-pro-BNP and ejection fraction, not influenced by blood pressure values was observed in both genders: patients with vs without arterial hypertension r=-0.4, p<0.0001 vs. r=-0.442, p=0.0011; female patients with vs. without arterial hypertension r=-0.29, p=0.010 vs. r=-0.42, p=0.05; male patients with vs. without arterial hypertension r=-0.52, p=0.0001 vs. r=-0.44, p=0.01. When the medication administered to heart failure patients with and without arterial hypertension was analyzed, the only significant differences noticed were involving digitalis (21.6 vs. 39.6%, p=0.01) and ARBs (46.3 vs. 24.5%, p=0.005). There were no statistically significant differences regarding administration of diuretics (86.6 vs. 88.7%, p=NS), ACEIs (56 vs. 43.4%, p=0.08), beta-blockers (75.4 vs. 64.2%, p=0.08) and nitrates (47.8 vs. 39.6%, p=NS).

**Conclusion:** Hypertensive patients with heart failure have a different profile compared to those without arterial hypertension. This implies a special approach in the evaluation and therapy recommended for this high risk population.

#### P452

##### Risk score for incident heart failure: a subject-level meta-analysis from the heart omics in ageing database

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Heart failure (HF) is a syndrome that leads to a diminished quality of life and costly hospital admissions, affecting especially the elderly. The Heart 'Omics' in Ageing (HOMAGE) database was used as a resource to conduct a subject-level meta-analysis to identify risk factors associated with new-onset HF and to develop a risk score for HF. Two population-based studies and two studies including patients at risk for cardiovascular disease were included. Time-to-event analysis was conducted by using Cox proportional hazard models stratified by study. A point-based

risk score for assessment of 5-year HF risk in each cohort was derived from the Cox regression model which was evaluated for discrimination (area under the receiver operating characteristic curve [AUC]) and calibration (Grønnesby-Borgan  $\chi^2$  statistic). In the population cohort, during a follow-up of 6.2 years, 589 participants out of 4438 subjects (mean age 73.4 ± 3.8 years, 51% women) developed HF. In the patient cohort 25059 patients at risk for cardiovascular disease were included (mean age 65.9 ± 9.2 years, 30% women) of which 526 developed HF. Sex (male), higher age, higher body mass index, higher systolic and lower diastolic blood pressure (only in the population cohort), higher heart rate, lower estimated glomerular filtration rate (eGFR), smoking, history of CV disease and use of antihypertensive medication were detected as significant predictors of incident HF. The 5-year HF risk associated with each point total, derived from the Cox model risk estimates of the population cohort, ranged from less than 1% risk for a point total of ≤ 0, to more than 30% risk for point totals above 13. In the patient cohort, a point total of 1 or less corresponds to a 5-year HF risk of < 1%, while the risk amounts to 30% or more for a point total of ≥ 15. To estimate HF risk in a general and patient population, two risk score models were developed from clinically relevant parameters to aid in risk stratification and contribute to future prevention.

#### P453

##### Did the incidence of chronic heart failure among patients attending cardiovascular rehabilitation program change in last 7 years

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**Introduction:** Many trials have shown that >70% of patients with heart failure had an ischaemic heart disease. Medical therapy with or without myocardial revascularisation (coronary angioplasty or bypass surgery) apparently does not provide maximum benefit for these group of patients.

**Purpose:** To review experience of our institution in incidence of chronic heart failure /CHF/ among patients who refer to in hospital cardiovascular /CV/ rehabilitation program after cardiac /bypass/ surgery or after myocardial infarction.

**Methods and Results:** We analyzed our clinical database from 2007-2015 and compare data. In the period of 2007-2015 we admitted 4373 patients after myocardial infarction and 3421 patients after bypass surgery for in hospital cardiac rehabilitation. The age structure over time has not changed. Mostly patients were in two age groups: from 55-64 year (31.15%) and from 65-74 year (33.18%). There were 6149 /78, 9%/ men and 1645 /21,1%/ women. Rehabilitation program lasted for 21 days and includes a physical examination of patients (blood pressure measurement, control of heart rate, recording an electrocardiogram), blood was sampled for analysis, risk factors were noted, education (about risk factors and dietary measures) and aerobic training with telemetric monitoring. We analyzed the data every 4 years /at 2007, at 2011 and at 2015/. During 2007, in our institute, we rehabilitated 1446 (92.57%) patients after myocardial infarction /MI/ and 116 (7.42%) patients after aortocoronary bypass surgery /ACB/. At 2011, there were 570 (57.1%) patients after MI and 546 (48.9%) after ACB. At 2015 rehabilitation after MI included 488 (52.75%) patients and 437 (47,25%) patients after ACB. Heart failure is defined as a reduction in global ejection fraction less than 40% /EF <40%/. At 2007 most patients attending CV rehabilitation were patients after myocardial infarction. Over the years, the number of patients after myocardial infarction and after cardiac bypass surgery is almost equalized with approximately the same representation of heart failure. There were 26,5% of patients with chronic heart failure on cardiovascular rehabilitation in 2007, 25,9% patients with CHR in 2011 and 27,83% patients with CHR in 2015. There were no significant differences in incidence in CHF among groups (t=0,760; p > 0,05).

**Conclusion:** new developments in diagnostics and treatment of patients with ischemic heart disease, despite efforts, did not have significant effect on reducing the incidence of chronic heart failure in patients with ischemic heart disease who attended the cardiovascular rehabilitation program in our institute.

#### P454

##### "Recovered" left ventricular ejection fraction: a different class of heart failure based on clinical characteristics?

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**Background:** Advances in pharmacological therapy, devices and surgery are responsible for a non-negligible number of patients with heart failure (HF) and reduced left ventricular ejection fraction (LVEF) whose systolic function improve significantly, even sometimes to normal or almost-normal values. The existence of a third class of HF beyond reduced- and preserved- LVEF HF has already been proposed.

**Objective:** To analyse the proportion, clinical characteristics and magnitude of improvement of patients with LVEF below 45% at baseline that increase it to a LVEF ≥45%, after one year of follow-up at a multidisciplinary HF Unit.

**Patients and Method:** LVEF at first visit and at one-year follow-up were assessed by echocardiography in 1063 patients (72.7% men; mean age 65.6 ± 11.9 years,

range 30-96 years). Aetiology of HF was mainly ischemic heart disease (52.2%), followed by dilated cardiomyopathy (14%), valvular disease (8.7%) and hypertensive cardiomyopathy (8.6%). Mean LVEF was  $32.8\% \pm 12.6$ . Most patients were in NYHA functional class II (68.3%) and III (25%). Patients were classified into three groups: 1) LVEF <45% at baseline and  $\geq 45\%$  at one year ("recovered HF", n=237); 2) LVEF  $\geq 45\%$  at baseline ("preserved HF" [HFpEF], n=145); and 3) LVEF <45% both, at first and at one-year visits ("reduced HF" [HFrEF], n=681).

**Results:** As expected, HFpEF patients were older ( $68.3 \pm 13.5$  years vs.  $65.2 \pm 11.6$ ,  $p=0.003$ ), predominantly female (57.9% vs. 21.8%,  $p<0.001$ ) and of non-ischemic aetiology (76.5% vs. 43.2%), had more atrial fibrillation (43.4% vs. 16.7%,  $p<0.001$ ), and were in worse NYHA functional class (37.2% III/IV vs 24%,  $p=0.001$ ), as compared with all patients with LVEF <45% at baseline. Recovered HF patients (as compared with HFrEF) were younger ( $63.4 \pm 12.4$  years vs.  $65.8 \pm 11.3$ ,  $p=0.007$ ), with more proportion of female sex (30.4% vs. 16%,  $p=0.001$ ), predominantly of non-ischemic aetiology (64.6% vs. 35.8%,  $p<0.001$ ), non-diabetic (66.7% vs. 59%,  $p=0.04$ ), had more atrial fibrillation (21.1% vs. 15.1%,  $p=0.03$ ), had less LBBB (7.6% vs. 16%,  $p=0.001$ ), had shorter HF duration (median 3 months [IQR 1-18] vs. 12 months [IQR 2-56],  $p<0.001$ ), and were in better NYHA functional class (19% III/IV vs. 26%,  $p=0.04$ ). Mean LVEF increase in patients with recovered HF was  $20.6 \pm 10.3$  points vs.  $3.4 \pm 10.3$  in HFrEF,  $p<0.001$ . Recovered HF patients also significantly differed from patients with HFpEF in age ( $p<0.001$ ), sex ( $p<0.001$ ), ischemic aetiology ( $p=0.01$ ), prevalence of atrial fibrillation ( $p<0.001$ ), duration of HF ( $p<0.001$ ), and NYHA functional class ( $p=0.001$ ).

**Conclusion:** Almost one quarter of ambulatory patients with HF showed LVEF "recovery" at one year of follow-up. Clinical characteristics of recovered HF patients significantly differed from HFrEF and HFpEF.

#### P455

##### Trends in epidemiology, clinical presentation and management of acute heart failure: insights from romanian cohorts of ESC-HF Pilot survey and ESC-HF-LT registry

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**Aim:** Temporal trends of epidemiological data on acute heart failure (AHF) are limited. We sought to assess changes in epidemiology, clinical presentation and management of AHF in Romania using data from two European registries conducted 3 years apart.

**Methods:** The European Society of Cardiology-Heart Failure Pilot study (ESC-HF pilot) and the European Society of Cardiology Long-Term Registry (ESC-HF-LT registry) were conducted during 2009-2010 and 2011-2013, respectively. Both registries were prospective, multicentric, observational surveys with 1-year follow-up and were largely representative for cardiological European community.

**Results:** Romanian sites have recruited a total number of 687 AHF patients in the two registries (358 in ESC-HF pilot and 329 in ESC-HF-LT registry). Median age of recruited patients increased from 69 (60-75) years in ESC-HF pilot to 71(61-78) years in ESC-HF-LT registry, and proportion of patients with HF and EF > 45% increased over time from 31% to 35%, trends similar to those reported by other European countries. 70% of AHF patients in both registries presented with chronic worsening HF and 30% with de novo HF. The use of life-prolonging, guideline-recommended medical therapies (GRMTs) increased over time (pre-admission use of ACE inhibitors/ARBs from 42% to 54%, beta-blockers from 34% to 45%, aldosterone antagonists from 25% to 34%). GRMTs increased substantially during hospitalization in both registries, and minimal variations were noticed during 1-year follow-up. The main intravenous therapies in both registries were diuretics (92% and 85%), followed by vasodilators (21.9% and 17.4%) and inotropes (7.6% and 17.2%), proportions similar to other European countries. While in-hospital mortality increased from 4.3% in ESC-HF pilot to 4.9% in ESC-HF-LT registry, 1-year all cause mortality remained similar, 24.3% vs 24.4%. 1-year HF related hospitalizations dropped from 18.8% in ESC-HF pilot to 15.2% in HF-LT registry. Furthermore, the composite outcome, 1-year all cause mortality and/or HF hospitalizations declined over time, from 39.1% to 35.8%.

**Conclusions:** Clinical profiles, in-hospital management and outcome of AHF patients in Romania were similar to other European countries, despite regional differences in healthcare systems. A temporal increase in the utilization of life-prolonging GRMTs therapies along with an improvement of 1-year outcome was observed.

#### P456

##### Accuracy of nurse-performed lung ultrasound in patients with acute dyspnea: a prospective observational study

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**Background:** In clinical practice lung ultrasound (LUS) is becoming an easy and reliable non-invasive tool for the evaluation of dyspnea. The aim of this study was to assess the accuracy of nurse-performed LUS, in particular, in the diagnosis of acute cardiogenic pulmonary congestion.

**Material and Methods:** We prospectively evaluated all the consecutive patients admitted for dyspnea in our Medicine Department between April and December 2015. At admission, serum BNP levels and LUS was performed by trained nurses blinded to clinical and laboratory data. The accuracy of nurse-performed LUS alone and combined with BNP for the diagnosis of acute cardiogenic dyspnea was calculated.

**Results:** 508 patients (41.6% men, mean age  $78.7 \pm 12.7$  years) were included in the study. Nurse-performed LUS alone had a sensitivity of 95.3% (95%CI 92.6-98.1%), a specificity of 88.2% (95%CI 84.0-92.4%), a positive predictive value of 87.9% (95%CI 83.7-92.2%) and a negative predictive value of 95.5% (95%CI 92.7-98.2%). The combination of nurse-performed LUS with BNP level (cut-off 400 pg/mL) resulted in a higher sensitivity (98.9%, 95%CI 97.4-100%), negative predictive value (98.8%, 95%CI 97.2-100%) and corresponding negative likelihood ratio (0.01, 95%CI 0.0, 0.07).

**Conclusion:** Nurse-performed LUS had a good accuracy in the diagnosis of acute cardiogenic dyspnea. Use of this technique in combination with BNP seems to be useful in ruling out cardiogenic dyspnea. Other studies are warranted to confirm our preliminary findings and to establish the role of this tool in other settings.

#### P457

##### Very low levels of circulating B-type natriuretic peptide constitute a risk for heart failure: a prospective population based cohort study

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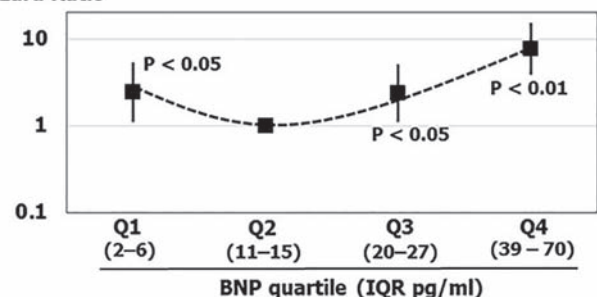
**Background:** The endogenous natriuretic peptide (NP) system plays an important role in enhancing renal sodium excretion and lowering cardiac afterload through its natriuretic and vasodilatory properties. Recent studies have suggested that chronic augmentation of the protective NP system in early stages of heart failure (HF) may ultimately prevent the progression of HF. However, no studies have demonstrated the risk of attenuation of the NP system for development of HF.

**Methods:** Subjects of this study were recruited from our general population. Baseline data including plasma B-type natriuretic peptide (BNP) levels were determined in 13,637 participants (mean age=64 yrs). Subjects were divided into quartiles (Qs) according to their baseline plasma BNP levels. Event free survival for HF events from entry into the study was estimated using the Kaplan-Meier method. A multivariate Cox regression analysis was performed to determine hazard ratios of plasma BNP quartiles for the onset of HF.

**Results:** During follow up (mean 9.0 years), 171 cases in the cohort had confirmed onset of HF (Framingham criteria). Although the follow up period was the same for all Qs, the event free rate in the second quartile (Q2) was the lowest (Q1 = 0.62%, Q2 = 0.26%, Q3 = 0.73%, Q4 = 3.41%). After adjustment for traditional cardiovascular risk factors (sex, age, body mass index, hypertension, diabetes, hypercholesterolemia, smoking, eGFR and atrial fibrillation), hazard ratios (HRs) for HF development among BNP quartiles revealed a J shaped pattern (Figure). The lowest Q1 (IQR 1.8 – 6.5 pg/ml) had a higher HR (2.43; 95% CI = 1.10 - 5.34) compared to the reference group (Q2;  $p<0.05$ ).

**Conclusion:** This cohort study suggests that very low levels of circulating BNP generate risk for future onset of HF in the general population. An impaired endogenous bioactive NPs system may be involved in the etiology of HF in certain subjects at risk.

#### Hazard Ratio



Multivariate HR among BNP quartiles



## EXERCISE TESTING &amp; TRAINING

## P458

**Exercise training heart failure rehabilitation program in Federal Almazov Medical Research Centre in Russia**

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In 2010 cardiologists of a Medical Research Centre in Russia proposed a new method for determination of exercise intensity for heart failure rehabilitation. We have marked four physiological stages during incremental physical exercise: LACTATE THRESHOLD, pH THRESHOLD, RESPIRATORY COMPENSATION POINT and AEROBIC LIMIT. Lactate threshold was determined when blood lactate level began to increase, pH-threshold was determined when blood pH level began to decrease. Respiratory compensation point (RCP) was determined when ventilation dramatically increase relative to carbon dioxide output (VE/VCO<sub>2</sub>). By continuous increase of work rate, oxygen consumption, up to a certain point, increases linearly and become stable – it is aerobic limit. This new concept of the division of physical exercises on the physiological phases helped us to develop the more precisely individualized physical rehabilitation program. First tree month HF patients trained 40-60 minutes every day on treadmill with exercise intensity observed at LT, every month after control CPET exercise intensity increased gradually. Other tree month patients trained 35-50 minutes every day on treadmill with exercise intensity that observed between LT and pH-T, every month after control CPET exercise intensity increased gradually. Before and after training 5 minutes morning exercises made. Since 2012 175 HF pts with III NYHA class participate in new individualized rehabilitation program. There was a significant increase in VO<sub>2</sub> and MLHFQ score after 32 weeks of training. In 15 patients after 32 weeks of aerobic exercises increase VO<sub>2</sub> reached 85-102% of maximum predicted values, which is normal. Such dynamics of oxygen consumption indicates, probably, the increase the number of mitochondria in muscle fibers of lower extremities. The survival rate in 175 HF patients (average age 53.5 ± 0.4, average NYHA class - 3.0, average LVEF - 40.8 ± 0.3%) was 81% in 3 years of follow-up.

**Conclusion:** Exercise training heart failure rehabilitation program proposed in a Medical Research Centre is safe and effective, increases exercise tolerance in HF patients, improves outcomes.

## P459

**The benefits of cardiac rehabilitation in coronary artery disease: does the weight matter?**

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**Background:** Cardiac rehabilitation programs (CRP) are medically supervised exercise-based protocols for patients (pts) who experience a cardiac event. It has been recognized that CRP improved coronary heart disease (CHD) risk factors (RF) and functional capacity. Obesity is a major CHD RF. On the other hand, obese pts may have some difficulties in CRP performance. The aim of this study was to compare obese and non-obese pts regarding their baseline clinical profile and response to a CRP.

**Methods:** We analysed data from a prospectively collected registry of 433 consecutive pts who underwent CRP after an acute coronary syndrome (ACS) from January 2009 to October 2015. Pts were divided in two groups according to their body mass index (BMI): BMI ≥ 30 kg/m<sup>2</sup> (obese) and BMI < 30 kg/m<sup>2</sup> (non-obese). Exercise performance was assessed using both duration and metabolic equivalents (METs) achieved in standard exercise test (ET) using Bruce protocol before and after CRP.

**Results:** Ninety-nine (22.9%) pts were obese. No differences concerning age (54.1 ± 10.1 vs 54.7 ± 9.6 years) or gender (79.8% vs. 86.7% males) were found between groups. Obese pts had a mean waist circumference 108.4 ± 6.1 cm in males and 102.1 ± 7.6 cm in females, while non-obese pts presented a mean waist circumference of 93.8 ± 5.5 in men and 81.5 ± 7.4 cm in women. Among CHD RF, hypertension and diabetes were more frequent in obese pts (64.6% vs. 40.1%, p < 0.001 and 29.6% vs. 16.3%, p = 0.003, respectively). Obese pts also showed higher levels of depression symptoms at admission (p = 0.005). The index coronary event affected 1 coronary artery in more than half of pts in both groups. Echocardiography showed a mean fractional ejection 55.5 ± 10.8% in obese pts and 51.7 ± 12.0% in other pts (p = 0.012). Baseline functional capacity was lower in obese group both in duration (7.05 ± 2.33 min vs 8.38 ± 2.23 min; p < 0.001) and intensity (7.67 ± 2.32 METs vs 8.91 ± 2.18 METs; p < 0.001). Both groups improved their functional capacity, but obese pts showed better results in duration (+36.7% vs. 28.8%, p = 0.043) and intensity (+32.4% vs. 25.9%, p = 0.079), the last without statistical significance.

**Conclusion:** Obesity is epidemic in western countries. It is tightly linked to CHD. Overweight should be a main focus in both primary and secondary prevention. CRP showed to improve exercise capacity in obese and can contribute to reduce morbidity and mortality in such important group of pts.

## P460

**Prediction of peak oxygen consumption in patients with heart failure using classification and regression trees**

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**The aim:** to determine factors with most significant impact on peak oxygen consumption (PVO<sub>2</sub>) in HF patients and create a model for PVO<sub>2</sub> prediction.

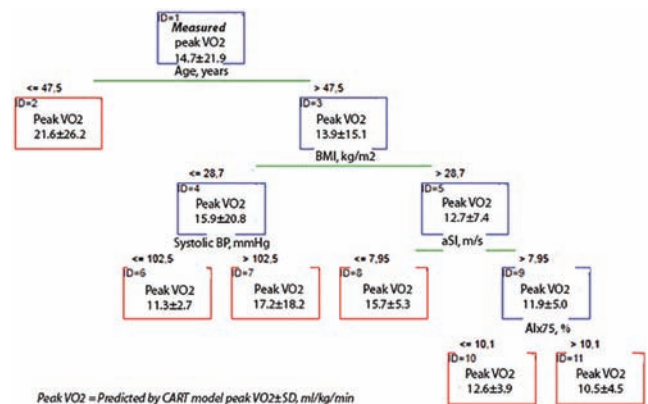
**Methods:** 91 patients with both reduced and preserved ejection fraction were consequently enrolled in the study (51.6% men; mean age 64.7 years; mean NYHA class 2.2 ± 0.8, mean NT-pro-BNP 563.6 pg/ml). All patients had undergone clinical and laboratory investigation; routine and tissue Doppler echocardiography, cardiopulmonary exercise testing and photoplethysmographic arterial stiffness analysis assessing augmentation index, corrected for a heart rate of 75 beats/min (Alx75, %), stiffness index (SI, m/s) and reflection index (RI, %). End-systolic elastance and effective arterial elastance were calculated. Factors with highest impact on peak VO<sub>2</sub> were identified by multivariate discriminant analysis of 49 clinical variables. Then Classification and regression trees (CART) allowing to predict PVO<sub>2</sub> were constructed using STATISTICA 11 software.

**Results:** relative ranks of different clinical characteristics with strongest influence on PVO<sub>2</sub> were determined by CART (see table). Of note, arterial stiffness characteristics affect PVO<sub>2</sub> more significantly than many "classical" factors. Simplified CART model for PVO<sub>2</sub> prediction is presented on the picture. Model validation in different limited HF patient population shown its affordable accuracy.

**Conclusions:** we construct CART model for PVO<sub>2</sub> prediction in exercise intolerant that include both classical factors and arterial stiffness characteristics.

Relative factors ranks estimated by CART

Clinical characteristics	Rank of influence on PVO <sub>2</sub>
Age, years	100
Body mass index, kg/m <sup>2</sup>	92
Systolic blood pressure, mmHg	57
LV ejection fraction, %	55
NT-pro-BNP, pg/ml	54
RI, %	47
Effective arterial elastance	44
E/E', mean	35
Alx75, %	34
SI, m/s	33
End-systolic elastance	31
Pulmonary artery systolic pressure, mmHg	27
Left atrial volume index, ml/m <sup>2</sup>	26


 CART model for PVO<sub>2</sub> prediction

## P461

**Aquatic exercise training is effective in maintaining exercise performance in trained heart failure patients**

Heart Foundation of Australia

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## P462

**High-intensity interval training combined with strength exercise effect on aorto-ventricular coupling in patients with chronic heart failure. A randomized phase iii clinical trial.**C Christina Chrysohou<sup>1</sup>; G Tsitsinakis<sup>1</sup>; A Aggelis<sup>1</sup>; E Herouvim<sup>1</sup>; D Tsiachris<sup>1</sup>; I Vogiatzis<sup>1</sup>; C Pitsavos<sup>1</sup>; N Koulouris<sup>1</sup>; C Stefanadis<sup>1</sup>; D Tousoulis<sup>1</sup><sup>1</sup>University of Athens, Athens, Greece

It is known that heart failure causes changes in cardiac mechanics, like an unfavorable alteration of ventricular/vascular coupling, which reflects arterial stiffness and has been related with adverse cardiovascular outcomes. Aim of this work was to evaluate the effect of high-intensity interval exercise (i.e. 30 sec at 100% of maximum workload, following by 30 sec at rest, 3 days per week at a 45 minutes working-out schedule, combined with aerobic and muscle strength training, for 12 weeks) on left ventricular function and aortic elastic properties of chronic heart failure patients.

**Methods:** a phase III clinical trial, that enrolled 100 consecutive eligible patients (NYHA II-IV, ejection fraction < 50%) randomly allocated in exercise and control group. Of then 72 patients completed the study (exercise group=33, 63+/- 9 years old, 88% men; control group: n=39, 56+/- 11 years of, 82% men). All patients underwent cardiopulmonary stress test, non-invasive high-fidelity tonometry of the radial artery, pulse pressure measurements by SphygmoCor device and echocardiography before and after the completion of the training program where diastolic indices were measured.**Results:** Both groups reported similar medical characteristics and physical activity status. General mixed effects models revealed that the intervention group reduced pulse wave velocity by 9% ( $p = 0.05$ ); Emv/Vp by 14% ( $p = 0.06$ ); E to A ratio by 24% ( $p = 0.024$ ); E to Emv by 8% ( $p = 0.05$ ); quality of life score increased by 66% ( $p = 0.003$ ); depression score decreased by 19% ( $p = 0.05$ ); augmentation index increased by 28% ( $p = 0.001$ ); VTI increased by 4% ( $p = 0.05$ ); 6 minutes walking distance increased by 13% ( $p = 0.05$ ); peak oxygen uptake increased by 28% ( $p = 0.001$ ); and peak power increased by 25% ( $p = 0.005$ ). There were no significant changes in the control group.**Conclusion:** Interval high intensity aerobic training, combined with strength exercise seems to benefit aortic dilatation capacity, left ventricular diastolic properties and increases augmentation index which reflects improved cardiac output. Those findings represent a beneficial effect of rehabilitation programs on arterial-ventricular coupling that boosts systolic pressure waveform and improved quality of life in chronic heart failure patients.

## P463

**Effects of short-time physical training in heart failure patients after surgical revascularization**D Marinkovic<sup>1</sup>; M Deljanin-Ilic<sup>2</sup>; B Ilic<sup>1</sup>; D Petrovic<sup>1</sup>; D Simonovic<sup>1</sup>; S Stojanovic<sup>1</sup>; S Ignjatovic<sup>1</sup><sup>1</sup>Institute for Treatment and Rehabilitation Niska Banja, Nis, Serbia; <sup>2</sup>University of Nis, Medical Faculty, Institute of Cardiology Niska Banja, Nis, Serbia**Aim:** To evaluate the effects of short-term physical training on physical exercise tolerance and level of markers of inflammation, neuro-humoral activation and endothelial function, in CHF patients after surgical revascularization.**Methods:** The study involved 43 patients (32 males); mean age  $60.3 \pm 5.7$  years, mean EF  $34.75 \pm 3.34\%$ , NYHA II and III, after surgical revascularization procedures. All patients were included in three-weeks rehabilitation program in the residential center, based on strictly controlled and individually prescribed physical training. Before and after rehabilitation, all patients were underwent exercise stress test, and from the veins blood samples, biochemical markers of inflammation, atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP) an endothelin (ET) were determined.**Results:** At the end of the study the hs-CRP and fibrinogen level were showed a decreasing trend (ns). After cardiovascular rehabilitation a significant reduction in white blood cells count was recorded ( $p = 0.028$ ). Erythrocyte sedimentation rate after rehabilitation was higher, but not significant. In all pts, the concentration of ANP and BNP was higher after 3 weeks compared to baseline values ( $p = 0.043$ ;  $p = 0.015$ ). In contrast, the value of endothelin after rehabilitation was lower than baseline value ( $p = 0.112$ ), but not significant. At end of this study, significantly higher serum HDL-cholesterol in CHF patients was found ( $p = 0.001$ ). Exercise tolerance was improved, as well as quality of life assessed by Minnesota Living With Heart Failure Questionnaire.**Conclusion:** CHF patients after surgical revascularization residential short-term training decreased the level of inflammatory status and ET and transitory increase ANP and BNP. Those positive effects are associated in significant increases of exercise tolerance and improve of quality of life.

## P464

**Monitoring of end-tidal pressure of carbon dioxide in patients with chronic heart failure and chronic obstructive pulmonary disease during walk test**KA Kira Ageeva<sup>1</sup>; VN Abrosimov<sup>1</sup><sup>1</sup>Ryazan State Academician Medical University, Therapy Department, Ryazan, Russian Federation**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 of 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 CO<sub>2</sub>. Significance of end-tidal CO<sub>2</sub> (PETCO<sub>2</sub>) is a constant, which shows the activity of respiratory system.**Methods:** We studied 52 patients with CHF in New York Heart Association (NYHA), age  $58 \pm 3,24$  years (25 patients (48,1%) in NYHA class II, 22 patients (4,3%) in NYHA class III, 5 patients (9,6%) in NYHA class IV). Also we studied 42 patients with COPD II-III, age  $60 \pm 3,48$  years (1st group - 22 patients (52,4%) with COPD II, 2nd group - 20 patients (47,6%) with COPD III). Control group 30 patients, age  $48 \pm 3,42$  years. 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 PETCO<sub>2</sub> in patients with CHF in NYHA class II was  $38,2 \pm 2,13$  mm Hg, in patients in NYHA class III was  $34,4 \pm 2,22$  mm Hg, in patients in NYHA class IV was  $32,4 \pm 1,14$  mm mm Hg. Significance of PETCO<sub>2</sub> in 1st group patients with COPD was  $36,2 \pm 2,43$  mm Hg, in 2nd group patients was  $34,1 \pm 1,22$  mm Hg. All patients performed 6MWT. The 6MWT distance in patients with CHF in NYHA class II was  $384 \pm 10,56$  m, in NYHA class III was  $290 \pm 17,24$  m, in NYHA class IV was  $142 \pm 3,51$  m. The 6MWT distance in 1st group patients with COPD was  $440 \pm 15,48$  m, in 2nd group was  $384 \pm 15,42$  m. There is reduction PETCO<sub>2</sub> in all patients with CHF during the 6MWT. PETCO<sub>2</sub> in patients with CHF in NYHA class II was  $33,34 \pm 2,51$  mm Hg, in NYHA class III was  $31,75 \pm 2,89$  mm Hg, in NYHA class IV was  $28,8 \pm 1,32$  mm Hg. 69,2% patients reported dyspnea as the main reason for a stop during the 6MWT. There is increase PETCO<sub>2</sub> in all patients with COPD during the 6MWT. After the 6MWT the significance of PETCO<sub>2</sub> in 1st group was  $43,21 \pm 2,81$  mm Hg, in 2nd group was  $45,05 \pm 3,26$  mm Hg. All patients reported dyspnea as the main reason for a stop during the execution 6MWT. When we analyzed the trend of PETCO<sub>2</sub> we found that these patients showed signs of periodic breathing than control group.**Conclusion:** Thus, capnography increases the diagnostic value of the 6MWT, helps to make interpretation of dyspnea in patients with CHF and COPD.

## P465

### Comparing exercise modalities in heart failure: a systematic review and meta-analysis

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**Background:** Several exercise modalities are suggested to improve exercise capacity and therefore prognosis in patients with heart failure (HF). Moreover, quality of life (QOL) and the functional modifications of the heart seem to be changeable with training. However, it is not clear which mode of physical activity is superior.

**Purpose:** In order to assess effect sizes of different exercise modalities, a systematic review and meta-analysis was performed according the PRISMA statement.

**Methods:** Randomized clinical trials in PubMed, Cochrane Library and Web of Science were selected. Primary outcome data were cardiorespiratory parameters i.e. peak oxygen uptake (peakVO<sub>2</sub>), ventilation over carbon dioxide slope (VE/VO<sub>2</sub>slope), oxygen uptake efficiency slope (OUES), exercise oscillatory ventilation (EOV), rest and peak pulmonary end-tidal CO<sub>2</sub> (PETCO<sub>2</sub>). Secondary variables were QOL, left ventricular ejection fraction (LVEF) and left ventricular end-diastolic diameter (LVEDD). Extracted data were pooled using random or fixed effects meta-analysis, if appropriate.

**Results:** Twenty RCTs (n=811) met the a-priori stated inclusion criteria. Studies were categorized into four different groups i.e. "interval training (IT1) versus IT and strength (IT1-S)" (n=156), "continuous training (CT) versus CT and strength (CT1-S)" (n=130), "IT2 versus CT2" (n=501) and "CT3 versus strength (S3)" (n=24). No significant random effects of exercise modality were revealed assessing VE/VO<sub>2</sub>slope. However, a trend was seen towards IT2 for peakVO<sub>2</sub> (P=0.099). Insufficient data were reported to assess the other primary parameters. There was a significant improvement in QOL with IT1-S (P<0.001). Comparing IT2 versus CT2, LVEDD and LVEF were significantly improved when applying IT2 (P<0.001).

**Conclusions:** There is some evidence to support high intensity interval training as effective to improve QOL, LVEF and LVEDD. Towards cardiorespiratory prognostic parameters however, it is not clear which training modality is outstanding. The fact that patients with HF are actively involved in whatever kind of exercise training seems to be enough to improve prognostic parameters, QOL and anatomic function.

## P466

### Effect of cardiac rehabilitation on glucose metabolism in patients with ischaemic heart failure

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**Aim:** Patients (pts) with cardiovascular diseases frequently have alterations in glucose metabolism (GM). Cardiac rehabilitation (CR) is effective in improving GM in diabetic pts. Our study aims to evaluate the effect of a CR program on GM of non-diabetic pts with schematic heart failure.

**Methods:** The study population included 524 consecutive patients admitted to our Cardiac Rehabilitation Unit with the diagnosis of heart failure and found to be diabetics. The gluco-metabolic state was evaluated by means of oral glucose tolerance test (OGTT) and HOMA index, the functional capacity was measured through the distance walked at six minute walking test (6mwt) both at baseline and before discharge.

**Results:** At baseline 85% of pts had Body Mass Index (BMI) of 25 or greater and 61% pts had normal fasting glucose (NFG). At baseline OGTT 17 pts (28,3%) had normal glucose tolerance, 25 (41,6%) had impaired glucose tolerance (IGT), and 18/60 (30,1%) were diabetic (DM). At the end of the CR program a significant reduction in BMI (29.8 ± 3.4 vs 29.0 ± 3.8 p 0.001) and waist circumference (81.0 ± 34.1 vs 79.1 ± 33.4 cm p 0.006) were observed. At discharge OGTT 64,7% of IGT pts had normal glucose tolerance (p 0.04), and 77% of DM pts resulted IGT. Overall there was a significant improvement in 2h glucose levels (170.2 ± 56.2 vs 146.8 ± 54.8; p 0.002), HOMA-R (2.6 ± 1.4 vs 1.8 ± 0.8, p 0.002) and distance walked at 6MWT (287 ± 107.9 vs 482 ± 117.8, p 0.001). IGT pts had a worst performance than pts with normal GM at baseline and discharge 6MWT (291.1 ± 83.4 vs 344,4 ± 87.1; p < 0.04; and 444.9 ± 102.3 vs 510.7 ± 84.7, p < 0.02 respectively). No difference was found between IGT and DM pts at baseline (291.1 ± 83.4 vs 264.7 ± 86.3 mts p > 0.05) and discharge 6MWT (444.9 ± 102.3 vs 457.8 ± 100 mts, p > 0.05). **Conclusion:** OGTT test is usefully to identify gluco-metabolic state in cardiac pts with NFG. Amongst non diabetic pts with heart failure those with IGT have a worse functional capacity than normal-glycemic ones. Cardiac rehabilitation programs improve GM and insulin resistance in cardiac pts with impaired OGTT.

## P467

### The relation between left atrial function and cardiac output during exercise in left heart disease patients: insights by combining cardiopulmonary exercise testing with stress echo

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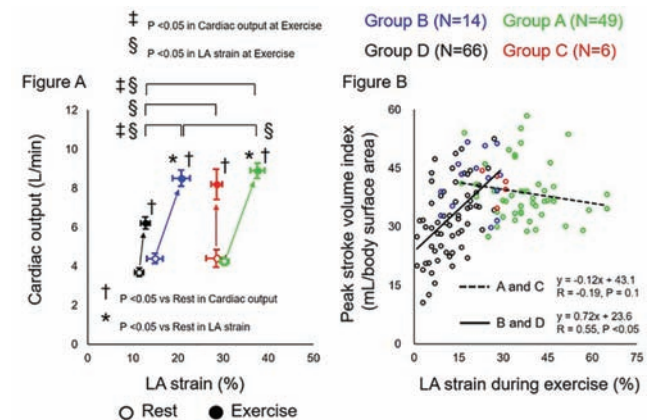
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**Background:** The hemodynamic response to exercise in left heart disease in relation to left atrial mechanics has never been studied. We aimed at investigating the link between left atrial function and cardiac output response during exercise.

**Methods:** 69 heart failure patients with reduced (n=46, HFrEF) and preserved (n=20, HFpEF) ejection fraction, 34 aortic stenosis (AS) patients, and 32 control subjects underwent cardiopulmonary exercise testing evaluation combined with Echo-Doppler with assessment of left atrial strain (LAS), measured at a similar stage of percent predicted VO<sub>2</sub>, and were divided into 4 groups according to LA volume index (LAVI) and LAS at rest.

**Results:** In group A (LAVI <34 ml/m<sup>2</sup>, LAS >23%, n=49) and B (LAVI <34 ml/m<sup>2</sup>, LAS ≤23%, n=14), LAS significantly increased during exercise (30.2 ± 5.7 vs 37.7 ± 10.9 and 14.8 ± 6.7 vs 20.6 ± 7.2%, P < 0.05, respectively) but no significant difference was observed in group C (LAVI ≥34 ml/m<sup>2</sup>, LAS >23%, n=6) and D (LAVI ≥34 ml/m<sup>2</sup>, LAS ≤23%, n=66) (28.5 ± 5.3 vs 28.5 ± 3 and 11.4 ± 5.7 vs 12.6 ± 7%). Looking at the two groups (B and D) with worse LAS, average LAS was the similar and no significant differences were observed in cardiac output at rest (3.7 ± 1.3 vs 4.4 ± 0.8 L/min) (Figure A). Nonetheless, in group D (36 HFrEF, 15 HFpEF, and 15 AS patients) compared to group B (1 HFrEF, 3 HFpEF, and 10 AS patients), LAS during exercise (P < 0.05) and cardiac output at peak exercise (6.2 ± 2.4 vs 8.5 ± 1.5 L/min, P < 0.05) were significantly lower (Figure A). LAS during exercise significantly correlated with peak stroke volume index in group B and D (R = 0.55, P < 0.05) and not in Group A and C (R = -0.19, P = 0.1) (Figure B).

**Conclusions:** In left heart disease patients, irrespective of etiology, an impaired LAS performance at rest is associated with a leftward shifted LAS vs CO response during exercise. Among this group of patients a dilated LA chamber defines the worse LAS vs CO relationship phenotype during exercise.



## P468

### Exercise intolerance can explain the obesity paradox in patients with systolic heart failure. Data from the Mecki Score Research Group

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**Background:** Obesity has been found to be protective in heart failure (HF), a finding leading to the concept of an obesity paradox. We hypothesized that a preserved cardiorespiratory fitness in obese HF patients may affect the relationship between survival and body mass index (BMI) and explain the obesity paradox in HF.

**Methods:** 4623 systolic HF patients (Left ventricular ejection fraction, [LVEF], 31.5 ± 9.5%, body mass index [BMI] 26.2 ± 3.6 kg/m<sup>2</sup>) were recruited and prospectively followed in 24 Italian HF centres belonging to MECKI Score Research Group. Besides full clinical examination, patients underwent maximal cardiopulmonary exercise test at study enrolment. Median follow-up was 1113 (553-1803) days. Study population was divided according to BMI (<25, 25-30, 25-30 kg/m<sup>2</sup>) and predicted peak oxygen consumption (peak VO<sub>2</sub>, <50%, 50-80%, >80%) [14]. Study endpoints were all-cause death and cardiovascular deaths including urgent cardiac transplant.



**Results:** All-cause and cardiovascular deaths occurred in 951 (28.6%, 57.4 per 1000 person/year) and 802 cases (17.4%, 48.4 per 1000 person/year), respectively. In the high BMI groups, several prognostic parameters presented better values [LVEF, peak VO<sub>2</sub>, ventilation/carbon-dioxide slope, renal function, haemoglobin ( $P < 0.01$ )] with respect to the lower BMI groups. Both BMI and peak VO<sub>2</sub> were significant positive predictors of longer survival: both higher BMI and peak VO<sub>2</sub> groups presented lower mortality ( $p < 0.001$ ). At multivariable analysis and using a matching procedure (age, gender, LVEF and peak VO<sub>2</sub>), the protective role of BMI disappeared.

**Conclusion:** Exercise tolerance affects the relationship between BMI and survival. The cardiorespiratory fitness mitigates the obesity paradox, observed in HF subjects.

## PROGNOSIS

### P469

#### Heart failure as a factor of unfavorable prognosis for women with myocardial infarction

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The study included 385 women with myocardial infarction (MI). Hospital mortality rate was 17.93%, 24-h mortality was 76.9%. The most frequent cause of death according to autopsy studies was cardiac arrest 95.65%. In 26.08% of the cases patients had myocardial rupture and hemotamponade. Multivariate regression analysis identified quantitative and qualitative factors affecting mortality in women. Factors affecting the men's risk of death in the hospital were congestive heart failure (CHF) (RR 17.7  $p = 0.0001$ ), VT / VF in the first day of MI (RR 13  $p = 0.01$ ), the SA and AV block (RR 8.1  $p = 0.05$ ), creatinin  $> 117$  mmol / l (RR 5.5  $p = 0.0005$ ), potassium  $< 4.15$  mmol / l (RR 3.8  $p = 0.0005$ ), sodium  $< 136.5$  mmol / l (RR 3.37  $p = 0.0001$ ), glucose  $> 9$  mmol / l (RR 3.27  $p = 0.003$ ). All survived women were divided into age groups: young till 44 years, middle age of 45-59 years, elderly - 60 years are more senior. During correlation analysis ( $p < 0.0001$ ) it was found link between heart failure with the presence and duration of a history of CHD, both stable angina and previous MI, also found significant ( $p < 0.001$ ) CHF with the presence and duration of diabetes. No significant differences according to age for NT-proBNP, determined on the 5th day of MI, was found, however, drew the attention of higher average value of this indicator in all age groups: a group of young women in 1036  $9 \pm 15.1$  pg / ml, medium - 1053.9  $\pm 8.1$  pg / ml and the elderly - 1082.3  $\pm 12.9$  pg / ml, respectively. In all age groups was detected significantly higher levels of neutrophils in the development of CHF (Killip's I 4.55  $\pm 0.2 \times 10^9$  / l Killip's IV 7.74  $\pm 0.5 \times 10^9$  / l). NT-proBNP level was significantly higher ( $p = 0.03$ ) in patients with angina before MI. It was found a positive relationship between the level of NT-proBNP and CK MB ( $r = 0.64$   $p = 0.03$ ), the absolute number of monocytes in the first day of MI ( $r = 0.46$   $p = 0.02$ ), CRP levels ( $p = 0.01$ ), as well as the development of left ventricular aneurysms ( $p = 0.02$ ) and a negative - the level of erythrocytes on the first day of MI ( $r = -0.58$   $p = 0.02$ ). Development of acute HF was associated with higher levels of glucose ( $p = 0.02$ ) and creatinin ( $p = 0.01$ ) in the first day of the MI, and the presence of anemia ( $p = 0.003$ ). The findings suggest that NT-proBNP, hyperglycemia and anemia is directly related to the vastness of myocardial lesion, one adverse remodeling in the development of MI and CHF, which are more common in older women with MI. In women the highest predictive value had acute heart failure and rhythm and conduction disturbances.

### P470

#### Serum markers of endothelial dysfunction and long-term prognosis in patients, hospitalized with acute decompensated chronic heart failure

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**Objective:** to estimate the link between serum endothelial dysfunction (ED) markers and poor outcomes in acute decompensated chronic heart failure (ADCHF) patients after discharge

**Materials and Methods:** The study included 60 ADCHF patients with sinus rhythm, mean age 69  $\pm 10$  years, 35 women (58%), treated with standard ADCHF therapy. The control group included 20 patients with compensated CHF (NYHA class II or III), compatible in age, gender, heart failure functional class, without being hospitalized within 3 months before enrollment. On admission, besides standard clinical examination, echocardiography, brachial artery diameter was measured 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%. Plasma vWF:Ag and serum levels of E-1, sICAM, sVCAM and -reactive protein (CRP) were also estimated at baseline. Follow-up period was 12 months. All ADCHF patients were contacted by phone for end-points (rehospitalization and/or death) 12 months after discharge.

**Results:** All ADCHF patients had severe endothelial dysfunction ED, compared with controls, with baseline FMD ratio of  $-2.15 \pm 2.86\%$  and  $9.00 \pm 1.47\%$  ( $< 0.001$ ), respectively. Also levels of vWF:Ag, -1, sICAM-1, sVCAM-1 and CRP were significantly higher in ADCHF patients than in the control group: vWF:Ag  $1.82 \pm 0.40$  vs.  $0.99 \pm 0.22$  U/ml ( $= 0.002$ ), E-1  $3.1 \pm 0.5$  vs.  $1.3 \pm 0.4$  fmol/ml ( $= 0.005$ ), sICAM-1  $430 \pm 81$  vs.  $224 \pm 16$  ng/ml ( $= 0.004$ ), sVCAM-1  $1999 \pm 192$  vs.  $789 \pm 62$  ng/ml ( $= 0.001$ ), and CRP  $9 \pm 7$   $3 \pm 1$  mg/dl ( $< 0.001$ ), respectively. Despite the received treatment, within 12 months after hospitalization due to ADCHF, 38(63%) patients had combined end points, 13(22%) of them died. Multiple regression analysis showed significant correlation between low baseline FMD ratio ( $\beta = -0.29$ ,  $p = 0.021$ ), high levels of ET-1 ( $\beta = 0.32$ ,  $p = 0.015$ ), sVCAM-1 ( $\beta = 0.41$ ,  $p < 0.001$ ) and CRP ( $\beta = 0.35$ ,  $p = 0.005$ ) and poor long-term prognosis.

**Conclusion:** In ADCHF patients and sinus rhythm low FMD ratio and high levels of ET-1, sVCAM-1 and RPat baseline is connected with poor prognosis after discharge

### P471

#### Cancer patients and the extended follow-up analysis in electrocardiograms

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**Background:** Cardiovascular impairment frequently occurs in patients with advanced cancer and has been shown to lead to reduced exercise capacity and quality of life. Before we showed that using patient's electrocardiograms, the resting heart rate had significant prognostic value. This is the two-year extended follow-up.

**Methods:** We enrolled 145 patients with histologically confirmed cancer (age 59  $\pm 10$  yrs, 56% men, body mass index [BMI]  $24 \pm 5$  kg/m<sup>2</sup>, tumor stage I/II/III/IV 11/10/32/46%) from 2005 through to 2010, and 59 healthy controls (age 60  $\pm 11$  yrs, 54% men, BMI  $26 \pm 4$  kg/m<sup>2</sup>). The cancer group consisted of 72 patients with pancreatic, 36 with colorectal, and 37 with non-small cell lung cancer. At baseline, a thorough cardiology assessment was performed including a resting ECG. Patients were followed through hospital record and telephone interviews in January 2016. Of 63 patients that were alive when our study was censored in February 2014, 37 patients could be reached in January 2015 and detailed information was acquired. Of those, 13 patients had passed away which raised the all-cause mortality to 95 (66%) during a mean follow-up of 33 months.

**Results:** The cancer patient's mean resting heart rate at baseline was 79  $\pm 14$  beats per minute (bpm), that of control subjects' was 70  $\pm 13$  bpm ( $p < 0.0001$ ). In total, 60% of all cancer patients presented with a resting heart rate  $\geq 75$  bpm, compared to 27% of healthy controls ( $p < 0.0001$ ). As a sensitivity analysis, we excluded control subjects who were taking a beta-blocker. Resting heart rate remained increased in cancer patients versus controls ( $p < 0.0001$ ). We found that resting heart rate, cancer diagnosis, BMI, surgical intervention, hemoglobin, serum potassium, and medication with anticoagulants all predicted survival in univariate analyses (all  $p < 0.05$ ). Cancer patients with heart rate  $\geq 75$  bpm had increased mortality compared to patients with heart rate  $< 75$  (HR 1.69 [1.10-2.60],  $p = 0.016$ ). Resting heart rate remained an independent predictor of survival in a multivariate model adjusting for all univariate significant parameters deemed clinically relevant including diagnosis, use of anticoagulation, surgery, BMI, hemoglobin, and serum potassium (HR 1.62 [1.04-2.52],  $p = 0.032$ ). In a second model we additionally included sex and age of the patients and the effect stayed significant (HR 1.62 [1.04-2.52],  $p = 0.035$ ).

**Conclusion:** The strong predictive value of the resting heart rate in advanced pancreatic, colorectal and non-small cell lung-cancer cancer is underlined by our long time follow-up.

### P472

#### Abnormal liver function predicts death and readmissions after acute decompensated cardiac failure

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**Background:** there are several risk factors and scores to predict outcomes after acute decompensated heart failure (ADHF). Regarding blood biomarkers, high sensitive troponin and impairment renal function are one of the most widely studied. Nevertheless, abnormal liver function tests (LFT) during hospitalization could help to identify high risk patient after ADHF admission and may be added as a tool to conventional and well known biomarkers.

**Objective:** to evaluate the association between abnormal LFT and death/heart transplantation and hospital readmission due ADHF in patients (pts) with ADHF at

180 days of follow up.

**Methods:** 223 consecutive pts admitted with ADHF between January-2013 and August-2014 were selected; Patients' basic characteristic data including sex, age, past medical history, medications, as well as blood exam results, were analyzed. Renal function impairment was defined by a  $>0,3$  mg/dl in creatinin value and abnormal liver function as an any upper limit increment in alanine aminotransferase, aspartyl aminotransferase, total bilirubin and/or alkaline phosphatase. The primary endpoint was death/heart transplantation and hospital readmission due ADHF at 180 days. Logistic regression analysis was used to evaluate factors associated to death.  $P < 0.05$  was considered statistically significant.

**Results:** mean age was 79 years old (DS  $\pm$  11) and 60% (134 pts) were male, mean left ventricle ejection fraction was 40% (IQR25-75: 29-59) and 43% (97 pts) had an ischemic etiology; abnormal LFT was present in 62% (138 pts) at admission and previous renal failure was recorded in 37% (83 pts); during in-hospital, 68% (153 pts) and 46% (104 pts) developed any liver enzyme enrichment or renal function impairment, respectively. There were 77 events (34%) during follow up. Regression analysis showed that highest bilirubin levels (OR 1,87, CI95%: 1,22-2,85,  $p < 0,004$ ) was the only variable associated to events among others LFT variations and factors like high sensitive troponin levels or renal impairment function.

**Conclusions:** high bilirubin levels were associated to death/heart transplantation and hospital readmission due heart failure in patients (pts) with ADHF. This easy variable may help to identify a high risk population and therefore to make a closer follow up.

#### P473

##### Comparative prognostic role of 3C-HF score across different age and ejection fraction in community-based HF population.

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**Background:** The estimates of 3C-HF score across different age range, and EF- HF groups (LVEF  $< 50\%$  - HFREF, LVEF  $\geq 50\%$  - HFpEF) is unknown. Aim: We investigate the predictive role of 3C-HF score in an epidemiological setting of community-based population according to age and HF phenotypes.

**Methods:** From October 2009 to December 2013 we studied consecutive ambulatory patients with HF whose ejection fraction had been assessed. We examined and compared the performance of 3C-HF score with Receiver Operating Characteristic for 1 year mortality and overall hospitalizations according to age categories (years):  $< 65$  ( $n = 203$ ), 65-74 ( $n = 519$ ), and 75-84 ( $n = 1012$ ),  $\geq 85$  ( $n = 570$ ).

**Results:** A total 2,321 HF patients (mean age  $78 \pm 8$ , 57% men) were included. Of these: 914 (41%) patients were identified as HFREF and 1,380 (59%) patients as HFpEF. At a follow-up of  $28 \pm 14$  months, 179 (10%) patients died. Of these 87 (11%) had HFREF, and 89 (7%) had HFpEF ( $p = 0,01$ ). There was a high burden of morbidity with 1030 (49%) patients presenting overall hospitalizations (441, 53% HFREF vs 589, 47% HFpEF;  $p < 0,001$ ). Older patients (75-84 years and  $\geq 85$  years) had higher prevalence of comorbidities ( $4.2 \pm 2.5$ ) with higher frequency of severe functional impairment (NYHA III-IV, 56%). Overall, the 3C-HF score showed a good 1-year mortality prediction irrespective of EF-HF groups (AUC 0,73-HFREF, AUC 0,72-HFpEF). The 3C-HF score prediction increased across age subgroups, and achieved its best prediction in elderly patients (aged 75-84 years-AUC 0.81; aged  $\geq 85$  years-AUC 0.83). However, 3C-HF score performed a lower prediction in HF patients young adult (aged  $< 65$  years) (ROC curve 0.56). This trend was maintained unchanged both in HFREF and in HFpEF. Similar results were confirmed for 1 - year overall hospitalizations.

**Conclusion:** The 3C-HF score prediction increased according to age, achieving the best prognostic prediction in HF older patients irrespective of HF phenotypes. The best estimate of 1-year mortality and morbidity of 3C-HF score in elderly population could be related to the sensitivity of this score to comorbidity burden typical of elderly population.

#### P474

##### MELD-XI score is associated with high risk clinical profile and outcome in acute heart failure

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**Background:** liver and renal abnormalities may be found in patients (pts) with advanced heart failure. The Model of End-Stage Liver Disease Excluding INR (MELD-XI) score allows functional risk stratification of HF pts on and off anti-coagulation awaiting heart transplantation and/or with left ventricular assist device. However, the impact of MELD-XI on the prognosis of HF pts with a less severe disease remains unclear.

**Objective:** to evaluate the value of MELD-XI for identifying high-risk pts and to evaluate the prognostic value for predicting mortality during hospitalization and death/hospital readmission due to acute decompensated heart failure (ADHF) at 180 days in pts hospitalized with ADHF.

**Methods:** 224 consecutive pts admitted with ADHF between January-2013 and August-2014 were selected. A MELD-XI score (5.116log (total bilirubin)+11.766log (creatinine)+9.44) was graded and pts were stratified by MELD-XI quartiles (Q1 to Q4). Patients' basic characteristic data including sex, age, past medical history, medications, as well as blood exam results, were analyzed. Complex therapy was defined as the needing of intra-aortic balloon pump, mechanical ventilation or hemodialysis;  $P < 0.05$  was considered statistically significant.

**Results:** mean age was 79 years old (DS  $\pm$  11) and 60% (134 pts) were male, mean left ventricle ejection fraction was 40% (IQR25-75: 29-59) and 43% (97 pts) had an ischemic etiology; median MELD-XI was 12,2 (IQR 25-75: 8,1-16. There were 16 (7,1%) deaths during hospitalization and 77 (34%) events (death/rehospitalization due to ADHF) during follow up. The highest MELD-XI quartile was associated with a lower left ventricle ejection fraction: Q4 median 34% (IQR25-75: 21-50%) versus 53% (IQR 37-60),  $p > 0,001$ . At admission, the highest MELD-XI quartile was associated with more prevalence of cardiogenic shock: Q4: 21% versus Q1: 0%,  $p < 0,001$ . During hospitalization, the MELD-XI score was associated with more inotropic use: Q4: 21% versus Q1: 0%,  $p < 0,001$ , more complex therapy use: Q4: 17% versus Q1: 0%  $p = 0,001$  and longer length of hospital stay: Q4: 7 days (IQR25-75: 4-15) versus Q1: 5 days (IQR25-75: 4-8)  $p = 0,02$ . Hospital mortality was higher in the highest MELD-XI quartile: Q4: 14% versus Q1: 1,8%,  $p = 0,03$  and death/hospital readmission due to DAHF at 180 days: Q4 56% versus Q1: 24%,  $p = 0,001$ .

**Conclusions:** the MELD-XI scoring system, a marker of liver and renal function, can identify high-risk pts at admission. The use of MELD-XI score for risk stratification may help to identify populations with poor outcome during hospitalization and higher risk of death or rehospitalizations during follow-up who will require rapid implementation of an aggressive treatment.

#### P475

##### Association of right bundle branch block with ST-elevation myocardial infarction and need for ventricular assist device and cardiac transplantation

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**Background/Introduction:** Right bundle branch block (RBBB) at the time of acute myocardial infarction is associated with increased mortality. Ventricular assist devices and/or cardiac transplantation are used for treatment in left ventricular dysfunction following myocardial infarction and may prevent death.

**Purpose:** To evaluate the relationship between right bundle branch block at ST-elevation myocardial infarction (STEMI) and subsequent left ventricular assist device (LVAD) therapy and/or cardiac transplantation.

**Methods:** We use a prospective cohort of 3900 STEMI cases treated with primary percutaneous coronary intervention (PCI) from 2002-2012. We excluded 71 repeat primary PCI cases and 55 patients with LBBB. We used multivariate logistic regression to determine if RBBB was associated with subsequent LVAD therapy, cardiac transplantation, and death at or before 1 year.

**Results:** On the initial presenting ECG with STEMI, normal QRS conduction was present in 3515 patients and RBBB in 259 patients. 6 patients received LVAD: 5 patients subsequently undergoing cardiac transplantation, and 1 patient died following LVAD. A total of 12 patients underwent cardiac transplantation. Following primary PCI for STEMI, 7 of 3515 patients (0.20%) with initial normal QRS and 6 of 259 patients (2.3%) with RBBB underwent LVAD and/or cardiac transplantation. Compared with normal QRS, RBBB was associated with LVAD and/or cardiac transplantation at 1 year (OR 9.86, 95%CI 3.11-31.29). RBBB was associated with the composite outcome of LVAD and/or cardiac transplantation or death at 1 year (adjusted OR 4.62, 95%CI 3.28-6.52).

**Conclusion:** The presence of RBBB at the time of STEMI diagnosis was associated with the subsequent need for treatment with LVAD or cardiac transplantation, but the absolute number of events was low.

#### P476

##### Low body mass index with acute heart failure is independently associated with high in-hospital mortality in community-based registry; KICKOFF Registry.

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**Background:** Elevated body mass index (BMI) is a major risk factor for the development of heart failure (HF), but association with low BMI and in-hospital mortality or social backgrounds have not been well documented.

**Purpose:** The purpose of this study is to identify the association of low BMI with in-hospital mortality and social backgrounds in acute heart failure (AHF) patients (pts).

**Methods:** We have enrolled 281 inpatients with AHF in the KICKOFF Registry (13

hospitals in Japan). The KICKOFF Registry is a community-based survey of HF pts. We compared the clinical characteristics, in-hospital mortality, and social backgrounds between HF patients (pts) with BMI <18kg/m<sup>2</sup> (low BMI; n=53) and the other pts (control; n=228).

**Results:** The low BMI were older and had longer length of hospitalization than control (84.5±9.0 vs. 76.8±11.8 years of age; p<0.01, 33.2±28.8 vs. 24.3±22.3 days; p=0.02, respectively). There was no significant difference in gender of male (41.5% vs. 49.6%; p=0.29). The low BMI had more valvular disease (47.2% vs. 30.7%; p=0.02), but less hypertension, diabetes or dyslipidemia (43.4% vs. 75.0%; p<0.01, 17.0% vs. 31.6%; p=0.03, 18.9% vs. 36.0%; p=0.01, respectively). The low BMI were more likely to need support by others; less by living alone (18.9% vs. 30.7%; p<0.01), more using long-term care insurance and dementia (71.7% vs. 41.2%; p<0.01, 45.2% vs. 25.0%; p<0.01, respectively). In the low BMI, there was higher in-hospital mortality than control (32.1% vs. 8.3%; p<0.01). After the adjustment by age, gender, history of heart failure, ischemic heart disease, valvular disease, hypertension, diabetes, dyslipidemia, atrial fibrillation and chronic kidney disease in multiple logistic regression models, low BMI was independently associated with high in-hospital mortality (adjusted odds ratio 5.94; 95% confidential interval 2.38-15.43; p<0.01).

**Conclusion:** Low BMI pts with HF were older, and needed more support by other person. There was more social frailty in low BMI pts. Low BMI was independently associated with high in-hospital mortality.

#### P477

##### Reasons why patients with chronic heart failure at very low risk for mortality die

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**Background:** A proper prognostic stratification is crucial for organizing an effective clinical management and treatment decision-making in patients with chronic heart failure (CHF). In this study, we selected and characterized a sub-group of CHF patients at very low risk for death with the aim to assess predictors of death in subjects with an expected probability of 1-year mortality near to 5%.

**Methods:** Among the best accessible models, we used the Cardiac and Comorbid Conditions HF (3C-HF) Score to identify patients with CHF with the best mid-term prognosis. We selected patients belonging to the lowest quartile of 3C-HF score (<9 points).

**Results:** We recruited 1777 consecutive CHF patients at 3 Italian Cardiology Units. Median age was 76±10 years, 43% were female, 32% had preserved ejection fraction. Subjects belonging to the lowest quartile of 3C-HF score were 609 (34% of total population). During a median follow-up of 21 [12-40] months, 48 of these patients (8%) unexpectedly died, and 561 (92%) survived. The variables that contributed to survival prediction emerged by Cox regression multivariate analysis were older age (HR 1.03[CI 1.00-1.07]; p=0.04), male gender (HR 2.93[CI 1.50-5.51]; p=0.002) and a higher degree of renal dysfunction (HR 0.96[CI 0.94-0.98]; p<0.001).

**Conclusions:** The prognostic stratification of CHF patients by 3C-HF score allows in daily practice to select patients at different outcome and to identify the factors associated with death in outliers at very low risk who should survive at mid-term follow-up. The reasons why these patients do not outlive the matching part of subjects who expectedly survive are related to the maintenance of a satisfactory renal function together with unmodifiable conditions such as older age and male gender.

#### P478

##### Prognostic impact of identification of patients with diffuse aneurysmatic coronary artery disease.

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**Aim:** Diffuse aneurysmatic coronary artery disease (ANCAD) involving both coronary arteries is a rare variant of CAD with limited and controversial data on prognosis and pathophysiology. Micro vessel disease, micro thrombosis and infarction resulting in chronic heart failure are discussed as risks and targets of treatment. The clinical value of novel diagnostic approaches is partly related to prognosis. We evaluated the prognostic impact of ANCAD in a small stratified long-term study cohort comprising two control groups, controls without CAD and patients with significant coronary stenosis without ectasia (SCAD).

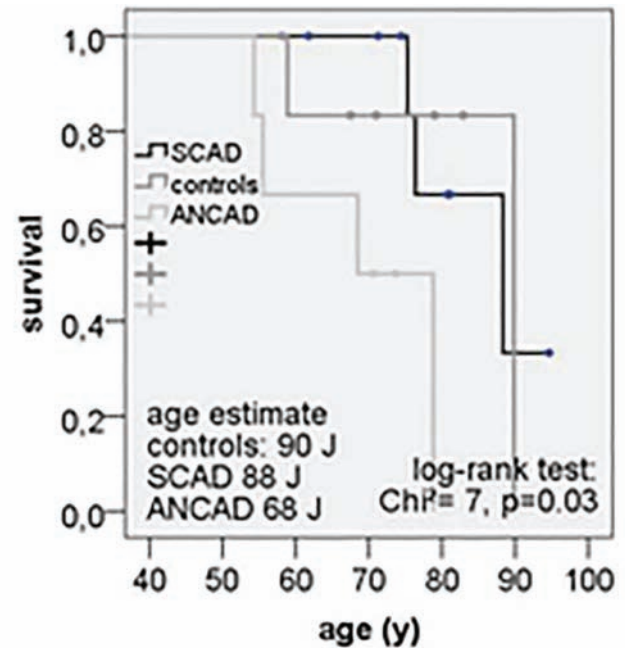
**Methods:** Patients with ANCAD (n=6; age: 50±10 y, 1 f), with CAD ruled out by angiography (controls) (n=8; age: 53±14y, 5 f) and with SCAD (n=9; age: 59±10y, 3 f) were selected by review of coronary angiograms performed between 1990 and 1994. The burden of stenosis was quantified by the Gensini score. Risk factors including total cholesterol and ejection fraction (EF) were collected. The last censoring of survival during follow-up was performed 2013.

**Results:** Mean follow-up was 18 y. At study inclusion the ANCAD patients had a

lower EF with history of myocardial infarction (47±10%) than controls (65±7%) and CAD patients (58±10%) in spite of younger age. Cholesterol (228±48 mg/dL), body mass index (27±4 kg/m<sup>2</sup>) and number of risk factors (2±1) were not significantly different between groups. The Gensini score did not differ between ANCAD (33±31) and SCAD (23±28). Survival analysis (fig) demonstrates a significantly reduced lifespan in ANCAD patients compared to SCAD.

**Conclusion:**

The lifespan of patients with ANCAD appears to be significantly reduced (20 y) as compared with SCAD in spite of a similar risk profile and burden of stenosis. These high risk patients should be identified at young age to initiate early diagnosis and treatment of micro vessel disease and evolving chronic heart failure. Novel diagnostic approaches may be useful for early detection and treatment.



Survival

#### P479

##### Prediction of mortality for heart failure patients using intelligent machine learning method

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**Background and objectives:** The prediction of prognosis in heart failure remains challenge. Risk stratification is therefore important for individual patient in terms of prognostic estimation and medical regimen planning. We hypothesized that a predictive model by using intelligent machine learning (ML) with medical data, blood test, and echocardiographic imaging would be a sensitive way to predict 1-year mortality in heart failure.

**Material and Methods:** Prospective longitudinal single-centre study of 526 patients hospitalized for heart failure. All patients underwent standard two-dimensional, Doppler echocardiography, and tissue Doppler echocardiography to characterize left ventricular (LV) dimension, structure, global and regional contractile function. A total of 157 variables were used in model building, including patient demographics, clinical vital signs, lab results, and imaging biomarkers. An ensemble-based ML method was implemented where artificial neural network was chosen as its base learner. Step-wise logistic regression was also used to build a predictive model and compared to the ML model. The outcome was assessed by hierarchical censoring of death.

**Results:** 526 HF patients [median age (IQR): 70 (60-78) years] were recruited, with 81 (15.4%) meeting the primary outcome. The ML model produced an area under the curve (AUC) of 0.88 (95% confidence interval [CI], 0.83-0.93), and a cutoff score of 55 gave a sensitivity of 82.7% (95% CI, 74.5%-91.0%), specificity of 78.0% (95% CI, 74.1%-81.8%), positive predictive value (PPV) of 40.6% (95% CI, 33.1%-48.1%), and negative predictive value (NPV) of 96.1% (95% CI, 94.1%-98.1%). The logistic regression model achieved an AUC of 0.78 (95% CI, 0.72-0.84), and at the cut-off score of 0.17 a sensitivity of 67.9% (95% CI, 57.7%-78.1%), specificity of 76.4%



(95% CI, 72.5%-80.3%), PPV of 34.4% (95% CI, 27.0%-41.7%), and NPV of 92.9% (95% CI, 90.3%-95.5%) (all  $p < 0.05$ ).

**Conclusion:** Intelligent ML method demonstrated better performance than logistic regression modeling in prediction of 1-year mortality in heart failure patients.

#### P480

##### Clinical implications of new-onset left bundle branch block after transcatheter aortic valve implantation

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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 394 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 162 patients (41.1%) immediately after TAVI and persisted at hospital discharge. After follow-up of  $2.37 \pm 1.9$  years, there were no differences in mortality rate between the N-LBBB and no N-LBBB groups (46.4% vs. 39.7%; adjusted-hazard ratio: 1.31 [95% confidence interval (CI): 0.811 to 2.141];  $p = 0.161$ ). There were no differences between groups regarding cardiovascular mortality HR=0.39 (95% CI 0.140-1.09),  $p = 0.071$ , rehospitalizations for heart failure HR=0.88 (95% CI 0.336-2.318),  $p = 0.800$ . Only 4 patients with N-LBBB required PPI during the follow-up period. There were 4 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:  $62.3 \pm 9$  vs.  $64.7 \pm 8$ ,  $p = 0.020$ ;  $53.4 \pm 25$  vs.  $55.6 \pm 24$ ,  $p = 0.853$  and  $61.6 \pm 7$  vs.  $64 \pm 8$ ,  $p = 0.214$ , respectively). N-LBBB was also not associated with a poorer New York Heart Association functional class at follow-up ( $1.78 \pm 0.6$  vs.  $1.68 \pm 0.6$ ,  $p = 0.199$ ). 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.

#### P481

##### Length of hospital stay in acute heart failure and risk of early readmission

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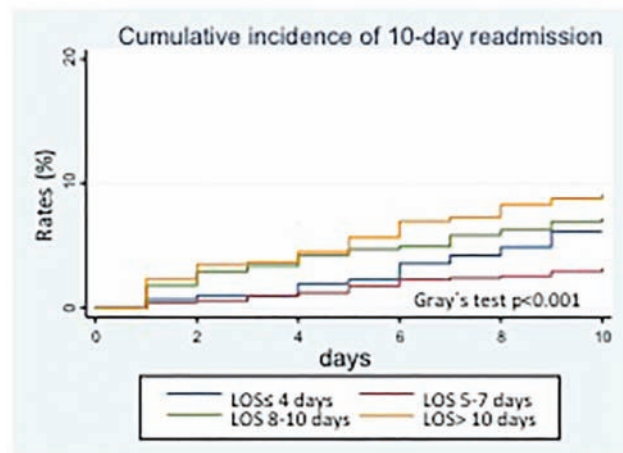
**Background:** Optimal length of stay in patients admitted for acute heart failure (AHF) remains controversial. Longer hospitalizations are associated with higher risk of complications, but little is known about the prognostic implication of short hospitalizations.

**Purpose:** To evaluate the relationship between length of stay (LOS) and risk of 10-day readmission in patients discharged for AHF.

**Methods:** we included 2361 consecutive patients admitted with AHF diagnosis in a third level hospital (2004-2014). We excluded 119 in-hospital deaths and 132 who were scheduled for cardiac surgery during index admission. Final study sample included 2110 patients. LOS was categorized: LOS1 ( $\leq 4$  days), LOS2 (5-7 days), LOS3 (8-10 days) and LOS4 ( $> 10$  days). Cox regression analysis adapted for competing events (death) was used to evaluate the independent association between LOS and the risk of unplanned 10-day readmission.

**Results:** Median LOS was 7 days (IQR=5-11). At 10-days, 130 patients (6,16%) were readmitted. Cumulative incidence of readmission among LOS categories showed a U-shaped pattern with lower rates for those in LOS2 (LOS1=6.1%, LOS2=3.2%, LOS3=7.2%, LOS4=9.1%, ( $p < 0.001$ ) as shown in figure 1. In the multivariate analysis, the U-shaped curve remained significant ( $p = 0.006$ ). Compared to LOS2, short LOS ( $\leq 4$ days) showed and increased risk of 10-days readmission (HR=1.94, CI 95%: 1.06-3.54,  $p = 0.031$ ). Similarly, more prolonged admissions (LOS3 and LOS4) also exhibited a higher risk (HR=2.18, CI 95%:1.28-3.71,  $p = 0.004$ , and HR=2.45, CI 95%: 1.49-4.04,  $p < 0.001$ , respectively).

**Conclusion:** LOS in patients with AHF is related to the risk of 10-day readmission. Higher risk was found for both short and prolonged stays.



#### P482

##### The CHA2DS2-VASc score as a predictor for high mortality in hospitalised heart failure patients

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**Objective:** Atrial fibrillation (AF) is common in patients with heart failure (HF). CHA2DS2-VASc score was originally employed as a risk assessment tool for stroke in patients with AF; however, it has recently been used to predict not only stroke but also various cardiovascular diseases beyond the original AF field. We aimed to verify the CHA2DS2-VASc score as a risk assessment tool to predict mortality in patients with HF.

**Methods:** Consecutive 1,011 patients admitted for treatment of HF were divided into three groups based on their CHA2DS2-VASc scores: a low score group (CHA2DS2-VASc score 1-3, n=317), moderate score group (CHA2DS2-VASc score 4-6, n=549) and high score group (CHA2DS2-VASc score 7-9, n=145). Of the 1,011 HF patients, 387 (38.3%) had AF. We compared patient characteristics among the three groups and prospectively followed for all-cause mortality.

**Results:** Although left ventricular ejection fraction was similar among all three groups, all-cause mortality was higher in the high and moderate score groups than in the low score group (37.9% and 29.3% vs. 15.1%, log-rank  $P < 0.001$ ). Furthermore, all-cause mortalities were significantly higher in the moderate and high score groups than in the low score groups ( $P < 0.001$ ) in the HF patients, irrespective of the presence or absence of AF ( $P < 0.01$ , respectively). In the multivariable Cox proportional hazard analysis, the CHA2DS2-VASc score was an independent predictor of all-cause mortality (all HF patients: hazard ratio (HR) 1.203,  $P < 0.001$ ; HF patients with AF: HR 1.152,  $P = 0.009$ ; HF patients without AF: HR 1.228,  $P < 0.001$ ).

**Conclusion:** The CHA2DS2-VASc score was an independent predictor of all-cause mortality in HF patients with or without AF. This comprehensive risk assessment score may help identify HF patients who are at high risk for mortality and optimize risk reducing treatment in HF patient.

#### P483

##### Prognostic importance of heart rate, and effect of sacubitril/valsartan according to heart rate, in PARADIGM-HF

Novartis Pharmaceuticals

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**Background:** Heart rate (HR) has emerged as an important prognostic marker in heart failure with reduced ejection fraction (HF-REF). Whether it is independently predictive of natriuretic peptides is unknown. We evaluated the prognostic importance of HR in the Prospective comparison of ARNI with ACEI to Determine Impact on Global Mortality and morbidity in Heart Failure trial (PARADIGM-HF) and examined the effect of sacubitril/valsartan (LCZ696), compared with enalapril, according to HR in this trial.

**Purpose:** To examine the prognostic importance of HR in conjunction with natriuretic peptides in HF-REF and the effect of sacubitril/valsartan compared with enalapril according to baseline HR in patients with HF-REF.

**Methods:** Baseline HR was added to a multivariable predictive model including age, sex, renal function, LVEF, prior myocardial infarction and HF hospitalization, as well as NT pro BNP. We estimated the risk of the primary composite endpoint (cardiovascular death or heart failure hospitalization) and all-cause death according to HR considered as either a categorical or continuous variable. We also examined the effect of randomized treatment according to HR.

**Results:** HR data were available in 8399 PARADIGM-HF patients. HR was not an independent predictor of outcome in patients with atrial fibrillation (n=2223). The relationship between HR (tertiles) and outcome in patients with sinus rhythm is shown in the table. In these patients, each 10 bpm increase in HR was associated with an 8 (3-14)% increase in adjusted risk of death from any cause and 8 (3-12%) increase risk of the primary composite endpoint. The effect of sacubitril/valsartan compared with enalapril was consistent for all outcomes across HR tertiles and when HR was considered as a continuous variable. In patients with a HR  $\geq 70$  bpm in sinus rhythm, the sacubitril/valsartan vs. enalapril hazard ratios for the primary endpoint and all-cause mortality were 0.79 (0.69-0.90) and 0.82 (0.70-0.95), respectively.

**Conclusions:** HR is adds incremental prognostic information to other prognostic variables, including NT proBNP. LCZ696 is equally effective, irrespective of HR (and whether the rhythm is sinus or atrial fibrillation/flutter).

	Adjusted hazard ratio	Tertile 1 - reference group ( $\leq 66$ bpm)	Tertile 2 (67-76 bpm)	Tertile 3 ( $\geq 77$ bpm)
Primary endpoint	1.00	1.00	1.19 (1.05, 1.35)	1.24 (1.09, 1.43)
CV death	1.00	1.00	1.19 (1.01, 1.40)	1.24 (1.04, 1.47)
HF hospitalization	1.00	1.00	1.18 (0.99, 1.39)	1.37 (1.15, 1.63)
All-cause mortality	1.00	1.00	1.23 (1.07, 1.42)	1.27 (1.08, 1.48)

Association between heart rate and outcome (tertile analysis)

**P484**

**A new tissue Doppler index to predict malignant ventricular arrhythmic events in patients with heart failure**

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**Background:** Recent studies demonstrated that a new tissue Doppler index, E/(E'xS'), including the ratio between early diastolic transmitral and mitral annular velocity (E/E'), and the systolic mitral annular velocity (S'), is a good echocardiographic predictor of cardiovascular events (atrial fibrillation, hospital readmission and cardiac death).

**Purpose:** We investigated the value of E/(E'xS') ratio to predict malignant ventricular arrhythmic events in patients with heart failure (HF).

**Methods:** In this prospective study, 300 consecutive outpatients with HF, in sinus rhythm, with optimal medical treatment, were analysed. Echocardiography was performed at 1.6  $\pm$  0.4 months after hospital discharge and E/(E'xS') ratio was determined. The average of the velocities from the septal and lateral site of the mitral annulus was used for the analysis. Patients with inadequate echocardiographic images, significant primary valvular heart disease, acute coronary syndrome in the last 40 days, coronary artery by-pass graft before baseline echocardiographic examination, congenital heart disease, and patients undergoing ventricular pacing were excluded. The end point included sudden cardiac death, ventricular fibrillation and sustained ventricular tachycardia (VA/SCD).

**Results:** Mean left ventricular ejection fraction of our patients was 39  $\pm$  14%. During follow-up period (36  $\pm$  9 months) VA/SCD occurred in 48 patients (16%). Mean E/(E'xS') was 3.85  $\pm$  1.49 in those patients, while it was 2.04  $\pm$  0.92 in the rest (p < 0.001). The area under the Receiver Operating Characteristic curve for E/(E'xS') to predict VA/SCD was 0.82 (95% confidence interval = 0.74-0.91, p < 0.001). The optimal E/(E'xS') cut-off was 2.84 (79% sensitivity, 80% specificity). Of our patients, 87 (29%) presented E/(E'xS') > 2.84 and 213 (71%) presented E/(E'xS')  $\leq$  2.84. VA/SCD was significantly higher in the group of patients with E/(E'xS') > 2.84 than in the group with E/(E'xS')  $\leq$  2.84: 38 events (43.7%) versus 10 events (4.7%), p < 0.001. Kaplan-Meier analysis (Figure 1) showed that the event-free survival rate during follow-up was significantly higher in the group of patients with E/(E'xS')  $\leq$  2.84 (log rank, p < 0.001).

**Conclusions:** In patients with HF, E/(E'xS') ratio is an important predictor of malignant ventricular arrhythmic events and may improve cardiovascular risk stratification.

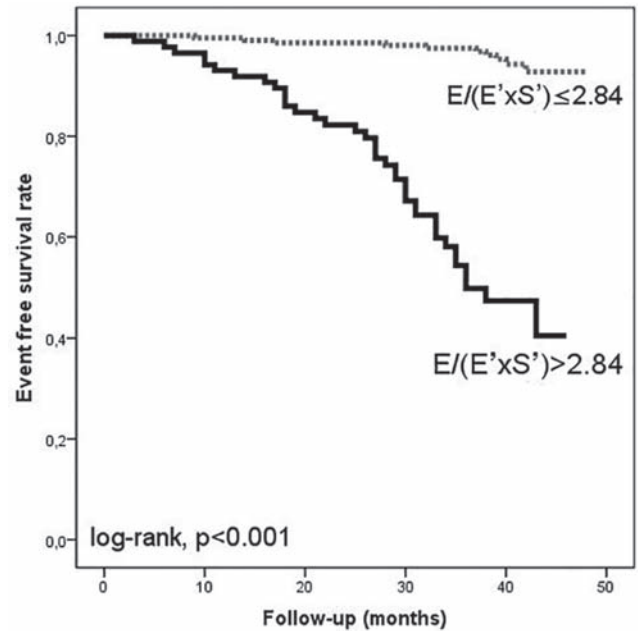


Figure 1. Kaplan-Meier analysis.

**P485**

**Impacts of baseline lipid levels on clinical outcomes in patients with acute decompensated heart failure**

Research of Korea Centers for Disease Control and Prevention  
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**Background:** Prior studies have suggested that low serum cholesterol level is associated with increased mortality in patients with heart failure, but there still have been controversies on the relationship between lipid levels and the outcomes of acute decompensated heart failure (ADHF). Therefore, the aim of this study was to evaluate the impact of baseline lipid levels on mortality in a nationwide cohort study of ADHF patients.

**Methods:** A total of 5,625 ADHF patients enrolled in the present registry were divided into 4 groups according to the quartile distribution of total cholesterol (TC), serum low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglyceride (TG) level; the lowest quartile (Q1), second quartile (Q2), third quartile (Q3), the highest quartile (Q4). TC: Q1 < 121, Q2 121-147, Q3 147-178, Q4 > 178 mg/dL, LDL-C: Q1 < 66.7, Q2: 66.7-90.1, Q3 90.1-115.6, Q4 > 115.6 mg/dL, HDL-C: Q1 < 32, Q2 32-40, Q3 40-49, Q4 > 48 mg/dL, TG: Q1 < 64, Q2 64-85, Q3 85-117, Q4 > 117mg/dL. In-hospital death and 1-year mortality were compared among the quartile groups of each lipid profile.

**Results:** In-hospital death was highest in the lowest quartile and gradually decreased as the quartile increasing for TC (Q1 6.8% vs. Q2 4.2% vs. Q3 4.4% vs. Q4 3.5%, linear p < 0.0001) and for HDL-C (Q1 7.7% vs. Q2 3.6% vs. Q3 2.8% vs. Q4 2.3%, linear p < 0.0001), but LDL-C and TG quartile were not associated with in-hospital death. One year mortality was highest in the lowest quartile and gradually decreased as the quartile increasing for TC (Q1 21.4% vs. Q2 18.0% vs. Q3 14.8% vs. Q4 13.3%, linear p < 0.0001), LDL-C (Q1 18.6% vs. Q2 15.5% vs. Q3 15.0% vs. Q4 12.8%, linear p = 0.003), and TG (Q1 19.3% vs. Q2 16.7% vs. Q3 14.6% vs. Q4 11.7%, linear p < 0.0001). Although HDL-C quartile did not show significant linear association on 1-year mortality, the lowest quartile of HDL-C showed significantly higher 1-year mortality than other quartiles on Kaplan-Meier survival analysis (p = 0.032 by log-rank test).

**Conclusion:** Low serum TC and HDL-C are significantly associated with in-hospital death and low serum TC, LDL-C, HDL-C, and TG are significant predictor of 1-year mortality in patients with ADHF. The results of the present study suggested that

the measurement of baseline lipid levels would be simple and useful for predicting adverse clinical outcomes in patients with ADHF.

## PULMONARY HYPERTENSION

### P486

#### Severe pulmonary artery hypertension in stenosis of left main coronary artery with left ventricular dysfunction: a case report

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This case report describes a man 78 year old, who presented a rapidly progressive dyspnea in patient with dyslipidemia, obesity, obstructive sleep apnea syndrome by being treated with C-PAP at night. Since about 2 months complained progressive worsening dyspnea for minimal effort and a few episodes of breathlessness at rest with nocturnal paroxysms. Echocardiographic exam showed left ventricle hypokinetic (FE 38%) with akinesia of posterior wall; right atrial dilatation; mild mitral regurgitation; TAPSE 18 mm and signs of severe pulmonary hypertension (PAPs 90 mmHg; actpo 77ms). CT chest: no signs of TEP, not evident parenchymal lesions or interstitial lung disease, expansion of trunk pulmonary artery. Work up for the common other secondary causes of pulmonary hypertension was negative. Blood tests (CBC, liver function, renal profile, coagulation) all substantially within the limits. Coronary angiography and right catheterization was performed and showed severe atherosclerosis of left main trunk, the right coronary artery and circumflex with the absence of significant stenosis. At the right catheterization: severe pulmonary hypertension (mPAP 42 mmHg; PVR 4.8 U.W) with postcapillary component (PCW 17 mmHg) and the systolic gradient (GTP) was 25mm/hg Fig. Excluded from the surgery option, was placed indication to perform Echo-stress to evaluate indication to a revascularization procedure. This examination revealed: Akinesia (Basic) rear, anterolateral hypokinesia and basal inferior; after infusion of the stressor is reduced coronary reserve observed in absence of ischemic induction. It was placed a medicated stent in the trunk of left main coronary artery with excellent result. After 6 months, right heart catheterization highlighted a PCW reduction and indication to specific therapy. Ambrisentan tablets 5mg /die was started with benefit (NYHA II) The right heart catheterization is necessary to confirm the diagnosis and to measure the systolic (GTP) and diastolic transpulmonary gradient (DPG); these could target patients who can benefit from specific treatment. Although not included in the vast majority of PAH vasodilator therapy clinical trials, vasodilator therapy may be of clinical benefit in a few carefully selected patients with left-sided cardiac disease. In patients over 55 years we recommend coronary angiography for the possibility of coexistence of coronary heart disease.

### P487

#### The advanced functional class and the variables of poor prognosis in pulmonary hypertension

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**Introduction:** Pulmonary arterial hypertension (PAH) is a multifactorial disease associated with high morbidity and mortality. However, the diagnosis and therapeutic strategies used in most of the Argentinean regions are poorly known. The advanced functional class (FC) is an indicator of poor prognosis and one of the therapeutic goals.

**Aims:** 1-To determine the impact of advanced FC in patients with PAH on established markers of poor prognosis, such as clinical, biomarker, hemodynamic, and echocardiographic parameter 2-To compare treatment strategies between an advanced and non advanced FC

**Method:** Between July 2014 and May 2015, 170 patients with confirmed PAH were prospectively included in a multicenter, collaborative, observational registry by 60 investigators from 20 provinces in Argentina. Inclusion criteria were as follows: 1-patients over three months of age; 2-mean pulmonary arterial pressure (mPAP) at rest  $\geq 25$  mmHg by right heart catheterization (RHC) and 3 - clinical stability in the absence of hospitalization in last month. WHO FC III or IV at diagnosis was defined as advanced (AFC) whereas WHO FC I or II were considered as non advanced (NAFC)

**Results:** Mean age was 50.5 years (SD 18) and 79% were female. According with the Nice classification, the distribution was: idiopathic 51.6%, inherited 1.6%, drugs

2.4%, connective tissue disease 15.3%, portal hypertension 1.6% and congenital heart disease 27.4%. WHO FC at initial diagnosis was: I: 3%; II: 27%; III: 45% and IV: 25% and during follow-up was: I: 19%, II 54%, III 21% and IV 6% ( $p < 0.001$ ). AFC at initial diagnosis was 70% and during follow up 27% ( $p < 0.001$ ). Clinical manifestations in AFC compared with NAFC was: syncope 11 vs 13% (NS); heart failure 30 vs 4% ( $p < 0.001$ ); BNP 372 vs 158 pg/ml (0.02), NT-proBNP 1595 vs 668 pg/ml (0.012), TAPSE 17.2 vs 19.3 mm (0.032), pericardial effusion 18 vs 10% ( $p = 0.020$ ); 6MWT 367 vs 373 (NS); CI 2.6 vs 2.8 (NS); RAP 12.3 vs 10 mm Hg (NS). PAH targeted drugs in AFC was = None in 26.7%, Monotherapy in 31.4% and Combined therapy in 41.9%.

**Conclusion:** In our registry of PAH, we observed a high percentage of patients with AFC (70%) at initial diagnosis and a significant decrease during follow-up (27%). Advanced FC at initial diagnosis was significantly associated with other variables of poor prognosis. These findings emphasize the need for strategies for early detection and therapy.

### P488

#### Functional capacity is predicted by right atrial volume in patients with pulmonary arterial hypertension. A cardiac magnetic resonance study

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**Background:** Right heart function is of clinical importance in patients with pulmonary arterial hypertension (PAH). There is however scarce data on the role of right atrial (RA) indices in the evaluation of functional capacity of PAH patients. The aim of our study was to investigate the relationship of RA size and volume as assessed by cardiac magnetic resonance (CMR) with exercise capacity assessed by 6-minute walk test (6MWT) distance in adult patients with PAH.

**Materials and methods:** This was a cross sectional study including patients with PAH. All patients underwent CMR (Avanto Siemens 1.5T) and 6MWT at the same day. RA volumes were assessed in end-systole (RAESV) and end-diastole (RAEDV) according to Simpson's rule. 4-chamber view was used for the determination of RA area.

**Results:** Our study included 21 patients with PAH (9 with idiopathic PAH, 10 with PAH associated with connective tissue disease and 2 with portopulmonary arterial hypertension, mean age  $54.5 \pm 12.9$  years) that walked  $449.0 \pm 104.4$ m. After controlling for confounding parameters, a direct linear correlation between distance walked in 6MWT and RAESV, RAEDV, RA area in end-systole and end-diastole (Table). Multivariate regression analysis showed that RAESV was an independent predictor of distance walked in 6MWT.

**Conclusion:** RAESV is a predictor of functional capacity in PAH.

Predictors of functional capacity in PAH

		Univariate	Multivariable		
		regression	regression		
		r	p	B	p
Age (years)	54.5 $\pm$ 12.9				
BSA (m <sup>2</sup> )	1.8 $\pm$ 0.2				
Distance (m)	449.0 $\pm$ 104.4				
LVEF (%)	66.7 $\pm$ 8.2	0.02			
			> 0.05		
CO (l/min)	5.4 $\pm$ 1.2	0.217			
			> 0.05		
RVEF (%)	49.9 $\pm$ 13.3	0.198			
			> 0.05		
RAED area (cm <sup>2</sup> )	21.5 $\pm$ 8.2	-0.462	0.005		
RAES area (cm <sup>2</sup> )	28.6 $\pm$ 8.2	-0.536	0.001		
RAESV (cm <sup>3</sup> )	116.7 $\pm$ 53.4	-0.595		0.522	0.015
			< 0.0001		
RAEDV (cm <sup>3</sup> )	76.7 $\pm$ 46.3	-0.462	0.005		

BSA: body surface index, LVEF: left ventricular ejection fraction, CO: cardiac output, RVEF: right ventricular ejection fraction, RAEDarea: right atrial end diastolic area, RAESarea: right atrial end systolic area, RAESV: right atrial end systolic volume, RAEDV: right atrial end diastolic volume



## P489

**Pulmonary hypertension role in hospitalizations in Spain: (2005-2013)**

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**Objective:** The aim of this study was to assess clinical characteristics, in-hospital admission caused by pulmonary hypertension (PH) in internal medicine wards.

**Materials and Methods:** Data from the Spanish National Minimum Basic Data Set (MBDS) of discharged admissions who were initially diagnosed of PH (from all internal medicine (IM) departments of Spanish National Health Care System hospitals between 2005 and 2013 were analysed (ICD-9: 416.8, 416.0). A descriptive data analysis was conducted comparing the administrative variables of all admissions in internal medicine with and without PH. A multivariate logistic regression analysis was performed, taking hospital mortality and hospital readmissions as dependent variables, and age, gender, comorbidity according to the Charlson comorbidity index (CHCI) and PH as independent variables.

**Results:** A total of 5.258.542 admissions in internal medicine were identified, of whom 205.038 were coded with PH. PH were more common in >75 years old patients (77.79 ± 10 vs 72.03 ± 17); p < 0.0001) and women (60% vs 47%; p < 0.0001). Among the comorbidities assessed, PH was more associated to the diagnosis of heart failure (64% vs 22%; p < 0.0001), atrial fibrillation (53% vs 21%; p < 0.0001), obesity (13% vs 8%; p < 0.0001), COPD (51% vs 36%; p < 0.0001) anaemia (24% vs 17%; p < 0.0001) and chronic renal dysfunction (20% vs 11%; p < 0.0001). Hospital readmissions due to any cause in patients with PH was 18% vs 14% in non-PH patients (p < 0.0001). PH maintained statistical significance in the regression model for readmissions: OR 1.336 (95% CI 1.282-1.393; p < 0.0001) after adjusting for gender, age, and CHCI.

**Conclusions:** In Spain, PH is an independent risk factor for hospital re-admission in internal medicine wards. In hospitalization, PH was mostly coded in elderly patients with comorbidities such as chronic heart failure, atrial fibrillation and pulmonary disease.

## P490

**S TWEAK content in platelets is lowered in patients with pulmonary arterial hypertension**

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**Background:** Pulmonary arterial hypertension (PAH) is a progressive disease characterized by proliferative changes in pulmonary arteries, which lead to deterioration in cardiopulmonary function. There is growing evidence suggesting that soluble tumor necrosis factor-like weak inducer of apoptosis (sTWEAK) could be involved in PAH development and progression. We hypothesized that circulating platelets may be an important source of sTWEAK and patients with PAH may present altered amount of TWEAK in platelets.

**Methods:** We enrolled 11 stable patients (48 ± 20 years old, 7 females) with confirmed diagnosis of PAH and 15 healthy controls matched for age and sex (46 ± 15 years old, 8 females). We obtained total blood sTWEAK capacity (serum) and sTWEAK present in circulating plasma (EDTA as anticoagulant). Platelets were isolated from citrate plasma by repeated centrifugation and homogenized in PBS for analysis of sTWEAK content.

**Results:** Most PAH patients had WHO class III (81.8%, n=9). Mean pulmonary artery pressure obtained during right heart catheterization was 60.4 ± 26 mmHg. Maximal exercise capacity was significantly limited with the average peak VO<sub>2</sub> of 16.46 ± 7 ml/kg/min in PAH vs 30.8 ± 8.3 ml/kg/min in the control cohort, p < 0.0001. PAH group also manifested significant ventilatory inefficiency characterized by elevated VE/VCO<sub>2</sub> slope (48.48 ± 12.8 vs 24.6 ± 3.9, p < 0.0001). Patients with PAH presented significantly lower serum sTWEAK levels comparing to control subjects (184.8 ± 58 vs 257 ± 86 pg/ml, p = 0.027). Furthermore, there were no significant differences in sTWEAK concentrations in EDTA plasma samples (86.2 ± 36 pg/ml in PAH vs 90.3 ± 27.8 pg/ml in controls). The concentration of sTWEAK content in platelets was significantly lower in PAH group than in platelets of patients from control group (141.43 ± 16.76 vs 346.86 ± 54.73, p = 0.0008). PAH group presented lower number of platelets (182 ± 58 vs 242.6 ± 57.8 \*1000/mcl, p = 0.008), however sTWEAK concentration in platelet lysates did not correlate with thrombocytes levels neither in PAH nor control groups, suggesting diminished platelet storage capacity in PAH patients. Difference between concentration of sTWEAK in serum and in EDTA plasma (released sTWEAK during clotting) was lower in PAH group (88 ± 61.6 vs 166.6 ± 86.1 pg/ml, p = 0.02). Interestingly, in combined PAH and healthy controls group (n=26) sTWEAK levels in platelets correlated positively with sTWEAK concentrations in EDTA plasma samples (r = 0.4, p = 0.04). Conclusions Patients diagnosed with pulmonary arterial hypertension present diminished storage capacity in platelets as well as lower serum sTWEAK concentrations. Platelets seem to be a major source of sTWEAK and could have an impact on pathophysiology of PAH, however the exact role of this phenomenon remains to be established.

## P491

**Incremental benefit of echocardiographic imaging and cardiopulmonary exercise test in prognostic evaluation of idiopathic pulmonary arterial hypertension**

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**Background:** In idiopathic pulmonary arterial hypertension (IPAH) survival is strongly associated to right ventricle (RV) function.

**Purpose:** The aim of the study was to evaluate the incremental prognostic value of echocardiographic and cardiopulmonary exercise testing (CPET) on long-term prognosis compared to traditional clinical and hemodynamic parameters. Methods. One hundred-thirty naïve IPAH patients were enrolled in our centre and prospectively followed-up for the presence of clinical worsening (CW). Baseline evaluation included clinical, hemodynamic, echocardiographic and CPET parameters. Cox regression modeling with c-statistic evaluation was realized and internal validation of the Cox analysis based on bootstrapping was considered.

**Results:** During a mean period of 528 ± 304 days, 54 patients presented CW (53%). Among demographic, clinical and hemodynamic parameters, WHO functional class and cardiac index remained independent predictors of CW (Model-1). Adding echocardiographic and CPET variables (model-2) peak O<sub>2</sub> pulse and RV fractional area change (RVFAC) resulted the only independent factors, significantly improving the power of the prognostic model (AUC: 0.81 vs 0.66, respectively; p = 0.005). Combining together the ROC cut-off values of O<sub>2</sub> pulse and RVFAC, patients with high RVFAC/high O<sub>2</sub> pulse had significantly a better prognosis compared with the others. Patients with low RVFAC/low O<sub>2</sub> pulse and high RVFAC/low O<sub>2</sub> pulse showed 99.8 and 29.4 increase in the hazard ratio, respectively, compared with high RVFAC/high O<sub>2</sub> pulse (p = 0.0001).

**Conclusions:** RVFAC and O<sub>2</sub> pulse evaluation are able to increase the power of the prognostic model, allowing clinicians to identify at an early stage patients with normal RV systolic function at higher risk of right heart failure before hemodynamic instability appearing.

## RIGHT VENTRICULAR FUNCTION

## P492

**Characteristics and outcome of patients with isolated right heart failure in acute heart failure syndrome**

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**Background:** Though dysfunction of right ventricle itself can lead to heart failure (HF) with typical symptoms and signs, right HF has been out of picture till lately under the presumption that right heart is a secondary player in the interaction of HF where left ventricle has taken the initiative. Yet, the significance of right HF in determining clinical outcomes has recently become the subject of increasing interest. Purpose We sought to assess the prevalence, clinical characteristics, and outcome of isolated right HF in patients hospitalized for acute heart failure syndrome (AHFS).

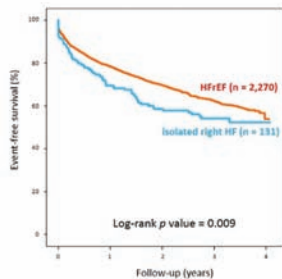
**Methods:** We prospectively enrolled 5,625 consecutive patients hospitalized for AHFS in Korea from 2011 to 2014 (the Korean Acute Heart Failure [KorAHF] registry). They were classified by the ESC guidelines and patients with isolated right HF were compared to those with left heart failure with reduced ejection fraction (HFrEF) to describe their unique features and outcomes.

**Results:** In KorAHF registry, 131 patients (2.3%) were hospitalized for isolated right HF. Compared with heart failure and reduced LV ejection fraction group (HFrEF group, n = 2,270), isolated right HF group was younger (64.0 vs. 66.5 years, p = 0.008) and female dominant (55.0 % vs. 38.6%, p < 0.001). Cor pulmonale (12.2%) and pulmonary thromboembolism (11.5%) were two major causes of isolated right HF, while ischemia was the leading cause of HFrEF (41.2%). At admission, isolated right HF group had significantly lower blood pressure (systolic 118.8 vs. 126.9 mmHg, p < 0.001, diastolic 71.7 vs. 78.9 mmHg, p = 0.014), hemoglobin (12.4 vs. 12.9 g/dL, p < 0.001), and serum sodium level (132.6 vs. 137.4 mmol/L, p = 0.008). There was no significant difference in intensive medical care between the groups during admission. In-hospital mortality was twice as high in isolated right HF group than in HFrEF group (8.1% vs. 3.7%, p = 0.041). Pump failure was the leading cause of in-hospital death in both group. The post-discharge 1-year mortality was significantly higher in isolated right HF group (31.3% vs. 21.6%, p = 0.008). Systolic blood pressure <90 mmHg (adjusted HR 3.18, 95% CI 1.03 – 9.82, p = 0.044), serum albumin <3.5 g/dL (adjusted HR 3.24, 95% CI 1.51 – 6.95, p = 0.003) and serum sodium <135 mmol/L (adjusted HR 3.63, 95% CI 1.73 – 7.62,

$p=0.001$ ) on admission, and hemodialysis during admission (adjusted HR 7.72, 95% CI 2.23 – 26.66,  $p < 0.001$ ) were independent predictors for 1-year mortality in isolated right HF group.

**Conclusions:** Our analysis reveals that patients with isolated right HF admitted for acute symptoms aggravation have worse clinical prognosis and several unique features, including lower blood pressure and serum sodium levels compared to those with left heart failure. This result provides a new insight for isolated right HF, which may make a step forward to develop its proper management strategy.

Survival curves in patients with isolated right HF vs. HFrEF



Kaplan-Meier Survival Curve

#### P493

##### Discordance of right atrial pressure and pulmonary capillary wedge pressure correlate significantly with impaired exercise tolerance and predict refractory heart failure

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**Background:** Right atrial pressure (RAP) is usually correlated to pulmonary capillary wedge pressure (PCWP). On the other hand, higher RAP/PCWP ratio was known as a risk of adverse outcomes. However, it is not clear whether higher RAP/PCWP ratio is associated with impaired exercise tolerance.

**Methods:** We investigated consecutive 35 patients with chronic heart failure due to dilated cardiomyopathy who received right heart catheterization (RHC) and cardiopulmonary exercise testing (CPET) at in-patient setting (around the same time as RHC) and out-patient setting (around 3 months after first CPET). We defined patients as discordant group (Group D) whose mean RAP (mRAP) was over 5mmHg and RAP/PCWP ratio was over 0.5, and the rest as concordant group (Group C). We compared patients characteristics, background, parameters obtained from right heart catheterization (PCWP, RAP, and cardiac index), echocardiogram, and CPET ((peak VO<sub>2</sub>/W, VE/VCO<sub>2</sub> slope, and work rate (VO<sub>2</sub>-WR relationship)) at in-patient and out-patient setting between groups.

**Results:** Six patients were divided into Group D. There were no significant differences in age, gender, LVEF, estimated GFR between two groups. NYHA functional class ( $p=0.0009$ ) and BNP level were higher ( $p=0.025$ ) in Group D. Exercise tolerance was significantly lower ( $p=0.036$ ) in Group D, and work rate was tended to be impaired in Group D ( $p=0.069$ ). And also exercise tolerance remained impaired at chronic phase in Group D ( $p=0.016$ ).

**Conclusion:** This study indicated that patients with higher RAP/PCWP ratio show lower exercise tolerance and predict refractory heart failure. We have to investigate more and make sure of this fact.

	Discordant	Concordant	p value
Number	6	29	
Age (years)	55.6 ± 14.9	51.9 ± 13.7	0.58
LVEF (%)	29.8 ± 8.5	31.3 ± 9.0	0.66
mean PCWP (mmHg)	15.0 ± 5.2	15.4 ± 11.1	0.78
mean RAP	10.5 ± 2.8	3.6 ± 3.7	0.0007
Cardiac Index (L/min/m <sup>2</sup> )	2.2 ± 0.6	2.1 ± 0.4	0.91
Peak VO <sub>2</sub> /W (ml/kg/min)	14.2 ± 3.3	18.5 ± 4.2	0.036
Peak VO <sub>2</sub> /W (ml/kg/min)	1.4 ± 4.0	3.5 ± 4.2	0.13
VO <sub>2</sub> /WR (ml/kg/min)	8.4 ± 1.6	9.9 ± 1.9	0.069
(VO <sub>2</sub> /WR) (ml/kg/min)	1.0 ± 1.7	0.4 ± 1.2	0.71

#### P494

##### The Tei index: a possible tool in assessing pulmonary embolism severity

This work was supported by CREDO Project - ID: 49182

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**Introduction:** The right ventricular (RV) myocardial performance (Tei) index is a global estimate of both systolic and diastolic function of the right ventricle. However, the value of the Tei index as a tool in the evaluation of the severity of pulmonary embolism (PE) has not been well investigated.

**Objective:** The objective of this observational retrospective study was to investigate the possible correlation between the RV Tei index and the early mortality risk of PE, as evaluated by validated clinical risk scores, imaging tests and cardiac laboratory biomarkers.

**Methods:** 50 patients diagnosed with acute PE by computed spiral tomography pulmonary angiography and classified as being at high, intermediate or low risk of early mortality were included in our study. All study population underwent a comprehensive echocardiographic study including tissue Doppler imaging (TDI) within first 12 hours of admission, with focus on different RV signs of pressure overload. The Tei index was measured by means of TDI, using the formula: (Tricuspid Valve Closure to Opening Time (ms) - RV Ejection time (ms)) / RV Ejection time (ms). Patients with concomitant cardiac or respiratory disease that could present signs of RV overload or dysfunction due to comorbidities were excluded from the study.

**Results:** In our study group, the patient risk categories were as follows: 21 patients were in the low early mortality risk category, 24 patients were in the intermediate risk category, and 5 patients in the high risk category. In this population, Tei index values of  $> 0.5$  were powerful indicators of non-low risk category ( $p < 0.005$ ). However, in the  $> 0.5$  category, Tei index values were unable to discriminate between intermediate and high risk of early mortality (no statistical significance).

**Conclusion:** Tei index accurately predicted patients that were at non-low early mortality risk, with a cut-off value of  $> 0.5$ , thus with a possible clinical impact in the process of decision making of whether to admit or discharge the patient. However, in our study group, it was unable to differentiate between intermediate and high risk patients, probably due to the low number of high risk patients.

#### P495

##### Use of ivabradine in patients with chronic cor pulmonale and right heart failure.

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Cor pulmonale is associated with development of right heart failure and tachycardia. Heart rate more than 70 beats per minute increases myocardial oxygen demand so it provokes myocardial ischemia. Prescription of beta-blockers in order to decrease heart rate is limited in patients with cor pulmonale due to their influence on hyperresponsiveness of airways.

**Purpose :** To investigate the influence of ivabradine on hemodynamics and HR in patients with chronic cor pulmonale.

**Material and methods:** 72 patients (38 men and 34 women, 41,3 ± 3,8 years of age) with chronic cor pulmonale on a background of COPD and bronchial asthma (non severe clinical course) without ischemic heart disease were examined. Patients were divided into 2 groups according to prescription of ivabradine in addition to basic treatment. The 1st group-36 patients with basic treatment of chronic cor pulmonale – Ca channel blockers (diltiazem), ACE inhibitors, low doses of loop diuretics; 2nd group-36 patients that were prescribed ivabradine 7,5 mg BD in addition to the basic treatment. All patients underwent a transthoracic echocardiography in A4C in dynamics of treatment within 12 weeks.

**Results:** Results of investigation are shown in the Table 1. It was found that patients of the second group that were taking ivabradine had statistically more significant tendency to normalization of structure-functional data of the right heart chambers due to significant decreasing of the heart rate.

**Conclusion:** Heart rate control has a big influence on the processes of heart remodeling. Thus, early prescription of ivabradine in patients with cor pulmonale could prevent worsening of right heart failure.

Tab.1 Data results

	1 group		2 group	
	Before	After	Before	After
PV Base diameter RVD1,cm	3,31 ± 0,28	3,23 ± 0,23	3,36 ± 0,19	3,18 ± 0,34*
PV Mid diameter, RVD2,cm	3,82 ± 0,12	3,71 ± 0,17*	3,73 ± 0,20	3,52 ± 0,18*
PV Longitudal diameter, RVD3, cm	8,48 ± 0,21	8,18 ± 0,25*	8,51 ± 0,17	8,15 ± 0,08*
PA diameter, cm	2,37 ± 0,18	2,23 ± 0,10*	2,40 ± 0,17	2,17 ± 0,09*
EF % (M mode)	43,2 ± 5,1	50,1 ± 3,2*	44,3 ± 6,2	53,4 ± 2,8*
PpA, mm Hg	30,2 ± 2,1	27,4 ± 1,5*	31,3 ± 2,2	26,1 ± 1,3*
RVWT, cm	0,69 ± 0,14	0,64 ± 0,18	0,68 ± 0,13	0,63 ± 0,15
Myocardial performance index (Index Tei)	0,41 ± 0,15	0,32 ± 0,17*	0,42 ± 0,17	0,30 ± 0,19*
Heart rate, beats per minute	108 ± 8	94 ± 6*	110 ± 6	86 ± 5*

\* - P <0,05 comparing 1st and 2nd groups before and after treatment.

**P496**  
**Comparison of echocardiography and cardiac magnetic resonance imaging in the evaluation of the right ventricle**

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**Introduction:** The physiological impact of the right ventricle has long been underestimated. Thus, the RV maintains adequate pulmonary perfusion and ensure low systemic blood pressure to prevent organ's congestion. However, the RV dysfunction may affect the left ventricular function, not only through direct mechanical interactions but also, by limiting the left ventricular pre-filling volumes. In our study, we aimed to compare echocardiography and cardiac magnetic resonance (CMR) imaging in the assessment of the RV during heart failure.

**Patients and results:** Thirty patients were collected, consecutively, during their hospitalization for heart failure in our department. CMR and echocardiography were realized during hospitalization. The right ventricular function was assessed by echocardiography using the tricuspid annular plane systolic excursion (TAPSE) and the pulsed wave doppler tissue imaging systolic velocity (S'), and by CMR using the mesures of the right ventricular volumes and ejection fraction. Finally, 43% of patients had RV dilation in bi-dimensional echocardiography versus 13% in CMR with poor correlation between the 2 exams (r=0.20, p=0.18). We found also, a poor correlation between echocardiography and CMR for the assessment of the right ventricular function (r=0.17). Indeed, 36.7% of the patients had impaired right ventricular function on echocardiography versus 26% on cardiac magnetic resonance.

**Conclusion:** Right ventricular dilation and dysfunction are independent risk factors of mortality and cardiovascular events, this is particularly, important in case of heart failure. The assessment of the RV should be considered in the evaluation of the prognosis of cardiomyopathies. CMR imaging represents a good alternative, if the RV cannot be well studied by echocardiography.

**HYPERTENSION / LV HYPERTROPHY/ RENAL DENERVATION**

**P497**

**Percutaneous stenting for aortic coarctation in children and adults: is it a valid option?**

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**Background:** Coarctation of the aorta (COA) accounts for 5-8% of all congenital heart defects. Traditionally, treatment for this condition is surgical. However, stenting for native or recurrent COA has become an important therapeutic strategy. The aim of this study was to evaluate the procedural safety and efficacy along with immediate and midterm results of stent implantation for either native or recurrent COA in children and adults.

**Methods:** We retrospectively reviewed the medical records of patients aged > 5 years who were submitted to endovascular treatment of COA in a tertiary care center between April 2009 and November 2015. Clinical, demographic and catheterization data were collected. Diagnosis of COA was based upon a combination of clinical signs, noninvasive imaging or invasive gradients measurements. Successful outcome was defined as peak systolic pressure gradient after stent implantation <20 mmHg.

**Results:** Forty-one patients underwent percutaneous repair of COA, 24% were associated with bicuspid aortic valve. The procedure was successful in 40 patients, all using femoral approach. Median age was 20 years (6 - 54), 73.2% were men, 73% had a native COA and 22% had a previous surgical repair of COA. Isolated balloon angioplasty was performed in one patient and one stent was inserted in the remaining cases, 93% were covered stents. The mean pre-procedural pressure gradient was 49 ± 15 mmHg and the mean post procedural pressure gradient was 11 ± 8 mmHg (p < 0.001). Acute complications were found in 28% of the procedures and included: 4 stent migrations, 1 sub-optimal stent expansion (but with no significant systolic gradient) and 5 complications related with femoral access vessel, 3 of whom required vascular surgery. Mean follow-up time was 35 ± 25 months. All patients were symptom free except one, who required reintervention with balloon angioplasty 20 months after the initial procedure. Comparing with pre-procedure antihypertensive therapy, the intervention led to discontinuation or reduction of therapy in 52% of cases (p = 0.002). Recurrent post-surgical COA was significantly associated with maintenance of antihypertensive medications (p = 0.004) and no other associations were found, namely age at intervention, gender or body mass index.

**Conclusions:** Stent implantation of native or recurrent COA is safe and effective in children and adult patients. Abnormal blood pressure values are not unusual, and blood pressure monitoring is mandatory after the procedure. Midterm follow-up suggests that the treatment is durable and may be considered an alternative to surgical repair, although a longer follow up is needed.

**P498**

**Silent hypertension in normotensive subjects is a major risk factor for LVH**

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**Purpose:** Elevated BP is a well-known risk factor for left ventricular hypertrophy (LVH), which might lead to heart failure. We have reported, previously, that abnormal

Table 60827

	526 (22%), no Medications, no Comorbidities regardless of BP					
	NT	Pre-HTN	HTN	A	B	C
SBP <120 DBP <80		SBP 120-139 or DBP 80-89	SBP ≥ 140 or DBP ≥ 90	SBP 120-129 DBP <80	SBP 130-139 DBP <80	SBP 140+ DBP <80
	281 (53%)	179 (34%)	66 (13%)	81 (15%)	25 (5%)	12 (2%)
Abnormal BPrisePME	29 (10%)	45 (25%)	40 (61%)	19 (23%)	10 (40%)	5 (42%)
LVH	17 (6%)	19 (11%)	15 (23%)	5 (6%)	5 (20%)	5 (42%)
Abnormal BPrisePME and LVH	2 (7%)	8 (18%)	12 (30%)	3 (16%)	2 (20%)	3 (60%)



rise in BP post mild exercise (BPrisePME) is associated with structural and functional abnormalities. The purpose of this study was to assess whether abnormal rise in BPrisePME in normotensive subjects is associated with LVH, which ultimately might lead to heart failure.

**Methods:** We screened 2406 asymptomatic subjects, age 20-79, for CVD risk using ECVDRS, which consists of 10 tests: large (C1) and small (C2) artery stiffness, blood pressure (BP) at rest and post mild exercise (PME), Carotid Intima Media Thickness (CIMT), abdominal aorta and left ventricle ultrasound (LVUS), retinal photography, microalbuminuria, ECG, and pro-BNP. Abnormal blood pressure rise post mild exercise (BPrisePME) was defined as systolic BP rise >30mmHg post 3-min-walk at 7% elevation, 2.5mph. Normotension (NT), pre-hypertension (pre-HTN), and hypertension (HTN) were defined according to JCN7 criteria.

**Results:** Among the 2406 subjects (1258 Female and 1148 Male), 1679 were not taking any CV medication. Among these, 526 subjects had no comorbidities, regardless of BP values. These subjects were divided into 6 groups, NT, Pre-HTN, HTN, and according to their systolic BP values (SBP), in groups A, B and C respectively. Results are shown in Table.

**Conclusions:** Based on our data,

1. LVH is present even in asymptomatic normotensive subjects with no CV comorbidities and not taking any medications.

2. 7% of normotensive subjects who have abnormal BPrisePME, have LVH.

Accordingly, we recommend screening for abnormal rise in BP post mild exercise in all subjects and initiating appropriate treatment to avoid progression to LVH with well-known deleterious consequences, including heart failure.

#### P499

##### Longitudinal and orthostatic changes of blood pressure predict dementia

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**Background:** The role of blood pressure (BP) variability in dementia is arguable. The aim of this study was to analyse how resting and orthostatic BP changes relate to incident dementia over a long-term follow-up.

**Methods:** In a prospective population-based project, 18,240 study participants (mean age: 45±7 years, 63% male) were examined with resting and orthostatic BP measurement at baseline (1974-92) and re-examined after 23±4 years (mean age: 68±6 years) with resting BP (2002-2006). A total of 428 participants (2.3%) were diagnosed with dementia through Dec 31, 2009. The association of resting and orthostatic BP changes with the risk of dementia was studied using multivariable-adjusted Cox regression models controlling for traditional risk factors.

**Results:** At baseline diastolic BP (DBP) decrease on standing was predictive of dementia (Hazard ratio (HR) per 10 mmHg: 1.22; 95% confidence interval (CI), 1.01-1.44, p=0.036). At re-examination, higher SBP and DBP lowered risk of dementia (HR per 10 mmHg: 0.94; 95% CI, 0.89-0.99, p=0.011; and 0.87; 0.78-0.96, p=0.006, respectively). SBP decrease between baseline and re-examination (4th quartile; -7±12mmHg) indicated increased risk of dementia (HR: 1.46; 95%CI, 1.11-1.93, p=0.008) compared with reference group (1st quartile; +44±13mmHg), as also did pronounced DBP decrease (4th quartile; -15±7mmHg) compared with reference group (1st quartile; +15±7mmHg); HR: 1.54; 95%CI, 1.14-2.08, p=0.005.

**Conclusion:** Diastolic BP decrease on standing in the middle age, decline in BP between middle- and advanced age, and lower BP in advanced age are independent risk factors of developing dementia.

Table 60834

	526 (22%), no Medications, no Comorbidities regardless of BP	Pre-HTN	HTN	A	B	C
	NT			SBP 120-129 DBP <80	SBP 130-139 DBP <80	SBP 140+ DBP <80
Abnormal CIMT	281 (53%)	179 (34%)	66 (13%)	81 (15%)	25 (5%)	12 (2%)
Abnormal C2	55 (20%)	64 (36%)	30 (45%)	29 (36%)	12 (48%)	10 (83%)
Abnormal BPrisePME	42 (15%)	33 (18%)	24 (36%)	12 (15%)	8 (32%)	6 (50%)
Normal BPrisePME	29 (10%)	45 (25%)	40 (61%)	19 (23%)	10 (40%)	5 (42%)
LVH	252 (90%)	134 (75%)	26 (39%)	62 (77%)	15 (60%)	7 (58%)
Abnormal BPrisePME and LVH	17 (6%)	19 (11%)	15 (23%)	5 (6%)	5 (20%)	5 (42%)
Normal BPrisePME and LVH	2 (7%)	8 (18%)	12 (30%)	3 (16%)	2 (20%)	3 (60%)
	15 (6%)	11 (8%)	3 (12%)	2 (3%)	3 (20%)	2 (29%)

#### P500

##### Abnormal rise in BP is associated with increased prevalence of LVH even in asymptomatic pre-hypertensive subjects

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**Purpose:** The purpose of this study was to assert whether abnormal rise in BP post mild exercise (BPrisePME) in pre-hypertension and hypertension is associated with increased prevalence in left ventricular hypertrophy (LVH).

**Methods:** We screened 2406 asymptomatic subjects, age 20-79, for CVD risk using ECVDRS, which consists of 10 tests: large (C1) and small (C2) artery stiffness, blood pressure (BP) at rest and post mild exercise (PME), Carotid Intima Media Thickness (CIMT), abdominal aorta and left ventricle ultrasound (LVUS), retinal photography, microalbuminuria, ECG, and pro-BNP. Abnormal blood pressure rise post mild exercise (BPrisePME) was defined as systolic BP rise >30mmHg post 3-min-walk at 7% elevation, 2.5mph. Normotension (NT), pre-hypertension (pre-HTN), and hypertension (HTN) were defined according to JCN7 criteria.

**Results:** Among the 2406 subjects (1258 Female and 1148 Male), 1679 were not taking any CV medication. Among these, 526 subjects had no comorbidities, regardless of BP values. These subjects were divided into 6 groups, NT, Pre-HTN, HTN, and according to their systolic BP values (SBP), in groups A, B and C respectively. Prevalence of abnormal structural and functional abnormalities are shown in Table.

**Conclusions:** Based on our data, abnormal rise in BP post mild exercise in pre-hypertension and hypertension is associated with increased prevalence in LVH as compared with normal control. Accordingly, we advocate screening for abnormal rise in BP post mild exercise in all subjects for identification of those at high risk for developing LVH with well-known grave consequences. Early detection and implication of appropriate treatment is better than late cure.

#### P501

##### Inter-arm blood pressure difference: the prevalence and characteristics in Korean general population

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**Background:** An increased inter-arm systolic blood pressure difference (IBPD) is an easily determined physical examination finding and a significant IBPD has recently been associated with worse cardiovascular outcome. But the prevalence of IBPD in Asian population is unknown and the relationship between IBPD and blood pressure (BP) variability is not yet determined. Method A representative population was selected by list-assisted random-digit dialing method from a city. The BP of two arms was simultaneously measured using validated automatic BP measurement devices for 3 times and an increased IBPD was defined as ≥10mmHg using the average of 3 BP differences obtained simultaneously in both arms.

**Results:** We recruited 497 subjects in this study, and 10 subjects were excluded because of inadequate ABPM measurements. Mean age was 46.9±9.4 years and 309 participants were female (63.4%). Overall systolic BP and diastolic BP were 118.5±13.4 mmHg and 75.1±10.3 mmHg and mean systolic IBPD was 5.7±4.0mmHg. Of the 487 subjects, 66 subjects (13.6%) had an increased IBPD. Compared with those with normal IBPD, subjects with increased systolic IBPD showed higher clinic BP (127.2±13.7 vs. 117.2±12.8 mmHg in systolic BP, P<0.001; 78.7±11.2 vs. 74.6±10.1 mmHg in diastolic BP, P=0.002), higher

24-hour systolic BP (118.5 ± 12.0 vs. 115.6 ± 10.8 mmHg, P=0.045) and higher 24-hour pulse pressure (42.4 ± 7.4 vs. 40.2 ± 6.5 mmHg, P=0.012). The subjects with increased systolic IBPD showed higher 24-hour BP variability; increased standard deviation of daytime BPs, increased weighted standard deviation of BPs, increased coefficient of variation of daytime BPs and increased average real variability of both 24-hour BPs and daytime BPs (Table). There was no significant difference in nighttime dipping pattern of increased IBPD subjects.

**Conclusion:** In this community-based cohort, an increased IBPD is common and associated with an increased short-term BP variability.

	All patients (n=487)	Systolic IABPD (+) (n=66)	Systolic IABPD (-) (n=421)	P-value
<b>BP profiles</b>				
24 hour SBP (mmHg)	118.0 ± 11.0	118.5 ± 12.0	115.6 ± 10.8	0.045
24 hour DBP (mmHg)	75.3 ± 10.2	76.3 ± 11.8	74.4 ± 9.9	0.491
24 hour PP (mmHg)	42.7 ± 8.7	42.4 ± 7.4	40.2 ± 6.5	0.012
Daytime SBP (mmHg)	119.3 ± 11.7	121.5 ± 12.5	118.9 ± 11.1	0.002
Daytime DBP (mmHg)	78.3 ± 10.8	78.8 ± 12.1	76.4 ± 10.5	0.800
Daytime PP (mmHg)	40.9 ± 7.5	42.9 ± 8.2	40.5 ± 7.3	0.019
Nighttime SBP (mmHg)	109.1 ± 12.2	112.0 ± 13.1	108.6 ± 12.0	0.035
Nighttime DBP (mmHg)	69.3 ± 10.7	70.8 ± 11.8	69.1 ± 10.5	0.226
Nighttime PP (mmHg)	39.8 ± 6.8	41.4 ± 7.1	39.5 ± 6.7	0.008
<b>24 hour BP variability</b>				
SD of 24 hour SBP (mmHg)	12.1 ± 3.2	12.7 ± 3.6	12.0 ± 3.2	0.106
SD of 24 hour DBP (mmHg)	10.2 ± 2.4	10.3 ± 2.3	10.2 ± 2.4	0.866
wSD of 24 hour SBP (mmHg)	10.3 ± 3.0	11.3 ± 3.6	10.2 ± 2.9	0.006
wSD of 24 hour DBP (mmHg)	8.7 ± 2.1	9.2 ± 2.2	8.6 ± 2.1	0.046
CV of 24 hour SBP (mmHg)	10.3 ± 2.5	10.7 ± 2.7	10.4 ± 2.5	0.338
CV of 24 hour DBP (mmHg)	11.8 ± 2.5	11.4 ± 2.3	11.8 ± 2.5	0.658
ARV of 24 hour SBP (mmHg)	9.3 ± 2.4	9.9 ± 2.9	9.2 ± 2.3	0.029
ARV of 24 hour DBP (mmHg)	8.3 ± 1.8	8.7 ± 2.0	8.2 ± 1.8	0.030
<b>Daytime BP variability</b>				
SD of daytime SBP (mmHg)	10.9 ± 3.9	12.2 ± 4.5	10.8 ± 3.8	0.007
SD of daytime DBP (mmHg)	9.1 ± 2.7	9.9 ± 2.9	9.0 ± 2.6	0.016
CV of daytime SBP (mmHg)	9.2 ± 3.0	10.0 ± 3.4	9.0 ± 3.0	0.019
CV of daytime DBP (mmHg)	11.7 ± 3.3	12.6 ± 3.4	11.8 ± 3.3	0.019
ARV of daytime SBP (mmHg)	9.5 ± 3.6	10.6 ± 4.4	9.3 ± 3.5	0.008
ARV of daytime DBP (mmHg)	8.4 ± 2.5	9.2 ± 2.8	8.3 ± 2.5	0.005

**P502**

**Incremental rise in blood pressure from normotensive to hypertensive is a major risk factor for LVH**

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**Purpose:** Hypertension is a major CV risk factor for left ventricular hypertrophy (LVH) and heart failure. The purpose of this study was to assess whether abnormal rise in BP post mild exercise (BPrisePME) might be the culprit and the clue for early detection of LVH in pre-hypertensive and hypertensive subjects.

**Methods:** We screened 2406 asymptomatic subjects, age 20-79, for CVD risk using ECVDRS, which consists of 10 tests: large (C1) and small (C2) artery stiffness, blood pressure (BP) at rest and post mild exercise (PME), Carotid Intima Media Thickness ? (CIMT), abdominal aorta and left ventricle ultrasound (LVUS), retinal photography, microalbuminuria, ECG, and pro-BNP. Abnormal blood pressure rise post mild exercise (BPrisePME) was defined as systolic BP rise >30mmHg post 3-min-walk at 7% elevation, 2.5mph. Normotension (NT), pre-hypertension (pre-HTN), and hypertension (HTN) were defined according to JCN7 criteria.

**Results:** Among the 2406 subjects (1258 Female and 1148 Male), 1679 were not taking any CV medication. Among these, 526 subjects had no comorbidities, regardless of BP values. These subjects were divided into 6 groups, NT, Pre-HTN, HTN, and according to their systolic BP values (SBP), in groups A, B and C respectively. Prevalence of abnormal structural and functional abnormalities are shown in Table.

	526 (22%), no Medications, no Comorbidities regardless of BP	NT	Pre-HTN	HTN	A SBP 120-129 DBP <80	B SBP 130-139 DBP <80	C SBP 140+ DBP <80
Abnormal CIMT	281 (53%)	55 (20%)	179 (34%)	66 (13%)	81 (15%)	25 (5%)	12 (2%)
Abnormal C2	42 (15%)	29 (36%)	33 (18%)	24 (36%)	29 (36%)	12 (48%)	10 (83%)
Abnormal BPrisePME	29 (10%)	45 (25%)	45 (25%)	40 (61%)	19 (23%)	10 (40%)	5 (42%)
Normal BPrisePME	252 (90%)	134 (75%)	134 (75%)	26 (39%)	62 (77%)	15 (60%)	7 (58%)
LVH	17 (6%)	19 (11%)	19 (11%)	15 (23%)	5 (6%)	5 (20%)	5 (42%)
Abnormal BPrisePME and LVH	2 (7%)	8 (18%)	8 (18%)	12 (30%)	3 (16%)	2 (20%)	3 (60%)

**Conclusions:** Based on our data, incremental rise in BP for normotension to hypertension is associated with increased prevalence of LVH.

Accordingly, we advocate screening for abnormal rise in BP regardless of the baseline BP status, to identify those at high risk for LVH and, ultimately, heart failure.

**HFPEF - HEART FAILURE WITH PRESERVED EJECTION FRACTION**

**P504**

**Hidden under metabolic syndrome: do many patients already have unrecognized HFpEF?**

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**Background:** Heart failure with preserved ejection fraction (HFpEF) is an epidemic problem associated with high morbidity and mortality rates. The importance of metabolic syndrome (MetS) in patients who already have diagnosed heart failure is widely discussed. However, there is a lack of knowledge on early development and diagnosis of HFpEF in metabolic syndrome.

**Purpose:** We hypothesised that a significant number of patients with MetS already have occult, undiagnosed HFpEF.

**Methods:** We evaluated 153 patients (mean age 57.59 ± 8.69, 46.15% males, 53.85% females) with MetS: 115 patients were enrolled from the Lithuanian High Cardiovascular Risk primary prevention programme prospectively, and 38 patients retrospectively. Retrospective patients with HFpEF were referred to cardiopulmonary stress testing for differential diagnosis of dyspnea, and were enrolled as they satisfied MetS criteria and had left ventricle ejection fraction >55%. Subjects were classified as having MetS if they met three or more criteria of the National Cholesterol Education Program. Patients were only included if they had satisfactory cardiac ultrasound, cardiopulmonary stress assessments and required laboratory tests. We considered patients as having HFpEF if during cardiopulmonary test the peak VO2 was ≤90% of predicted or/and BNP was 35 pmol/l or more. The t-test was used for comparison.

**Results:** Number of patients with reduced predicted VO2 n=116 (75.82%), with increased BNP n=95 (62.09%), with both reduced predicted VO2 and increased BNP n=76 (49.67%).

**Conclusions:** A significant number of metabolic syndrome patients have undiagnosed HFpEF. Therefore, there is a need for comprehensive future researches on this topic. BNP was better discriminator for the presence of HFpEF than VO2 in MetS patients.

## Results

	Total prospective group, n = 115	Prospective group without HFpEF, n = 44 (38.26%)	Prospective group with HFpEF, n = 71 (61.74%)	Retrospective group with HFpEF, n = 38 (47.5%)	P value
BNP (pmol/l)	25.96 ± 19.02	16.22 ± 6.58	32.00 ± 21.58	191.21 ± 249.78	0.00036
Peak VO <sub>2</sub> (% of predicted)	90.91 ± 15.41	102.5 ± 7.67	83.73 ± 14.62	79.80 ± 22.14	0.32735
LVMI (g/m <sup>2</sup> )	95.45 ± 23.17	100.26 ± 22.86	95.70 ± 23.35	110.65 ± 30.86	0.01131
LVMI, men (g/m <sup>2</sup> )	100.58 ± 27.27	103.86 ± 27.86	95.56 ± 26.49	119.07 ± 25.54	0.3704
LVMI, women (g/m <sup>2</sup> )	95.89 ± 20.88	96.33 ± 15.43	95.74 ± 22.70	104.52 ± 33.44	0.00323
E/E'	10.18 ± 2.36	10.38 ± 2.33	10.05 ± 2.38	11.55 ± 4.65	0.18218
Normal diastolic function (%)	15.65	15.91	15.49	2.36	
Pseudonormal diastolic function (%)	58.26	61.36	56.34	52.63	
Restrictive diastolic function (%)	10.44	13.64	8.45	5.26	
LVH (%)	62.61	54.55	60.56	68.4	

LVMI-left ventricular mass index, LVH-left ventricular hypertrophy.

## P505

## Gender disparity in heart failure patients with preserved ejection fraction

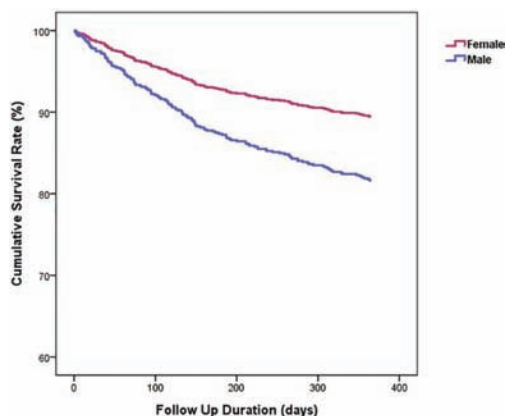
J-H Ju-Hee Lee<sup>1</sup>; H-R Kang<sup>1</sup>; D-H Bae<sup>1</sup>; S-M Kim<sup>1</sup>; S-Y Lee<sup>1</sup>; J-W Bae<sup>1</sup>; K-K Hwang<sup>1</sup>; D-W Kim<sup>1</sup>; M-C Cho<sup>1</sup>

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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 HF clinical trials. And there are few data regarding the gender disparity in HF especially in patients with HF with preserved ejection fraction (HFpEF). **METHODS** We evaluated the HFpEF patients hospitalized for ADHF in ten regionally-representative tertiary university hospitals who registered in the Korean Acute Heart Failure (KorAHF) Registry from March 2011 to February 2014. HFpEF defined as EF ≥45%.

**Results:** A total of 5,625 patients were recruited and 1,769 patients (31.4%) were classified as HFpEF. Mean age was 72.0 ± 13.3 and 1,052 patients (59.5%) were male. Mean follow up duration was 787 ± 400 days. Women were older and showed higher prevalence of hypertension, valvular heart disease and atrial fibrillation and lower prevalence of previous MI and coronary revascularization. At baseline echocardiography, women showed higher LV EF, but they showed higher LA volume index, E/e' ratio and RV systolic pressure. Despite the higher EF, mean NYHA functional class of women was worse at baseline and NYHA functional class III and IV patients were more prevalent in women. But the improvement in mean NYHA functional class after treatment was significant in both genders. The use of ACE inhibitor, ARB, beta blocker and aldosterone antagonist was equal in both genders. Although the unadjusted in-hospital mortality and overall mortality were comparable, the adjusted in-hospital mortality and overall mortality were significantly higher in male.

**Conclusions:** There were significant gender disparity in baseline characteristics, clinical presentation and co-morbidity in HFpEF patients. The differences of gender can affect the prognosis variously, so we emphasize the importance of the approach concerning these differences.



## P506

## Which measurement of blood pressure is more associated with ejection fraction preserved heart failure without hypertension: central blood pressure or peripheral blood pressure?

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**Background:** Peripheral systolic blood pressure (pSBP) has been used to predict ejection fraction preserved heart failure (HFpEF). However, the assessment of superiority between pSBP and central SBP (SBP2) to predict ASCVD in patients without hypertension (HTN) has not been fully established.

**Methods:** Two hundred and twenty patients (male:female ratio 115:105, mean age 54.2 ± 14.7 years) without HTN were enrolled from subjects who simultaneously received transthoracic echocardiography and non-invasively semiautomated radial artery applanation tonometry in the Department of Internal Medicine of our Hospital, from July 2011 to May 2015. Moreover, the area under the receiver operating characteristic curve (AUC) of SBP2 was compared with that of SBP to identify HFpEF.

**Results:** Thirty nine subjects (male:female ratio 20:19, mean age 65.9 ± 11.3 years) were diagnosed as HFpEF according to ESC guidelines for diagnosis and treatment of heart failure 2012. HFpEF patients had significantly higher pSBP (131 ± 20mmHg vs 126 ± 14mmHg), SBP2 (125 ± 21mmHg vs 116 ± 16mmHg) and pulse pressure (54 ± 19mmHg vs 49 ± 11mmHg) than the patients without HFpEF. After multivariate analysis after adjusted for age, gender, body mass index, fasting plasma glucose, diabetes, lipid profiles, antihypertensive medication and lipid-lowering medication, SBP2 ( $\beta = 0.231$ , 95% CI 1.036 to 1.289,  $p = 0.010$ ) or pSBP ( $\beta = 0.887$ , 95% CI 0.800 to 0.982,  $p = 0.021$ ) were associated with HFpEF. In addition, AUC (0.639) of pSBP was significantly greater than that of SBP2 to identify HFpEF. ( $P = 0.007$ ).

**Conclusions:** Central blood pressure is superior to pSBP in identifying HFpEF, although both peripheral and central SBP are associated with HFpEF in patients without hypertension.

## P507

## Heart rate response and functional capacity in patients with advanced heart failure with preserved ejection fraction

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**Background:** The mechanisms of exercise intolerance in heart failure with preserved ejection fraction (HFpEF) are not yet elucidated. Chronotropic incompetence has emerged as a potential mechanism.

**Purpose:** We aimed to evaluate the relationship between heart rate (HR) response to exercise and functional capacity in advanced HFpEF patients.

**Methods:** We prospectively studied 40 HFpEF patients [50% NYHA III, 55% female, age (mean ± SD) 71.6 ± 8.6 years and 40% atrial fibrillation]. Functional performance was assessed by peak oxygen consumption (peak VO<sub>2</sub>).

**Results:** The mean (SD) peak VO<sub>2</sub> was 10.2 ± 3.1 mL/min/kg. Following chronotropic parameters were calculated: Delta-HR (HR at peak exercise - HR at rest), chronotropic index (CI) = (HR at peak exercise - resting HR) / [(220 - age) - resting HR] and CI according to the equation developed by Keteyian (CIK) as HR at peak exercise - HR at rest / [(119 + (HR at rest/2) - (age/2) - 5) - HR at



rest)]. In a bivariate setting, peak VO<sub>2</sub> was positively and significantly correlated with Delta-HR ( $r=0.33$ ,  $p=0.037$ ) and borderline with CI and CIK ( $r=0.30$ ,  $p=0.055$  and  $r=0.31$ ,  $p=0.050$ , respectively). In a multivariable linear regression analysis chronotropic parameters were associated with peak VO<sub>2</sub>. For increase in 10 bpm in Delta-HR and 0.1-unit increase in CI and CIK there was an associated increase in the mean of peak VO<sub>2</sub> of 0.32 mL/kg/min ( $p=0.040$ ), 0.27 mL/kg/min ( $p=0.015$ ) and 0.15 mL/kg/min ( $p=0.016$ ), respectively.

**Conclusion:** In patients with advanced HFpEF, the HR response to exercise was positively associated to patient's functional capacity.

See Figure 1. Functional form of the adjusted association among different chronotropic indexes and peak oxygen consumption. Variables modeled with fractional polynomials. Delta-HR, absolute difference between heart rate (HR) at peak exercise and HR at baseline; CI, chronotropic index, a measure of chronotropic response based on the Astrand formula; CIK, chronotropic index according to the equation of Keteyian; peak VO<sub>2</sub>, peak oxygen consumption.

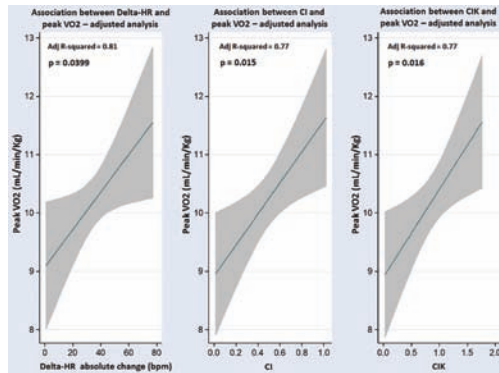


Figure 1

## P508

### Evidence of pericardial abnormalities with potential haemodynamic significance is frequent in HFpEF patients: causality or causality?

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**Background:** Due to obvious practical difficulties for invasive haemodynamic assessment the frequency of cardiac chamber compression from concomitant pericardial disease contributing to diastolic dysfunction (DD) in HFpEF patients is unknown.

**Purpose:** To evaluate by means of non-invasive methods how often patients with stage C HFpEF exhibit evidence of anatomical pericardial involvement and/or ultrasound functional abnormalities that, although not diagnostic of a definite cardiac compressive syndrome, may suppose a superimposed compromise of the myocardial diastolic function.

**Methods:** 207 patients with stage C HFpEF were retrospectively studied. Their clinical and ultrasound parameters and results of thoracic CT and cardiac MRI were recorded. Study subgroups were designed according to classical patterns of DD (I, II, III and IV). Categorical variables included the following signs of probable cardiac compression (SPCC): 1. Jugular veins distension and/or Kussmaul sign, if not serious pulmonary hypertension present (<40 mm Hg), 2. Moderate to severe pericardial effusion (> 10 mm) accompanied by RA collapse or paradoxical pulse; 3. Calcification or thickening (> 3 mm) of the pericardium with corresponding heart wall flattening, interventricular septal bounce or pericardial knock sound; 4. Respiratory variation of early transmitral flow > 25%; and 5. Estimated RA pressure > 15 mmHg (providing PSP <40 mmHg) along with typical abnormalities of the venous inflow (non collapse of IVC on inspiration ± hepatic veins expiratory reversal). Clinical outcome was analyzed by means of logistic regression.

**Results:** At least one SPCC was found in 28 cases (13.5%). Remarkably, while 21 out of 101 patients with types III/IV DD (20.7%) showed some SPCC, only 7 of the remaining (6.6%) evinced SPCC suggesting diastolic compromise of pericardial origin. Detection of 2 or more SPCC independently increased the risk of death or hospitalization from HF decompensation.

**Conclusion:** Significant pericardial involvement with possible haemodynamic transcendence is frequently seen in HFpEF patients with types II and IV DD, and it may represent an important independent risk factor. SPCC could be being underestimated in clinical practice thus avoiding the implementation of specific decompressive therapies in HFpEF.

## P509

### Defining the phenotype of stage B HFPEF progressers

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**Intro:** Asymptomatic Left Ventricular Diastolic Dysfunction (LVDD) is defined as evidence of diastolic dysfunction, but normal systolic function, in the absence of the signs and symptoms of the clinical syndrome of heart failure (HF). The ACC/AHA define this clinical entity as Stage B Heart Failure. Our understanding of who is at greatest risk of progressing from Stage B HFPEF remains limited. We report a longitudinal analysis of progression from Stage B to identify a higher risk phenotype.

**Methods:** The STOP-HF Screening Service recruits patients at risk of developing heart failure. Criteria requires age > 40 and at least one of the following: (1) hypertension medicated for > 1 month; (2) dyslipidaemia (TC>5.0mmol/l and/or LDL>3.0mmol/l); (3) BMI>30; (4) vascular disease; (5) diabetes; (6) arrhythmia requiring therapy; (7) moderate to severe valvular disease. Those with established HF or left ventricular systolic dysfunction are not recruited.

We include 609 individuals with Stage B HFPEF in this analysis. Individuals who progressed from Stage B HFPEF to heart failure were classified as Stage B Progressers. Median follow-up for Progressers from time of baseline BNP to diagnosis of HF was 5.5 years. We define Stage B HFPEF as patients who are asymptomatic with Doppler-echocardiographic evidence of significant LVDD (LAVI>34ml/m<sup>2</sup> and septal E prime <10mm). We define HFPEF as the presence of typical clinical signs and symptoms of the HF syndrome in the presence of a raised BNP with the aforementioned echocardiographic features. Baseline demography, medical and clinical parameters were recorded along with echocardiographic parameters, and biomarkers (including BNP). Comparison between subgroup was calculated according to appropriate statistical analysis.

**Results:** 28 of 609 were Stage B Progressers (4.6% over a Median of 5.5years). 40.8% of the Stage B cohort compared with 60.7% of Stage B Progressers were female. Median BNP at baseline was 28.3 pg/ml in the Stage B group compared with 102 pg/ml in Stage B Progressers. Median Age in the Stage B group was 66.7 at baseline, and 71.0 in the Stage B Progressers.

**Conclusion:** Our data suggests a high risk Stage B phenotype for the development of HF, comprising older age, female gender and higher baseline BNP. This higher risk cohort may be best suited to intervention strategies directed at prevention of HFPEF.

## P510

### Predictors of mortality in acute de novo heart failure with preserved ejection fraction in long-term follow-up

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**Background:** Chronic heart failure with preserved ejection fraction (HFpEF) is reported to have a similar prognosis to heart failure with reduced ejection fraction. However, studies about acute de novo HFpEF have not been established.

**Purpose:** We sought to determine risk factors for all-causes mortality in patients with acute de novo HFpEF, including echocardiographic parameters, especially, left atrial size and pulmonary hypertension, which reflect chronic hemodynamic status of left ventricular diastolic dysfunction.

**Methods:** We enrolled consecutively 495 patients (mean age, 72 ± 13 years; 65% female) with acute de novo HFpEF, who were admitted to our hospital. Patient underwent echocardiography and assay of biomarkers (B-type natriuretic peptide, myoglobin etc.). Cox proportional-hazards model was used to assess risk factors for all-causes mortality.

**Results:** All-causes mortality was 43% over a median follow-up of 4.4 years. On univariate analysis, old age, female, diabetes mellitus, low body mass index, high TR pressure gradient, high inferior vena cava size, high BNP, low sodium level and high myoglobin were associated with all-causes mortality. After adjustment for covariates, Cox regression analysis revealed that old age ( $P < 0.001$ ), low BMI ( $P < 0.001$ ), high BNP ( $P = 0.003$ ), low sodium ( $P = 0.01$ ) and high myoglobin ( $P = 0.001$ ) were independently associated with all-causes mortality. But, echocardiographic parameters such as left atrial size, TR pressure gradient and IVC size were not related to mortality.

**Conclusions:** Our study confirmed that age, BMI, BNP, sodium and myoglobin level were independent risk factors for all-cause mortality of acute de novo HFpEF. But, echocardiographic parameters reflecting left ventricular diastolic dysfunction failed to show clinical relevance.

## P511

**Body mass index and adverse outcomes in heart failure patients with preserved ejection fraction**

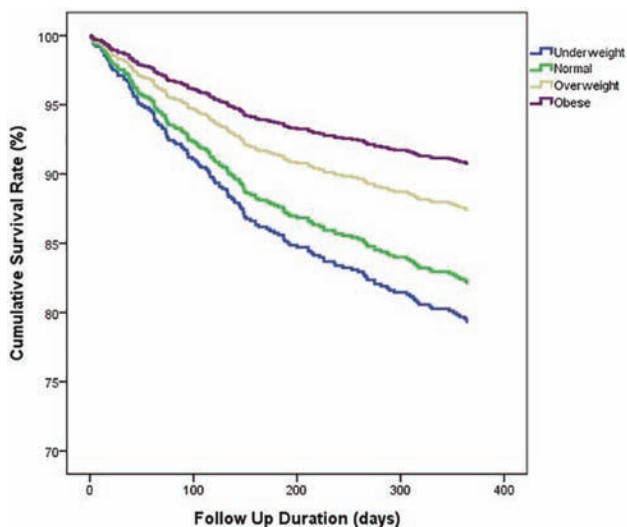
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**Background:** Obesity is a major risk factor for incident heart failure (HF). Paradoxically, in HF with reduced ejection fraction (HFrEF), a high body mass index (BMI) appears to be beneficial. However, there are few data regarding the relationship between BMI and outcomes in HF with preserved ejection fraction (HFpEF). Method We evaluated the HFpEF patients hospitalized for ADHF in ten regionally-representative tertiary university hospitals who registered in the Korean Acute Heart Failure (KorAHF) Registry from March 2011 to February 2014. HFpEF defined as EF  $\geq$ 45% and BMI were categorized according to WHO criteria for Asian (<18.5, 18.5 to 22.9, 23 to 24.9, and  $\geq$ 25 Kg/m<sup>2</sup>).

**Results:** Among the 5,625 patients who were registered at KorAHF Registry, 1,769 patients (31.4%) were classified as HFpEF. Mean age was 72.0  $\pm$  13.3 and 717 patients (40.5%) were male. Mean follow up duration was 787  $\pm$  400 days. The patients were categorized to underweight (BMI <18.5 Kg/m<sup>2</sup>, 207 patients, 11.8%), normal (18.5  $\leq$  BMI <23 Kg/m<sup>2</sup>, 731 patients, 41.6%), overweight (23  $\leq$  BMI <25 Kg/m<sup>2</sup>, 355 patients, 20.2%) and obese (BMI  $\geq$ 25 Kg/m<sup>2</sup>, 466 patients, 26.5%). Patients with higher BMI were younger, more often men, and more likely to have hypertension and diabetes. Obese patients showed the lowest mortality. In multivariate analysis adjustment for 14 risk variables including age, sex, and N-terminal pro-brain natriuretic peptide, the hazard ratio for the mortality was increased in patients with lower BMI. (Figure).

**Conclusion:** Obesity is common in HFpEF patients and is accompanied by multiple differences in clinical characteristics. Independent of other key prognostic variables, there was a significant obesity-paradox in relationship between BMI and mortality in HFpEF.



## P512

**Gender specific treatment effects of Spironolactone in Diastolic Heart Failure: Insight from ALDO-DHF**

Federal Ministry of Education and Research Grant 01GI0205 (clinical trial program Aldo-DHF [FKZ 01KG0506])

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**Background:** Women are approximately two times more likely than men to develop HFpEF, a common condition without established therapy. Aldosterone stimulation may contribute to the progression of HFpEF. Long-term aldosterone receptor blockade in the randomized controlled ALDO-DHF trial improved left ventricular diastolic function in these patients. We aimed to assess differences in baseline

characteristics, cardiovascular structure and function and gender specific treatment effects of spironolactone in HFpEF.

**Methods:** This is a secondary, post-hoc analysis of the ALDO-DHF. Subjects were stratified according to sex. Clinical characteristics and cardiac structure and function were compared between men and women. Efficacy endpoints that reached significance in the comparison of Spironolactone vs. Placebo in ALDO-DHF were assessed in ANCOVA models for interaction of sex, treatment.

**Results:** 422 subjects (221 female) were studied. Mean age was 67 years. At baseline male vs female subjects differed significantly ( $p < 0.001$ ), e.g. in NYHA class, Maximal workload, Peak VO<sub>2</sub>, 6MWT distance, LV diameter, LV mass index, LAVI and SF 36 physical functioning score. Also, RR systolic ( $p = 0.015$ ) and Mean arterial pressure ( $p = 0.005$ ) differed significantly between subjects at baseline. In regard to effect of spironolactone vs. placebo, Systolic RR and Mean arterial pressure changed significantly from baseline to follow-up in both sex ( $p < 0.001$ , respectively), with no significant difference between both sex (ANCOVA  $p = 0.079$  and  $p = 0.93$  respectively). Change in pulse pressure was -0.8 (95% CI -4.4 to 2.6,  $p = 0.64$ ) in men and -8.2 (95% CI -11.6 to -4.9,  $p < 0.001$ ) in women,  $p = 0.003$  for interaction of sex and treatment,  $p = 0.043$  after Bonferroni-adjustment.

**Conclusion:** We observe distinct sex-differences in baseline clinical characteristics, structure and function in the ALDO-DHF population. A marked decrease of pulse pressure in women was documented. This finding may bear notable medical consequences.

## BASIC SCIENCE: ACUTE HEAT FAILURE

## P514

**Heart failure in women and their pathophysiological factor**

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**Abstract:** Heart failure can occur in any age, no depend on sex, but in men and women the mechanism, even if is the same, the fact is that the compromise on pumping function is different. AIM We realized a follow-up with 100 female patients during hospitalization with heart failure as a mean diagnostic. These are patient between 60 and 75 years old, with different pathologies: diabetes mellitus, arterial hypertension, obesity, atrial fibrillation, and hypothyroidism. We observed their treatment comparing with a control group (100 men in heart failure) by administering vasodilator and diuretic drugs. Performed echocardiography doppler control, daily renal function, NT pro BNP levels control, oxide nitric response.

**Results:** We observed that ventricular dilation, hypertrophy as tachycardia is more typical in men. Our group demonstrated very fast response to beta blockers and diuretics. The ejection fraction increased in 10-15% faster than in control group. Oxide nitric had not the result we expected. But in men the effect is very high. NT pro BNP levels no were increased as a control group. Recovering renal function in women during heart failure depends on risk factors as diabetes mellitus, obesity, more characteristics for women.

**Conclusions:** In women heart failure has the same mechanism that in men, but more of the cardiac compensatory mechanisms during heart failure as Frank-Starling mechanism, ventricular dilation or hypertrophy and tachycardia present more complications in men; women recover sinus rhythm faster than men, hypertrophy is not characteristic and dilation recovers EF as pumping function is near normal. We do not observed increased sympathetic adrenergic activity in our patients and increased vagal activity to heart. Renin-angiotensin-aldosterone and antidiuretic hormone systems in women is compensated by vasoconstriction improving ventricular stroke volume by reducing afterload on the ventricle.

Table 3. NT-pro BN characteristics

NT-proBNP cutoff value of 125 pg/mL had the best sensitivity-to-specificity ratio and NPV to rule out asymptomatic LV moderate to severe diastolic or systolic dysfunction in patients at risk for heart failure:

1. Men younger than 60 years (sensitivity, 87.5%; specificity, 92.7%; NPV, 99.5%; positive predictive value [PPV], 33.3%)
2. Women younger than 60 years (sensitivity, 100%; specificity, 84.1%; NPV, 100%; PPV, 33.3%)
3. Men at least age 60 years (sensitivity, 100%; specificity, 77.1%; NPV, 100%; PPV, 32.5%)
4. Women at least age 60 years (sensitivity, 100%; specificity, 69.9%; NPV, 100%; PPV, 21%)

## P515

**Cardiorenal effects of intravenous thrx-215409, a novel neprilysin inhibitor, in a canine model of acute heart failure**

Funded by Theravance Biopharma  
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**Introduction:** Acute heart failure (AHF) episodes are associated with unacceptably high mortality and rehospitalisation rates despite treatment with conventional therapies including furosemide (FUR). Adverse consequences of AHF may be related to inadequate compensation by protective endogenous neurohormonal systems including natriuretic peptides (NP) such as atrial NP, brain NP and C-type NP which are degraded by the enzyme neprilysin (NEP). Acute NEP inhibition elevates the levels of endogenous NP which could offer short and long-term therapeutic benefit by exerting protective cardiorenal effects, neurohormonal inhibition and end-organ protection.

**Purpose:** To assess the haemodynamic, renal and neurohormonal effects of intravenous (IV) THRX-215409 (THRX), a potent and selective NEP inhibitor, when co-administered with FUR in a canine model of AHF.

**Methods:** Mongrel dogs, paced 10 days at 240 beats per min, were anaesthetised and instrumented for assessment of hemodynamic and renal function. After a 30-min baseline, dogs were treated IV with vehicle (V), FUR (0.1 mg/kg/hr) or THRX (3 mg/kg/hr) + FUR (0.1 mg/kg/hr) for two 30 min treatment periods, followed by a 30 min recovery.

**Results:** THRX + FUR increased urinary cGMP output to a significantly greater magnitude than FUR ( $47711 \pm 13519$  vs  $25481 \pm 3382$  moles/30 min;  $p < 0.01$ ), which was consistent with NEP target engagement. THRX + FUR reduced left ventricular end-diastolic pressure to a significantly greater extent than FUR alone (change from baseline:  $-8 \pm 2$  vs  $-5 \pm 1$  mmHg,  $p < 0.05$ ) without altering mean arterial pressure (MAP;  $-3 \pm 3$  vs  $4 \pm 6$  mmHg). THRX + FUR produced a significant increase in glomerular filtration rate (GFR) relative to FUR ( $20 \pm 13$  vs  $-1 \pm 7$  mL/min,  $p < 0.05$ ). THRX + FUR and FUR produced similar diuretic ( $38 \pm 10$  vs  $39 \pm 10$  mL/30 min) and natriuretic ( $4.8 \pm 1.6$  vs  $5.2 \pm 1.5$  moles/30min) effects. THRX + FUR, compared to FUR, produced significantly greater decreases in plasma renin activity (change from baseline:  $-3 \pm 1$  vs  $2 \pm 1$  ng/mL/hr,  $p < 0.005$ ) and plasma angiotensin II levels ( $-48 \pm 20$  vs  $41 \pm 15$  pg/mL,  $p < 0.005$ ). FUR and THRX + FUR had similar effects on renal blood flow, cardiac output, plasma norepinephrine and aldosterone levels.

**Conclusion:** In a canine model of AHF, THRX + FUR is more effective than FUR alone at reducing ventricular filling pressures, suppressing renin-angiotensin system activity and improving GFR. The salutary cardiorenal effects of THRX were accompanied by preservation of the renal effects of FUR and had no impact on MAP. These preclinical findings support clinical investigation of the efficacy of THRX-215409 in AHF.

## P516

**Short and long-term prognostic Impact of QRS duration at baseline in acute heart failure population: insight from HEARTS**

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**Objective:** Predictors of mortality in heart failure (HF) are widely studied and examined in order to utilize therapeutics and interventions preventing undesired outcomes. Interventricular conduction delays, defined as prolonged QRS duration ( $> 120$ ms), have been shown to affect outcomes in HF population, however, there is limited data with wider QRS during in HF patients. Therefore, we evaluated the association between QRS duration of ( $\geq 150$ ms) and short and long term outcomes in HF cohort.

**Methods & Results:** Data was gathered from the HEART function Assessment Registry Trial in Saudi Arabia (HEARTS). A national multicenter project, studying clinical features, management, short- and long-term outcomes, and mortality predictors in patients admitted with acute decompensated heart failure (ADHF). The registry enrolled 2609 ADHF patients admitted to 18 hospitals in Saudi Arabia between October 2009 and December 2010, and followed mortality rates until January 2013. Registering 2609 patients with diagnosed and de novo HF. The cohort was divided into two groups. Group 1 were patients with a QRS duration of  $\geq 150$ ms at baseline. Group 2 were patients with QRS duration  $< 150$ ms in duration. The first group (QRS duration  $\geq 150$ ms  $n = 116$ ) showed an independent association with worse clinical outcomes and higher adjusted in-hospital, 1-year, 2-year and 3-year mortality rates 15.52%, 37.93%, 43.97% and 44.83% respectively. Compared to the second group (QRS duration  $< 150$ ms  $n = 2489$ ) 6.11%, 18.64%, 22.62 and 23.38% respectively ( $p < 0.001$ ). These findings were independent of the morphology of the QRS at baseline.

**Conclusion:** QRS duration wider than 150ms at baseline is strongly associated with increased short and long-term mortality in HF population. Moreover, greater QRS width proportionately increases the association with worse outcomes.

## P517

**Suppressive effect of epigallocatechin 3-O-gallate on endoglin molecular regulation in myocardial fibrosis in vitro and in vivo**

Shin Kong Wu Ho-Su Memorial Hospital (Taipei, Taiwan) to Lin, CM (grant number: SKH-8302-102-0501)

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**Background:** Epigallocatechin-3-O-gallate (EGCG), derived from green tea, has been studied extensively because of its diverse physiological and pharmacological properties.

**Purpose:** This study evaluates the protective effect of EGCG on angiotensin II (Ang II)-induced endoglin expression in vitro and in vivo.

**Materials and Methods:** Cardiac fibroblasts (CFs) from the thoracic aorta of adult Wistar rats were cultured and induced with Ang II. Western blotting, Northern blotting, real-time PCR, and promoter activity assay were performed. Through in vivo AMI-related myocardial fibrosis study, immunohistochemical and confocal analyses were performed, and hemodynamic monitoring data were measured.

**Results:** Ang II increased endoglin expression significantly as compared with control cells. The specific extracellular signal-regulated kinase inhibitor SP600125 (JNK inhibitor), EGCG (100 mM), and c-Jun N-terminal kinase (JNK) siRNA attenuated endoglin proteins following Ang II induction. In addition, pretreated Ang II-induced endoglin with EGCG diminished the binding activity of AP-1 by EMSA. Moreover, the luciferase assay results revealed that EGCG suppressed the endoglin promoter activity in Ang II-induced CFs by AP-1 binding. Finally, EGCG and the JNK inhibitor (SP600125) were found to have attenuated endoglin expression significantly in Ang II-induced CFs, as determined through confocal microscopy. Following in vivo AMI-related myocardial fibrosis study, as well as immunohistochemical and confocal analyses, after treatment with endoglin siRNA and EGCG (50 mg/kg), the area of myocardial fibrosis reduced by 53.4% and 64.5%, and attenuated the left ventricular end-diastolic and systolic dimensions, friction shortening in hemodynamic monitor.

**Conclusions:** Epigallocatechin-3-O-gallate (EGCG) attenuated the endoglin expression and myocardial fibrosis in vitro and in vivo, the novel suppressive effect was mediated through JNK/ AP-1 pathway.

## P518

**Family support and self-care behaviors in individuals with heart failure: an integrative review**

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**Objective:** The purpose of this review is examine and synthesize recent literature regarding the relationship between social support and self-care behaviors in individuals with heart failure(HF).

**Background:** self-care is an important factor in maintaining health and well-being for individuals with heart failure. self-care behaviors are an integral component of self-care, and maybe impacted by the disease process of heart failure. However, family support may positively influence an individual's self-care behaviors by associated with activities associated with maintaining heart failure-related treatment regimens. This review will synthesize the current knowledge related to the influence of social support on heart failure self-care behaviors.

**Design:** Using and integrative review method, a review of current empirical literature was conducted utilizing CINAHL, Science Direct, and PubMed computerized databases for a period of January 2004 to December 2014.

**Results:** Family support appears to have a positive relationship on heart failure self-care behaviors, can also provide a variety of real and perceived resources including emotional support, instrumental support or tangible. Family plays an important role in helping people to maintain positive self-care behaviors. Despite the multidimensionality of the concept, should be focus on a support and often emotional support for self-care behaviors in heart failure patients.

**conclusion:** Family support is effective in engaging and decision- making related to self care behaviors in HF patients and self-confidence is a potential mediator of this relationship.

## P519

**Predictive model for in-hospital outcome in ST elevated myocardial infarction complicated with acute heart failure**

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**Introduction:** Acute ST elevated myocardial infarction (STEMI) represents often the underlying condition for the development of acute heart failure (AHF). The aim of this



study was to develop predictive model for in-hospital outcome in patients presenting with acute STEMI and AHF, after primary percutaneous coronary intervention (pPCI).

**Methods:** A total of 1495 patients with STEMI were admitted to our hospital and treated with pPCI during 36 months. In this study we analyzed 45 (3.01%) of them, which were presented with symptoms and clinical signs of AHF. Each patient was initially described using 386 attributes (clinical and demographic characteristics, biochemical analysis of blood parameters, echocardiographic parameters, and diagnosis codes). Model induction and evaluation was conducted within the widely used Waikato Environment for Knowledge Discovery.

**Results:** The in-hospital mortality was 26.67%. Mean age was  $65.87 \pm 10.84$ . Survivors were younger ( $64 \pm 10.88$  vs.  $68.33 \pm 10.81$ ,  $p=0.363$ ). Most subjects were male, 60.00%. Regarding to gender there wasn't statistically significant difference in those with in-hospital mortality (male 18.5% vs. female 38.9%,  $p=0.175$ ). There was 68.9% with previously hypertension, 53.4% diabetics and 46.63% with preserved left ventricular ejection fraction ( $\geq 45\%$ ). Model for predicting in-hospital mortality was developed by boosting the Decision Stumps machine learning algorithm (accuracy 82.2%, AUC=0.856). It is one of the simplest weak classifiers, which is a one-level decision tree. Boosting trained an army of Decision Stumps which each focus on one part of the characteristics of the data. Features selected as most important were: Left Ventricular Internal Diameter at end diastole (in survivors  $5.29 \pm 0.34$  vs. in those with lethal outcome  $5.49 \pm 0.578$ ;  $p=0.373$ ), Right Ventricular Systolic Pressure (lower values in survivors  $36.83 \pm 2.18$  vs.  $39.28 \pm 10.06$ ;  $p=0.566$ ), Fibrinogen (lower values in survivors  $3.44 \pm 0.722$  vs.  $4.94 \pm 1.62$ ;  $p<0.005$ ), Sedimentation (higher in those with lethal outcome  $10$  vs.  $34.83 \pm 22.79$ ;  $p=0.304$ ), time elapsed from pain occurrence to admission to hospital ( $334.29 \pm 283.25$  in survivors vs.  $223.89 \pm 153.70$  in those with lethal outcome;  $p=0.169$ ), Mitral Regurgitation (MR) (severe MR in 11.1% of patients) and present QS complexes (in 34.2% of patients).

**Conclusion:** Although selected features are not all statistically significant as standalone predictors, machine learning algorithm utilized their combination, so predictive model for in-hospital outcome with good predictive performances has been made and ready for usage in clinical practice.

## P520

### Predicting the development of cardiogenic shock in myocardial infarction

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**Purpose:** To develop a mathematical formula to calculate the risk of developing cardiogenic shock in patients with AMI.

**Methods:** We examined 55 patients with mi aged 56-85 years. The first group consisted of 29 patients (14 men and 15 women) at the age of  $66.8 \pm 1.2$  years, complicated by cardiogenic shock, second - 26 patients (15 men and 11 women) at the age of  $66.4 \pm 1.0$  years without cardiogenic shock. All admission underwent standard laboratory tests with dynamic assessment of the level of troponin I, D-dimer. Repeatedly recorded 12-lead ECG was performed the echocardiography, the coronary angiography on the unit of General Electric, was measured central hemodynamic parameters. The

**Results:** Patients in compared groups were matched for age, both groups were dominated by men. In the first and second groups of more than 60% of patients with IMPT (at 65.5% and 61.5%, respectively,  $p<0.05$ ). Patients with back, they were almost 2 times more in the 1st group (CABG) than in the second (10 (34.4%), against 5(19.2%), with 2/3 of them involved the right ventricle. More than 60% (62.2%) patients in the CABG group and 61.5% in the group without CABG was performed revascularization ISA. The "symptom-balloon" in the group with CABG when INT was 2 times longer and amounted to 420 minutes than in those without CABG (210,  $p<0.05$ ), which was an important factor determining the development of complications. Thrombolytic therapy is carried out 10 (52.6%) patients with INT in the 1st group and 6 (37.5%) patients of the second group. PCI completed 18(62%) patients of the first group and 14(53.8 percent) in the second. Pharmacoinvasive strategy (TLT+PCI) due to non-delivery of the patient in the first 120 minutes were used in 5(27.2%) patients of the first group and 4(15.4 %) second. Most patients of the 1st group, they developed in the first day, admission CABG were signs in 8(27.5%) patients. The garden in the first group at admission was less than during the second (96.5 % against 138.4,  $p<0.01$ ). To predict the development of shock on the obtained data was applied stepwise discriminant analysis selected the most important predictors of the development of CABG. For these factors amounted to equations linear discriminant functions for each group. To predict outcome in new patients of the equation 2 is calculated: Shock(+)= $-308,4 + 0,22 \cdot AD(p) + 4,47 \cdot Sat + 0,44 \cdot GFR - 0,32 \cdot Troponin + 0,61 \cdot Creatinine - 0,0011 \cdot income + 6,37 \cdot Potassium + 0,37 \cdot Glucose + 0,32 \cdot Hemoglobin$ ; Shock(-)= $-288,0 + 0,16 \cdot AD(p) + 4,21 \cdot Sat + 0,49 \cdot GFR - 0,22 \cdot Troponin + 0,66 \cdot Creatinine - 0,0014 \cdot income + 7,66 \cdot Potassium + 0,28 \cdot Glucose + 0,29 \cdot Hemoglobin$ . Each patient can be assigned to the group corresponding to the maximum value of the function, with a probability of 83.6 per cent.

**Conclusions:** Thus, a multivariate mathematical model based on the method of discriminant analysis to predict the development of shock.

## BASIC SCIENCE: CARDIOMYOPATHY

### P521

#### Endothelial leptin receptor signalling contributes to the development of cardiac hypertrophy and fibrosis following chronic pressure overload in mice

Deutsche Forschungsgemeinschaft

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**Background:** The adipokine leptin and its receptors are expressed in the heart, and leptin has been shown to promote cardiomyocyte hypertrophy and collagen production in fibroblasts. Leptin expression in cardiomyocytes increases after mechanical stretch, and heart failure in humans is associated with elevated serum leptin levels. In the past, it has been difficult to dissect any direct effects of leptin on the heart from those associated with its role in body weight regulation. Endothelial cells play an important role during cardiac remodelling processes, among others via secretion of paracrine factors acting on cardiomyocytes and other cells in the heart.

**Purpose:** To determine the role of endothelial leptin signalling for the cardiac remodelling in response to chronically increased pressure overload.

**Methods:** Cardiac hypertrophy was induced by transverse aortic constriction (TAC) in mice with inducible, endothelial-specific deletion of leptin receptors (End.LepR-KO) and controls (End.LepR-WT).

**Results:** Western blot analysis confirmed reduced leptin receptor expression in endothelial cells isolated from End.LepR-KO mice ( $24 \pm 5.1\%$  of controls). Survival after TAC did not differ between genotypes: i.e. 17 out of 37 (46%) End.LepR-WT and 14 out of 30 (47%) End.LepR-KO mice died within the observation period of 20 weeks ( $P=0.304$ ). Echocardiography revealed that endothelial leptin receptor deletion improved LV function ( $P<0.01$ ) and was associated with reduced LV dilation ( $P<0.01$ ) and cardiac hypertrophy ( $P<0.001$ ). Histological analysis demonstrated a significantly greater mean cardiomyocyte cross-sectional area in banded hearts from End.LepR-WT compared to End.LepR-KO mice ( $P<0.05$ ) as well as increased cardiac fibrosis, as determined by Masson trichrome ( $P<0.05$ ) and sirius red ( $P<0.01$ ) staining, whereas the number of CD31-positive endothelial cells was reduced ( $P=0.056$ ). Western blot analysis confirmed elevated leptin protein levels in banded hearts of WT mice (1.3-fold increase vs. sham), however, activated LepR signalling was observed only in End.LepR-WT mice and blunted in their End.LepR-KO counterparts, as indicated by reduced levels of phosphorylated STAT3 and total SOCS3 expression. Moreover, significantly increased cardiac levels of VCAM1 in End.LepR-WT, but not in End.LepR-KO mice suggested that endothelial leptin receptor deletion protects against the development of endothelial dysfunction. In line with the more pronounced cardiac hypertrophy observed echocardiographically and histologically in End.LepR-WT mice, cardiac levels of mTOR were significantly increased ( $2.4 \pm 0.6$ -fold change vs. sham), but not in End.LepR-KO mice ( $0.9 \pm 0.1$ -fold change vs. sham;  $P<0.05$ ).

**Conclusions:** Our findings suggest that activation of leptin signalling in endothelial cells, for example by elevated leptin produced in hypertrophic cardiomyocytes, contributes to pathological cardiac remodelling following chronic pressure overload.

### P522

#### Histologic and histometric characterization of myocardial fibrosis in end-stage hypertrophic cardiomyopathy: a clinical-pathological study of 30 explanted hearts

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**Background:** Myocardial fibrosis is frequently found by cardiovascular magnetic resonance (CMR) in hypertrophic cardiomyopathy (HCM), particularly in End-Stage HCM (ES-HCM) and showed to carry an ominous prognosis. Nonetheless, extent and distribution of fibrosis were never pathologically characterized.

**Objectives:** To assess overall amount, base-to-apex, circumferential and epicardial/endocardial distribution, pattern and type of myocardial fibrosis in a group of transplanted ES-HCM. To evaluate quantitative relationship between CMR and histometric assessment of fibrosis (subgroup analysis).

**Methods:** For each heart, a whole midventricular short-axis section (subdivided into 10 samples), three samples from basal and three from apical level were considered. Histomorphometric analysis was carried out.

**Results:** Thirty hearts examined. Overall Fibrosis: 37.3%. Left-Ventricular (LV) base-to-apex distribution (% of assessed myocardium): 31.9% basal, 43% medium and 46.2% apical level. Midventricular short-axis section: circumferential distribution (% of overall fibrosis within the section): anterior, anterolateral, inferolateral, inferior LV walls (11.9%; 15.8%; 7.0%; 24.3% respectively); anterior, medium and posterior septum (11%, 10.7%, 11.4% respectively); anterior and inferior Right-Ventricular walls (3.4%, 4.5% respectively). Midventricular short-axis section: epicardial-endocardial distribution (% of overall fibrosis within the section): trabecular 26.1%; subendocardial 20.2%; midwall 33.4%; subepicardial 20.3%. Main patterns identified: midwall 33.3%, transmural 23.3%, midwall and subepicardial 23.3%, midwall and subendocardial 20%. Fibrosis Type: replacement 53.3%, mixed 33.3% and perimycocyte interstitial fibrosis 13.3%. Comparison LGE-histological quantification of fibrosis: mean difference = 11%.

**Conclusions:** In hearts of ES-HCM undergoing heart transplantation the amount of myocardial fibrosis was very marked; there was a clear growing base-to-apex gradient. The most represented pattern was midwall, while subendocardium and subepicardium were never exclusively involved. The LV inferior and anterior walls and the entire septum are maximally affected, whereas the inferolateral wall was significantly spared. Replacement fibrosis was the predominant type and it was marked and typical of older patients. There was a good correlation between LGE-CMR and histometric quantification of fibrosis. These observations have numerous potential implications on the understanding of the HCM pathophysiology and on interpretation of imaging techniques.

## P523

### miR-181a mediates the effects of the CB1 inhibition on cardiac remodelling

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**Purpose:** The endocannabinoid system is increasingly studied in the cardiac field due to its role in fibrosis, inflammation and cell fate modulation. The deregulation of this system has been implicated in myocardial infarction (MI) and consequent heart failure development. A recent study suggests cannabinoid receptor 1 (CB1) inhibition to improve cardiac function and to reduce adverse remodelling in response to cardiac stress, but the exact underlying molecular mechanisms of these beneficial effects remain unknown. MicroRNAs (miRNAs, miRs) provide a complex layer of post-transcriptional regulation modulating key biological processes such as tissue remodelling in heart failure. The aim of the present study was to explore microRNA pathways in the chronic effect of CB1 receptor inhibition after angiotensin-fibrosis induction and left ventricular remodelling.

**Methods and Results:** Adverse cardiac remodelling was induced in mice by chronic administration of Angiotensin II (AngII, 1.5 mg/kg/day) with osmotic minipumps for 14 days. Treatment with CB1 antagonist, or vehicle was delivered every second day during the AngII administration period. Hemodynamic parameters were measured by echocardiography and cardiac pressure-volume catheter and tissue samples were taken for molecular and histological analysis. After two weeks of AngII infusion, left ventricular dysfunction was prevented by CB1 antagonist treatment. This was shown by significantly improvements of the myocardial performance index and end-diastolic pressure values. At the tissue level, anti-fibrotic effects of CB1 antagonist treatment were confirmed histologically and by expression analysis of pro-fibrotic genes. These beneficial effects were also observed in CB1 KO mice and in an aging mouse model. The particular role of tissue fibroblast in AngII-induced cardiac fibrosis was further explored. Primary cardiac fibroblasts (CF) from each experimental group were isolated and analysed by next generation deep RNA sequencing to identify differentially regulated microRNAs. MicroRNA-181a was downregulated by in vivo AngII delivery and vice versa upregulated after CB1 antagonist treatment. Foxb1 (a direct target of miR-181a) was differentially regulated, suggesting a possible mechanism of action for the benefits of CB1 receptor inhibition. Mir-181a KO mice confirm these results on a functional and molecular level.

**Conclusion:** We found that in AngII-induced cardiac remodelling, LV function is preserved by chronic CB1 antagonist treatment and that cardiac fibrosis is reduced with concomitant downregulation of pro-fibrotic genes. Also, CF-enriched miR-181a seems to be sensitive to CB1 antagonist treatment, thereby affecting cardiac fibrosis. The current study employs a novel concept regarding chronic CB1 inhibitor treatment and may provide important details and novel targets for anti-fibrotic approaches in heart failure.

## P524

### Pharmacological inhibition of sphingosine 1-phosphate receptor 2 (S1pr2) ameliorates pressure overload-induced cardiac hypertrophy and fibrosis in mice

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**Background:** S1P, a bioactive sphingolipid metabolite, tightly regulates cardiovascular functions via its receptors. It has been shown that S1P/S1Pr2 signaling regulated heart and vascular development. However, it is unknown whether S1pr2 regulates cardiac remodeling in pressure overload-induced heart failure. We aimed to investigate the effect of pharmacological inhibition of S1pr2 by JTE013 in a mouse model of pressure overloaded-induced cardiac hypertrophy.

**Methods:** We performed transverse aortic constriction (TAC) to induce pressure overload-induced cardiac remodeling in mice. We treated operated mice with 5 mg/kg/day S1pr2 antagonist, JTE013, or placebo (DMSO) i.p., respectively. We performed echocardiography to investigate cardiac hypertrophy and cardiac function. We also carried out histological analysis to study cardiac remodeling in TAC model.

**Results:** Echocardiography showed obvious myocardial hypertrophy in the TAC mice following 8 weeks of pressure overload of the heart (corrected LV Mass (AW): 71.83 ± 10.32 Sham group vs. 124.98 ± 10.81 TAC-DMSO group. P < 0.05), which is confirmed by measurement of heart weight (heart weight/body weight: 0.0059 ± 0.0002 Sham group vs. 0.0099 ± 0.0007 TAC-DMSO group. P < 0.05) and histological analysis of cardiomyocyte cross-sectional area (114 ± 3.1 square micrometer Sham group vs. 393 ± 12.2 square micrometer TAC-DMSO group. P < 0.05). Cardiac function was significantly reduced in TAC mice (ejection fraction (EF%): 75.23 ± 1.84 Sham group vs. 41.16 ± 5.33 TAC-DMSO group. P < 0.05). S1pr2 antagonist, JTE013, significantly attenuated cardiac hypertrophy (corrected LV Mass (AW): 124.98 ± 10.81 TAC-DMSO group vs. 91.98 ± 8.06 TAC-JTE013 group. P < 0.05), which was verified by post mortem analysis (heart weight/body weight: 0.0099 ± 0.0007 TAC-DMSO group vs. 0.0079 ± 0.0003 TAC-JTE013 group. P < 0.05; cardiomyocyte cross-sectional area: 393 ± 12.2 square micrometer TAC-DMSO group vs. 245 ± 15.6 square micrometer TAC-JTE013 group. P < 0.05), while JTE013 moderately improved cardiac function in pressure overloaded heart failure (ejection fraction (EF%): 41.16 ± 5.33 TAC-DMSO group vs. 49.01 ± 0.47 TAC-JTE013 group. P > 0.05). Our further Masson's Trichrome staining and Picro Sirius Red staining showed that cardiac fibrosis and collagen deposition in myocardium were significantly reduce in TAC-JTE013 group compared to TAC-DMSO group.

**Conclusions:** Our results demonstrate that inhibition of S1pr2 ameliorates cardiac hypertrophy and cardiac fibrosis in pressure overload-induced heart failure, suggesting that S1pr2 negatively regulates cardiac remodeling in chronic heart failure.

## P525

### Association of angiotensin-converting enzyme polymorphism with phenotype of hypertrophic cardiomyopathy

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**Introduction:** The factors that determine the morphological characteristics and the clinical course of patients with hypertrophic cardiomyopathy (HCM) are still unclear. Genetic polymorphisms may have influence on the different phenotypes found in these patients. The angiotensin-converting enzyme (ACE) gene deletion/insertion polymorphism, which has three distinct genotypes (II, ID, and DD) have been associated with differences phenotypic in HCM.

**Objectives:** The aim of this study was to determine the frequency of ACE genetic polymorphism in the population of patients of our University Hospital and to correlate with the types of hypertrophic cardiomyopathy.

**Methods:** We selected 43 consecutive patients with HCM from the Cardiomyopathy Unit, our University Hospital, and a State University. Echocardiographic 2D studies were performed according to the recommendations of the American Society of Echocardiography and DNA was extracted from blood samples for the polymerase chain reaction.

**Results:** We analyzed 43 patients with HCM (53.4% males and 46.6% females). ACE genotype DD was found in 23.2%, 16.2% ACE genotype II and 60.4% ACE genotype ID. Among the patients, 51.1% have non-obstructive asymmetric septal hypertrophy (NOASH), 27.9% obstructive asymmetric septal hypertrophy (OASH), 11.6% apical hypertrophic form and 9.3% other forms of HCM. Among patients with ACE genotype DD 40% have OASH, 30% NOASH, 20% apical form and 10% others types of hypertrophy. Patients with ACE genotype DI, 23% have OASH, 57.6% NOASH, 7.6% apical form and 11.5% others types. And with ACE genotype II, 28.5% have OASH, 57.1% NOASH, 14.2% apical form and none have another form of hypertrophy.

**Conclusion:** We observed that the ACE genotype DI was more frequent in HCM patients, followed by ACE genotype DD and ACE genotype II. These results are similar to the current available medical literature. The ACE genotype DI is more related to non-obstructive asymmetric septal hypertrophy. The ACE genotypes DD and II do not have any predominant form of hypertrophy.

## P526

### Study of a mouse with proximal titin A-band truncation reveals disease mechanisms and modifiers of titin dilated cardiomyopathy

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**Purpose:** 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 regulates sarcomere assembly, contraction, relaxation and signaling. Truncating mutations are overrepresented in the A-band. We engineered mice with titin A-band truncation (TTNΔA) and assessed cardiac phenotype and transcriptional profile.

**Results:** TTNΔA mice were generated by introducing lox-P sites flanking exons 276-277 and crossing with E1a-Cre mice, causing a frameshift and a premature stop codon in the TTN proximal A-band. 28 heterozygous intercrosses produced 120 pups: none were homozygous TTNΔA. Genotyping (n = 125) revealed homozygous embryos at E8.5 - E10.5, with fetal demise at E10.5. Heterozygous male and female mice (age 6-80 weeks) were viable, fertile and not different from wild type (WT) in appearance, activity, or echocardiographic phenotype. Pregnant heterozygous females showed no echocardiographic phenotype and produced similar litter size as WT. Transcriptional changes (RNA sequencing) and local sarcomere lesions (electron microscopy) at baseline (age 6-8 weeks, males) suggested that TTNΔA pre-disposed to disease. Voluntary cage-wheel running (two months) (n = 5-8 per study, males), angiotensin II or isoproterenol infusion (two weeks) evoked no echocardiographic differences in TTNΔA compared to WT. Double heterozygous TTNΔA LMNA knock-out, TTNΔA MYH6 F764L knock-in and TTNΔA PLN R9C transgenic mutation mice showed no exacerbation of DCM. Interestingly, upon thoracic aortic constriction (TAC, four weeks) TTNΔA mice showed exacerbated DCM and congestive heart failure. RNA sequencing of TTNΔA vs. WT TAC hearts showed differential expression (fold change > 1.5 / < 0.67, p < 0.001) of 1465 transcripts. Total TTN transcripts were reduced and mutant transcripts half that of WT transcripts (digital PCR) in TTNΔA TAC hearts, with no detection of mutant protein (titin gels and titin immunoblotting). rAAV9 delivery to WT pups in vivo (n = 12-15) of TTN RNAi targeting the TTN exon 276-277 junction, reduced TTN mRNA and protein to 30% and resulted in mortality and severe DCM, with degradation of myofibrils (electron microscopy). Pathway analyses of differentially expressed transcripts in TTNΔA TAC and TTN RNAi, i.e. titin DCM, implicated cardiotoxic pathways. Calcineurin-NFAT and TGFβ/Smad signaling were identified as central players in titin DCM, along with titin-associated mechanosensors FHL1 and ANKRD1 (pathway analyses and immunoblotting).

**Conclusions:** Homozygous TTNΔA mutation is embryonically lethal, while heterozygous mice show overt DCM upon pressure overload. TTNΔA transcripts are expressed but do not yield detectable mutant protein, suggesting haploinsufficiency as disease mechanism. Reduced titin level is sufficient to cause DCM.

## P527

### Lack of growth differentiation factor 15 aggravates adverse cardiac remodeling upon pressure-overload in mice

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**Background/introduction:** Growth differentiation factor 15 (GDF15) is a distant member of the TGF-β family. Under homeostatic conditions GDF15 is not highly expressed, however, upon injury GDF15 levels robustly increase. GDF15 influences many processes including inflammation, apoptosis and fibrosis. In a mouse model of myocardial infarction, GDF15 deficiency results in increased incidence of cardiac rupture. This detrimental effect on the healing process is most likely related to an exacerbated inflammatory response. In heart failure (HF) patients, GDF15 plasma levels are increased and high GDF15 levels are associated with a higher mortality. Despite this association, a causal role of GDF15 in adverse cardiac remodeling leading to HF is currently not very well established. We therefore aimed to study the role of GDF15 in a mouse model of non-ischemic HF development.

**Methods:** GDF15 knock-out (KO) mice and wild type (WT) mice underwent trans aortic constriction (TAC) with a 27 gauge needle. Correct placement of the TAC was confirmed by Doppler measurements of the carotid flow ratios. Cardiac function

and geometry was assessed using echo at baseline, 7, 28 and 42 days after TAC. At day 42 immunohistochemistry was performed to study cardiomyocyte hypertrophy (WGA) and influx of different leukocyte subtypes. Flow cytometry was performed at 42 days after TAC on cardiac lymph nodes (LN), blood and spleen to study the effect of GDF15 deficiency on leukocyte subtypes.

**Results:** GDF15 KO mice have significantly increased end diastolic volume (EDV) and end systolic volume (ESV) after 6 weeks of TAC compared to WT mice (EDV: 93 μl versus 64 μl, ESV: 72 μl versus 38 μl, p < 0.05). The increase of ESV is already present 7 days after TAC. GDF15 KO mice show increased heart weight/body weight ratios after 42 days of TAC compared to WT mice. (7.0 mg/g versus 9.2 mg/g, p < 0.01) Though this observation implies increased cardiac hypertrophy in GDF15 KO mice, we did not observe a difference in cardiomyocyte hypertrophy. Flow cytometry did not show any alterations in the amount or activation status of leukocytes in the blood, LN or spleen after 42 days of TAC. Conclusions GDF15 deficiency aggravates adverse cardiac remodeling upon pressure-overload. Volume increase, both EDV and ESV is accelerated in GDF15 KO mice compared to WT mice. These changes are already present after 7 days of TAC. Increased heart weight/body weight ratio in GDF15 KO mice is not related to an increased volume of individual cardiomyocytes. More in depth analyses are needed to provide a mechanistic explanation for the worsening of cardiac function in GDF15 KO mice.

## P528

### Bergamot polyphenols protect against doxorubicin-induced cardiomyopathy reducing ROS production and promoting myocyte survival

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**Background:** Doxorubicin (DOXO) is one of the most widely used antineoplastic drugs. Despite its highly beneficial effects against several neoplasias, the clinical use of DOXO has the serious drawback of cardiotoxicity, which over time causes a cardiomyopathy that leads to congestive heart failure. The molecular pathogenesis of anthracycline cardiotoxicity remains highly controversial, although the oxidative stress-based hypothesis involving intramyocardial production of reactive oxygen species (ROS) has obtained great interest. In this regard, dietary polyphenols, in particular flavonoids, play a cardiovascular protecting role due to their pleiotropic anti-oxidative and anti-inflammatory effects.

**Purpose:** Thus, we have investigated whether a rich mixture of flavonoids extracted from Bergamot (Citrus Bergamia Risso et Poiteau), the bergamot-derived polyphenolic fraction (BPF), could attenuate DOXO-induced cardiomyopathy in vivo.

**Results:** Here we show that BPF was able to prevent DOXO-induced LV impairment and myocardial strain dysfunction. Indeed, echocardiographic assessment demonstrated that BPF administration in DOXO+BPF group significantly reduced LV end-systolic diameter (LVESd), LV end-diastolic diameter (LVEDd), improving both ejection fraction (EF) and fractional shortening (FS) compared to DOXO-treated rats. BPF was also able to prevent time-to-Peak (TPK) delay of cardiac strain and strain rate and dyssynchrony of radial motion in short axis when compared to DOXO group.

Histological analysis of DOXO+BPF-treated rats revealed a significant reduction of myocyte apoptosis, accompanied by a decrease in reactive myocyte hypertrophy and myocardial fibrosis compared to DOXO-treated rats. Moreover, cardiomyocytes isolated from DOXO-treated rats showed a slight increase in Akt phosphorylation which was associated with a strikingly increase in p38 phosphorylation compared to control rats. Importantly, phospho-Akt was significantly increased by BPF co-treatment, which, at the same time, reduced p38 phosphorylation compared to DOXO-treated rats.

Finally, we found that BPF significantly prevent 8-OHdG (marker of oxidative damage of DNA) nuclear accumulation in cardiac tissue and counteracts the increase in lipid peroxidation, tyrosine nitration of cardiomyocytes isolated from DOXO-treated rats.

**Conclusion:** BPF reduces DOXO-induced cardiotoxicity by decreasing ROS production and myocyte apoptosis that lead to a significant improvement of cardiac function. These data suggest that BPF may be used as a promising cardioprotective agent in patients undergoing anthracycline chemotherapy.

## P529

### Programmed cell death-1 antigen as a potential mechanism of the pathogenesis of idiopathic dilated cardiomyopathy

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**Introduction:** Programmed cell death-1 (PD-1), is expressed on activated T cells, and delivers inhibitory signals. Little is known about the role of cellular immunity in the pathogenesis in idiopathic dilated cardiomyopathy (IDCM). The aim of the study was to assess an expression of PD-1 on CD4+ T and CD8+ T lymphocytes in patients with IDCM.

**Material and methods:** We studied 50 IDCM patients and 20 healthy persons. Mononuclear cells were isolated from peripheral blood, incubated with appropriate fluorochrome-conjugated monoclonal antibodies and analyzed with a flow cytometer.

**Results:** Increased proportion of PD-1+ cells was detected from CD4+ T cells in patients than in controls ( $6.98 \pm 3.29\%$  vs.  $4.82 \pm 1.37\%$ ,  $p < 0.001$ ). Similarly, the expression of PD-1 in CD8+ T cells was also significantly upregulated in IDCM patients compared with controls ( $7.02 \pm 1.03\%$  vs.  $3.99 \pm 1.32\%$ ,  $p < 0.001$ ). Patients with ejection fraction lower than 30% had higher frequencies of both PD-1+ lymphocyte subsets than other patients ( $13.06 \pm 4.92\%$  vs.  $5.93 \pm 1.75\%$ ,  $p < 0.001$ ).

**Conclusions:** The study identified that expression of PD-1 was upregulated on CD4+ T and CD8+ T cells from IDCM patients. Moreover the percentage of PD-1+ cells was extremely high in patients with low ejection fraction. Our data suggest a potential mechanism of the pathogenesis of IDCM.

### P530

#### CaMKII beta isoform induced dilated cardiomyopathy and heart failure

CIHR

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The calcium calmodulin dependent protein kinase II b4 isoform (CaMKIIb4) is a muscle specific isoform of the CaMKII family of protein kinases which is also expressed at low levels in myocardium. CaMKIIb4 isoform is the most abundant and its activation is implicated in cardiac hypertrophy/failure. We generated transgenic (tg) mice lines with specific expression of CaMKIIb4 in postnatal myocardium to examine its impact on structure and function. Echocardiography indicated a dose and time dependent depression of fractional shortening, ejection fraction and cardiac output in tg mice. In high CaMKIIb4 expressers a marked increase in left ventricular internal diameter and a decrease in wall thickness with a ~70% decrease in cardiac function was noted at 6 weeks post birth. The level of CaMKIIb4 activation (phosphoThr-287) impacted the severity and temporal appearance of myocardial dysfunction in tg mice. qPCR analysis indicated that the fetal gene program was activated and Western blot analysis indicated that the expression of proteins involved in calcium transport at the SR were significantly depressed in Tg myocardium. CaMKIIb4 also inhibited the activity of CaMKII $\delta$  and resulted in a unique dilated cardiomyopathy. These data suggest that a cross talk between specific CaMKII isoforms induces distinct cardiomyopathies.

### P531

#### Assessment of peripheral blood T, NK and NKT-like cells in patients with idiopathic dilated cardiomyopathy

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**Introduction:** Although chronic myocardial inflammatory process mediated by viral/bacterial and autoimmune factors has been postulated in the pathogenesis of idiopathic dilated cardiomyopathy (IDCM), the role of immune mechanisms still remains unclear.

The aim of the study was to assess the frequencies of peripheral blood T, NK and NKT-like cells in patients with IDCM.

**Material and methods:** We studied 50 IDCM patients and 20 healthy persons. Percentages of NK and NKT-like cells were evaluated with flow cytometry using monoclonal antibodies: anti-CD3/FITC, CD16/CD56/PE, CD45/PerCP (BD Biosciences), which allowed for simultaneous assessment of CD3+T lymphocytes and NK (CD16+CD56+) cells. During analysis, the CD3+CD16+CD56+ population was also determined. Immunofluorescence studies on T cell subsets were performed using a combination of the following mAbs: CD3/FITC, CD19/PE, CD8/FITC, CD4/PE, purchased from R&D Systems. Statistical analysis of the results was conducted using Statistica 9.0. A value  $p$  less than 0.05 was considered statistically significant.

**Results:** The mean frequency of CD3+CD56+CD16+ NKT-like cells in the peripheral blood of patients with IDCM was  $10.93\% \pm 11.02\%$  and this value was significantly lower in comparison to the control group ( $21.15\% \pm 9.08\%$ ,  $p = 0.0005$ ). The mean percentage of CD56+CD16+ NK cells in the group of patients was  $14.67\% \pm 6.89\%$ , and was significantly higher compared to the healthy controls ( $4.71\% \pm 2.99\%$ ,  $p = 0.000002$ ). The mean percentage of CD3+ T lymphocytes in the peripheral blood of patients with IDCM was  $67.91\% \pm 16.56\%$  and was significantly higher in comparison to the control group ( $51.7\% \pm 24.12\%$ ,  $p = 0.02$ ). The mean percentage

of CD8+ T lymphocytes in the study group was  $28.89\% \pm 11.68\%$  and was significantly higher in comparison to the healthy controls ( $18.72\% \pm 6.86\%$ ,  $p = 0.001$ ).

**Conclusions:** Our findings of the abnormalities in immune cells distribution in peripheral blood of IDCM patients suggest that IDCM development and progression is related to the dysregulation of the immune system.

### P532

#### Patients with diabetes mellitus subjected to PCI during hospitalisation.

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The aim of investigation was to reveal clinical - demographic characteristics of patients (pts) with non-ST-elevation acute coronary syndrome (NSTEMI-ACS) and diabetes mellitus (DM) subjected to PCI during hospitalization in 2014 - 2015.

**Methods:** We observed 120 pts with NSTEMI-ACS, among them DM in 27 (23%) pts. Monitoring of patients continued 6-18 months.

**Results:** Among 27 pts with NSTEMI-ACS and DM prevailed aged group 60-69 years, 59% (16) males. Smoking was registered in 4 (15%) pts with NSTEMI-ACS and DM (less than in non-diabetic NSTEMI-ACS pts,  $p = 0.002$ ). The following risk factors were observed: arterial hypertension - 93% (25) pts, BMI  $\geq 25$  - 93% (25) pts, family history of cardiovascular disease - 19 (70%) pts (more frequent than in non-diabetic NSTEMI-ACS pts,  $p = 0.002$ ). Previous myocardial infarction was in 37% (10) of pts, 10 pts (37%) had previous PCI. Pts received oral hypoglycemic drugs (80.0%), insulin (20%). Ischemic changes of ECG were determined in 56% (15) pts. The level of troponin T at admission  $> 0.05$  ng/ml was detected in 56% of pts. The level of glucose at admission was  $9.3 \pm 0.7$  mmol/l (in pts without DM -  $5.7 \pm 0.14$  mmol/l). Average LDL-C level was  $3.0 \pm 0.2$  mmol/l, LDL  $> 1.8$  mmol/l was registered in 78% (21) of pts. All admitted pts received anticoagulants and dual antiplatelet therapy (aspirin in conjunction with either clopidogrel or ticagrelor),  $\beta$ -blockers, statins. In pts with NSTEMI-ACS and type 2 DM risk of adverse cardiovascular events during hospitalization (GRACE) was higher ( $p = 0.038$ ) than in those without DM. Coronary stenosis  $> 55\%$  revealed in 100% of patients, multivessel disease in 81% (22) pts, in 6 (22%) pts was determined stent stenosis de novo. One-vessel coronary disease was revealed in 7.5% of pts, two-vessel disease - 15.8% pts. Balloon angioplasty with stenting was performed in all pts. In pts with NSTEMI-ACS unstable angina was diagnosed in 60 pts, myocardial infarction was revealed in 60 pts. During hospitalization there were no lethal outcomes, one case of non-fatal ischemic stroke was observed on the 2-d day of hospitalization, in 2 pts was registered non-fatal myocardial infarction, in 1 patient - early postmyocardial infarction. In 3 non-diabetic NSTEMI-ACS pts unstable angina was observed, in 2 pts - early postmyocardial infarction. The development of combined end point (death from myocardial infarction, unstable angina, myocardial infarction) in pts with NSTEMI-ACS and DM was significantly earlier than in non-diabetic NSTEMI-ACS pts ( $p < 0.008$ ). Thus, risk of cardiovascular events during hospitalization and observation (6-18 months) in pts with NSTEMI-ACS and DM was significantly higher than in non-diabetic NSTEMI-ACS pts. So, DM is considered to be an important risk factor of ischemic heart disease progression.

### P533

#### Microrna-155 promotes myocardial microvascular endothelial activation in septic cardiomyopathy

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**Purpose:** Septic cardiomyopathy remains a leading cause of death in critically ill patients and its pathophysiology remains poorly understood. Myocardial edema and inflammatory cell recruitment to interstitial space are proposed mechanisms underlying sepsis-induced contractile dysfunction. In previous experiments we have localized miR-155 expression in septic myocardium mainly to the microvascular (MV) endothelial cells. The aim of this work was to evaluate the role of miR-155 in myocardial endothelial activation.

**Methods:** 1) Experimental sepsis was induced using LPS injection in WT ( $n = 20$ ) and miR-155 $^{-/-}$  (KO;  $n = 20$ ) male mice. Cardiac function was evaluated through echocardiography. Myocardial expression of NOS, PKG activity and cGMP and NOx content was evaluated. Cardiac MV permeability was assessed with Evans blue-albumin leaking and myocardial water content. Mouse cardiac MV endothelial cells (MCMVEC) were isolated with FACS. Quantification of miR-155, cytokine mRNA profile and adhesion molecules was performed. 2) Human cardiac MV endothelial cells (HCMVEC) were transfected with anti-miR-155 or scramble LNA probe and incubated with LPS (100ng/mL) or vehicle for 24h. Evaluation of cytokine mRNA profile, NOS expression, NOx and adhesion molecules was performed. Monocyte adhesion assay was performed using Dil-stained THP1 cells. 3) MiR-155 expression, inflammatory cell infiltration and interstitial space area were assessed in post-mortem myocardial samples from septic shock patients ( $n = 28$ ).

**Results:** LPS exposure increased miR-155 expression in the myocardium, MCMVEC and HCMVEC. KO mice presented with attenuated LPS-induced cardiac dysfunction, MV permeability, NOS2 expression, PKG activity and cGMP and NOx levels, compared with WT. KO MCMVEC presented with attenuated LPS-induced cytokine expression and adhesion molecules, compared with WT cells. Mir-155 inhibition in HCMVEC prevented LPS-induced overexpression of cytokines and adhesion molecules, nitric oxide production and monocyte adhesion, through SOCS1-mediated inhibition of STAT3 and NF-κB signaling pathways. In human samples, miR-155 expression correlated with leukocyte infiltration and interstitial area fraction.

**Conclusions:** Endothelial miR-155 is upregulated in septic cardiomyopathy. MiR-155 knockout attenuates LPS-induced myocardial dysfunction, edema and MV permeability. In EC, miR-155 inhibition blunted LPS-induced nitric oxide production, cytokine and cell adhesion molecules overexpression. Our results suggest an important role of endothelial miR-155 in septic cardiomyopathy and reinforces its attractiveness as a therapeutic target.

**P534**

**Distinct cardiac response to chronic pressure-overload in type 1 and type 2 diabetic rats**

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**Introduction:** Diabetic cardiomyopathy is characterized by myocardial changes in the left ventricle (LV) induced by diabetes mellitus (DM) even in the absence of other comorbidities. The pathophysiology differs in type 1 DM (DM1) and type 2 DM (DM2) individuals: DM1 induces predominantly systolic alterations while DM2 triggers mostly diastolic dysfunction. However, the exact underlying mechanisms remain unclear. The association between DM and pressure overload, such as in hypertension or valve stenosis, is frequent and accelerates the cardiac injuries imposed by DM. We aim to evaluate biventricular structural and functional changes in DM1 and DM2 rats subjected to chronic pressure-overload (CPO).

**Methods:** Wistar rats with 7 weeks were distributed into 2 groups: DM1 (streptozotocin 60mg/kg; control group CTRL1) and DM2 (hypercaloric diet group; control group CTRL2 regular diet). Half of these animals were subjected to CPO by aortic banding (DM1+BA e DM2+BA). 8 weeks later heart biventricular function was evaluated and samples were collected to molecular and morpho-histological studies and isolated cardiomyocytes functional evaluation.

**Results:** As previously described the DM1 and DM2 induced remodeling in both ventricles with cardiac hypertrophy and increased fibrosis deposition. The simultaneous presence of CPO resulted in the elevation of LV systolic pressure. However, compared with DM2, DM1 promoted a higher increase of fibrosis, increased RV passive tension and impaired of LV relaxation. On the other hand DM2 impacted especially the RV, promoting increased systolic pressure and impaired relaxation. When combined with CPO, DM2 aggravated cardiac hypertrophy and myocardial stiffness, as assessed by LV cardiomyocytes passive tension and end-diastolic pressure.

**Conclusions:** This study demonstrates that both types of diabetes induce distinct cardiac alterations per se and when combined with chronic pressure overload. DM1 promoted a more pronounced extracellular matrix remodeling (cardiomyocyte hypertrophy and fibrosis deposition) when compared with DM2, whereas DM2 had a higher impact in myocardium function, either from LV and RV. The concomitant presence of CPO worsens the myocardium deposition of fibrosis promoted by DM1, having no impact on DM2.

**P535**

**Use of two-dimensional "2D" stain imaging for early detection of iron overload cardiomyopathy in polytransfused patients.**

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**Introduction:** Iron overload cardiomyopathy in polytransfused patients is characterized by a restrictive cardiomyopathy with early diastolic dysfunction and a late systolic dysfunction.

**Purpose:** The aim of this study is to determine the value of the two-dimensional "2D" stain imaging in the early detection and screening of iron overload cardiomyopathy.

**Methods:** This is a case-control study comparing eleven polytransfused patients followed at Hedi Chaker's hematology department and twenty apparently healthy patients randomly selected. All patients underwent conventional transthoracic echocardiography with an analysis of myocardial deformation "speckle-tracking" or two-dimensional "2D" stain imaging in the cardiology department of the same hospital.

**Results:** Our patients mean age was 58.4 years (19, 80) with a sex ratio of 1.75. Diseases treated in the long-term by transfusions was myelodysplastic syndrome in 8 cases, thalassemia major in 2 cases and myelofibrosis in one case. All patients received more than 20 red blood cells units. The majority of patients were asymptomatic (10/11). Mean left ventricular ejection function was 59.9%. The S wave in the lateral mitral annulus was 9.7 ± 2.1 cm/s. Diastolic function was preserved in 10 patients. The global longitudinal strain was -18.5 % ± 3.2 with a significant difference from the control group (-20.8% ± 2.05), p = 0.02. There is a significant correlation between the number of red blood cells units received and the global longitudinal strain (p = 0.019).

**Conclusion:** The two-dimensional "2D" stain imaging is a new noninvasive technique that can better assess the real state of left ventricular function. In our study we found a significant decrease in global longitudinal strain in polytransfused patients compared to controls. Our results confirm the value of this new technique in the early detection of iron overload cardiomyopathy.

**P536**

**Resveratrol attenuates diastolic dysfunction by reducing cardiac fibrosis in a model of doxorubicin cardiomyopathy**

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**Background:** Clinical benefits of doxorubicin (DOXO) are limited by cardiotoxicity that has been linked to oxidative stress, cardiomyocyte death and increased fibrosis. Diastolic dysfunction that represents less studied aspect of anthracycline cardiomyopathy, results in part from increased myocardial fibrosis and stiffness. ROS trigger not only cardiomyocyte death with reactive inflammation and fibrosis but also mediate TGF-β-dependent cardiac fibroblasts activation.

**Purpose:** To determine whether resveratrol (RES), a direct SIRT1 activator, might improve cardiac function by interfering with adverse myocardial remodeling resulted from myocyte loss and activation of pro-fibrotic pathways in a model of DOXO cardiomyopathy.

**Methods:** F344 rats received a total of 15 mg/kg DOXO over 2 weeks or DOXO and RES (2.5 mg/kg/day).

**Results:** In DOX-treated rats, increased myocardial stiffness correlated with fibroblast activation and collagen deposition. Treatment with RES resulted in reduced fibrosis and fibroblast activation and, most importantly, reduced the mortality rate. Co-treatment with RES significantly ameliorated end-diastolic pressure/volume relationship and improved ±dP/dt, indices of diastolic function. The activation of p53 and the level of myocyte death were reduced by RES. Myocardial upregulation of BNP was counteracted by RES administration. Interestingly, cardiac fibroblasts isolated from DOXO-treated rats had elevated levels of TGF-β and an increased phospho-SMAD3/SMAD3 ratio. The expression of fibroblast activate protein 1α and α-SMA, markers of activated fibroblasts was also augmented showing that in vivo exposure to DOXO generates pro-fibrotic population of activated cardiac fibroblasts. In contrast, RES determined decreased levels of TGF-β and phospho-SMAD3/SMAD3.

**Conclusions:** Our study indicates that SIRT1 activation supports animal survival and cardiac function by interfering with myocyte loss and interstitial fibroblast activation that contribute to DOXO-induced myocardial remodeling.

Structural and functional data	CTRL1		DM1-BA		DM2-BA	
	mean ± SEM	range	mean ± SEM	range	mean ± SEM	range
Heart wt (g/100g)	3.28±0.07	3.04-3.54	3.33±0.10	3.04-3.58	3.49±0.10	3.24-3.77
LV wt (g/100g)	0.79±0.07	0.62-0.94	0.82±0.07	0.67-0.97	0.89±0.10	0.72-1.07
RV wt (g/100g)	0.47±0.03	0.37-0.58	0.49±0.04	0.39-0.61	0.51±0.05	0.41-0.67
LV wall thickness (mm)	1.17±0.03	1.05-1.29	1.21±0.04	1.08-1.34	1.25±0.05	1.12-1.38
RV wall thickness (mm)	0.84±0.02	0.74-0.94	0.86±0.03	0.76-0.96	0.88±0.04	0.78-1.00
LV end-diastolic volume (ml)	2.68±0.12	2.27-3.09	2.73±0.13	2.32-3.14	2.78±0.14	2.37-3.19
RV end-diastolic volume (ml)	1.45±0.07	1.25-1.65	1.48±0.08	1.28-1.68	1.51±0.09	1.31-1.71
LV stroke volume (ml)	1.45±0.07	1.25-1.65	1.48±0.08	1.28-1.68	1.51±0.09	1.31-1.71
RV stroke volume (ml)	0.84±0.04	0.74-0.94	0.86±0.05	0.76-0.96	0.88±0.06	0.78-1.00
LV end-systolic volume (ml)	1.23±0.05	1.02-1.42	1.25±0.06	1.04-1.44	1.27±0.07	1.06-1.46
RV end-systolic volume (ml)	0.61±0.03	0.51-0.71	0.62±0.04	0.52-0.72	0.63±0.05	0.53-0.73
LV fractional shortening (%)	33.9±1.2	28.2-39.6	34.1±1.3	28.4-39.8	34.3±1.4	28.6-40.0
RV fractional shortening (%)	20.7±0.8	17.4-24.0	20.8±0.9	17.5-24.1	20.9±1.0	17.6-24.2
LV end-diastolic pressure (mmHg)	11.7±0.4	9.1-14.3	12.1±0.5	9.5-14.7	12.5±0.6	9.9-15.1
RV end-diastolic pressure (mmHg)	10.8±0.3	8.2-13.4	11.2±0.4	8.6-14.0	11.6±0.5	9.0-14.4
LV end-systolic pressure (mmHg)	117.5±4.0	91.0-144.0	118.2±4.1	91.5-144.5	118.9±4.2	92.0-145.0
RV end-systolic pressure (mmHg)	118.4±3.2	91.8-145.0	119.1±3.3	92.2-145.5	119.8±3.4	92.5-146.0
LV dP/dt (mmHg/s)	2780±87	2242-334	2824±90	2248-336	2868±93	2250-338
RV dP/dt (mmHg/s)	1395±10	1310-153	1412±11	1325-154	1429±12	1338-155
LV passive tension (mmHg)	18.8±1.0	15.7-22.0	19.2±1.1	16.1-22.1	19.6±1.2	16.2-22.2
RV passive tension (mmHg)	11.8±1.2	8.4-16.2	12.2±1.3	8.7-16.3	12.6±1.4	9.1-16.4
LV active tension (mmHg)	96.7±3.1	84.2-108.4	97.0±3.2	84.5-108.5	97.3±3.3	84.8-108.6
RV active tension (mmHg)	57.9±2.0	49.4-66.4	58.2±2.1	49.7-66.5	58.5±2.2	49.9-66.6
LV compliance (ml/mmHg)	0.21±0.01	0.18-0.24	0.21±0.01	0.18-0.24	0.21±0.01	0.18-0.24
RV compliance (ml/mmHg)	0.15±0.01	0.13-0.17	0.15±0.01	0.13-0.17	0.15±0.01	0.13-0.17

## P537

**Blocking the N-terminal domain of midkine attenuates acute inflammation and prevents pathological remodelling and heart failure in experimental autoimmune myocarditis**S Stefan Brunner<sup>1</sup>; L Weckbach<sup>1</sup>; A Uhl<sup>1</sup>; U Grabmaier<sup>1</sup><sup>1</sup>University Hospital Grosshadern, Munich, Germany

Rationale: Midkine plays a critical role for the recruitment of polymorphonuclear cells. Nevertheless, its role in acute myocarditis and progression to inflammatory dilated cardiomyopathy (IDCM) has not been clearly defined.

**Objective:** To investigate the effect of an antibody against midkine on inflammatory cell recruitment and disease progression in the mouse model of Experimental Autoimmune Myocarditis (EAM).

**Methods and Results:** EAM was induced by immunization of BALB/c mice with heart-specific myosin-alpha heavy chain peptide together with Complete Freund's adjuvant. An antibody directed versus the N-terminal domain of midkine was administered from day 0 until day 21. As evidenced by histopathology, EAM severity scores at peak of inflammation were significantly reduced in antibody-treated mice. Accordingly, flow cytometry revealed reduction of CD45+ cells as well as distinct subsets such as monocytes/macrophages, polymorphonuclear cells and T cells. Further, antibody-treatment protected mice from progressive cardiac fibrosis and heart failure at later stages. Interestingly, treatment with an antibody directed versus the C-terminal domain of midkine did not attenuate acute inflammation during EAM.

**Conclusion:** Our findings provide in vivo evidence, that blocking the N-terminal but not the C-terminal midkine domain attenuates acute inflammation and prevents pathological remodelling and heart failure progression after acute myocarditis.

## P538

**The role of autophagy in alcoholic cardiomyopathy**

PON03PE\_00078\_1; PON03PE\_00078\_2

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Alcoholic cardiomyopathy represents one of the major clinical complications in chronic alcoholics being accompanied by significant impairment of the myocardial structure, cardiac remodeling and cardiomyocyte hypertrophy. On the other hand, chronic alcohol consumption, leads to alterations of mitochondrial structure and function in cardiac cells, decreased protein synthesis, impairment of the myofibrillar architecture, myocardial contractile dysfunctions and dilatation of the sarcoplasmic reticulum. Besides these evidences, the pathophysiological mechanism underlying cardiomyocyte alterations subsequent to chronic exposure to ethanol still remains to be elucidated. An exaggerated, ROS-dependent autophagic response has been suggested at the early stages of alcoholic cardiomyopathy, though the mechanism is still unclear. Here we investigated on the potential role of overproduction of ROS and autophagy in rat cultured cardiomyocytes undergoing chronic alcohol exposure.

Chronic exposure of H9c2 cardiomyocytes to ethanol (500 and 1000  $\mu$ M) failed to produce direct impairment of cell viability as detected by trypan blue and MTT assay, thus confirming previous data showing that ethanol exposure leads to cell death at higher concentrations. However, the effect of ethanol was accompanied by significant dose-dependent increase of ROS generation in cardiomyocytes. Moreover, immunoblot experiments indicated that a 500 and 1000  $\mu$ M ethanol exposure for 12 days caused a statistically significant dose-dependent increase of Beclin 1 expression compared to the control, thus indicating that autophagic response occurs early in the development of ethanol-induced cardiomyopathy at sublethal ethanol concentrations. The relationship between ROS overproduction and the occurrence of autophagy due to ethanol exposure was confirmed by experiments carried out in the presence of the peroxynitrite decomposition catalyst MnTBAP. Indeed pre-treatment of H9c2 cells with MnTBAP decreased ROS levels as well as ethanol-induced autophagy is expressed by the decrease of Beclin 1 expression.

Thus, our data showed that chronic ethanol exposure of cultured cardiomyocytes causes ROS accumulation which supports protective autophagy. This effect occurs in the absence of cardiomyocyte death, suggesting a reversible stage of the disease. Exhausting protective autophagy leads to further oxidative stress and finally, apoptotic death of cardiomyocytes, thereby generating alcoholic cardiomyopathy and the subsequent heart failure.

## P539

**Toxic effects produced by acute exposure to methylmercury in cardiomyocyte**

PON03Pe\_00078\_1; PON03Pe\_00078\_2

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Methylmercury is the most common and toxic form of organic mercury. In particular, fish products are the main source of methylmercury in the diet. For decades, the toxic effects of mercury were associated mainly with neurological disorders and nephropathy. Recent studies have suggested that methylmercury exposure leads to an increased risk of cardiovascular disease, increased vascular resistance alongside with an elevation of blood pressure.

The mechanism of mercury-induced cardiotoxicity is not fully elucidated. However, an increased oxidative stress via NADPH oxidase activation has been suggested to play a role.

Here, we investigated on the toxic effects subsequent to acute exposure to methylmercury in cardiomyocytes. In particular we found that exposure of the cell line H9c2 to methylmercury (0.5, 1, 5, 10, 25, 50, 75 and 100  $\mu$ M) for 24 hours produced a dose-dependent cell death. Flow cytometric analysis showed that the treatment with methylmercury at lower concentration (25  $\mu$ M) determined early apoptotic death; higher concentrations (75 and 100  $\mu$ M) of methylmercury produced a late apoptosis. This was confirmed by detection of caspase 3, a biomarker of apoptotic cell death, which was overexpressed after exposure of cardiomyocytes methylmercury, (25 e 50  $\mu$ M). Moreover, methylmercury 10 and 25  $\mu$ M produced an arrest in phase S/G2M of cardiomyocyte cell cycle, thus confirming heavy metal-related cardiomyocytes to undergo apoptotic cell death.

Thus, methylmercury leads to apoptotic cell death accompanied by oxidative stress and this may represent the basis for a better understanding and treatment of heavy metal-related cardiomyopathy.

## P540

**Peripartum cardiomyopathy : clinical pictures and prognosis about 10 cases**H Habiba Drissa<sup>1</sup>; MERIEM Drissa<sup>1</sup>; MERIEM Drissa<sup>1</sup>; MERIEM Drissa<sup>1</sup>; MERIEM Drissa<sup>1</sup>; MERIEM Drissa<sup>1</sup>; MEHDI Cheour<sup>1</sup>; MEHDI Cheour<sup>1</sup>; MEHDI Cheour<sup>1</sup>; MEHDI Cheour<sup>1</sup>; HAJER Malek<sup>1</sup>; HAJER Malek<sup>1</sup>; HAJER Malek<sup>1</sup>; HAJER Malek<sup>1</sup>; HAJER Malek<sup>1</sup><sup>1</sup>La Rabta University Hospital, adults cardiology, Tunis, Tunisia

**Introduction:** Peripartum Cardiomyopathy (PPCM) is a rare type of heart failure of unknown cause occurring late in pregnancy or in the postpartum period. Unfortunately, PPCM is a disease whose underlying etiology and natural history remain completely understood. only a few case series have been published to date

**Purpose:** is to describe the clinical pictures and prognosis of PCCM Results we reported a cases of 10 women hospitalized in a department hospital , the mean age was 32 years ,7 patients were multiparous. Caesarean section was performed in 6 cases , 2 patients had severe preeclampsia. The main presenting symptom was congestive heart failure with acute pulmonary edema. Only in one case. Electrocardiogram (ECG) showed tachycardia ; Furthermore, in all the ten cases, cardiac ultrasound showed a left ventricular diastolic diameter of more than 58 mm and a shortening fraction of or less than 25 %(25-40%). The treatment administered to these patients included bed rest, oxygen ,Intravenous diuretics , than converting enzyme inhibitors. In one case, circulatory support for hemodynamic instability in spite of inotropic therapy was required. Six patients got well with clinical recovery and echocardiography normalization of left ventricular parameters but 3 women had persistent signs of chronic heart failure and ultrasound signs of left ventricular dysfunction. We reported one case of death due to a refractory heart failure.

**Conclusion:** PCCM is an uncommon complication of pregnancy with unknown cause and potentially life-threatening complications. Echocardiography appears to be extremely valuable in diagnosing PPCM, formulating prognosis of recovery and following the course of the disease which is still a mystery.

## P541

**Role of S100A8 and S100A9 alarmins in Cocksackievirus B3-induced myocarditis**I Mueller<sup>1</sup>; S Van Linthout<sup>1</sup>; T Vogl<sup>2</sup>; B Pieske<sup>3</sup>; C Tschoepe<sup>3</sup>

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**Background:** The alarmins S100A8 and S100A9 are danger-associated molecular pattern molecules and have been shown to be of importance in several cardiovascular disorders. Their role in myocarditis has not been explored yet.

**Purpose:** The aim of the present study was to investigate the role of S100A8/S100A9 in biopsy-proven myocarditis patients and in experimental CVB3-induced myocarditis.

**Methods:** S100A8/A9 serum concentrations (ng/ml) were evaluated in myocarditis (n=8) and control (n=11) patients. S100A8 and S100A9 mRNA expression was analyzed in endomyocardial biopsies (EMBs) of CVB3+ patients (n=5), who eliminated the virus over time. S100A9 knock down (-/-) and wild-type (wt) C57BL/6



mice were i.p. infected with 5 x 10 and 5 p.f.u. of CVB3. A subgroup of S100A9<sup>-/-</sup> CVB3 mice was additionally i.p. injected with S100A8 every 2 days. Seven days after infection, mice were hemodynamically characterized and left ventricles (LV) were isolated. To further assess the role of both alarmins, CVB3-infected HL-1 cardiomyocytes and cardiac fibroblasts were supplemented with S100A8 or S100A9.

**Results:** S100A8/9 serum concentrations were 2.2-fold ( $p < 0.05$ ) higher in myocarditis versus control patients. S100A8 and S100A9 mRNA expression in EMBs dropped over time in CVB3+ patients who spontaneously healed, whereas LV S100A8 and S100A9 mRNA expression was 13.4-fold and 12.1-fold higher in CVB3-infected vs control mice ( $p < 0.0005$ ). S100A9<sup>-/-</sup> CVB3 mice exhibited an improved LV function compared to CVB3 wt mice. CVB3 copy number was 2.3-fold ( $p < 0.05$ ) lower in S100A9<sup>-/-</sup> CVB3 mice compared to their wt CVB3 littermates. S100A9<sup>-/-</sup> CVB3 mice further displayed 2.9-fold and 2.1-fold lower LV myeloperoxidase activity and Ly6G mRNA levels versus CVB3 wt mice ( $p < 0.05$ ), as well as 2.2-fold and 1.3-fold lower LV Ly6c mRNA expression and CD68+ cells in S100A9<sup>-/-</sup> CVB3 vs CVB3 wt mice, respectively ( $p < 0.05$ ). LV NOX1 and RAGE mRNA levels were 3.3-fold and 2.2-fold decreased in S100A9<sup>-/-</sup> CVB3 vs wt CVB3 mice ( $p < 0.05$ ). I.p. application of S100A8 in S100A9<sup>-/-</sup> CVB3 mice induced the CVB3 copy number by 5.0-fold ( $p < 0.05$ ) vs S100A9<sup>-/-</sup> CVB3 mice. S100A8 and S100A9 supplementation led to a 1.8-fold and 1.7-fold ( $p < 0.0005$ ) increase in CVB3 copy number in HL-1 cells, respectively, and both to a 1.2-fold ( $p < 0.05$ ) induction in CVB3 mRNA expression in cardiac fibroblasts.

**Conclusions:** The cardiac S1008/A9 system is upregulated in human and murine myocarditis, thereby increasing oxidative stress and reducing anti-viral mechanisms. We conclude that S100A8/A9 could be an important therapeutic target for the treatment of myocarditis.

#### P542

##### **NOD2 knock down improves left ventricular function and attenuates NLRP3 inflammasome activity in experimental Coxsackievirus B3-induced myocarditis**

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**Introduction:** The cytoplasmatic pattern recognition receptor, nucleotide binding oligomerization domain 2 (NOD2), belongs to the innate immune system and is among others responsible for the recognition of single stranded (ss) RNA.

**Purpose:** With Coxsackievirus B3 (CVB3) being a ssRNA virus and the recent evidence that the NOD2 target, NLRP3 is of importance in the pathogenesis of CVB3-induced myocarditis, we wanted to unravel the role of NOD2 in CVB3-induced myocarditis.

**Methods:** Gene expression was analyzed on endomyocardial biopsies taken from CVB3+ patients who spontaneously eliminated CVB3 (n=6). NOD2 knockdown (-/-) mice and wild-type (wt) C57BL/6 mice were i.p. infected with 5x10<sup>6</sup> p.f.u. of CVB3. Seven days after infection, mice were hemodynamically characterized and left ventricles (LV) were isolated. NOD2 was knocked down in HL-1 cells via NOD2 siRNA. HL-1 cells transfected with scrambled (scr) siRNA served as controls.

**Results:** Endomyocardial biopsy NOD2 and NLRP3 mRNA expression decreased by 2.5-fold and 2.2-fold over time in patients, which spontaneously eliminated CVB3, respectively ( $p < 0.05$ ). Furthermore, LV NOD2 mRNA expression was 2.3-fold ( $p < 0.0005$ ) increased in CVB3-infected versus control mice. NOD2<sup>-/-</sup> mice were rescued from the detrimental CVB3-mediated effects as shown by a reduced cardiac inflammation (less cardiac infiltrates, suppression of pro-inflammatory cytokines and TLR4 signaling), cardiac fibrosis, apoptosis, 12.5-fold ( $p < 0.05$ ) lower CVB3 copy number, and an improved LV function in NOD2<sup>-/-</sup> CVB3 compared to wt CVB3 mice. In agreement, the CVB3-induced inflammatory response, CVB3 copy number and apoptosis were less pronounced in CVB3-infected NOD2 siRNA versus CVB3 scr siRNA HL-1 cardiomyocytes. Both in vivo and in vitro, NOD2<sup>-/-</sup> was associated with a decrease in CVB3-induced NLRP3 expression and activity as evidenced by lower ASC expression, caspase 1 activity and/or IL-1 expression in CVB3 NOD2<sup>-/-</sup> versus CVB3 wt mice and CVB3 NOD2 siRNA versus CVB3 scr siRNA HL-1 cells.

**Conclusions:** NOD2 is involved in the pathology of acute CVB3 myocarditis. Its inhibition exerts cardiobeneficial effects, indicating that modulation of NOD2 represents a promising therapeutic strategy to treat viral myocarditis.

#### P543

##### **Cannabidiol is a novel treatment for autoimmune myocarditis**

Intramural Program of NIH/NIAAA

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**Introduction:** Myocarditis is a major cause of heart failure and sudden cardiac death in young adults and adolescents. Many cases of myocarditis are associated with autoimmune processes in which cardiac myosin is a major autoantigen. Conventional immunosuppressive therapies often provide unsatisfactory results and are associated with adverse toxicities during the treatment of autoimmune myocarditis. Cannabidiol (CBD) is a non-psychoactive constituent of Marijuana which exerts anti-inflammatory effects independent from classical cannabinoid receptors. Recently 80 clinical trials have been reported investigating the effects of CBD in various diseases from inflammatory bowel disease to graft-versus-host disease. CBD-based formulations are used for the management of multiple sclerosis in numerous countries, and CBD also received FDA approval for the treatment of refractory childhood epilepsy and glioblastoma multiforme.

**Purpose:** Herein, using a well-established mouse model of experimental autoimmune myocarditis (EAM), we studied the potential beneficial effects of CBD on T cell-mediated inflammation, cardiomyocyte cell death, fibrosis and myocardial dysfunction.

**Methods:** EAM was induced by immunization with cardiac myosin emulsified in adjuvant in our mice. Fibrotic remodeling and cardiac inflammation were investigated by qRT-PCR, histological and immunohistochemical tools. Detailed myocardial systolic and diastolic function were examined by invasive hemodynamic measurements by using pressure-volume conductance microtip catheter system.

**Results:** EAM was characterized by marked myocardial T cell-infiltration, profound inflammatory response, fibrosis (Sirius Red staining:  $5.33 \pm 0.59$  vs.  $1.00 \pm 0.15$  in controls; fold change) and oxidative stress (4-hydroxynonenal (4-HNE) content:  $4.29 \pm 0.78$  vs.  $1.00 \pm 0.28$  in controls; fold change) accompanied by marked attenuation of both systolic (end systolic pressure-volume relationship (ESPVR):  $1.78 \pm 0.19$  vs.  $8.39 \pm 1.21$  in controls) and diastolic (end diastolic PVR (EDPVR):  $0.27 \pm 0.05$  vs.  $0.09 \pm 0.02$  in controls) cardiac functions. Chronic treatment with CBD largely attenuated the CD3+ and CD4+ mediated inflammatory response and injury, myocardial fibrosis (Sirius Red staining:  $2.07 \pm 0.97$ ), oxidative stress (4-HNE:  $2.54 \pm 0.12$ ) and cardiac dysfunction in mice (ESPVR:  $3.33 \pm 0.54$ ; EDPVR:  $0.16 \pm 0.02$ ).

**Conclusion:** CBD may represent a promising novel treatment for management of autoimmune myocarditis and possibly other autoimmune disorders, and organ transplantation.

#### P544

##### **Intracoronary infusion of allogeneic cardiosphere-derived cells attenuates myocardial inflammation and prevents depression of systolic function in rats with autoimmune myocarditis**

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**Background:** Myocarditis is a potentially lethal inflammatory cardiomyopathy without effective treatment. Cardiosphere-derived cells (CDCs) have been shown to exert cardioprotective, regenerative and immunomodulatory effects in ischemic cardiomyopathy. However, the effect of CDC administration in hearts with myocarditis is unknown.

**Purpose:** To investigate the effects of intracoronary infusion of allogeneic CDCs in rats with autoimmune myocarditis.

**Methods:** Allogeneic CDCs were grown from hearts explanted from healthy Lewis rats. Autoimmune myocarditis was induced in Lewis rats by subcutaneous footpad injection of purified porcine cardiac myosin mixed with complete Freund's adjuvant on days 1 and 7. On day 10, rats with autoimmune myocarditis underwent lateral thoracotomy and were subsequently randomized to undergo global intracoronary infusion of 500,000 allogeneic CDCs (n=6) or vehicle solution (n=8). Global intracoronary infusion was achieved through infusion of cells or vehicle solution into the left ventricular cavity during brief aortic clamping. Rats were followed for 3 weeks post-infusion and underwent cardiac echocardiography on day 1, day 10 (prior to infusion) and day 28 (3 weeks post-infusion). Afterwards, rats were euthanized, hearts were explanted and underwent histology. Myocardial lymphomononuclear infiltration was assessed by whole-field microscopy after hematoxylin eosin staining.

**Results:** Subcutaneous footpad injection of purified porcine cardiac myosin mixed with complete Freund's adjuvant induced histologically-confirmed autoimmune myocarditis in 14/14 rats. Left ventricular ejection fraction was comparable on day 1 ( $83.4 \pm 1.5\%$  vs  $83.3 \pm 4.2\%$ ,  $p = 0.95$ ) and on day 10 ( $81.1 \pm 5.8\%$  vs  $78.7 \pm 5.8\%$ ,  $p = 0.57$ ) between the 2 groups. Intracoronary infusion of allogeneic CDCs prevented myocarditis-induced functional depression and resulted in significantly higher left ventricular ejection fraction at 3 weeks post-infusion compared to control animals ( $84.9\% \pm 0.9\%$  vs  $61.3 \pm 8.4\%$ ,  $p = 0.02$ ). Allogeneic CDC therapy resulted in dramatic attenuation of lymphomononuclear infiltration at 3 weeks post-infusion compared to control animals ( $8.1\% \pm 7.2\%$  vs  $21.5 \pm 3.8\%$  of the myocardium infiltrated by inflammatory cells,  $p = 0.03$ )

**Conclusions:** Global intracoronary infusion of allogeneic CDCs dramatically attenuates myocardial inflammation and prevents depression of systolic function in rats with autoimmune myocarditis.

## BASIC SCIENCE: CO-MORBIDITIES

### P545

#### Enalapril, eplerenone or their combination: finding the best paradigm to protect against Doxorubicin-Induced Cardiotoxicity

Swiss Heart Foundation, Pfizer

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**Introduction:** Anticancer therapy with anthracyclines such as Doxorubicin (Dox) is complicated by the generation of reactive oxygen species (ROS) in cardiomyocytes, causing early and late cardiac dysfunction. Dox treatment is associated with activation of the renin-angiotensin-aldosterone system which may further increase ROS load and fibrosis upon activation of the mineralocorticoid receptor (MR) by aldosterone.

**Purpose:** Using mice, we assessed the ability of MR blockade, ACE inhibition or their combination to protect against Dox-induced cardiotoxicity (DIC).

**Methods:** Acute and chronic DIC were induced in C57Bl6 male wild type (WT) mice by a single injection of Dox (15 mg/kg) or five weekly injections of Dox (4 mg/kg), respectively. MR blockade was achieved in WT mice with an Eplerenone-enriched diet and in transgenic mice by deleting the MR gene specifically in cardiomyocytes (MR KO). ACE inhibition was provided by adding Enalapril in drinking water. Left ventricular (LV) systolic function was assessed by 2D echocardiography and magnetic resonance imaging and diastolic function by Doppler imaging. Changes in gene expression levels were assessed by qPCR and activation of stress-sensing pathways assessed by western blot. Plasma aldosterone levels were measured by LC-MS and radio-immunoassay.

**Results:** Acute and chronic models of DIC both triggered body weight loss as well as cardiac atrophy, which was associated with reduced cardiomyocyte cell size and decreased activation of mTOR and Rps6. DIC was further characterized in both models by cardiac diastolic and systolic dysfunction, as shown by decreased mitral inflow velocities and decreased cardiac output, respectively. MR blockade with Eplerenone was not sufficient to prevent cardiac dysfunction. It drastically increased plasma aldosterone levels and was associated with an increased expression of CTGF and of angiotensin II (AngII) receptor type I, suggesting that an interplay between aldosterone and AngII signaling diverts the effect of MR blockade. Enalapril treatment, however, decreased the severity of both diastolic and systolic dysfunction in the chronic model of DIC. Combination of Enalapril and Eplerenone lowered cardiac dysfunction and further decreased aldosterone and CTGF levels.

**Conclusions:** Our data show that blocking MR with Eplerenone does not prevent DIC in mice. However, blocking AngII production with Enalapril limits the severity of cardiac dysfunction in a clinically relevant model of chronic DIC. Our results suggest that Enalapril or Enalapril and Eplerenone combination in human may protect against DIC.

### P546

#### Ranolazine protects from trastuzumab cardiomyopathy

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**Purpose:** The anti-cancer anti-ErbB2 Trastuzumab (T) is used to treat HER2 positive breast cancer, but unfortunately can produce cardiac dysfunction. The mechanisms of cardiotoxicity have not been fully elucidated, but oxidative stress may play an important role. The late INa inhibitor Ranolazine (R) protects from doxorubicin-induced oxidative stress and cardiac dysfunction as we have previously described. Here, we hypothesize that treatment with R reduces T cardiotoxicity.

**Methods:** To assess toxicity in vitro, rat H9C2 cardiomyoblasts and human fetal cardiomyocytes were pretreated with R (1 and 10  $\mu$ M) for 72 hours and then treated with T (200 nM) for additional 72 hours. Cell viability was determined by cell counts and MTT assays. To evaluate cardiac function in vivo, fractional shortening (FS) and ejection fraction (EF) were measured by M-mode echocardiography and radial and longitudinal strain (RS and LS) were measured using 2D speckle-tracking echocardiography in C57BL6 mice, 2-4 months old, pretreated with R (305 mg/kg/day, a

dose comparable with that used clinically in humans of 750 mg twice daily) per os for 3 days. R was then administered for additional 7 days, alone and in combination with T (2.25 mg/kg/day ip), according to our well established protocol. We have evaluated tissue expression of BNP (brain natriuretic peptide) and MMP2 (matrix metalloproteinase 2) by reverse transcription-polymerase chain reaction (RT-PCR) analysis on heart tissue.

**Results:** R reduced T toxicity in H9C2 cardiomyoblasts and human fetal cardiomyocytes as evidenced by higher viability rate of cells treated with R+T than cells treated with T alone ( $p < 0.01$ ). In our in vivo studies, after 7 days with T, FS, EF, RS and LS decreased. Interestingly, in mice treated with R+T, the reduction in cardiac function was milder: FS was  $59 \pm 3\%$ , EF was  $90 \pm 2\%$ , RS was  $39.6 \pm 2$ , LS was  $-20.5 \pm 0.9$   $p < 0.05$  respectively, vs T alone. R prevents the increased expression of BNP and MMP2 ( $p < 0.05$ ) on heart tissue.

**Conclusions:** In our mouse model, T produces LV dysfunction and R reduces T cardiotoxic effects. We plan to test R as a cardioprotective agent with other antineoplastic cardiotoxic drugs in our experimental models and to define the mechanisms of cardioprotection.

### P547

#### Sildenafil treatment in a rat model of cancer cachexia

Piano di azione e coesione PONricerca e competitività  
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**Background:** Cachexia, or wasting syndrome, is a complex metabolic disorder which has been shown to occur in late stages of chronic disease including end-stage cancer characterized by involuntary weight loss caused by an ongoing wasting of skeletal muscle and depletion of adipose tissue. Cachexia affects 50-80% of cancer patients and is responsible for 30% of their death. Given that, brown adipose tissue (BAT) plays a key role in thermogenesis and energy balance, increased thermogenesis in brown fat during cancer cachexia indicates that metabolically active adipose tissue contributes to the imbalanced energy homeostasis involved in catabolic wasting. Cachexia also affects the cardiac muscle, indeed, the atrophy of the heart and impairment of cardiac function consequently increases mortality. Anti-cachectic therapy in patients with cancer cachexia is, so far, limited to nutritional support. Sildenafil, a selective inhibitor of the the enzyme phosphodiesterase-5 (PDE5), responsible for the breakdown of cGMP has been shown to induce myocardial protective effects and to improve energy balance in a variety of experimental models. We hypothesized that sildenafil ameliorates the wasting process and the heart function in the Yoshida hepatoma tumor model.

**Methods:** In this study the effects of sildenafil were tested in cachectic tumour-bearing rats (Yoshida AH-130 ascites hepatoma). Rats were treated daily with 30mg/kg/d of sildenafil or vehicle starting one day after tumor-inoculation, and for a period of 16 days. Body weight and body composition were assessed at baseline and at the end of the study. Cardiac function was analyzed by echocardiography at baseline and at day 11.

**Results:** Treatment with 30mg/kg/d of sildenafil attenuated the loss of body weight and the wasting of fat mass. Administration of 30mg/kg/d of sildenafil protected the heart from general atrophy. Tumor-bearing rats displayed cardiac dysfunction, as indicated by the significant impairment of the left ventricular ejection fraction (LVEF) as well as the left ventricular fractional shortening (LVFS). In contrast, sildenafil improved cardiac dysfunction. Although sildenafil did not reduce the loss of lean body mass, it was able to protect from adipose tissue depletion.

**Conclusions:** The animals carrying the ascites hepatoma AH-130, treated with Sildenafil showed, an attenuation of fat adipose tissue. In addition, the drug showed an improvement of the cardiac function probably due to an antagonism of cardiac atrophy subsequent to cancer-induced cachexia. Larger studies, with longer follow-up and molecular analysis, are required in order to get better insight of the pathophysiological mechanisms underlying sildenafil related cardioprotection.

### P548

#### Enhanced-autophagy by exenatide mitigates doxorubicin-induced cardiotoxicity in vitro and in vivo

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**Background:** Exenatide, glucagon-like peptide-1 analogue, mitigates myocardial injury caused by ischemia/reperfusion injury via survival signaling pathway. We investigated that exenatide would also provide a protective effect in doxorubicin-induced cardiotoxicity.

**Methods:** H9c2 cardiomyocytes were incubated after treatment with doxorubicin (DOX, 1, 10  $\mu$ M) or pre-treatment with exenatide (3, 30 nM) followed by DOX in vitro. Incubated cells were measured with cell viability and autophagosome staining. In vivo, SD rat was treated with exenatide (10  $\mu$ g/kg, subcutaneous injection) or

control saline 1 hour prior to every DOX (accumulative dose, 20 mg/kg) intraperitoneal injection, and left ventricular (LV) function and performance were assessed by echocardiography. Western blot, TUNEL staining and ROS study to determine the intracellular changes. Autophagic process was visualized by Cyto-ID staining in H9c2.

**Results:** In vivo, echocardiography shows that reduced LV function by DOX treatment was significantly improved by pre-treatment of exenatide. Doxorubicin significantly increased myocyte apoptosis by TUNEL and ratio of activated caspase-3, which also decreased by pre-treatment exenatide. However, the oxidative stress in cardiac tissue and serum did not significant differ between each groups. Autophagic markers, LC3 II, Beclin, and ATG5 signal increased in exenatide combination group. Also, number of autophagosomes increased appreciably with more exenatide pre-treated H9c2 cells than DOX treated cells. When suppress the formation of autophagosome by Bafilomycin A1, apoptosis regulated under the exenatide-mediated autophagy inhibition in H9c2.

**Conclusion:** Exenatide reduces DOX-induced cardiomyocytes apoptosis by upregulating autophagy and improves cardiac function. These novel results highlight the therapeutic potential of exenatide to prevent doxorubicin cardiotoxicity.

#### P549

##### TLR4 and TLR2 detection method from peripheral human blood for early detection of doxorubicin induced cardiotoxicity

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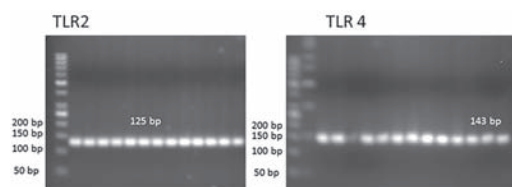
**Background/introduction:** -Reducing mortality and morbidity in cancer patients with current therapies is a major breakthrough in the treatment of cancer patients. Through their mechanisms of action, cancer treatments can have significant cardiovascular adverse effects that can cause cardiomyopathy and heart failure with reduced survival benefit and considerable decrease in the use of antineoplastic therapy.

**Purpose:** The purpose of this study is to assess the role of TLR2 and TLR 4 gene expression as an early marker for the risk of doxorubicin induced cardiomyopathy in correlation with early diastolic dysfunction in patients treated with doxorubicin.

**Methods:** Our study included 25 consecutive patients who received treatment with doxorubicin for hematological malignancies (leukemia, lymphomas or multiple myeloma), aged 18-65 years old, with a survival probability > 6 months and with left ventricular ejection fraction > 50% who expressed their informed consent. Exclusion criteria consisted of previous anthracycline therapy, previous radiotherapy, history of heart failure or chronic renal failure, atrial fibrillation or other significant arrhythmias, pregnancy. In all patients, in fasting state, a blood sample was drawn for the assessment of TLR2 and TLR4 gene expression. Gene expression was assessed by qRT PCR using the following steps: blood collection (3 ml of blood), RNA isolation, cDNA reverse transcription, qRT PCR and quantification of the relative expression. Patient's blood was drawn directly in Tempus™ Blood RNA Tube (4342792 Applied Biosystems). At enrolment all patients were evaluated clinically, an ECG and an echocardiography were performed. Echocardiographic parameters recorded (determined on a Siemens Acuson X300 machine) were those of left ventricular diastolic and systolic function (ventricular volumes, ejection fraction, pulsed and tissue Doppler analysis).

**Results:** - The average amount of gene expression units was 0.113 for TLR4 (range 0.059-0.753) and 0.218 for TLR2 (range 0.046-0.269). The mean mRNA extracted quantity was 113,571  $\mu\text{g}/\mu\text{l}$ . As for the diastolic function parameters, criteria for diastolic dysfunction were present after 6 months in 16 patients (64%). In these patients the mean values for TLR4 were 0,1198625 and for TLR2 0,16454 gene expression units. As for the diastolic function parameters, criteria for diastolic dysfunction were present after 6 months in 16 patients (64%). In these patients the mean value for TLR2 was  $0.30 \pm 0.19$  and for TLR4  $0.15 \pm 0.04$ . The corresponding values for the patients who did not develop diastolic dysfunction were  $0.16 \pm 0.07$  for TLR2 ( $p = 0.01$ ) and  $0.11 \pm 0.10$  for TLR4 ( $p = 0.2$ ).

**Conclusion:** - Our study suggests that TLR4 and TLR2 expression is higher in patients under doxorubicin therapy which develop diastolic dysfunction. This may suggest a predisposition to myocardial involvement, a higher sensitivity to doxorubicin cardiac effects.



qRT-PCR (O'RangeRuler™ 50 bp DNA Ladder)

## BASIC SCIENCE: METABOLISM / DIABETES MELLITUS / OBESITY

#### P550

##### Modulation of cardiac structure by epicardial adipose tissue

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**Introduction:** Diastolic heart failure (DHF) is recognized an important cause of cardiovascular mortality and morbidity reaching approximately 50% of heart failure cases. Several risk factors, such as obesity, are associated with its development. 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 (EAT) can act in a paracrine manner directly on the myocardium and influence their structure and function. In this work we aim to characterize the profile of EAT under conditions of DHF and to evaluate their possible changes in cardiac structure.

**Methods:** EAT of 20-weeks-old lean and obese ZSF1 rats was collected for: 1) separation of proteins to mass spectrometry (MS) identification, 2) adipokines' expression, 3) adipocytes fibrosis and cross-sectional area assessment and 4) for 24h DMEM incubation to obtain conditioned medium. Successively, 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:** In EAT of the obese ZSF1, MS-results presents decreased levels of 3-ketoacyl-CoA thiolase protein enzyme as a compensatory mechanism in order to inhibit fatty acid oxidation and increase lumican and collagen-alpha-1(I) proteins suggesting a link between inflammation caused by obesity and increases of adipose tissue extracellular matrix. The histological and molecular studies of EAT revealed hypertrophy of adipocytes in obese animals ( $1505 \pm 80.01 \mu\text{m}^2$  vs.  $7595 \pm 265.5 \mu\text{m}^2$ ,  $p < 0.0001$ ) without fibrosis, as well as a significantly increase in expression of several adipokines. Among these overexpressed adipokines are visfatin ( $0.42 \pm 0.18 \text{AU}$  vs.  $1.4 \pm 0.33 \text{AU}$ ,  $p < 0.05$ ), leptin ( $0.12 \pm 0.032 \text{AU}$  vs.  $0.93 \pm 0.18 \text{AU}$ ,  $p < 0.0001$ ), apelin ( $0.08 \pm 0.03 \text{AU}$  vs.  $0.24 \pm 0.04 \text{AU}$ ,  $p < 0.05$ ) and chemerin ( $0.33 \pm 0.096 \text{AU}$  vs.  $0.90 \pm 0.16 \text{AU}$ ,  $p < 0.05$ ) that are involved in fibrosis and hypertrophic pathways. In organotypic cultures, conditioned media from obese ZSF1 EAT rats 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:** Obesity promotes significant alterations in EAT which alter the myocardial structure, inducing collagen deposition and cardiomyocyte hypertrophy.

#### P551

##### Insulin signaling exacerbates heart failure via an IRS1-Akt1 signaling module that is independent of IRS2

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**Background:** Generalized insulin resistance exacerbates heart failure, and heart failure is an insulin resistant state. We recently reported that pressure overload cardiac hypertrophy (POH) leads to activation of Insulin Receptor (IR) tyrosine kinase activity in cardiomyocytes and that reducing cardiomyocyte insulin signaling prevented heart failure in a mouse model of POH.

**Objectives:** To further explore the signaling mechanisms responsible for this phenomenon we generated mice with cardiomyocyte-restricted deficiency of IRS1 and IRS2 respectively and induced POH using transverse aortic constriction (TAC). Results Following TAC, wildtype (WT) controls developed POH and heart failure characterized by hyperactivation of Akt1 (2.01fold,  $p < 0.05$ ) but not Akt2, which was accompanied by increased myocardial fibrosis (+46.0% vs. WT Sham,  $p < 0.05$ ). Remarkably, following TAC, IRS1 deficient hearts were completely resistant to cardiac hypertrophy and maintained normal left ventricular (LV) function. Akt1 activation and increased fibrosis were also absent. In contrast, IRS2 KO hearts developed an exacerbation of the WT phenotype, which was prevented by haploinsufficiency of Akt1. We then examined LV tissue from failing human hearts, obtained at the time of implantation of a left ventricular assist device, and compared insulin signaling with LV tissue obtained from normal donor hearts. Failing human hearts exhibited increased IRS1 (+73.7%,  $p < 0.05$ ) but not increased IRS2 phosphorylation. Hyperactivation of Akt1 (+84.4%  $p < 0.05$ ), was observed in failing human hearts, but Akt2 phosphorylation was normal. Conclusion Taken together these data define a critical



role for an IR-IRS1-Akt1 signaling module in exacerbating LV remodeling in the failing heart and provides a molecular mechanism linking insulin resistance and heart failure.

## P552

### MR antagonists protect against diet induced obesity and cardiac inflammation in mice, through browning of the adipose tissue and modulation of autophagy

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**Background:** Obesity is a key factor in the development of insulin resistance (IR), cardiovascular disease, hypertension, type 2 diabetes etc. Given the near epidemic incidence of obesity in western society there is a clear need for effective treatment options. Mineralocorticoid receptor (MR) blockade has shown significant promise in transgenic mouse models of obesity in limiting IR and adipocyte dysfunction, a disease that is independent of classical MR actions (renal).

**Purpose:** Metabolic effects of MR antagonists were investigated on adipose tissue and heart in mice fed a high fat diet (HFD).

**Methods:** Female 10-week-old C57Bl6 mice were fed with normal chow or a HFD for 12 weeks. Mice fed HFD were concomitantly treated for 12 weeks with drospirenone (DRSP, 6 mg/Kg/day), a potent MR antagonist with antiadipogenic activity, or spironolactone (SPIRO, 20 mg/kg/day). Magnetic Resonance Imaging (MRI) and PET/CT imaging were used to analyse fat tissue mass and metabolic activity. Gene expression analysis was performed by real time RT-PCR. Autophagy was investigated by western blot for LC3.

**Results:** DRSP and SPIRO prevented weight gain and white fat mass expansion induced by HFD in parametrial, perivescical, and inguinal depots without affecting interscapular fat pad weight. Mice fed HFD showed no increase in heart or kidney weight and tissue fibrosis. Cardiac macrophage recruitment and osteopontin staining was increased in hearts of HFD-fed mice and reversed by both MR antagonists. Moreover, both DRSP and SPIRO prevented the impaired glucose tolerance in mice fed HFD, and countered HFD-induced up-regulation of WAT markers transcripts and adipocyte hypertrophy. Importantly, MR antagonists increased uncoupling protein 1 (UCP-1) positive brown-like adipocyte content in WAT, and improved metabolic activity of adipose tissue, as indicated by PET/CT imaging. In keeping with this, MR antagonism significantly increased expression of brown-like adipocyte marker genes (PRDM16, CIDEA, ADRB3, UCP-1) in all WAT depots analysed. In exploring the mechanism, we demonstrated that MR antagonism induced brown adipose tissue (BAT) markers, and reduced the autophagic rate, a key remodelling process in adipocyte differentiation, in WAT depots in vivo as well as in primary cultured adipocytes.

**Conclusions:** We conclude that adipocyte MR regulates BAT-like remodeling of WAT through modulation of autophagy. MR blockade therefore has promise as a novel therapeutic option for the prevention of metabolic dysfunctions and the cardiac consequences of obesity.

## P553

### Role of mitochondrial translocator protein (TSPO) in oxidative damage in heart and skeletal muscle

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Obesity, mainly its abdominal form, is considered a relevant risk factor not only in type 2 diabetes, lipid disorders and hypertension but also in the development of coronary artery disease. During the past decade, evidence has been collected showing that among patients with type 2 diabetes and cardiovascular comorbidity, overweight and obese patients had a lower mortality compared with normal-weight subjects. These paradoxical findings are known as the "obesity paradox". In our experimental model, rats were fed with a normocaloric diet (NPD group) or with a high fat diet (HFD group), respectively. One month later, streptozocin (STZ, 35 mg/Kg, i.p.) was administered in a subgroup of both NPD and HFD rats to induce diabetes and the sacrifice was carried out after sixty days. Our results revealed that diabetic rats fed with a normocaloric diet (NPD+STZ) showed a significant loss of muscle tissue compared to the corresponding controls (NPD). On the other hand, hyperlipidemic diabetic rats (HFD+STZ) as well as HFD rats, didn't show any significant difference in lean mass composition. In addition, the impairment of body mass observed in hyperglycemic rats was associated with a decreased cardiac function, less pronounced in HFD+STZ rats. This effect was accompanied by a down-expression of mitochondrial Translocator Protein (TSPO) in hyperlipidemic

diabetic rats as compared with controls. TSPO plays a central role in the regulation of mitochondrial function modulating the crosstalk between Inner Membrane Anion Channel (IMAC) and Permeability Transition Pore (PTP) in the mitochondrion. To date, the role of TSPO in preventing mitochondrial dysfunction and apoptosis is unclear. In response to oxidative stress and impairment of intracellular antioxidant systems, TSPO down-regulation might represent a defensive mechanism of cardiomyocyte aimed to prevent the opening of PTP. TSPO has also been associated with cholesterol import into mitochondria, a key step in steroidogenesis; as a consequence, its down-regulation can further reduce PTP opening induced by mitochondrial cholesterol accumulation and oxysterol overproduction. Despite of TSPO down-expression, in HFD+STZ rats we observed an increase in plasmatic levels of cholesterol derived- allopregnanolone probably involved in the protection of heart and skeletal muscle tissues by oxidative damage. The discussion over the molecular mechanisms underlying the obesity paradox cannot lead to an underestimation of obesity as a crucial risk factor for the development of cardiovascular and metabolic diseases; however, the preservation of cardiac and muscle tissues from mitochondrial-induced oxidative damage observed in HFD+STZ rats suggests the need of further investigations aimed to identify new therapeutic strategies in cardiovascular diseases.

## P554

### Role of matrix metalloproteinases in cardiac dysfunction induced by oxidative stress in a rat model of diabetes

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Diabetes is a metabolic, heterogeneous disorder caused by obesity, sedentary lifestyle and hypercaloric dietary supply and frequently related to genetic susceptibility. Hyperglycaemia and hyperlipidemia represent the most important risk factors for cardiovascular diseases which are the leading cause of death among people with diabetes. Despite this evidence, to date, the exact role of hyperglycaemia and hyperlipidemia in diabetic cardiomyopathy is not well established. To better clarify this aspect, rats were fed with a normocaloric diet (NPD group) or with a high fat diet (HFD group), respectively. One month later, streptozocin (STZ, 35 mg/Kg, i.p.) was administered in a subgroup of both NPD and HFD rats to induce diabetes. After a period of 60 days, we observed that hyperglycaemia or hypercholesterolemia significantly increased the diameter of the left ventricular chamber in diastole (LVEDd) and in systole (LVESd) and these pathological conditions reduced ejection fraction (EF) and fractional shortening (FS) compared to control (NPD). Unexpectedly, cardiac dysfunction was less marked in diabetic rats fed with an hyperlipidemic diet (HFD+STZ) suggesting an adaptive response to injury of diabetic heart in the presence of hyperlipidemia. This response was characterized by a modulation of matrix metalloproteinases (MMPs), a family of zinc-dependent endopeptidases responsible for both physiological and pathophysiological tissue remodeling. In particular, we observed an activation of all myocardial MMP-2 isoforms (intracellular full-length-MMP-2, N-terminal truncated intracellular MMP-2 and extracellular MMP-2) in NPD as well as in HFD and HFD+STZ rats as paragoned with diabetic rats not affected by hyperlipidemia. On the other hand, N-terminal truncated intracellular MMP-2 (NT-MMP-2) and MMP-9 activities appeared comparable in NPD and in diabetic hyperlipidemic rats. Recent evidence shows that NTT-MMP-2 activity impairs heart muscle function reducing calcium transients without affecting the structure of myofibrils, as occurred after full-length-MMP-2 activation. As a consequence, in HFD+STZ rats, the enhanced activity of NTT-MMP-2 among all MMP-2 isoforms and restored MMP-9 activity suggest their involvement in a myocardial remodeling to preserve cardiac function and integrity in response to oxidative stress induced by diabetes. In conclusion, our results highlight the importance of MMPs as a potential pharmacological target in order to counteract myocardial oxidative damage in diabetes.

## P555

### Effect of hyperlipidaemia and hyperglycaemia on modulation of apoptotic cell death in diabetic cardiomyopathy

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Diabetes is a metabolic, heterogeneous disorder characterized by a complex pathogenesis which can be related to genetic susceptibility, obesity, sedentary lifestyle and hypercaloric dietary supply. Hyperglycaemia and hyperlipidaemia are the most

important risk factors for cardiovascular diseases which are the leading cause of death among people with diabetes. Despite this evidence, to date, the exact role of hyperglycaemia and hyperlipidaemia in the onset of cardiovascular diseases is not well established.

To better clarify mechanisms underlying these metabolic dysfunctions, rats were fed with a normocaloric diet (NPD group) or with a high fat diet (HFD group), respectively. One month later, streptozocin (STZ, 35 mg/Kg, i.p.) was administered in a subgroup of both NPD and HFD rats to induce diabetes. After a period of 60 days, we observed that hyperglycaemia or hypercholesterolemia significantly increased the diameter of the left ventricular chamber in diastole (LVEDd) and in systole (LVESd) and these pathological conditions reduced ejection fraction (EF) and fractional shortening (FS) compared to control (NPD). Unexpectedly, cardiac dysfunction was less marked in diabetic rats fed with an hyperlipidemic diet (HFD+STZ) suggesting an adaptative response to injury of diabetic heart in the presence of hyperlipidaemia. Growing evidence shows that the development of left ventricular dysfunction in diabetes is induced by myocardial injury which is characterized by mitochondrial dysfunction and altered myocardial metabolism. In particular, oxidative stress appears to play a very important role in tissue damage as we observed in diabetic rats fed with normocaloric diet (NPD+STZ) showing an overexpression of myocardial NADPH oxidase compared to control. On the other hand, the concomitant presence of both pathological conditions in HFD+STZ rats induced a down-expression of myocardial NADPH oxidase compared to NPD+STZ animals as well as an increased expression of Bcl-2 suggesting an improved mitochondrial function and a down-regulation of apoptosis. However, we also revealed an enhancement of cytosolic cytochrome c levels in HFD+STZ rats as compared with other groups. As a consequence, here we hypothesize that cytochrome c release from mitochondria to cytosol represents an early event caused by free radicals overproduction in cardiomyocytes of HFD rats. This detrimental event is probably compensated by enhanced Bcl-2 levels in response to later STZ-induced hyperglycaemia, suggesting a role for Bcl-2 in promoting cell survival after release of cytochrome c. In conclusion, our results highlight the importance to prevent free radicals-induced diabetic cardiomyopathy and represent a new insight in order to counteract oxidative damage and to improve cardiac dysfunction in diabetes.

## BASIC SCIENCE: BIOMARKERS

### P556

#### New interesting targets for heart failure therapy in the natriuretic peptide clearance system- could type c natriuretic peptide receptor be as promising as neprilysin?

Institute of Cardiology Research Grant

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**Background:** Since the introduction of new molecules targeting neprilysin (NEP) and natriuretic peptide (NP) receptors for the treatment of heart failure the interest in molecular mechanisms governing clearance of natriuretic peptides has also increased. NEP, a membrane-bound metallo-endopeptidase, degrades a variety of peptide hormones, including natriuretic peptides, while type C natriuretic peptide receptor (NPR-C) is a clearance receptor for NPs with some signalling properties of its own associated with adenylyl cyclase and phospholipase C transduction pathways. It binds NPs on the cell surface, internalizes them and delivers to lysosomes for degradation.

**Goal:** This study aimed to demonstrate the changes in natriuretic peptide clearance system (NEP and NPR-C) taking place in a failing human heart.

**Methods:** NEP and NPR-C levels were measured using ELISA in cardiac tissues of 43 heart failure patients referred for heart transplantation and 12 healthy donor hearts not allotted to transplantation. Cardiac NPR-C expression was also assessed with rtPCR for mRNA expression. NEP activity was assayed using fluorimetry.

**Results:** In failing hearts the levels of NPR-C mRNA were significantly increased (fold change: 2.93;  $p = 0.0000131$ ) in the presence of significantly reduced NPR-C protein levels (7.5 vs. 4.8 ng/mg of protein;  $p = 0.0014$ ). NEP levels did not differ between healthy and failing heart tissues (respectively: 205.7 vs. 218.5 ng/mg of protein;  $p = 0.4181$ ). However, neprilysin activity was significantly increased in cardiac tissues obtained from heart failure patients (1951.8 vs. 5424.1 F/10  $\mu$ g of protein/30 min;  $p < 0.0002$ ).

**Conclusions:** Augmented production of natriuretic peptides in heart failure induces changes to their clearance system through a positive feedback loop, leading to increased transcription of NPR-C mRNA in cardiac cells. Lower levels of NPR-C protein in heart failure reflect its increased activity as a clearance receptor (binding the molecules, internalization and lysosomal fusion) since the receptor is removed from the cell surface and degraded together with its ligand. The neprilysin system also adapts to increased concentrations of NPs. While NEP expression remains unchanged, the activity of neprilysin appears to be significantly increased in failing

hearts. Both of these mechanisms contribute to reduction of antifibrotic and anti-hypertrophic activity of NPs. While neprilysin inhibitors are extensively investigated and their anti-remodeling properties were already demonstrated, NPR-C remains a potential therapeutic target of heart failure treatment that has been somewhat neglected to date.

### P557

#### A preliminary study on carbon-based nanotubes gelatin scaffold for cardiac tissue regeneration

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**Introduction:** A realistic goal for cardiac muscle engineering is the design of a scaffold able to mimic both the tissue-specific architecture and mechanical properties as well as the main physiological functions.

**Purpose:** Aim of this study was the set up of gelatin and carbon nanotubes (CNT) scaffolds for cardiac tissue engineering applications.

**Methods:** Gelatin-based scaffolds (Sc) and CNT in percentage of 0.3% and 0.9% ( $n = 12$ ), cross-linked with genepin 0.2%, were prepared. H9c2 cell line was cultured for 10 days in DMEM, supplemented with 10% of FBS (C10%,  $n = 10$ ). Myoblast differentiation was induced by adding 1% FBS (C1%,  $n = 6$ ), while cardiac phenotype by 10 nM all trans-retinoic acid (CRA,  $n = 6$ ). Cell viability, cytotoxicity, phenotype differentiation and immunohistochemical assay were performed. After 10 days cells and Sc were collected in tri-reagent and RNA was extracted for Real-Time PCR analysis (CFX-96 Real-Time PCR detection systems, Bio-Rad). In order to evaluate cardiac phenotype, the natriuretic peptide (NP) and endothelin (ET) system were studied. To confirm cellular interaction by gap junction formation, connexin (CX)-43 was measured.

**Results:** Immunohistochemistry study revealed that C1% showed the presence of elongated myotubes, typical of skeletal phenotype and dissimilar from myoblast of control condition. CRA was induced to cardiac phenotype showing round and multinucleated nuclei. Data were also confirmed by a significantly increased expression of NP system in CRA with respect to C10% and C1% except for NP receptor-C that significantly decreased in CRA. Furthermore, CRA revealed an increased of both ET-A and ET-B receptors in parallel with a decreased ET-1 expression with respect to C10% and C1%. In CNT Sc cell viability was similar both at 0.3% than and 0.9% and resulted decreased at 3 days probably for adapting at the Sc. NP and ET system expression decreased in CNT0.3% and CNT0.9% with respect to C10% ,as well as CX43 mRNA ( $p < 0.01$ ), mainly due to a lacking of complete differentiation in cardiac phenotype during these few days.

**Conclusions:** In this study the addition of retinoic acid during serum reduction favours a cardiac phenotype at the expense of skeletal muscle trans-differentiation, confirmed by NP and ET system expression. Moreover, the lacking of a complete differentiation of cells on CNT-Sc highlights the need of more day of culture to realize this process. Nevertheless further analysis on novel biomaterials to enhance cell growth/proliferation and to support the damaged heart will be needed to bring heart tissue engineering into clinical application, these results are an useful starting point to develop new Sc-based biomaterials.

### P558

#### Cardioprotective effects of sitagliptin against doxorubicin-induced cardiotoxicity in rats

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**Background:** There is a large body of evidence suggesting that inhibitors of dipeptidyl peptidase-4 (DPP-4), such as sitagliptin, may exhibit beneficial effects against different inflammatory disorders.

**Purpose:** This investigation was conducted to elucidate the potential ability of sitagliptin to counteract the injurious effects of doxorubicin (DOX) in cardiac tissue.

**Methods:** Male Wistar rats were pretreated with sitagliptin for 10 days then treated with a single dose of DOX (20 mg/kg, i.p). Electrocardiography, biochemical estimation of serum and tissue markers, histo- and immunopathological examinations were done.

**Results:** have shown that supplementation with sitagliptin resulted in significant improvement of cardiac function with contaminant decrease in serum markers of DOX-induced cardiotoxicity. These results were supported by the histopathological **Results:** Furthermore, a marked protection against oxidative stress was evident through reduction of lipid peroxidation and prevention of reduced glutathione content depletion and superoxide dismutase activity reduction in cardiac tissue of rats pretreated with sitagliptin in combination with DOX. Moreover, sitagliptin ameliorated the activation of in nuclear factor kappa-B and the release of inflammatory cytokines tumour necrosis factor-alpha and nitric oxide. Finally, sitagliptin

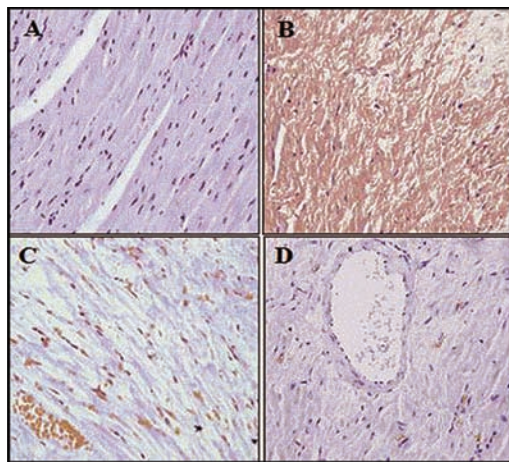
attenuated DOX-induced increase in the expression of pro-apoptotic protein Bax and in the apoptotic marker, caspase-3.

**Conclusions:** these data indicate that sitagliptin pretreatment could alleviate DOX-induced cardiotoxicity via reducing oxidative damage and its subsequent inflammation and apoptosis.

(0.141±/-11µM/L vs 0.22±/-12µM/L in volunteers; n=38 and 48). HbNO was significantly correlated with endothelial function (ENDO-PAT) and (inversely) correlated with major cardiovascular risk factors. We conclude that HbNO reflects exposure of RBCs to NO in vivo and is sensitive to oxidative degradation by H2O2. HbNO could be developed as a biomarker of NO bioavailability and/or oxidative stress ex vivo.

Groups	HR (bpm)	R-R interval (ms)	QRS duration (ms)	QTc interval (ms)	R wave voltage (mv)
Control	363.3 ± 11.09	145 ± 8.5	47.5 ± 3.2	145 ± 8.6	0.69 ± 0.033
DOX	273 ± 6.03***	267.5 ± 6.3***	88.8 ± 8.4***	231.9 ± 9.3***	0.43 ± 0.017***
Sitagliptin (10 mg/kg) + DOX	322.9 ± 9.9***	235.6 ± 6.1***##	63.1 ± 6.1#	170.8 ± 3.5###	0.5 ± 0.023***
Sitagliptin (20 mg/kg) + DOX	350 ± 10.6###	190.7 ± 3.5***###	56.9 ± 5.5##	151.8 ± 9.7###	0.62 ± 0.016###

Table 1. Effects of doxorubicin with/without sitagliptin pretreatment on ECG parameters



4Effects of doxorubicin (DOX) with/witho

**P559**

**Nitric oxide forms a paramagnetic compound with hemoglobin in venous erythrocytes that reflects vascular no bioavailability in vivo and is quantifiable by electron paramagnetic resonance spectroscopy**

FNRS-FRIA

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Nitric oxide bioavailability reflects severity of endothelial dysfunction in metabolic and cardiovascular diseases, but its quantification in circulating blood remains a challenge. NO can form paramagnetic iron-nitrosyl complexes with hemoglobin (5-coordinate- $\alpha$ -HbNO) in erythrocytes (RBCs) representing bioavailability of vascular endothelial function and NO in vivo. We observed the HbNO complex in RBCs from mouse, rat and human venous blood and we developed a modified subtraction method using EPR spectroscopy to quantify it. The HbNO circulating concentration is ~425nM in rodents and ~92nM in human venous blood. RBCs contain endothelial nitric oxide synthase (eNOS) protein. We measured, using NOS and arginase inhibitors, nitrite/nitrate production and HbNO formation in human, eNOS(+/+) and eNOS(-/-) mice RBCs. Nitrite and HbNO signals increased after arginase inhibition and were abrogated after NOS inhibition in human and eNOS(+/+) RBCs but insensitive to modulators in eNOS(-/-). However, HbNO signal from freshly drawn venous RBCs was minimally sensitive to NOS inhibitors ex vivo suggesting a minor contribution of erythrocytic NOS to HbNO complex compared with vascular endothelial NOS or other NO sources. Next, we determined that HbNO signal is influenced by physico-chemical determinants. The HbNO formation, upon exogenous NO donor exposure, was significantly higher in hypoxic condition (1% O<sub>2</sub>: 0.018±/-0.002µM compared to room air 0.0036±/-0.0004µM HbNO/NO donor µM). The stability of pre-formed HbNO was higher after 30min under hypoxia (17±/-0.4% degradation vs 49±/-0.2% at room air), at 20°C (16±/-0.3% degradation vs 30±/-0.1% at 37°C) and under acidic pH (32±/-1% vs 62±/-0.7% at physiological pH). HbNO signal is significantly preserved by RBCs incubation with catalase (2µM HbNO/L vs 0.5µM HbNO/L in untreated controls) whereas superoxide dismutase had minimal effect. Conversely, catalase inhibition highly increased ROS formation. This suggested that HbNO formation is sensitive to oxidative degradation, possibly by H<sub>2</sub>O<sub>2</sub>. Finally, we compared circulating HbNO levels in venous RBCs from healthy volunteers or patients with cardiovascular diseases and found decreased HbNO in patients

**P560**

**Circular RNAs in heart failure: identification of MICRA as a novel biomarker of left ventricular dysfunction**

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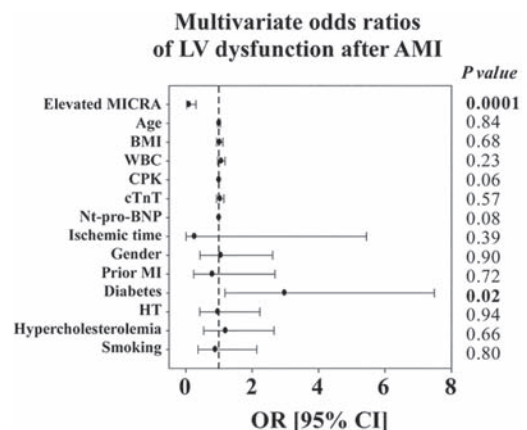
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**Background/Introduction:** Prediction of the development of left ventricular (LV) dysfunction after acute myocardial infarction (AMI) is challenging. Existing biomarkers such as brain natriuretic peptides have serious limitations due to lack of specificity and stability in the few hours following AMI. Therefore, novel biomarkers are needed to improve the identification of patients at risk of LV dysfunction after AMI. Both microRNAs and long noncoding RNAs circulating in the bloodstream have shown some potential to predict outcome after AMI. Whether circular RNAs (circRNAs), a novel class of long noncoding RNAs formed by back splicing, constitute a reservoir of cardiac biomarkers is unknown.

**Purpose:** To address the ability of circRNAs to predict outcome after AMI.

**Methods:** Expression levels of a circRNA called MICRA for Myocardial Infarction-associated Circular RnA were measured by quantitative PCR in peripheral blood cells obtained at reperfusion in a test cohort of 409 AMI patients and a validation cohort of 145 additional AMI patients. The capacity of MICRA to predict LV dysfunction (4-month LV ejection fraction <40%) was determined using univariate and multivariable analyses. Blood samples from 87 healthy volunteers and human LV biopsies from 22 failing hearts and 5 control hearts were also used. Results- In the test cohort, MICRA was down-regulated in AMI patients compared to healthy volunteers (P = 0.003) and was mostly expressed by lymphocytes. MICRA was a univariate predictor of 4-month LV dysfunction (P < 0.001). In multivariable analyses, MICRA was the strongest predictor of LV dysfunction (P = 0.0001; Figure). Patients with low levels of MICRA were at high risk of LV dysfunction (odds ratio 0.09 [95% confidence interval (CI) 0.03-0.31]). MICRA provided an additive predictive value, as demonstrated by a decrease in model deviance (P < 0.001) and an integrated discrimination improvement of 7%, 95% CI [2-12]. The predictive value of MICRA was confirmed in the validation cohort (odds ratio 0.03 [0.001-0.96]). Finally, MICRA was detected in the left ventricles of failing human hearts (P < 0.01).

**Conclusions:** We identified MICRA, a novel circRNA predicting LV dysfunction after AMI. This finding motivates further investigation of the biomarker and therapeutic value of circRNAs.





## P561

### Circulating miR-122-5p and miR-124a-3p predict outcome after out-of-hospital cardiac arrest. a sub-study of the target temperature management (TTM) trial

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**Background:** Heart failure is a frequent underlying cause of cardiac arrest. MicroRNAs (miRNAs) are small nucleotides with biomarker value in various cardiovascular contexts. Previous small-scale studies suggested that miRNAs might be useful indicators of outcome after cardiac arrest.

**Purpose:** To determine the prognostic value of miRNAs in a large cohort of comatose survivors of out-of-hospital cardiac arrest (OHCA).

**Methods:** The Target Temperature Management (TTM) trial addressed the potential benefit of TTM at 33°C vs. 36°C on outcome after OHCA. In this sub-study, circulating levels of 5 miRNAs (Table) were measured in serum samples from 579 TTM patients, 48h after return of spontaneous circulation. The primary and secondary end-points were poor neurological outcome at 6 months and survival at the end of the trial, respectively.

**Results:** Forty-eight percent of the patients had a poor neurological outcome or were dead at 6 months, presenting lower miR-122-5p and higher miR-124a-3p levels compared to good outcome patients (both  $p < 0.001$ ). This was independent of targeted temperature management regimen. Both miRNAs were significant univariable predictors of neurological outcome (odds ratios 0.68 [0.54-0.86] for miR-122-5p and 5.75 [3.97-8.34] for miR-124a-3p). In multivariable analyses including neuron-specific enolase, miR-122-5p and miR-124a-3p were independent predictors of neurological outcome (Table) and generated an integrated discrimination improvement of 0.03 ( $p < 0.001$ ). In Cox proportional hazards models, miR-122-5p and miR-124a-3p were significant predictors of death (hazards ratios 0.67 [0.52-0.86] and 2.53 [1.94-3.28]).

**Conclusion:** Low levels of miR-122-5p and high levels of miR-124a-3p predict poor neurological outcome and mortality after OHCA.

#### Odds ratio of poor neurological outcome

Parameter	OR	95% CI	p-value
Neuron-specific enolase	1.04	1.01-1.07	0.003
Log miR-21-5p	1.43	0.84-2.43	0.19
Log miR-122-5p	0.38	0.22-0.65	< 0.001
Log miR-124a-3p	4.94	2.63-9.29	< 0.001
Log miR-181a-5p	0.66	0.37-1.18	0.16
Log miR-221-3p	0.69	0.41-1.18	0.17

Other variables in the model: age, gender, time from cardiac arrest to return of spontaneous circulation, bystander cardiopulmonary resuscitation, first monitored rhythm, shock on admission, lactate levels and targeted temperature management regimen.

## P562

### Galectin 3 plasma levels at baseline correlate with poor clinical outcome in patients with peripartum cardiomyopathy

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**Background: and objective:** Peripartum cardiomyopathy (PPCM) is characterized by new onset of heart failure in late pregnancy and up to the first six months postpartum. Galectin 3 is a  $\beta$ -galactoside-binding lectin protein that is required for transforming growth factor (TGF)- $\beta$  pathway-mediated myofibroblast activation leading to cardiac fibrosis. This matricellular protein was described as a prognostic biomarker in heart failure patients. We aimed to determine whether galectin 3 and cardiac fibrosis are associated with poor outcome in PPCM patients.

**Methods and Results:** In this single centre prospective study, we enrolled 37 PPCM patients and 10 age-matched healthy subjects. All patients received ACE inhibitors and beta-adrenergic blocking agents. Plasma NT-proBNP and Galectin 3 levels were measured at baseline. Echocardiograms were performed at baseline and six months postpartum. Poor outcome in PPCM patients was defined by NYHA  $\geq 3$  or death.

At baseline, PPCM patients had significantly higher NT-proBNP and Galectin 3 levels than healthy controls ( $p < 0.001$  and  $p < 0.05$ , respectively). Six months postpartum, four patients did not improve their cardiac function (EF,  $26.7 \pm 7.4\%$ ) and seven died. Baseline NT-proBNP ( $3865.6 \pm 1039$  vs.  $1730.1 \pm 245$  pmol/l,  $p = 0.035$ ) and Galectin 3 ( $15.72 \pm 0.91$  vs.  $8.75 \pm 0.69$  ng/ml,  $p = 0.02$ ) levels were significantly higher in patients with poor outcome compared to patients that improved their cardiac function (EF,  $45.7 \pm 11.3\%$ ).

**Conclusion:** NT-proBNP and Galectin 3 levels were increased in the plasma of PPCM subjects who had poor outcome 6 months after delivery. Galectin 3 may be a clinically useful biomarker that identifies a subset of PPCM patients at highest risk of myocardial dysfunction due to fibrosis. These findings should be confirmed in a larger cohort and could lead to specific therapeutic intervention.

## P563

### Role of galectin-3 and plasma B-type natriuretic peptide in predicting prognosis in discharged heart failure patients

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In discharged HF patients the combination of galectin-3 and NT-proBNP seemed to be the best predictor for short-term (60-day) mortality. Furthermore, galectin-3 demonstrated to be a robust independent marker of cardiovascular mid-term (18-month) outcome in HF patients. The objective of this study was to analyse the value of a single, pre-discharge determination of plasma galectin-3 alone and in correlation with plasma BNP in predicting mid-term clinical outcome in HF patients discharged after an acute decompensated heart failure (ADHF) episode.

**Methods:** all HF subjects discharged alive after an ADHF episode were enrolled in an out-patient clinic follow-up. All patients underwent a determination of BNP and galectin-3, a 6-minute walk test (6MWT) and a transthoracic echocardiogram within 48 hours upon hospital discharge. Death by any cause, cardiac transplantation and worsening heart failure requiring readmission to the hospital were considered cardiovascular events. Data regarding the occurrence of cardiovascular events were collected from multiple sources in all patients.

**Results:** eighty-three patients (67 males, age 73 ys old) were analysed (mean follow-up  $11.6 \pm 5.2$  months; range 3-22 months). During the follow-up 38 events (45.7%) were scheduled (13 cardiac deaths, 35 re-hospitalisation for ADHF). Main differences between the events group vs no-events group are described in Table 1. CHF patients who suffered an event are more impaired in renal function and showed an higher plasma BNP and Gal-3 at pre-discharge evaluation. Choosing adequate cut-off points (BNP  $\geq 500$  pg/ml and Gal-3  $\geq 17.6$  ng/ml), the Kaplan-Meier curves depicted the powerful stratification using BNP+Gal-3 in predicting clinical course at mid-term follow-up (Fig 1) (log rank 5.65;  $p = 0.017$ ).

**Conclusion:** adding Gal-3 to BNP, a single pre-discharge strategy testing seemed to obtain a satisfactorily predictive value in alive HF patients discharged after an ADHF episode.

Tab 1

	No-event group (45pts)	Event group (38 pts)	p
Age	72.6 $\pm$ 11.6	74 $\pm$ 7.4	0.5
Galectin-3 (pg/ml)	19.1 $\pm$ 10.5	24.4 $\pm$ 10.9	0.03
LVEF (%)	40.7 $\pm$ 15.8	33.8 $\pm$ 16.4	0.07
Creatinine	1.3 $\pm$ 0.9	1.4 $\pm$ 0.7	0.5
6MinWalkingTest (m)	374.4 $\pm$ 186.2	287.2 $\pm$ 102.2	0.01
Glomerular Filtration Rate	70.3 $\pm$ 17.3	58.8 $\pm$ 22.6	0.05
Haemoglobin (gr/dl)	13.2 $\pm$ 2.4	12.7 $\pm$ 2.1	0.6
BNP (pg/ml)	681.5 $\pm$ 569.5	1357.5 $\pm$ 1229.2	0.003

LVEF = left ventricular ejection fraction; BNP=brain natriuretic peptide.

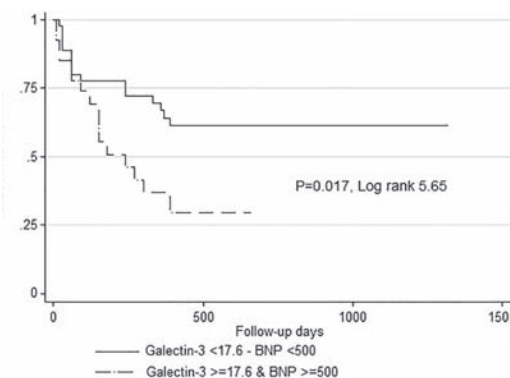


Fig 1

## P564

### Osteopontin could be a predictor of severity in patients with corepulmonale and patients with left sided heart failure?

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**Objectives:** to measure osteopontin levels in patients with corepulmonale and patients with left sided heart failure and correlate these levels with pulmonary artery systolic pressure and ejection fraction respectively.

**Background:** Many biomarkers were recently investigated as possible diagnostic and prognostic makers in left sided and right sided heart failure.

**Methods:** The study included 75 subjects, divided in three groups : 20 patient in group 1 suffering from left sided heart failure, 23 patients in group 2 suffering from right sided heart failure and cor pulmonale, 20 healthy persons in control group and 12 patients were excluded. All individuals were subjected to thorough history taking, clinical examination, conventional transthoracic echocardiography, osteopontin and brain natriuretic peptide plasma levels measurement.

**Results:** osteopontine and BNP plasma levels were significantly higher in left sided heart failure patients as well as in patients with corepulmonale compared with control group (patients with corepulmonale have the highest values ). There was significant negative correlation between osteopontine and EF( $r=-0.681, p=0.001$ ) and significant positive relationship between osteopontine and NYHA class in patients with left sided heart failure( $r=0.605, p=0.002$ ). In patients with corepulmonale, there was insignificant positive correlation between osteopontin and PASP ( $r=0.311, p=0.148$ ).

**Conclusion:** osteopontin levels were significantly increased in patients with left sided heart failure and correlated with ejection fraction and NYHA class. Also increased significantly in patients with corepulmonale and right sided failure but the correlation with pulmonary artery systolic pressure was non significant.

## P565

### Prevention of rehospitalization for heart failure through site visits on Italy territory using an equipped vehicle with POCT brain natriuretic peptide(BNP) + bioimpedance vector analysis (BIVA)

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**Background:** Prevention of rehospitalization for Heart failure is a major worldwide issue. The objective of this study was to evaluate if outside hospital medical visits in several Italian areas using an itinerant vehicle equipped with BNP and BIVA would be helpful in identifying patients at risk for rehospitalization for HF.

**Methods:** This was an observational study by using a medicalized vehicle traveling through 11 cities in Italy during the heart failure ESCHA awareness week of 2015. All studied patients underwent into the vehicle: 1.Health questionnaire to test the presence of symptoms of heart failure; 2.Physical examination with vital signs assessment; 3. POCT BNP Test measurement (pg/ml) (AleretM Heart Check) and 4.BIVA(EFG)assessment. Patients were followed up by phone call 90 and 180 days after in order to check the occurrence of events (death, rehospitalization and needs for Cardiology urgent visit).

**Results:** 100 patients (M/F 56/44), mean age  $67.69 \pm 13.13$  years were enrolled. On the basis of recorded data patients were divided into four groups: group 1, patients without heart failure (36%); group 2, patients with unrecognized heart failure (21%); group 3, patients with controlled chronic heart failure (19.4%); group 4, patients with heart failure not controlled by therapy (23.6%). In group 1,2,3 and 4 : median values of [IQR] of BIVA and BNP were:73.7%[73.-73.9] and 52.0[35.0-91.0]; 79%[76.3-81.5]

and 270[189.7-383]; 73.7%[73.5-73.8] and 132.5[73-221]; and 80.9%[77.6-84.9] and 241[151.7-460.2] respectively. There was a significant difference within the groups both for BIVA and for BNP: group1 vs group2 ( $p < 0.0001$ ); group1 vs group4 ( $p < 0.0001$ ); group2 vs group3 ( $p < 0.0001$ ); group 3 vs group4 ( $p < 0.0001$ ). A direct correlation was found between BNP and Hydration% ( $r=0.34, p < 0.003$ ), and a significant inverse correlation between BNP and reactance ( $r=-0.38, p < 0.001$ ). In all studied population the combination of BNP+BIVA showed to have good prognostic power for future events with an AUC 0.78 ( $p < 0.001$ ). In the group 4: the value of the BNP (with a cut-off  $> 211$  pg/ml) showed to be as a prognostic factor for future events with an AUC 0.90 ( $p < 0.0001$ ); while at BIVA analysis: hydration percentage (with a cut-off  $> 82\%$ ) and reactance (with a cut-off  $< 29.2$  ohm) resulted to be have prognostic role for future events with AUCs of 0.82 ( $p < 0.001$ ) and 0.78 ( $p < 0.006$ ) respectively.

**Conclusion:** In patients with HF, on site preventive, examination using POCT BNP+BIVA seems to be useful to identify those subjects apparently asymptomatic and in stable condition but at risk for future events. This initiative could be useful for primary heart failure prevention and better management in order to avoid rehospitalizations for worsening heart failure.

## P566

### Diagnostic and prognostic value of BNP, NGAL, ST2 AND TnIhs in patients with hypertensive crisis in the emergency department

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**Introduction:** Hypertensive Crisis are one of the most common and frequent cause of visits for patients referring to Emergency Department (ED). There are few studies in literature investigating the diagnostic and prognostic role of biomarkers in patients with hypertensive crisis.

**Purpose:** Aim of this study was to investigate the diagnostic and prognostic role of Brain Natriuretic Peptide (BNP), Neutrophil Gelatinase-Associated Lipocaline (NGAL), suppression of tumorigenicity 2 (ST2) and high sensitive Troponin I (TnIhs) in patients with hypertensive crisis, and to evaluate their possible role in the differential diagnosis between hypertensive emergencies or urgencies.

**Methods:** This was a prospective observational study in hypertensive crisis patients (Systolic Blood Pressure  $> 180$  mmHg and/or Diastolic Blood Pressure  $> 120$  mmHg), presenting to the ED of Sant'Andrea University Hospital of Rome from August 2014 to February 2015. At ED arrival BNP, NGAL, ST2 and TnIhs blood values were measured.

**Results:** 73 patients (M/F 40/35; mean age  $66.39 \pm 14.05$  years) with hypertensive crisis (34 hypertensive emergencies; 39 hypertensive urgencies) were enrolled. In hypertensive emergencies the final diagnosis were: acute ischemic coronary disease (8/34, 24%), acute pulmonary edema (8/34, 24%), acute cerebrovascular disease (13/34, 38%), acute renal failure (5/34, 14%). Compared to patients with hypertensive urgencies, patients with hypertensive emergencies showed significantly higher levels of biomarkers (BNP  $358.36 \pm 504.68$  vs  $43.80 \pm 36.94$  pg/ml ( $p=0.001$ ); NGAL  $85.55 \pm 75.33$  vs  $53.40 \pm 22.23$  ng/ml ( $p=0.04$ ); TnIhs  $11.80 [3.34 - 3.67]$  pg/ml vs  $3.75 [2.2 - 8]$  pg/ml ( $p < 0.0007$ ). ST2 levels were not different in the two subgroups of patients: ST2  $31.55 [21.5 - 51.7]$  ng/ml e  $31.5 [19.42 - 51.07]$  ng/ml ( $p=0.66$ ). We analyzed biomarkers prognostic value in terms of probability of rehospitalization: BNP showed a significant prognostic value (AUC 0.744,  $p < 0.0001$ ), similar to the combination of the three biomarkers (AUC 0.672,  $p < 0.03$ ).

**Conclusions:** BNP, NGAL and TnIhs seem to be potential useful biomarkers in distinguishing hypertensive emergencies from urgencies in Emergency Department. Moreover, BNP seems to have a good prognostic value for rehospitalization in patients with hypertensive emergencies from the ED.

## P567

### Features of N-terminal of the prohormone brain natriuretic peptide plasma level in patients with arterial hypertension and chronic heart failure with a preserved left ventricular ejection fraction

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Purpose of research is to study the characteristics of N-terminal of the prohormone brain natriuretic peptide plasma level (NT-proBNP) in patients with arterial hypertension (AH) and heart failure with a preserved left ventricular ejection fraction (HFpEF).

**Research methods:** 346 men, average age  $46.68 \pm 10.44$  year were surveyed and divided into groups: group 1 - patients with hypertension without HF (n=180); group 2 - patients with AH and HFpEF (n=86). Healthy men with normal blood pressure, without CH (n=80) representative by age were included in a control group. All patients underwent echocardiography, daily monitoring of arterial pressure, NT-proBNP plasma level was determined with enzyme-linked immunosorbent assay (ELISA method).

**Results:** the highest NT-proBNP was in the patients of the first group with 1 degree of hypertension in comparison with patients with 2 and 3 degree of

AH, the control and the second group of patients. Correlation analysis of the data in group 1 showed an inverse correlation between NT-proBNP and the degree of hypertension ( $r=-0,624$ ;  $p=0,023$ ). In group 2 this correlation was not established ( $r=0,151$ ;  $p=0,294$ ). NT-proBNP in group 2 correlated with functional class of chronic heart failure ( $r=0,215$ ;  $p=0,049$ ) and diastolic filling: E ( $r=0,252$ ,  $p=0,05$ ), E/A ( $r=0,347$ ,  $p=0,018$ ). The level of natriuretic peptides was highest in the group "non-dipper", "night-peaker" and statistically significantly different from patients with an unchanged circadian blood pressure profile and the profile of the "over-dipper" as for systolic blood pressure, and the circadian profile of diastolic blood pressure.

**Conclusions:** The determination of natriuretic peptides in patients with arterial hypertension and chronic heart failure personifies the diagnosis of disease and prediction of cardiovascular events: a decrease in plasma levels of NT-proBNP in patients with arterial hypertension without HF is associated with higher degree of hypertension and the risk of defeat of target organs; in patients with chronic heart failure, regardless of the degree of hypertension, increased levels of natriuretic peptides indicates the severity of myocardial dysfunction and severity of chronic heart failure.

### P568

#### Exhaled breath analysis in diagnostics of heart failure with preserved ejection fraction

This study was supported by Russian Academy of Science  
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#### Background:

Heart failure (HF) is a leading cause of cardiovascular morbidity and mortality. The 5-year survival rate for all patients with heart failure, regardless of ejection fraction (EF), is less than 50%. Data from epidemiologic studies of heart failure with preserved EF (HF-PEF) find that the annual mortality is approximately 10%. The diagnosis of HF-PEF is more difficult than the diagnosis of HF with reduced EF (HF-REF). In our previous studies we found out that concentration of certain voluntary organic compounds (VOCs) in exhaled breath in patients (pts) with and without HF is differ.

#### Purpose:

The purpose of this study was to investigate exhaled breath in patient with HF-PEF. METHODS From October 2013 to September 2015 we enrolled 21 pts with HF-PEF in heart failure group and 16 pts without HF in control group. HF-PEF was diagnosed according ESC active guidelines. We collected fasting exhaled breath samples of all patients in 1L Tedlar bags. Exhaled breath was analyzed using PTR-MS (Compact PTR-MS, Ionicon, Austria).

**Results:** The baseline characteristics of pts are in the Table 1. In compare with control group several biomarkers were significantly higher in HF-PEF group. They are acetone, acetic aldehyde, ethanol, propylene. The median (interquartile range) concentration of acetone in HF-PEF group when compared to control group was 934 ppb [324-2432] vs 322 ppb [280-368],  $p=0,002$ ; acetic aldehyde 297 [213-441] vs 193 [177-231],  $p=0,004$ ; ethanol 18 [14-28] vs 10,6 [9-21],  $p=0,018$ ; propylene 343 [122-873] vs 124 [94-141],  $p=0,04$  respectively.

**Conclusion:** There are significant difference in exhaled breath between patients with HF-PEF and without heart failure. Further investigation is necessary to determine the correlation between these biomarkers and levels of natriuretic peptides.

#### Baseline characteristics.

	HF-PEF (n=21)	Control group (n=16)
Mean age (range), years	72 (60 - 75)	64 (38 - 70)
Male sex - n, %	10 (47,6%)	9 (56,3%)
Medical history		
Hypertension - n, %	21 (100%)	14 (87,6%)
Diabetes mellitus - n, %	8 (38,1%)	2 (12,5%)
Previous MI - n, %	10 (47,6%)	2 (12,5%)
Atrial fibrillation - n, %	13 (61,9%)	0
Mean EF, %	60 ± 7	69 ± 4

MI - myocardial infarction

### P569

#### Cardiac expression of NGAL is up-regulated in experimental cancer cachexia

Piano di azione e coesione ricerca e competitività PON 2007-2013

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**Introduction:** NGAL is commonly seen as a marker of kidney injury; however, it has also been associated with critically ill patients (heart failure, sepsis, multi-organ failure) and is thought to play a role in cancer cell motility.

**Study design and methods:** Here we compared the mRNA expression of NGAL in the heart of cachectic rats bearing the Yoshida hepatoma ( $n=16$ ) to that of the aldosterone antagonist spironolactone-treated (5 or 50 mg/kg/d,  $n=11$  and 9, respectively) rats as well as healthy controls ( $n=10$ ). Plasma levels of NGAL and aldosterone were assessed by ELISA. Tumor bearing rats lost  $45 \pm 4$ g body weight, while controls gain  $61 \pm 3$ g ( $p < 0.001$ ) after 16 days. Five mg/kg/d spironolactone reduced wasting ( $-25 \pm 10$ g) and 50mg/kg/d stopped weight loss ( $+0.5 \pm 16$ g,  $p < 0.05$ ). Cardiac NGAL mRNA expression was up-regulated by 93% compared to controls ( $p < 0.05$ ) and was reduced to control levels by 50 mg/kg/d spironolactone ( $p > 0.05$ ), while the 5mg/kg/d dose was not effective. Aldosterone was up-regulated from  $337 \pm 7$  pg/mL in controls to  $591 \pm 31$  pg/mL in the placebo group ( $p < 0.001$ ) and reduced to  $396 \pm 22$  pg/mL in animals treated with 50mg/kg/d spironolactone ( $p < 0.01$ ). Plasma levels of NGAL were increased in tumor-bearing rats ( $1462 \pm 360$  g/L) compared to controls ( $93 \pm 6$  g/L,  $p < 0.001$ ). High dose spironolactone reduced NGAL levels to  $530 \pm 77$  g/L ( $p < 0.05$  vs placebo). Cardiac function assessed by echocardiography was markedly improved by high dose spironolactone. Cardiac output on day 11 was decreased in the placebo group compared to control  $49 \pm 7$  mL/min vs  $80 \pm 7$  mL/min, respectively  $p < 0.01$ ). This functional impairment was reduced by high dose spironolactone ( $79 \pm 7$  mL/min,  $p < 0.01$  vs placebo), which may functionally reflect the reduction of NGAL mRNA in the heart and protein in plasma.

**Conclusion:** NGAL could potentially be used as a biomarker to assess cardiac impairment in cancer cachexia. However, more studies are needed to confirm our results.

### P570

#### Dependence of concentrations of heart failure biomarkers on ultrasound indicators of remodeling in subjects with myocardial infarction

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**Purpose:** To estimate the content of galectin-3 and its relationship with ultrasound indicators of remodeling in comparative aspect with N-terminal natriuretic propeptide (Nt-proBNP).

**Materials and methods:** We examined 87 subjects admitted with the diagnosis of ST-elevated myocardial infarction (STEMI). All the subjects underwent standard diagnostic methods in MI, including coronary angiography (CAG). On the 10th - 14th days of MI all the subjects underwent echocardiography under standard modes with left ventricle (LV) ejection fraction (EF) estimation and remodeling parameters such as LV end-diastolic dimension (EDD), LV end-systolic dimension (ESD). Galectin-3 was estimated by immunoenzyme method in blood serum in all the subjects on the 1st - 2nd days of the disease and in 81 subjects it was estimated in dynamics on the 10th - 14th days. The allowed values of this biomarker in blood serum are 0.0-2.28 ng/ml. Nt-proBNP level was estimated in 81 subjects on the 1st - 2nd days of MI and in 78 subjects on the 10th - 14th days of the disease. Reference range of this indicator in subjects younger than 75 years old is up to 125 pg/ml, older than 75 years old - up to 450 pg/ml. We used standard statistical methods of data processing.

**Results:** Evaluation of instrumental indicators showed that subjects with LV dilatation are characterized by higher ( $=0.01$ ) values of galectin-3 estimated on the 10th - 14th days of the disease ( $26.1 [11.9;42.9]$  ng/ml and  $10.6 [9.1;28.9]$  ng/ml respectively). These data were also confirmed by conducting a correlation analysis, thus we noted a positive correlation of galectin-3 estimated on the 10th - 14th days of MI with the values of LVEDD ( $r=0.39$ ;  $p=0.01$ ) and LVESD ( $r=0.4$ ;  $p < 0.01$ ). The presence in subjects of a reduced LVEF less than 40% was associated ( $=0.01$ ) with the increased value of galectin-3 on the 10th - 14th days of MI which was  $45.6 [44.8;52.8]$  ng/ml as compared to subjects with the preserved LVEF -  $15.5 [9.9;35.9]$  ng/ml. Nt-proBNP level didn't show any significant association with echocardiographic parameters.

**Conclusions:** Galectin-3 is more sensitive to ultrasound markers of acute myocardial remodeling as opposed to Nt-proBNP.



## BASIC SCIENCE: PATHOPHYSIOLOGY

## P571

**Low ambient temperature induces increased mortality, cardiac autonomic nervous system dysregulation and heart dysfunction in endotoxemic mice**

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**Purpose:** Induced therapeutic hypothermia is documented to be organ-protective including neuro- and cardiac protection. In contrast, spontaneously occurring hypothermia provokes several negative effects that rise concerns regarding potential detrimental effect of induced hypothermia, particularly during inflammation. Whereas septic patients with hypothermia suffer from higher incidence of organ dysfunction and increased mortality, underlying molecular mechanisms are barely elaborated.

**Methods:** Mice were acclimatized either to neutral ambient temperature of 30°C (normal ambient temperature group, NORM) or reduced ambient temperature of 26°C (reduced ambient temperature group, COOL). Thereafter, mice received LPS (10mg/g bw i.p.) and effects on survival, cardiac autonomic regulation (ANS, telemetry), left ventricle performance (Pressure-Volume-conductance) and stress-associated tissue injury and cell death in heart were studied at control, 3h, 24h, 3days & 7days post injection.

**Results:** Intriguingly, an enhanced sympathetic tone verified by heart rate (HR), HRV (heart rate variability), sympathetic tone activity and cardiac catecholamine release was found in mice kept at 26°C. Mortality rate of the COOL group was significantly increased (> 50%) after LPS-induced SIRS, compared to the NORM group (mortality rate < 10%). The evaluation of body temperature revealed a LPS-dependent induction of hypothermia in both groups, which was more pronounced in the COOL group by about 4°C. We further revealed that the cardiac contractility was transiently impaired in mice kept at 30°C with complete recovery after 7days, whereas animals of the COOL group developed a pronounced and prolonged myocardial dysfunction with reduced contractility compared to the NORM group. The reduced contractility of the COOL group was further confirmed by a reduced beta adrenergic pathway activity of heart tissue. Surprisingly, the level of inflammation in cardiac tissue from both groups was comparable, whereas the stress maker (HSP90) for tissue and organ injury known to be upregulated under catecholamine overstimulation was abundantly increased in COOL group. In addition, further evaluation of cardiac tissue revealed a higher level of stress-related inflammatory response (iNOS expression with enhanced nitrotyrosine formation), stress-induced damage (PARP) and cell death (Tunel positive) in mice from the COOL group.

**Conclusion:** Enhanced sympathetic activation induced by unsuitable ambient temperature provokes in LPS-induced SIRS mice significant effects including mortality rate and sustained heart failure.

## P572

**Effects of GRK5 gene removal in stress induced cardiomyopathy**

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**Background:** G protein coupled receptor kinase 5 (GRK5) is a ser/thr kinase involved in the regulation of the beta adrenergic receptors ( $\beta$ ARs) signaling and cardiac function. A genetic variant of GRK5 gene (L41Q polymorphism) is strongly associated with Stress Induced Cardiomyopathy, in which catecholaminergic stress plays a central role. We can induce SIC like regional akinesia in mice by intraperitoneal (i.p.) injection of a single dose (400 mg/kg) of isoprenaline (ISO), a non-selective beta adrenergic agonist.

**Purpose:** To evaluate the role of GRK5 in the pathogenesis of SIC.

**Methods:** In order to assess the effects of ISO on global and regional cardiac contractility we performed echocardiography (Vevo 770) in mice with gen deletion for GRK5 (GRK5KO) and C57BL/6J (WT) used as control. We calculated Ejection Fraction (EF) and Fractional Wall Thickening (FWT), defined as the ratio between wall thickness in systole and diastole, in basal condition and after stimulation with ISO. FWT was calculated in 18 different cardiac segments. Results were represented as variation of EF and FWT ( $\Delta$ EF% and  $\Delta$ FWT) respect to basal. At last, hearts were collected for biochemical analysis.

**Results:** In WT group after 2 hrs stimulation we observed a  $\Delta$ 25%  $\pm$  2% for EF, while the analysis of  $\Delta$ FWT evidenced a regional contractile impairment in 13/18 cardiac segments. In GRK5KO group after 2 hours stimulation we observed an higher  $\Delta$ EF% respect to WT ( $\Delta$ 52%  $\pm$  4%) while the analysis of  $\Delta$ FWT evidenced an impairment of contractility in only 9/18 cardiac segments. In particular, contractility impairment

was significantly higher in apical segments in WT group in comparison to GRK5KO group (6/6 in WT vs 3/6 in GRK5KO). To identify the role of regional  $\beta$ AR signaling we explored the localization to cardiac membranes of another GRKs classically associated to desensitization, GRK2. In membrane extracts from basal and apical sections of myocardium, in basal condition, GRK2 levels are higher in the apex of WT mice and ISO reduced such accumulation. Opposite, in GRK5 KO mice, GRK2 levels are lower in the apex in basal condition, compared with WT, and are recovered in response to ISO.

**Conclusion:** This data confirm the role played by catecholaminergic stress in SIC. GRK5 removal preserve left ventricular function in this condition, suggesting that  $\beta$ AR desensitization is involved in the pathogenesis of SIC. Moreover, SIC specific cardiac phenotype may be due to the different pattern of distribution of GRKs and  $\beta$ ARs.

## P573

**A-B crystallin reverses high titin-based stiffness in failing human cardiomyocytes**

FP7-Health-2010; MEDIA-261409

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**Background:** Increased diastolic stiffness is present in almost every heart failure patient and is caused by fibrotic changes of the extracellular matrix (ECM) and changes in the cardiomyocyte protein titin. **Purpose:** The purpose of this study was to determine the relative contributions of the ECM collagen and the cardiomyocyte titin to diastolic stiffness in failing human hearts. Moreover, different contributors to titin-based stiffness were explored.

**Methods:** Left ventricular tissue was procured during aortic valve replacement in patients with severe aortic stenosis (AS, n=7) or during cardiac catheterization in patients with dilated cardiomyopathy (DCM, n=3). Explanted donor hearts (n=8) served as controls. Myocardial strips were dissected and attached between a force transducer and a length motor to measure passive stiffness (Fpassive) caused by titin and collagen over a range of muscle stretches. After detaching all cardiomyocyte filaments with KCl and KI, stretches were repeated and the remaining Fpassive was collagen-based. In isolated, single cardiomyocytes, similar experiments were performed to further explore titin-based Fpassive. Cardiomyocytes subsequently underwent incubation with alkaline phosphatase to dephosphorylate titin, a prestretch in an acidic environment (to mimic failing myocardium) and, finally, incubated in  $\alpha$ -B crystallin. After each step, muscle stretches were repeated and Fpassive was determined. Also, another series of experiments were performed in AS samples to determine the effect of each individual step in the single cardiomyocyte experiments.

**Results:** Cardiomyocyte Fpassive was increased over the whole range of stretches in AS and DCM, whereas ECM Fpassive was only higher in failing hearts at higher muscle lengthening. Fpassive in donor samples increased after dephosphorylation, but not to levels observed in failing cardiomyocytes. Acidity and prestretch increased Fpassive in donor to reach levels observed in failing cardiomyocytes and this was normalized by  $\alpha$ -B crystallin. In single AS cardiomyocytes, prestretch was the key mechanism to increase Fpassive. In failing cardiomyocytes, irrespective of pretreatment,  $\alpha$ -B crystallin normalized Fpassive.

**Conclusion:** The ECM contributed to increased diastolic stiffness in failing myocardium, but only at higher muscle lengthening or at an advanced stage. Cardiomyocyte Fpassive was increased over a whole range of muscle stretches in failing myocardium. Changes in titin phosphorylation status were insufficient to explain the increased Fpassive in failing cardiomyocytes. These findings suggest that structural changes, such as titin aggregation under conditions of wear and tear lead to increased cardiomyocyte Fpassive and this was normalized by administration of  $\alpha$ -B crystallin.

## P574

**Cardiac dysfunction induced by ionizing radiation exposure: the mitochondrial side**

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**Background:** Exposure to ionizing radiation (IR) is a cause of cardiac dysfunction whose severity relates among other factors to the increased reactive oxygen species production (ROS). Mitochondria, being the primary source of radical oxygen species (ROS) and of energetic substrates for the myocardium, are the possible mechanisms of IR related cardiac dysfunction.

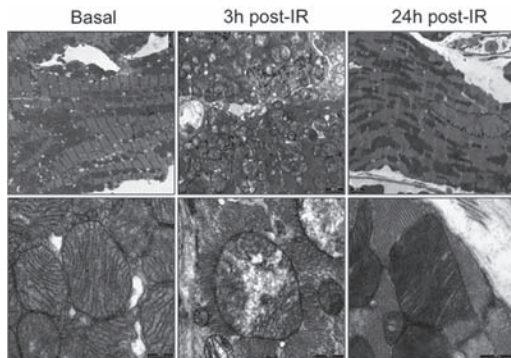
**Purpose:** To evaluate the possible involvement of mitochondria to mediate the effects of IR exposure on cardiac function.

**Methods:** In C57BL/6 mice subjected to IR exposure by X-ray (4 Gy), we performed

echocardiography at basal, and 3 and 24 hours post IR exposure. Mice were sacrificed and heart samples collected at each time point for analysis of mitochondria morphology by transmission electron microscopy (TEM) and biochemistry.

**Results:** At 3 h post-IR, we observed increased left ventricle diastolic diameter (LVdD:  $39.5 \pm 0.3$  vs  $35 \pm 0.15$  mm;  $p < 0.05$  vs Basal) with reduced ejection fraction (EF:  $45\% \pm 2$  vs  $66\% \pm 4$ ;  $p < 0.05$  vs Basal). At 24h post-MI, we found a recovered LVdD ( $36.2 \pm 0.4$  vs  $35 \pm 0.15$  mm; ns) and ameliorated cardiac contractile function (EF:  $60\% \pm 3$  vs  $66\% \pm 4$ ; ns). Morphological analysis by TEM (Fig 1) revealed that, at 3 hours post IR exposure, mitochondria were reduced in number, showing cristae disarrangement with intra-vacuolization and fragmentation. At 24 h post-IR mitochondria number and morphology are recovered with normal cristae and absence of vacuolization. Morphological changes were accompanied by molecular modifications involved in mitochondria induced apoptosis (Cyt C), mitophagy (p62) and mitochondrial mass (SOD). In particular, Cyt C release was dramatically increased into cytosolic fraction at 3 h post IR and reduced at 24 h. Similarly, p62 was increased in response to stress at 3 h with a partial reduction at 24 h. Inversely, SOD level was reduced at 3h but normalized at 24h as compared to basal, indicating recovering of mitochondrial mass. Mitochondria damage was also evaluated by expression of the different complexes (I to IV) composing the mitochondria respiratory chain through RT-PCR. At 3 h post-IR complex I,II,III and IV are all reduced as well ATPase expression. At 24 hours post-IR, complexes expression and ATPase were recovered.

**Conclusions:** IR induces an acute cardiomyopathy that is associated to an altered mitochondrial morphology and function.



Mito post IR

**P575**

**Biventricular remodelling in pressure overload: the role of adipose tissue and inflammation**

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**Purpose:** Evaluate the impact of left ventricle chronic pressure overload in both ventricles and the contribution of inflammatory mediators produced by the adipose tissues in the cardiac adaptations.

**Methods:** Wistar rats (65-85g) were randomly divided and submitted to ascending aortic constriction (AC group) or sham procedure (Sh group). Echocardiographic and hemodynamic evaluations were performed after 8 weeks and samples of myocardium, skeletal muscle and adipose tissue obtained for morpho-histological and molecular assessment.

**Results:** (Figure): As expected the AC group developed increased heart weight, left ventricle (LV) wall thickness, cardiomyocyte hypertrophy and elevated fibrosis content compared with the Sh group. The AC also promoted increased systolic pressure (Psyst), reduced contractile reserve (Pisovol) and myocardial stiffness (EDPVR) of LV. Interestingly the same structural adaptations were observed in the right ventricle (RV) of the animals with AC: cellular hypertrophy and fibrosis deposition. At the functional level these animal presented elevated Psyst beside increased TEI index and time of constant of isovolumetric relaxation (Tau) in the RV. Furthermore, although similar body weight in the 2 groups, the AC animals presented adipose tissue and skeletal muscle atrophy at cellular level. These structural alterations in the adipose tissue resulted in altered secretory profile with increased synthesis of pro-inflammatory molecules such as TNFα.

**Conclusions:** We observed that LV overload affect both ventricles before impairment of the systolic function. This condition also impacts other tissues at an early stage, stimulating skeletal muscle and adipose tissue atrophy. Mediating the bi-ventricular cardiac remodeling might be the pro-inflammatory environment promoted by the dysfunctional adipose tissue.

	Sh (n=13)	Ba (n=10)		Sh (n=13)	Ba (n=10)
Body weight (g)	320±3	322±5	Skeletal muscle		
Heart weight/TL (g/cm)	2.3±0.05	3.2±0.20*	Soleus (TL) (g/cm)	0.42±0.011	0.44±0.008
LV Cardiomyocyte CSA (µm <sup>2</sup> )	381±9	483±7*	Soleus CSA (µm <sup>2</sup> )	341±17.3	231±206*
Fibrosis (%)	4.7±0.38	7.6±0.84*	EDV (TL) (µm <sup>3</sup> )	0.37±0.020	0.34±0.018
WV (µm <sup>3</sup> /cm <sup>2</sup> )	45±2.9	60±1.9*	EDV CSA (µm <sup>2</sup> )	395±12.9	330±25.8*
Psyst (mmHg)	108±3.9	151±3.5*	Adipose tissue		
EDPVR	0.08±0.008	0.08±0.024*	Adipose tissue/TL (g/cm)	7.3±0.77	7.5±0.21
Pisovol (%)	70±4.7	47±5.4*	Adipocyte CSA (µm <sup>2</sup> )	225±2.7	281±2.8*
RV Cardiomyocyte CSA (µm <sup>2</sup> )	278±3.7	355±5.9*	TL (µm <sup>2</sup> /NA, AU)	0.03±0.020	0.07±0.014*
Fibrosis (%)	5.4±0.31	8.0±0.56*	IL1β (mRNA, AU)	0.06±0.014	0.28±0.12
TEI index	0.26±0.005	0.32±0.011*	Gas6m3 (mRNA, AU)	0.36±0.05	0.48±0.08
Psyst (mmHg)	22±0.79	27±0.94*	Resistin (mRNA, AU)	0.09±0.03	0.13±0.01
Tau (s)	8.4±1.34	12.8±1.25*			

\*vs Sham p<0.05.

AU: arbitrary units; BSA: body surface area; CSA: cross sectional area; EDV: end-diastolic volume; EDPVR: end-diastolic pressure-volume relationship; IL-1β: Interleukin 1 beta; IL-6: Interleukine 6; LV: left ventricle; Pisovol: systolic pressure in isovolumetric contraction; Psyst: Systolic pressure; RV: right ventricle; Tau: time of constant of isovolumetric relaxation; TL: tibia length; TNFα: tumor necrosis factor alpha.

Figure

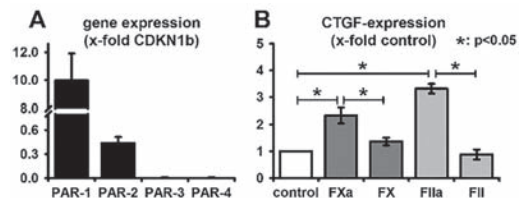
**P576**

**Recombinant factor Xa activates murine primary cardiac fibroblasts in vitro.**

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**Background:** Clinical data suggest that heart failure patients with coronary artery disease may benefit from pharmacological factor Xa-inhibition. A potential pathophysiological mechanism relates to protease activated receptor (PAR) mediated processes leading to adverse cardiac remodeling, as PARs are stimulated by a number of proteases including factors Xa and IIa. We aimed to investigate the contribution of cardiac fibroblasts and tested, whether they are activated by recombinant factors Xa and IIa.

**Methods and Results:** Using TaqMan-PCR we found PAR-1 highest expressed in primary murine cardiac fibroblasts, whereas PAR-2 was lower expressed and PAR-3 as well as PAR-4 expression was almost not detectable (Fig. A). When primary murine cardiac fibroblasts were incubated with recombinant factor Xa (1 U/ml, 24 hours), connective tissue growth factor (CTGF) expression (Fig. B, normalized to CDKN1b expression) increased significantly, while the inactive factor X did not alter CTGF expression. Similar results were found for the recombinant factor IIa (1 U/ml). **Conclusion:** PAR-1, a receptor potentially sensitive for factor Xa and IIa, is highly expressed on primary murine cardiac fibroblasts. Stimulation with recombinant factors Xa and IIa resulted in activation of these cells, indicating that cardiac fibroblasts may contribute to PAR mediated adverse cardiac remodeling in heart failure. This and a potential protective effect of pharmacological factor Xa-inhibition will be clarified in further mechanistic studies and animal models.



BASIC SCIENCE: PULMONARY HYPERTENSION

**P577**

**Exercise preconditioning increases endothelium-dependent dilatation of isolated pulmonary vessels in rats with hypoxic pulmonary hypertension**

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**Introduction:** One of the reasons of pulmonary hypertension is an imbalance between vasodilators and vasoconstrictors. The increase of endothelium-derived vasoconstrictors causes vessels wall thickening, increases pulmonary resistance and right ventricular systolic pressure. Exercise was shown to improve endothelial function (Mereles, 2006). The aim of the study was to test the hypothesis that exercise training will increase endothelium-dependent dilation of pulmonary vessels and reduce the degree of pulmonary hypertension.

**Methods and design:** Male Wistar rats were used. The procedures followed the FELASA/ICLAS for use of the laboratory animals (Guide for use of the laboratory animals, National Academy Press, Washington, D.C.1996). hPAH was induced by exposure to hypobaric hypoxia. Rats were housed in a hypobaric chamber at simulated altitude of 5000 m, 10 h a day, 2 wk. (O2 concentration reduced to 10%). The rats were divided into two groups: hPAH control (CPAH) and trained hPAH (TPAH). Rats underwent exercise training (aerobic swimming during 30 min.) for a period of

2 weeks to hypoxia. Right ventricular (RV) hypertrophy was calculated as RV weight /rat b. w. Systolic right ventricle pressure (RVSP) was measured. Perfusion pressure of isolated pulmonary and systemic (popliteal) artery to vasoconstrictor serotonin (10-9 – 10-5) was measured. Endothelium-dependent dilatation of isolated blood vessels caused by estradiol (10-9 – 10-5). Endothelium-independent vasodilatation caused by sodium nitroprusside (10-9 – 10-5M).

**Results:** Two weeks after hypoxia exposure all rats developed hPH and RVSP was higher by 26% in group TRAH compared with group CRAH. Pulmonary vessels of rats, which had exercise preconditioning demonstrated elevated vasodilatation to estradiol (106M, -58% vs. control -28%  $p < 0,05$ ) without changing responses to sodium nitroprusside (-91% vs 81%) and serotonin perfusion. In the arteries of the systemic circulation differences between groups were not found.

**Conclusions:** Aerobic exercise preconditioning (30 min. swimming) causes an increase in endothelium-dependent vasodilatation of isolated pulmonary vessels in rats with hypoxic pulmonary hypertension. However, this does not reduce the extent of the disease.

#### P578

##### Effects of aerobic exercise training on hypoxia-induced pulmonary hypertension and platelet count in male rats

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**Introduction:** Analysis of the influence of exercise training on the development of pulmonary hypertension has been for 40 years. However, the answer has not been received. It is shown that physical exercise can both positively and negatively influence on the disease. The result depends on the type of pulmonary hypertension, hemodynamic, age and others. Aim. We analyzed the role aerobic exercise training on the systolic right ventricle pressure, and platelet count in the male rats with hypoxia pulmonary hypertension (hPAH).

**Methods and design:** Male Wistar rats were used. The procedures followed the FELASA/ICLAS for use of the laboratory animals (Guide for use of the laboratory animals, National Academy Press, Washington, D.C.1996). hPAH was induced by exposure to hypobaric hypoxia. Rats were housed in a hypobaric chamber at simulated altitude of 5000 m, 10 h a day, 2 wk. (O<sub>2</sub> concentration reduced to 10%). The rats were divided into two groups: hPAN control (CPAH) and trained hPAH (TPAH). Rats underwent exercise training (aerobic swimming during 30 min.) for a period of 2 weeks to hypoxia. Right ventricular (RV) hypertrophy was calculated as RV weight /rat b. w. Systolic right ventricle pressure (SAP) was measured. Blood hematocrit (Hmt), hemoglobin (Hb) and platelet (PLT) were measured using a blood analyser Gemalait 1280 (Dikson Russia).

**Results:** Two weeks after hypoxia exposure both groups of male rats developed hPAH. However the degree of disease was different: the magnitude of RV hypertrophy was significantly greater in TRAH rats than in CPAH (7,02+ 0,29 vs. 5,86+0,30  $p < 0,05$ ). The degree of systolic right ventricle pressure in TRAH groups as the indicator of hPAH was high than in CPAH rats (74,8 ± 5,25 vs 59,3 ± 4,9 mm Hg;  $p < 0,05$ ). Hmt and Hb were similar in both groups. But PLT was higher in TRAH group than in CPAH group (449 vs 562 × 10<sup>9</sup>/L).

**Conclusions:** The two-week aerobic exercise training to hypoxia leads to an increase in the level of development of hypoxic pulmonary hypertension. It can be assumed that platelet activation and pulmonary vascular thrombosis plays a role in this effect.

## BASIC SCIENCE: RIGHT VENTRICULAR FUNCTION

#### P579

##### Effects of asthma severity on remodeling of right ventricular in patients with arterial hypertension

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**Background:** Bronchial asthma (BA) is a serious medical problem. It was found that the frequency of arterial hypertension (AH) detection in patients with asthma is about 30 %. Purpose of the study. The article analyzes peculiarities of progression of changes in the right ventricle (RV) in cases of different degrees of severity of BA at the background of AH.

**Material and methods:** 91 patients were involved in a study of 2008-2015 years with varying BA severity in the step of controllability associated with AH 1, 2 severity. Of these, 26 patients (29%) with mild BA (BAMAH), 34 (37%) with an average severity of BA (BAAAH), 31 (34%) - severity of severe BA (BASAH). A group of 30 patients with AH 1.2 degrees and a group of 32 people with BA were taken for a comparative analysis. All examined patients were outpatients and were taken adequately matched basic therapy on BA with inhaled corticosteroids (ICS). The patients used a  $\beta_2$ -agonists ( $\beta_2$ -AM) short action on demand. A group of patients with AH 1.2 degrees, n = 30, and a group with different degrees of BA in the stage of

control n = 32, were taken for comparative analysis. The diagnosis of AH and extent of increase the blood pressure (BP) - on the basis of criteria of WHO 2013. In groups of comparison there were no statistically significant distinctions of an average the BP, groups were comparable on age, sex and an experience of AH ( $p > 0,05$ ). All patients were performed the echocardiography on Acuson 128XP \ 10c (USA).

**Results:** Changes in the RV in patients with BA accompanied by AH and without it were similar. There were more unfavorable situations in case of combined pathology. The number of hypertrophy of the RV in patients with combined BA and AH was reliably higher. BA-1,9 ± 0,07cm, H-1,94 ± 0,05cm, BAMAH-3,83 ± 0,16cm, =0,01, BAAAH-5,2 ± 0,12cm, =0,002, =0,005, BASAH-10,45 ± 0,49cm, =0,0015, =0,0001.

**Conclusion:** Remodeling of the right parts of the heart in patients with BA with AH was similar. With isolated BA hypertrophy of the RV was revealed in several patients included in the group with severe BA. In cases of combined pathology hypertrophy of the RV was already revealed in mild degrees of bronchial obstruction. Obvious hypertrophy of the RV increased with increase of the severity of bronchial obstruction in patients with combined AH and BA.

#### P580

##### Cartilage oligomeric matrix protein (COMP) is a potential adaptive mechanism to the pressure overload in the right ventricle

LBI LVR

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**Objective:** Right ventricle (RV) is subjected to pressure overload in many clinical situations like pulmonary embolization and pulmonary arterial hypertension. The functional status of RV predicts survival of those patients. However, the mechanisms of RV adaptation to pressure overload are not fully investigated. The aim of our study was to investigate the role of COMP in the RV pressure overload model.

**Methods:** RV pressure overload was induced in wild-type (WT) or COMP knockout (KO) mice by pulmonary artery banding (PAB). Three weeks post-operation, mice were investigated by echocardiography and invasive hemodynamics. Subsequently, histology and gene expression analysis were performed on RV tissue samples. Cultured cardiac fibroblasts were stimulated by TGF $\beta$  and PDGF and COMP expression was analyzed by RT-PCR.

**Results:** PAB generated a significant pressure overload in WT mice (RV systolic pressure (RVSP) in PAB=48 ± 11 mm Hg vs. sham29 ± 5 mm Hg,  $p = 0,001$ ). Echocardiography showed thickened RV free wall, enlarged RV and reduced cardiac. Invasive hemodynamics revealed reduced contractility index, prolonged tau, and elevated EDP. Elevated expression of ANP, BNP and collagens was measured in RV tissue samples. Histologic examination revealed RV fibrosis. Elevated COMP expression was detected in RV tissue, which was localized to vimentin and DDR2 positive cells. PAB operation in COMP KO mice caused RVSP elevation comparable with RVSP in WT mice (COMP KO RVSP=50 ± 4 mm Hg,  $p = 0,15$  vs. WT PAB). However, COMP KO mice demonstrated worse survival after PAB operation. They demonstrated worsening of diastolic function compared to WT mice as evidenced by prolonged Tau ( $p = 0,012$  vs. WT PAB) and elevated RV EDP ( $p = 0,005$  vs. WT PAB). Higher degree of RV fibrosis was revealed by Masson's Trichrome staining in RV of COMP KO PAB operated mice. In the isolated cultured cardiac fibroblasts, stimulation by TGF $\beta$  but not PDGF caused increase in COMP expression.

**Summary:** RV in pressure overload model is characterized by systolic and diastolic dysfunction. Absence of COMP led to worse survival, deterioration of RV diastolic function and more pronounced RV fibrosis. Thus, COMP appears as an adaptive mechanism to pressure overload.

#### P581

##### Urocortin-2 attenuates right ventricular dysfunction in pulmonary arterial hypertension

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FCT-PTDC/DTP-FTO/0130/ 2012

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Urocortin(UCN)-2 is highly expressed in the cardiovascular system and has shown promising therapeutic effects in several studies in human and experimental heart failure. This study analysed the levels of UCN-2 in human and experimental pulmonary arterial hypertension (PAH), and the effects of UCN-2 treatment in an animal model of right ventricular (RV) failure, secondary to PAH.

Rats were submitted to monocrotaline (MCT, n=35)/vehicle (CTRL, n=27) administration, or pulmonary artery banding (PAB, n=13)/Sham (n=5). After 14 days, animals were randomly assigned to receive either UCN-2(5 $\mu$ g/Kg/day) or vehicle. Functional measurements were performed 23-25days after MCT or PAB, and



after euthanasia tissue was collected. Moreover, RV, lung and blood samples were collected from PAH patients (n=7) and non-PAH controls (n=6). Only significant data (mean  $\pm$  SEM,  $p < 0.05$ ) are given. Functional studies revealed that MCT group developed PAH, as shown by increased RV end-systolic pressure (MCT vs CTRL:  $60 \pm 3$  vs  $22 \pm 1$  mmHg), end-diastolic pressure ( $6.0 \pm 0.7$  vs  $3.7 \pm 0.3$  mmHg), and decreased ejection fraction ( $32 \pm 4$  vs  $75 \pm 3\%$ ) and pulmonary artery acceleration time ( $13.6 \pm 0.57$  vs  $25.7 \pm 2.61$  ms). UCN-2 treatment attenuated these changes ( $48 \pm 4$ ;  $4.3 \pm 0.3$  mmHg;  $60 \pm 3\%$  and  $20.0 \pm 1.11$  ms, respectively). Also, UCN-2 treated rats had higher survival rate (76 vs 44%) and exercise capacity (MCT vs CTRL vs MCT+UCN-2:  $219 \pm 88$  vs  $749 \pm 71$  vs  $573 \pm 88$  m). PAH rats presented RV hypertrophy as shown by the morpho-histological analysis (RV weight/tibia length ratio, MCT vs CTRL:  $0.08 \pm 0.00$  vs  $0.04 \pm 0.00$  g/cm; cardiomyocyte cross-sectional area:  $353 \pm 25$  vs  $234 \pm 25 \mu\text{m}^2$ ). UCN-2 therapy attenuated RV remodelling ( $0.06 \pm 0.00$  g/cm and  $283 \pm 22 \text{mm}^2$ , respectively). MCT-group isolated cardiomyocytes developed higher passive force compared to CTRL-group at the sarcomere lengths of 2.2 (MCT vs CTRL:  $5.09 \pm 1.14$  vs  $2.48 \pm 0.56 \text{N/m}^2$ ) and 2.3  $\mu\text{m}$  ( $8.10 \pm 1.77$  vs  $4.02 \pm 0.82 \text{N/m}^2$ ). UCN-2 restored passive force development ( $3.44 \pm 0.70$  and  $5.36 \pm 0.97 \text{N/m}^2$ , respectively). Plasmatic levels of UCN-2 were increased in MCT rats with decompensated RV function, compared to compensated RV ( $p = 0.0338$ ). PAB rats treated with UCN-2, showed RV-specific decrease in cardiomyocyte hypertrophy (PAB vs SHAM vs PAB+UCN-2:  $534 \pm 46$  vs  $280 \pm 29$  vs  $387 \pm 31 \mu\text{m}^2$ ) and fibrosis ( $11.96 \pm 1.2$  vs  $2.23 \pm 0.3$  vs  $2.66 \pm 0.2\%$ ). Moreover, UCN-2 levels in the buffy coat from blood of human PAH patients were higher than in controls ( $p = 0.035$ ), while a trend toward an up regulation was seen in the RV and Lung of PAH patients ( $p = 0.0663$  and  $p = 0.0734$ , respectively). UCN-2 levels are altered in human and experimental PAH. UCN-2 treatment attenuates PAH and RV dysfunction and increases survival in MCT-induced PAH, and has direct anti-remodelling effects on the pressure-overloaded RV. UCN-2 has a relevant role in the pathophysiology of PAH, and might be a new treatment option in this condition.

## P582

### Pulmonary hypertension induced right ventricular stiffness predicted by spectral transfer function analysis: an experimental study

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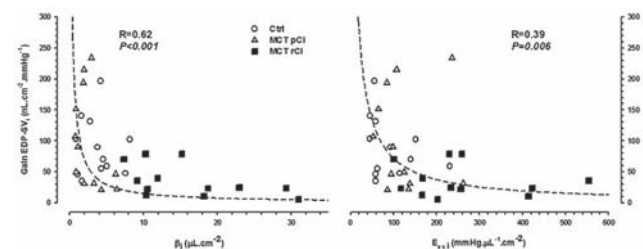
Recent clinical studies suggest right ventricular (RV) diastolic stiffness is an important prognosis determinant in pulmonary hypertension (PH). Impaired stroke volume (SV) variation induced by fluctuating RV end-diastolic pressure (EDP) during ventilation as assessed by spectral transfer function (STF) gain may enable detection of RV stiffness without the need for invasive pressure-volume (PV) recordings with inferior vena cava (IVC) occlusions.

Our aim was to evaluate the role of RV stiffness in disease progression in Monocrotaline-induced pulmonary hypertension (MCT) and to validate STF gain

between EDP and SV as a marker of RV stiffness. Seven-week old Wistar-Kyoto (WKY) randomly injected with 60 mg/Kg monocrotaline (MCT) or placebo were divided into three groups (12 rats each) according to their cardiac index (CI). Placebo-injected controls (Ctrl), MCT preserved CI (MCTpCI), and MCT reduced CI (MCTrCI). All underwent RV open-chest PV hemodynamic evaluation on the 24-34th day after MCT injection, under halogenate anesthesia and positive-pressure ventilation at constant inspiratory pressure. Beat-to-beat fluctuation in hemodynamic parameters during ventilation was assessed by STF. End diastolic stiffness ( $\beta_i$ ) and end-systolic elastance (Ees<sub>i</sub>) for indexed volumes were obtained from IVC occlusion. Additionally, indexed ventricular-vascular coupling (VVC<sub>i</sub>), indexed arterial elastance (Ea<sub>i</sub>), and preload-recruitable stroke work (PRSW) were calculated and correlated to CI to establish determinants of RV failure progression.

Ea<sub>i</sub> was found to be the strongest determinant of reduced CI, alongside with  $\beta_i$  ( $P < 0.001$ ) but not PRSW. MCTrCI showed higher  $\beta_i$  and Ees<sub>i</sub> compared with both Ctrl and MCTpCI ( $P < 0.05$ ), along with impaired RV STF gain between EDP and SV<sub>i</sub>, denoting impaired dynamic Frank-Starling mechanism. On multivariate analysis and analysis of covariance with group as dummy variable  $\beta_i$  and not Ees<sub>i</sub> or PRSW correlated with impaired STF gain from EDP to SV<sub>i</sub> ( $P < 0.001$ ). Receiver-Operating Characteristics curve analysis of STF gain between EDP and SV<sub>i</sub> showed an area under curve of 0.84 for higher  $\beta_i$  prediction ( $P < 0.001$ ).

Afterload and RV stiffness and not RV contractile function are the major players in RV failure progression. RV diastolic stiffness can be reasonably assessed by STF analysis between EDP and SV variation with respiration. Results suggest right heart catheterization-derived EDP and SV<sub>i</sub> or noninvasive surrogate variation with respiration as a prognostic tool to assess RV stiffness in PH.



Correlations of STF gains

## NURSING INVESTIGATOR AWARD

Sunday 22 May 2016 8:30–11:00

Location: Agora

618

**Mid-upper arm circumference is a better predictor of mortality than calf circumference in patients with heart failure.**K Kentaro Kamiya<sup>1</sup>; T Masuda<sup>2</sup>; Y Matsue<sup>3</sup>; N Hamazaki<sup>2</sup>; R Matsuzawa<sup>4</sup>; S Tanaka<sup>2</sup>; K Nozaki<sup>4</sup>; E Maekawa<sup>5</sup>; T Inomata<sup>3</sup>; J Ako<sup>5</sup><sup>1</sup>Kitasato University Hospital, Sagami-hara, Japan; <sup>2</sup>Department of Cardiovascular Medicine, Kitasato University Graduate School of Medical Sciences, Sagami-hara, Japan; <sup>3</sup>Department of Cardiology, Kameda Medical Center, Chiba, Japan;<sup>4</sup>Department of Rehabilitation, Kitasato University Hospital, Sagami-hara, Japan;<sup>5</sup>Department of Cardiovascular Medicine, Kitasato University School of Medicine, Sagami-hara, Japan

**Background:** Sarcopenia is one of the most powerful prognostic factors of heart failure (HF). Although decreased mid-upper arm circumference (MUAC) and calf circumference (CC) are known to reflect muscle mass and nutritional status, direct comparison remains to be elucidated. The purpose of this study was to investigate prognostic significance of MUAC and CC, and to compare their predict ability in patients with HF.

**Methods:** MUAC and CC were measured at the time of discharge in 570 admitted heart failure patients. Prognostic predictive ability of MUAC and CC were compared for all-cause mortality. C-indices were compared between 3 models: Seattle Heart Failure Model (SHFM) only, SHFM plus MUAC, and SHFM plus CC.

**Results:** Patients were mean age of 67.4 years old and 398 (70%) were male. During the mean follow-up period of 1.8 years, 70 deaths were observed. In the univariate analysis, MUAC and CC were significant predictors of mortality. After adjustment for other prognostic factors, MUAC (adjusted HR per SD increase: 0.47, 95% CI: 0.31 – 0.73;  $p < 0.01$ ) but not CC (adjusted HR per SD increase: 0.74, 95% CI: 0.49 – 1.11;  $p = 0.15$ ) predicted mortality. Likewise, MUAC but not CC showed complementary prognostic predictive capability to SHFM [C-index: SHFM only = 0.63, SHFM+MUAC = 0.71 ( $p = 0.008$  vs SHFM only), SHFM+CC = 0.67 ( $p = 0.133$  vs SHFM only)] (Figure).

**Conclusion:** The evaluation of MUAC could be used for risk stratification in patients with heart failure.

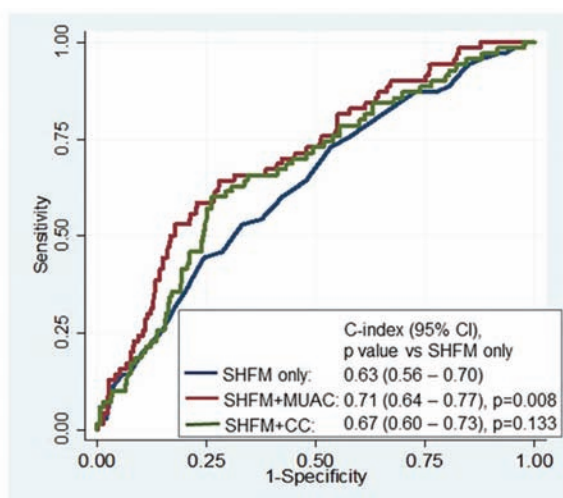


Fig. Comparison of C-index for all-cause mortality

619

**Utility and potential impact of a structured telephone support tool to facilitate a seamless program of composite nurse-led, face-to-face and structured telephone support management for heart failure.**

National Health and Medical Research Council of Australia

NA Emanuele<sup>1</sup>; Y Ahamed<sup>1</sup>; MJ Carrington<sup>1</sup>; D Thompson<sup>1</sup>; S Stewart<sup>1</sup><sup>1</sup>Australian Catholic University, Mary MacKillop Institute for Health Research, Victoria, Australia

**Background:** Structured Telephone Support (STS) in the management of chronic heart failure (CHF) is associated with improved health outcomes relative to standard care, but has been mainly applied as a substitute rather than adjunctive strategy in the management of the syndrome.

**Purpose:** To evaluate the utility and potential impact of the Green Amber Red Delineation of risk And Need in CHF (GARDIAN-CHF) and an integrated system of STS management (GARDIAN-Angel) as part of a multicentre, randomised trial of standard versus intensified management of recently hospitalised patients with CHF (the WHICH? II Trial).

**Methods:** Baseline profiling data used to categorise trial participants as low (green), medium (amber) or high (red) risk for recurrent morbidity and mortality via the GARDIAN-HF tool were analysed. The subsequent nature and consequences of initially applied STS via the GARDIAN-Angel surveillance system and team (via a national telephone call centre) were also analysed.

**Results:** 328 trial participants (aged  $74.7 \pm 10.8$  years), 42% female and 15% living remotely) were studied. The majority (57%) had CHF with reduced LVEF ( $31.4 \pm 9.4\%$ ). Delineation of increased risk was mediated via holistic/socio-demographic factors (22% had self-care deficits, management deficits (46%); and clinical instability at index hospitalisation (91%) then at 7-14 days (48%) indicative of increased surveillance/support with an elevated BNP recorded in 42% of all patients, irrespective of age. GARDIAN-HF profiling indicated that 4.3% (GREEN), 29% (AMBER), and 67% (RED Status) were at a low, medium and high risk of poor event-free survival. Subsequent assessment by the GARDIAN-Angel STS team in 5754 structured calls (62% capture with a mean call time of 12 minutes including 304 initial structured calls lasting a mean of 22 minutes), assessing patients for variation of their self-reported overall health and heart failure symptoms and consequently given an automated GREEN flag (35%), requiring no response, AMBER flag (53%), with issues requiring monitoring, and the remainder a RED flag (12%), indicating new clinical instability requiring immediate action by the home-based team. Calls revealed ongoing fatigue (62.4%), dyspnoea (43.4%) and pedal oedema (27.6%); with a further 12% and 3% reporting angina or any type of fall. The STS team confirmed that 44%, 46%, and 10% of flags were GREEN, AMBER and RED respectively, indicating occasional disagreement with the automated GARDIAN-Angel flag rating. Alternatively, 57 RED/Crisis flag calls (1% of all structured calls and in total of 34 patients) required a high priority response and 13 (22%) of these RED/Crisis calls were re-hospitalised.

**Conclusion:** These preliminary data demonstrate the utility and potential health impact of an integrated method to modulate STS according to individual need and risk.

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**Self-care confidence totally mediates the influence of simple attention and working memory on self-care in adults with heart failure**

National Institutes of Health, USA

E Ercole Vellone<sup>1</sup>; L Pancani<sup>2</sup>; A Greco<sup>2</sup>; M D'addario<sup>2</sup>; P Steca<sup>2</sup>; B Riegel<sup>3</sup><sup>1</sup>University Tor Vergata, School of Nursing, Rome, Italy; <sup>2</sup>University of Milan-Bicocca, Milan, Italy; <sup>3</sup>University of Pennsylvania, School of Nursing,

Philadelphia, United States of America

**Background:** Cognition is impaired in 25-50% of heart failure (HF) patients. Cognitive impairment may affect patients' abilities to perform HF self-care. The situation-specific theory of HF self-care proposes that self-care confidence may

mediate the relationship between cognition and self-care, but little is known about this issue.

**Purpose:** The purpose of this study was to test the hypothesis that self-care confidence mediates the relationship between specific cognitive domains (simple and complex attention, processing speed, working memory, and short-term memory) and HF self-care.

**Methods:** This was a secondary analysis of data from a longitudinal cohort comparative study. A sample of 280 adults with chronic HF were enrolled from 3 outpatient settings in the USA. Self-care was measured with the Self-Care of HF Index, which measures self-care maintenance (i.e., monitoring of HF symptoms and adherence to treatments), self-care management (i.e., recognizing and managing symptoms of HF exacerbation), and self-care confidence (i.e., confidence in each of the self-care processes). Cognition was measured with a battery of neuropsychological tests. Sociodemographic characteristics, illness duration, HF type, comorbidity, and NYHA functional class were measured. The mediation model was tested with structural equation modeling using baseline data.

**Results:** Patients were 62 (SD, 12.5) years old on average, mostly male (64.3%) and functionally compromised (NYHA class III, 58.6%). Most (93.2%) patients had at least 1 test in which they demonstrated impaired cognition. In mediation analysis, self-care confidence totally mediated the relationship between simple attention and self-care (self-care maintenance and management) and between working memory and self-care (self-care maintenance and management). Processing speed, complex attention, and short-term memory were neither mediated by self-care confidence nor had a significant relationship with self-care maintenance and management. However, short-term memory had a significant direct effect on self-care maintenance. The tested models had acceptable fit indices.

**Conclusions:** Results of this study suggest that self-care confidence might compensate for impaired cognition in HF patients. That is, patients with confidence in their ability to perform self-care may do well in spite of impaired cognition. Because cognitive impairment is so difficult to modify, interventions focused on self-care confidence might successfully improve self-care.

## 621

### Gait speed provides prognostic capability comparable to 6-min walk test in elderly patients with cardiovascular disease.

K Kamiya<sup>1</sup>; T Masuda<sup>2</sup>; Y Matsue<sup>3</sup>; N Hamazaki<sup>2</sup>; R Matsuzawa<sup>1</sup>; S Tanaka<sup>2</sup>; K Nozaki<sup>1</sup>; E Maekawa<sup>4</sup>; A Matsunaga<sup>2</sup>; J Ako<sup>4</sup>

<sup>1</sup>Department of Rehabilitation, Kitasato University Hospital, Sagamihara, Japan; <sup>2</sup>Department of Cardiovascular Medicine, Kitasato University Graduate School of Medical Sciences, Sagamihara, Japan; <sup>3</sup>Department of Cardiology, Kameda Medical Center, Chiba, Japan; <sup>4</sup>Department of Cardiovascular Medicine, Kitasato University School of Medicine, Sagamihara, Japan

**Background:** Although gait speed and 6-min walk (6MW) tests are applied as prognostic gauges for elderly cardiovascular disease (CVD) patients, few direct comparison studies have been conducted. The purpose of this study was to compare the prognostic predictive ability of gait speed and 6MW tests in CVD patients.

**Methods:** Usual gait speed (over a 10 meters) and 6MW were measured at the time of discharge in admitted elderly CVD patients ( $\geq 65$  years old). Prognostic predictive ability of gait speed and 6MW were compared for all-cause mortality.

**Results:** A total of 599 CVD patients ( $75 \pm 6$  years old, 65% male, 57% heart failure, 37% ischemic heart disease, and 6% others) were included. During the mean follow-up period of 1.9 years, 72 all-cause deaths were observed. After adjustment for confounding factors, both usual gait speed (adjusted hazard ratio per SD increase: 0.67, 95% CI: 0.50 to 0.89,  $P = 0.006$ ) and 6MW (adjusted hazard ratio per SD increase: 0.60, 95% CI: 0.45 to 0.81,  $P = 0.001$ ) were independent predictor of all-cause mortality. C-indices were 0.64 (95% CI: 0.57 to 0.71) for usual gait speed and 0.65 (95% CI: 0.58 to 0.72) for 6MW. There was no significant difference in c-indices between groups of gait speed and 6MW ( $P = 0.456$ ).

**Conclusion:** Gait speed and 6MW test showed similar prognostic predictive ability for all-cause mortality in elderly patients with CVD. Gait speed, which is an easily and non-invasively measurable metric, can be used as a risk stratification tool.

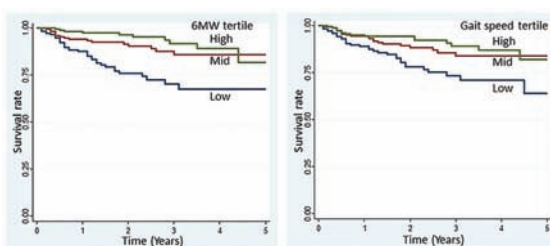


Fig. Six-minute walk distance and all-cause mortality

Fig. Usual gait speed and all-cause mortality

## 622

### Cost-analysis in the management of cardiac implanted electronic devices with remote monitoring: our experience

A Zanni<sup>1</sup>; C Sticozzi<sup>1</sup>; A Malagoli<sup>1</sup>; L Rossi<sup>1</sup>; U Corvi<sup>1</sup>; M Piepoli<sup>1</sup>; G Villani<sup>1</sup>  
<sup>1</sup>Guglielmo Da Saliceto Hospital, Department of Cardiology, Piacenza, Italy

**Introduction:** The implantation of cardiac electronic devices has increased exponentially over the last decade in response to widening indication. Follow-up of patients with cardiac implantable electronic devices (CIEDs) is challenging due to both their increasing volume and technical complexity. The devices equipped with the remote monitoring (RM) function are capable of providing on daily basis automatic information about the patient cardiac condition as well as the implant status without compromising the safety. New organizational models promote significant efficiencies regarding physician and technician personnel time. Accordingly, the RM is proposed to be a clinical practice for the follow-up.

**Purpose:** To assess the costs-analysis of the RM compared to standard follow-up of CIEDs.

**Methods:** In our institution 590 outpatients with chronic HF and single- or dual-chamber CIED implanted are followed through standard outpatient visits (group A, 295 patients) or by the RM (group B, 295 patients). In the group A planned visits are scheduled every 6 months with an increased frequency when the device approaches its end of service or in case of advisories; in the group B instead are scheduled one annual visit, transmissions every six months and alert notification. Each planned visit total cost € 19.16 (including medical equipment, clinical staff and maintenance of the outpatient areas). Physician and technician personnel time-consuming was assessed for both groups.

**Results:** During 18-months follow-up were performed 806 planned visits in group A compared to 304 in group B. Costs in group A was € 32.37 / patient per year compared to 30.1 € / patient per year in group B. The overall time-consuming by the physician and technician personnel in group A was 18.2 minutes per patient/ per year compared to 12.7 minutes per patient /per year for remote control in group B.

**Conclusions:** The device's RM allows effective optimization of healthcare resource consumption, allowing a reduction of the cost of follow-up.

## 623

### The lived experience of adults with heart failure: a phenomenological study

This study was founded by the Centre of Excellence for Nursing Scholarship Rome, Italy

M Marco Paturzo<sup>1</sup>; L Berto<sup>2</sup>; A Petruzzo<sup>1</sup>; A Mottola<sup>1</sup>; MZ Cohen<sup>3</sup>; R Alvaro<sup>1</sup>; E Vellone<sup>1</sup>

<sup>1</sup>University of Rome Tor Vergata, Biomedicine and Prevention, Rome, Italy;

<sup>2</sup>Ospedali Riuniti della Valdichiana Senese, Siena, Italy; <sup>3</sup>University of Nebraska Medical Center, Omaha, United States of America

**Background:** People with heart failure (HF), a major public health problem that continues to grow in Europe and the USA, have significant mortality, decreased quality of life and high hospitalization rates. Although a number of studies have been conducted on patients with HF, they have not given a rigorous comprehensive description of what it is like to live with HF

**Purpose:** The purpose of this study was to describe the lived experience of adults with heart failure (HF).

**Methods:** A hermeneutic phenomenological design was used. Thirty patients affected by HF were enrolled between February 2014 and July 2014 from an outpatient cardiovascular clinic in Italy. Phenomenological interviews took place at patients' homes, and the investigators analyzed verbatim transcripts. Data saturation was achieved, and participants to ensure data trustworthiness confirmed all extracted themes.

**Results:** The patients were mostly male (67%) with a mean age of 71 (SD 9.15) with a range of 48–86. Mostly were in NYHA class I-II (70%) and a mean illness duration in months of 66 (SD 57.72) Seven themes emerged from the phenomenological analysis: 1) important life changes; 2) social isolation caused by the illness; 3) anger and resignation associated with the disease; 4) relief from spirituality; 5) will to live; 6) uncertainty about the future and 7) the inescapability of disease and death.

**Conclusions:** The findings of this study provide an overview of the lived experiences of patients with HF, give new insights and reinforce the findings of previous research. Thoroughly understanding the lived experiences of patients with HF could play an important role in designing nursing care. The meaning that our patients attribute to their lived experience helps to create their needs, which are important to direct care. Family support and religious beliefs are an important source for HF patients to better manage their fears and cope with the future. Findings of this study provide nurses with a comprehensive description of what it is like to live with HF, which can be useful in helping to meet patients' needs more effectively and in tailoring interventions.

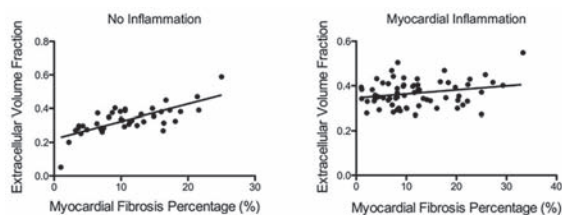


## MODERATED POSTER SESSION 2 - CARDIOMYOPATHY

Sunday 22 May 2016 10:00–11:00

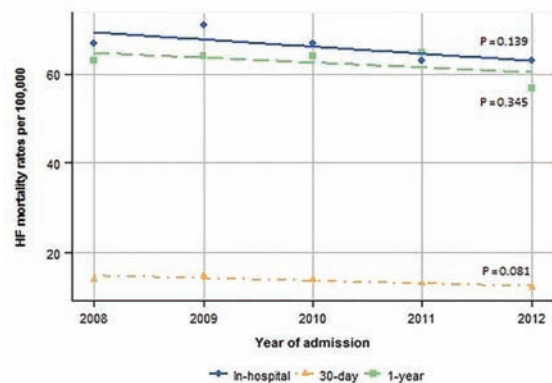
Location: Poster Area

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**Cardiac magnetic resonance derived extracellular volume fraction estimates myocardial fibrosis in patients with cardiomyopathy without inflammation but not in presence of significant inflammation**P Philipp Lurz<sup>1</sup>; D Lang<sup>1</sup>; C Luecke<sup>2</sup>; J Lurz<sup>1</sup>; K Rommel<sup>1</sup>; K Klingel<sup>3</sup>; M Gutberlet<sup>4</sup>; G Schuler<sup>4</sup><sup>1</sup>University of Leipzig, Heart Center, Department of Internal Medicine and Cardiology, Leipzig, Germany; <sup>2</sup>Heart Center of Leipzig, Diagnostic and Interventional Radiology, Leipzig, Germany; <sup>3</sup>University Hospital Tuebingen, Department of Molecular Pathology, Tuebingen, Germany; <sup>4</sup>Heart Center of Leipzig, Department of Paediatric Cardiology, Leipzig, Germany**Background:** The presence of diffuse fibrosis in non-ischemic cardiomyopathy is associated with unfavorable outcome. Endomyocardial biopsy (EMB) is the gold standard in quantifying the extend of fibrotic tissue. Recently, cardiac magnet resonance imaging (CMR) modalities such as T1 mapping and estimation of the extracellular volume fraction (ECV) have been suggested as non-invasive measurement strategies. However, it is uncertain whether ECV provides a valid estimate of diffuse fibrosis in the presence of other pathologies impacting on ECV such as myocardial edema.**Methods:** 107 consecutive patients with suspicion of inflammatory cardiomyopathy underwent CMR. Extracellular volume fraction was calculated from T1 times pre and post contrast. Furthermore, in all patients left ventricular (LV) endomyocardial biopsies (EMB) were taken. Quantification of fibrosis in EMB was realized using Masson-trichrome-stained slides and digital marking of fibrotic areas.**Results:** Significant inflammation was present in 66 patients, 41 exhibited no significant inflammation on EMB. There were no difference in age ( $45 \pm 14$  vs.  $45 \pm 15$  years;  $p=1.0$ ) or LV ejection fraction ( $37 \pm 17$  vs.  $36 \pm 18\%$ ;  $p=0.9$ ). Although LV collagen volume percentage was similar in both groups (inflammation  $12.3 \pm 17.8$  vs. non-inflammation  $11.4 \pm 7.9\%$ ;  $p=0.577$ ), ECV was significantly higher in patients with inflammation ( $0.37 \pm 0.06$ ) than in patients without inflammation ( $0.33 \pm 0.08\%$ ;  $p=0.02$ ). Importantly, ECV adequately estimated the degree of LV collagen volume percentage only in patients without inflammation ( $r=0.72$ ;  $p<0.0001$ ), but not in those with inflammation ( $r=0.24$ ;  $p=0.06$ ; Figure).**Conclusion:** These findings prove the theoretical concept of ECV as an estimate for diffuse fibrosis only in absence of other pathologies such as myocardial edema. This should be considered when ECV is used as a surrogate for diffuse fibrosis or predictor of outcome in cardiomyopathies.

Figure

625

**Survival after first heart failure hospitalization in slovenia between 2004 and 2012**D Daniel Omersa<sup>1</sup>; J Farkas<sup>1</sup>; I Erzen<sup>1</sup>; M Lainscak<sup>2</sup><sup>1</sup>National Institute of Public Health, Ljubljana, Slovenia; <sup>2</sup>General Hospital Celje, Department of Cardiology, Celje, Slovenia**Introduction:** Heart failure (HF) is a global health problem with excessive mortality and significant economic burden. There is limited data about post-hospitalization mortality, particularly for central and east European countries. Aim We aimed to evaluate mortality in patients with first heart failure related hospitalization in Slovenia.**Methods:** Slovenian national hospital discharge registry was searched for HF hospitalizations (HF coded in any diagnose fields) in all Slovenian residents  $\geq 20$  years between 2004 and 2012 and linked with National death registry; follow-up was censored at the end of 2013. First HF hospitalization was defined as the first HF hospitalization of an individual after 4 years of observational period. Trends of standardized mortality rates (in-hospital, 30-day and 1-year) were assessed using ANOVA. The effects of age, sex, admission year and different comorbidities were evaluated with multiple Cox proportional hazards model. Results Overall, 43,636 patients had first HF hospitalization between 2008 and 2012. The in-hospital mortality was 20.1%. In the remaining 34,865 patients, who were discharged alive, the 30-day and 1-year mortality was 3.8% and 18.0%, respectively. Between 2004 and 2012, in-hospital, 30-day and 1-year mortality rates per 100,000 have changed from 116 to 118, 36 to 32 and 181 to 166, respectively, whereas no significant trends were observed. Men, older patients, patients with myocardial infarction, diabetes mellitus, chronic kidney disease, chronic obstructive pulmonary disease and cancer had increased independent hazards for higher mortality. The most important variables in the model were higher age (HR = 1.826 per 10 year increase,  $P < 0.0001$ ) and cancer (HR = 2.303,  $P < 0.0001$ ).**Conclusion:** In recent years, mortality rates remained high where older patients and those with cancer had the highest mortality.

626

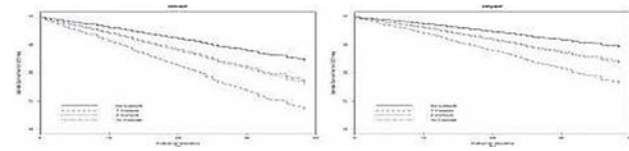
**Quantitative contributor of comorbidities in HF patients according to HF phenotypes.**A Iorio<sup>1</sup>; M Senni<sup>1</sup>; A Gavazzi<sup>1</sup>; C Concetta Di Nora<sup>2</sup>; S Poli<sup>2</sup>; E Zamboni<sup>2</sup>; G Barbati<sup>3</sup>; G Cioffi<sup>3</sup>; G Sinagra<sup>2</sup>; A Di Lenarda<sup>4</sup><sup>1</sup>Ospedale Papa Giovanni XXIII, Bergamo, Italy; <sup>2</sup>University Hospital Riuniti, Cardiovascular Department, Trieste, Italy; <sup>3</sup>Villa Bianca Hospital, Trento, Italy; <sup>4</sup>Cardiovascular Center A.S.S. 1 of Trieste, Trieste, Italy**Background:** Co-morbidities frequently accompany heart failure (HF), contributing to increased mortality and morbidity. However, the prognostic contributor of non cardiac comorbidities in HF according to EF- HF phenotypes is still widely unknown.

**Aim:** We compare prognostic contributor of co-morbidities in patients with chronic HF according to HF phenotypes (LVEF <50% - HFrEF, LVEF ≥50% - HFpEF) in community population.

**Methods:** From October 2009 to December 2013 we studied all consecutive HF patients whose ejection fraction (EF) had been assessed. Prognostic impact of 15 non cardiac comorbidity burden on mortality and morbidity was compared between EF-HF phenotypes using population attributable risks (PARs).

**Results:** A HF population consistent of 2314 patients (mean age 78 ± 8, 57% men), 941 (41%) HFrEF, 1373 (59%) HFpEF. Overall, there was a high rate of comorbidities (Median 3, IQR 2-4), with 1257 (54%) patients presenting ≥ 3 non-cardiac comorbidities. The high comorbidity rates occur similarly between EF-HF phenotypes. At a follow-up of 28 ± 14 months, 472 (20%) patients died, 225 (24%) with HFrEF, and 247 (18%) with HFpEF (p < 0.001). When we grouped HF patients for 1,2, ≥3 comorbidities, the latter was associated to a worse outcome (Figure 1). For overall population, prognostic implications of comorbidities (PARs) for mortality were: CKD=40%, anemia=41%, COPD=30%, diabetes=21%, PAD=20%, and <10% for all other co-morbidities. This trend was maintained unchanged by considering PARs between HF phenotypes for mortality and morbidity (HF, Cardiovascular and Non-Cardiovascular Hospitalizations).

**Conclusion:** In a community HF population, comorbidity burden contributed to high mortality and morbidity with similar quantitative effect across EF-HF phenotypes. These observations suggest that targeting of comorbidities could have a crucial role on prognosis irrespective of LVEF.



## 627

### Chagas' cardiomyopathy mortality in the 21st century: seven years prospective follow up

GE Germano Emilio Souza<sup>1</sup>; JL Vieira<sup>1</sup>; AT Casolato<sup>1</sup>; LR Moraes<sup>1</sup>; GA Braga<sup>1</sup>; VS Issa<sup>1</sup>; SM Ayub-Ferreira<sup>1</sup>; PR Chizzola<sup>1</sup>; EA Bocchi<sup>1</sup>; LM Pessoa De Melo<sup>2</sup>  
<sup>1</sup>Heart Institute -InCor, São Paulo, Brazil; <sup>2</sup>Servico de Hematologia e Hemoterapia, Sao Jose dos Campos, Brazil

**Background:** Chagas' cardiomyopathy is a neglected disease with poor prognosis. Most of prognostic information about this disease was produced through small cohorts or under suboptimal follow-up time.

**Purpose:** We sought to evaluate systolic heart failure prognosis according to its etiology: Chagas' cardiomyopathy(G1) versus non Chagas' cardiomyopathy(G2) in the 21st century, in a big sample and long term follow-up.

**Methods:** Cohort study. Non-randomized. Inclusion criteria: Left ventricle ejection fraction <45% and onset of symptoms time > 1 month. Two different serologic tests were performed to allocate patients either for CC group or NCC group. Exclusion criteria: varfarin or heparin anticoagulation, mechanic heart valve prothesis, neoplasia, pregnancy or puerperal state, strogenic therapy, ongoing infection, decompensated thyroid disease, extra-corporeal circulation, dialytic therapy, diagnosed coagulation disorders, congenital heart disease. All patients underwent clinical, eletrocardiographic, laboratorial and echocardiographic evaluation. Primary outcome was transplant-free survival. Secondary outcome was hospitalization-free survival. Sample size calculated for 90%power. P value significative if <0,05. Fischer's exact test for categoric variables; non-paired T-student test for parametric continuous variables and Mann-Whitney test for non-parametric continuous variables. Kaplan-Meier method and log-rank test were used for estimating outcomes and difference between groups, respectively.

**Results:** From January 2008 to april 2009, 287 patients were prospectively included (138 patients in CC group- G1 - and 149 in NCC group - G2). The mean follow-up time was 7.8years. G1 patients were younger, had lower body mass index, lower blood pressure and LVEF, and higher BNP levels. Hypertension, diabetes, tobacco use and dislipidemia were less frequent in G1. Previous stroke was more prevalent in G1. In G1 and G2, 5.6% and 6.8% of patients were lost for follow-up. Primary outcome was higher in G2 (59,2%) versus G1 (32,2%);log-rank=0,0001. Secondary outcome was also higher in G2 (38,8%) versus G1 (24,5%);log-rank = 0.0001.

**Conclusions:** Chagas' cardiomyopathy prognosis remains worse than non-Chagas' cardiomyopathy in the 21st century in this large sample after a long term follow-up.

## 628

### Clinical characteristics and long term outcome of peripartum cardiomyopathy in a resource limited setting.

MEPI funding through NIH Grant Number TW008881 and TW008905.

E T Gambahaya<sup>1</sup>; JG Hakim<sup>1</sup>; DP Kac<sup>2</sup>; GT Fana<sup>1</sup>; JA Matenga<sup>1</sup>

<sup>1</sup>University of Zimbabwe College of Health Sciences, Medicine, Harare, Zimbabwe;

<sup>2</sup>University of Colorado Denver, Cardiology, Denver, United States of America

**Introduction:** Peripartum cardiomyopathy (PPCM), a rare and potentially fatal complication of pregnancy occurs with a relatively high frequency in African women. However, there is limited data about the long term outcome of PPCM in African patients where diagnosis is often delayed with limited access to treatment.

**Objectives:** The primary objective was to evaluate clinical outcomes and risk factors for adverse outcomes among PPCM patients.

**Methods:** Patients with a diagnosis of PPCM were recruited prospectively and followed up for 2 years. Assessments included New York Heart Association (NYHA) functional class, clinical examination and echocardiograms at enrolment, at 6 and at 24 months follow-up. Baseline characteristics associated with the primary outcome (a composite of death, left ventricular ejection fraction (LVEF) <50%, NYHA functional class III/IV at 24 months) were identified.

**Results:** Forty-nine patients with a new diagnosis of PPCM were recruited at a tertiary care centre in Zimbabwe. The mean age was 28.1 ± 5.7 years. Approximately 1/3 were primigravid with a median parity of 2. In total, 17 (34.7%) had a history of pregnancy-induced hypertension and 2 (4%) were HIV positive. Six (12.2%) had left ventricular intramural thrombi at baseline. NYHA class improved from baseline to each time point (p < 0.001). Eight (16.3%) patients died within the 2 year follow up period including 7 (14.2%) within 6 months. LVEF improved from 29.3 ± 9.7% at baseline to 43.8 ± 15.4%, after 6 months (p < 0.001) and 42.7 ± 14.0% after 24 months (p < 0.001). Twenty-four (49.0%) patients fully recovered left ventricular function with 16 patients recovering within 6 months and a further 8 patients after 6 months. Twenty-six patients had an adverse outcome. Factors associated with an adverse outcome were lower maternal age (OR 0.82, 95% CI 0.72-0.95, p = 0.006), baseline NYHA class III/IV (OR 8.8, 95% CI 2.08-37.20, p = 0.003 and OR 24.0, 95% CI 2.33-247.37, p = 0.008 respectively), being primigravid (OR 0.20, 95% CI 0.05-0.72, p = 0.014), onset of symptoms after the postpartum period (OR 2.35, 95% CI 1.19-4.62, p = 0.014), increased left ventricular end diastolic dimensions (OR 1.11 95% CI 1.00-1.23, p = 0.049), and lower LVEF at baseline (OR 0.91 95% CI 0.84-0.98, p = 0.012).

**Conclusions:** A substantial proportion of African PPCM patients fully recovered left ventricular function. However, mortality and adverse outcomes were frequent. Lower maternal age, worse NYHA class, being primigravid, symptom onset after the postpartum period, increased LVDD, and reduced LVEF at baseline were associated with an adverse outcome.

## 629

### Clinical presentation and prognosis of patients with Chagas' cardiomyopathy during episodes of acute decompensated heart failure

L M Lina Marcela Gomez Madronero<sup>1</sup>; LR Moraes<sup>1</sup>; CB Terhoch<sup>1</sup>; HF Moreira<sup>1</sup>; SM Ayub-Ferreira<sup>1</sup>; MT Oliveira<sup>1</sup>; SG Lage<sup>1</sup>; VS Issa<sup>1</sup>; EA Bocchi<sup>1</sup>

<sup>1</sup>Heart Institute of the University of Sao Paulo (InCor), heart Failure, Sao Paulo, Brazil

**Introduction:** Chagas' disease is a major cause of heart failure in Latin America. However, few studies have analyzed the clinical presentation and prognosis of patients with Chagas during acute decompensated heart failure.

**Methods:** We analyzed a cohort of 409 patients admitted for decompensated heart failure in a tertiary hospital dedicated to cardiology from August 2013 through December 2015; we categorized the patients according to the presence of Chagas' etiology and compared clinical characteristics and prognosis.

**Results:** Mean age was 55.3 ± 15 years and 254 (62.1%) patients were male; left ventricle ejection fraction was 30 ± 12%; 102 (24.9%) patients had ischemic heart disease, 97 (23.7%) Chagas' cardiomyopathy, 74 (18.1%) idiopathic dilated cardiomyopathy and 48 (11.7%) hypertensive disease. At admission BNP level was 1486 ± 1297pg/dL and creatinine 1.96 ± 1.2mg/dL. During hospital admission 45 (11%) patients were submitted to heart transplant and 128 (31.3%) died.

As compared to other etiologies, patients with Chagas' disease had a smaller proportion of patients with history of hypertension (33% vs 58.7%, P < 0.001) and diabetes mellitus (14.4% vs 36.5%, P < 0.001), had lower heart rate at admission (75.2 ± 21.9 vs 86.2 ± 25.8, P < 0.001), were more hypotensive (systolic pressure of 92.3 ± 22.3 vs 100.8 ± 28.7, P = 0.009) and had more frequently ascites (31.3% vs 19.7%, P = 0.06) and hypoperfusion (47.4% vs 33.3%, P = 0.04). Echocardiographic data showed that Chagas' patients had lower ejection fraction (27 ± 9.1% vs 31 ± 12.6%, P = 0.004), larger left ventricle diastolic diameter (68.9 ± 8.8mm vs 65.3 ± 11.9, P = 0.008), lower pulmonary systolic pressure (43.9 ± 12.3 vs 48.6 ± 14mmHg, P = 0.01) and larger proportion of patients with right ventricular dysfunction (40.5% vs 66.3%, P = 0.002). Admission BNP was higher in patients with Chagas' (2033 ± 1574pg/ml vs 1315 ± 1148pg/ml, P < 0.001). The degree of organ dysfunction, measured by BUN, creatinine, sodium, bilirubin and hemoglobin was similar between groups. Prognostic data showed that Chagas'

patients received more frequently intraortic balloon pump (IABP) (34% vs 16.7%,  $P < 0.001$ ), were more frequently transplanted (21.6% vs 7.8%) and had lower mortality (27.8 vs 32.7,  $P = 0.01$ ).

**Conclusion:** Patients with Chagas markedly differ in their clinical and hemodynamic presentation. Despite more severe cardiac dysfunction and similar degree of organ damage, prognosis was better. IABP was effective in bridging patients until heart transplant. These data is important for therapeutic decision involving heart transplant and use of ventricular assist-devices in this setting.

**630**

**Riociguat - new therapeutic option in the management of cardiac amyloidosis**

Austrian fellowship grant, KLI 246, KLI 245 and the Austrian Society of Cardiology, the Österreichischer Herzfonds

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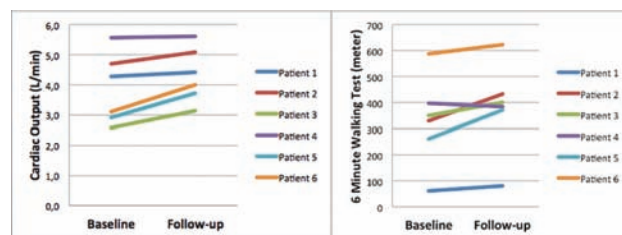
**Background:** Cardiac amyloidosis (CA) is a rare disease and represents the prototype of a restrictive cardiomyopathy. A vast majority of affected patients present with advanced heart failure and face significant morbidity and mortality. However, an effective therapy is still lacking and a diagnosis of CA precludes patients from participation in standard heart failure clinical trials. The soluble guanylate cyclase (sGC) -- stimulator riociguat, already approved for the treatment of precapillary pulmonary hypertension, has also been shown to have favorable hemodynamic effects in heart failure.

**Purpose:** We aimed to test the safety and efficacy of Riociguat in patients with cardiac amyloidosis.

**Methods:** CA was diagnosed based on cardiac magnetic resonance imaging and myocardial biopsy. Baseline work-up of patients and re-evaluation under therapy included the assessment of blood pressure, NYHA functional class, exercise capacity as measured by the 6-minute walk test (6MWT), serum NT-proBNP and invasively measured hemodynamic parameters.

**Results:** Six participants with wild-type transthyretin amyloidosis (83.3% male, 16.7% female, mean age 82.5 (73.0--85.8) years) were included in the named-patient use program. Follow-up was performed after a median of 4.5 months (3.0--7.0). Our preliminary findings indicate that application of riociguat in CA patients is safe. Systolic blood pressure 127 mmHg (116--147) vs. 116 (113--129) mmHg; ( $p = 0.345$ ) and diastolic blood pressure 87.0 mmHg (80.3--90.0) vs. 74.5 mmHg (66.3--80.8); ( $p = 0.058$ ) basically remained unchanged from baseline values. Despite a small patient number, considerable effects could be encountered with respect to outcome measures. At baseline three patients presented with NYHA II (50.0%) and three patients presented with NYHA III (50.0%). Under treatment three patients improved from NYHA III to NYHA II. The other patients remained clinically stable with no change in NYHA class; ( $p = 0.083$ ). 6MWT improved from 340m (210--444) to 392m (298--480); ( $p = 0.046$ ). NT-proBNP levels decreased from 4009pg/ml (1837--8360) to 3250pg/ml (1792--8576); ( $p = 0.753$ ). With regards to invasive hemodynamic parameters, cardiac output increased from 3.7l/min (2.8--4.9) to 4.2l/min (3.6--5.2); ( $p = 0.028$ ), mean pulmonary arterial pressure 33.0mmHg (29.0--39.5) vs. 32.0mmHg (27.5--39.5) and pulmonary arterywedge pressure 25.0mmHg (16.8--30.0) vs. 22.0mmHg (16.8--28.8) did not change under treatment.

**Conclusion:** Our preliminary data from a named patient use program indicate that riociguat treatment is safe in patients with CA. More information is necessary to support the evidence that riociguat may relieve the burden of disease associated with CA.



**631**

**Manifestation of delay peripartum cardiomyopathy in Taiwan: implications from 925 cases in ten year**

T H Tien Hsing Chen<sup>1</sup>; VCCWU Wu<sup>1</sup>

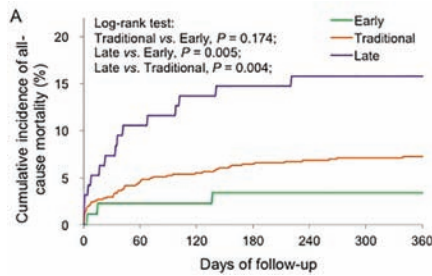
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**Background:** Relationship of onset and outcome in peripartum is not clear. Method: We identified all women hospitalized with HF 3 months before or 10 months after a delivery between January 1, 1997 and December 31, 2012. HF was initially screened for by International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes congestive heart failure (428.0,428.1,428.40, 428.41, 428.42, 428.43,428.9,425.4,425.9,674.5). We further categorized PPCM patients into 3 groups: (1) Early Diagnosis: PPCM diagnosed as early as 1st month till 9th month of pregnancy (2) Traditional Diagnosis: PPCM diagnosed as previously defined between one month prior to and 5th month post-delivery, and (3) Late Diagnosis: PPCM diagnosed from 6th month till 12th month post-delivery. Result: A total of 925 patients (30.4 ± 5.7 years old) satisfied our TNHIBD criteria as candidates of PPCM patients and were followed for a mean of 5.4 ± 4.1 years. There were 88 patients in the Early Diagnosis group, 742 patients in the Traditional Diagnosis group, and 95 patients in the Late Diagnosis group. There was significant difference in previous delivery ( $p = 0.046$ ), delivery type (abortion, vaginal delivery, and Cesarean section) at diagnosis of PPCM ( $p < 0.001$ ), multiparity at diagnosis of PPCM ( $p = 0.003$ ) among groups. For long-term outcome, patients in Late Diagnosis had highest all-cause mortality (18.2%), compared with patients in Traditional Diagnosis group (8.7%) and Early Diagnosis group (5.7%), and also highest mortality within 1 year (9.1%), compared with patients in Tradition Diagnosis group (3.8%) and Early Diagnosis group (2.3%). Conclusion: Late diagnosis of peripartum cardiomyopathy results in increased morbidity and mortality in pregnancy-associated heart failure.

6151 - Long-Term outcome 1 year after PPCM

Outcome	Number of event (%)		Adjusted hazard ratio and 95% CI		Traditional vs. Early		Late vs. Early		Late vs. Traditional	
	Early (n = 88)	Traditional (n = 742)	Late (n = 95)	P	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
HR (95% CI)	P		HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
New occurrence of dialysis	0 (0.0)	2 (0.3)	0 (0.0)	NA	NA	NA	NA	NA	NA	NA
Heart failure	5 (5.7)	22 (3.0)	6 (6.3)	0.63 (0.23-1.69)	0.354	1.59 (0.47-5.39)	0.456	2.54 (1.01-6.38)	0.047	
Acute myocardial infarction	0 (0.0)	1 (0.1)	0 (0.0)	NA	NA	NA	NA	NA	NA	
Heart transplant	0 (0.0)	4 (0.5)	1 (1.1)	NA	NA	NA	NA	1.49 (0.16-13.84)	0.725	
Cerebrovascular accident	0 (0.0)	3 (0.4)	1 (1.1)	NA	NA	NA	NA	1.96 (0.20-19.41)	0.567	
CV death revised	1 (1.1)	21 (2.8)	9 (9.5)	2.79 (0.37-20.89)	0.319	8.79 (1.08-71.27)	0.042	3.15 (1.40-7.11)	0.006	
MACE§	6 (6.8)	44 (5.9)	15 (15.8)	0.99 (0.42-2.35)	0.984	2.62 (0.99-6.92)	0.053	2.64 (1.44-4.83)	0.002	
All-cause mortality	3 (3.4)	54 (7.3)	15 (15.8)	2.27 (0.70-7.34)	0.170	4.94 (1.40-17.42)	0.013	2.17 (1.20-3.95)	0.011	





Time to death since PPCM diagnosis

632

**The presence of a truncating mutation in titin independently associates with arrhythmic burden in patients with dilated cardiomyopathy**

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**Background:** Dilated cardiomyopathy (DCM) can be associated with prognostically adverse arrhythmias at presentation. It is often unclear whether this is a marker of phenotypic severity or whether they reflect an independent pathophysiological process. We sought to establish whether truncating variants in the sarcomeric protein TTN (TTNtv), found in up to 20% of DCM, were associated with the occurrence of arrhythmic DCM at baseline independently of cardiac function.

**Methods:** 630 prospectively recruited DCM patients underwent cardiac MRI and were sequenced for TTNtv. The presence of confirmed ventricular tachycardia (VT), non-sustained ventricular tachycardia (NSVT) or atrial fibrillation (AF) at baseline was collected on all patients. Continuous and categorical variables were compared using Mann-Whitney/t-tests or Chi-squared tests as appropriate. Univariable and multivariable logistic regression models were used to identify variables that were independently associated with arrhythmic DCM status.

**Results:** 201 patients (32%) had evidence of AF, VT, or NSVT at baseline. These patients were more likely to be older, male, with worse cardiac function (age 63.4 years ± 11.6 vs 54.6 years ± 15.9, p < 0.0001; gender male n = 164 (81.6%) vs n = 266 (62.0%), p < 0.0001; baseline left ventricular ejection fraction 36.0% ± 12.2 vs 40.8% ± 12.6, p < 0.0001; baseline right ventricular ejection fraction 32.3% ± 13.6 vs 39.8% ± 13.4, p < 0.0001). TTNtv were found in 13.9% (n = 28) of patients with arrhythmias compared to 7.9% (n = 34) of patients without (p = 0.03). Age, gender and baseline left and right ventricular function were each predictive of arrhythmia status in univariate analysis. Adjusting for these variables, the presence of TTNtv was an independent predictor of arrhythmia status (odds ratio 3.01, p = 0.001) (Table 1).

**Conclusion:** Adjusting for age, gender and baseline cardiac function, the presence of a truncating variant in TTN is independently associated with atrial and ventricular arrhythmias. This suggests that arrhythmia status in DCM is not solely a reflection of phenotypic severity, which has implications for guiding patient management.

Table 1

Variable	Unadjusted analysis		Adjusted analysis		
	OR	P value	OR	P value	95% confidence interval
Age	1.04	< 0.0001	1.03	< 0.0001	1.03 to 1.06
Male Gender	2.71	< 0.0001	2.36	0.0003	1.50 to 3.77
Baseline left ventricular ejection fraction	0.97	< 0.0001	0.98	0.49	0.99 to 1.03
Baseline right ventricular ejection fraction	0.96	< 0.0001	0.97	< 0.0001	0.94 to 0.97
TTNtv positive	1.9	0.0198	3.01	0.001	1.57 to 5.83

Predictors of baseline arrhythmia status in DCM patients

633

**Two-dimensional strain echocardiography is superior to left ventricular ejection fraction in prediction of outcome in patients with left-sided infective endocarditis**

TKL was funded by grants from The Danish Heart Foundation  
 TK Trine Killeerich Lauridsen<sup>1</sup>; C Alhede<sup>1</sup>; AL Crowley<sup>2</sup>; J Kisslo<sup>2</sup>;  
 T Fritz-Hansen<sup>1</sup>; CT Larsen<sup>3</sup>; N Risum<sup>4</sup>; P Sogaard<sup>2</sup>; AL Dahl<sup>1</sup>; NE Bruun<sup>1</sup>  
<sup>1</sup>Gentofte University Hospital, Cardiology, Copenhagen, Denmark; <sup>2</sup>Duke University Medical Center, Cardiology, Durham, United States of America; <sup>3</sup>Roskilde Hospital, Cardiology, Roskilde, Denmark; <sup>4</sup>Rigshospitalet - Copenhagen University Hospital, Cardiology, Copenhagen, Denmark; <sup>5</sup>Aalborg University Hospital, Aalborg, Denmark

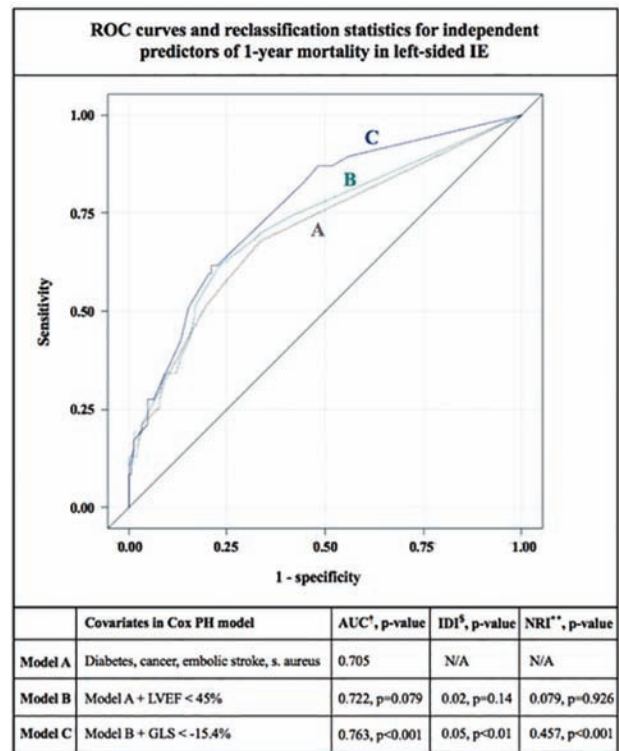
**Background:** Impaired cardiac function is the main predictor of poor outcome in infective endocarditis (IE). 2-dimensional (2D) global longitudinal strain (GLS) has proven superior in prediction of long-term outcome as compared to LVEF in valvular disease and heart failure in general. Whether measurements of cardiac deformation can predict survival in patients with IE has not previously been investigated.

**Purpose:** To determine whether 2D GLS is associated with long-term outcome and further to investigate whether GLS is superior to LVEF in risk stratification and prognosis of IE.

**Methods:** The study included consecutive patients with definite IE admitted between January 2006 and January 2014. Log-rank significance testing was applied to determine survival for LVEF and GLS, respectively. Cox models adjusted for surgery and reclassification statistics were applied to identify independent predictors of 1-year mortality.

**Results:** A cohort of 190 patients met eligibility criteria. LVEF and GLS were both prognostic markers of mortality. Independent predictors of 1-year mortality were s. aureus IE (HR:2.02; 95%CI 1.11–5.72, p=0.022), diabetes (HR:2.05; 95%CI 1.12–3.75, p=0.020), embolic stroke (HR:3.95; 95%CI 1.93–8.10, p < 0.001) and GLS < -15.4% (HR:2.95; 95%CI 1.52–5.72, p < 0.001). Adding GLS to known risk factors of IE resulted in significant increase of AUC (AUC = 0.722, p < 0.001).

**Conclusions:** Impairment of both LVEF and GLS was associated with long-term mortality in left-sided IE. GLS was superior to LVEF in both risk prediction and risk discrimination of patients with left-sided IE.



Independent predictors in IE

## CLINICAL CASE CORNER 2: CATCH ME, IF YOU CAN: CASES OF VERY FAST (OR SLOW) HEART - PART I

Sunday 22 May 2016 10:00–11:00

Location: Poster Area

634

### Palpitations in a young male scheduled for tonsillectomy

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<sup>1</sup>Erasmus Medical Center, Thoraxcenter, Department of Cardiology, Rotterdam, Netherlands; <sup>2</sup>Erasmus Medical Center, Department of Pathology, Rotterdam, Netherlands; <sup>3</sup>Erasmus Medical Center, Department of Clinical Genetics, Rotterdam, Netherlands

**Introduction and case-report description:** A 21-year old male scheduled for tonsillectomy due to recurrent pharyngitis was referred for analysis of an irregular heart rhythm. He had occasionally palpitations. He used a maximum of three units of alcohol weekly, but no drugs. His physical examination was unremarkable. ECG showed sinus rhythm with ventricular extrasystoles. Echocardiography revealed a diffuse hypokinetic left ventricle (LV) with an end-diastolic diameter of 58 mm, normal wall thickness and diastolic filling pressures. There was no valve pathology. The right ventricle (RV) dimensions and function were normal. Computer tomography revealed a normal coronary anatomy. Three months later he was admitted because of palpitations and pre-syncope. Rhythm observation revealed frequent episodes of polymorph non-sustained ventricular tachycardia. NT-proBNP and high-sensitivity troponin T were moderately increased (59 pmol/l and 584 ng/l, respectively). Thyroid function was normal.

**Description of the problem:** This young patient had symptomatic ventricular arrhythmias associated with an impaired LV function at normal loading conditions. Questions, problems or possible differential diagnosis: What is the differential diagnosis? What additional investigations should be performed? Should this patient receive an ICD?

**Answers and discussion:** Differential diagnosis includes infectious or auto-immune myocarditis, sarcoidosis, or arrhythmogenic cardiomyopathy. We performed a MRI that revealed a dilated LV with an ejection fraction of 45%, and linear midwall delayed enhancement in the interventricular septum. Endomyocardial biopsy of RV septum showed no active myocarditis, no granulomas, but extensive fibrosis. All immunologic markers were negative, including the anti-heart antibodies. Genetic testing showed a pathogenic frame-shift mutation in desmoplakin (DSP) gene, that was also found in his mother. He was treated with an angiotensin-converting enzyme inhibitor, a mineralocorticoid receptor antagonist and high dose beta-blocker. An ICD was implanted.

**Conclusions and implications for clinical practice:** Ventricular arrhythmias associated with impaired LV function at normal loading conditions in a young patient warrant additional examination, including myocardial biopsy and genetic testing. The phenotype associated with the pathogenic mutation of DSP can represent an arrhythmogenic left ventricular cardiomyopathy (ALVC). Cardiac screening of first-degree relatives revealed severely impaired LV function and ventricular arrhythmias in a younger sister. Several studies showed an increased risk for malignant ventricular arrhythmias in male patients with lamina A/C mutations. Whether this increased risk is present for other genetic mutations is unknown. In our patient the decision for ICD implantation was based on the burden of ventricular arrhythmias and the presence of an anatomic substrate, although there are no specific recommendations for this phenotype.

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### Sudden unexplained death in a young patient

M Juarez Fernandez<sup>1</sup>; MA Espinosa Castro<sup>1</sup>; I Sousa Casasnovas<sup>1</sup>; C Devesa Cordero<sup>1</sup>; V Gomez Carrillo<sup>1</sup>; M Martinez Selles<sup>1</sup>; R Yotti Alvarez<sup>1</sup>; F Fernandez Aviles<sup>1</sup>

<sup>1</sup>University Hospital Gregorio Maranon, cardiology, Madrid, Spain

**Introduction and case report:** A 22 year old man without medical history or family history of heart disease presented a cardiac arrest. Rhythm was analyzed with a semiautomatic defibrillator that detected a shockable rhythm and delivered electrical defibrillation. The patient recovered with an atrial fibrillation rhythm.

**Procedure:** The patient was admitted to our Cardiovascular Intensive Care Unit and hypothermia was performed. After completing the hypothermia and rewarming, he awakened without neurological sequelae. Atrial fibrillation persisted since admission so finally successful electrical cardioversion was performed. His electrocardiogram and Holter monitoring showed no other abnormalities. Further investigations (echocardiogram, coronary angiography, cardiac magnetic resonance, exercise stress test, flecainide and epinephrine test) were also normal.

In the absence of diagnosis an implantable cardioverter defibrillator (ICD) was implanted and genetic testing was performed with a NGS panel (76 genes) identifying a missense mutation in KCNQ1 gene, in exon 5 (R231H). Therefore the patient was diagnosed with Long QT Syndrome type I and he started beta blockers. Genetic counseling was given and genetic cascade was recommended to first-degree relatives.

**Differential diagnosis:** When facing a sudden death in a young patient without structural heart disease inherited channelopathies such as Long QT syndrome (LQTS), Brugada syndrome or catecholaminergic ventricular tachycardia need to be ruled out. Our patient's electrocardiogram showed neither Brugada nor LQTS findings. Provocative testing were normal. A clinical clue in this case was the finding of persistent atrial fibrillation which is rare after defibrillation of ventricular fibrillation in a young patient.

**Conclusions and implications for clinical practice:** In about a third of young patients with sudden cardiac death the etiology is not identified. In most the cause is an inherited arrhythmogenic disorder and the clinical-genetic study can diagnose up to 40 % of these. It is worth to perform a genetic testing in the unexplained cases in order to minimize the risk of recurrence or shocks after ICD implantation and to identify family members at risk in the case of hereditary diseases. In the case we present here, genetic testing has allowed the diagnosis of LQTS although electrocardiogram, exercise test and epinephrine test were normal. The R231H variant in KCNQ1 is related to LQTS type I and familial AF. This mutation has been described in several families with ventricular arrhythmias and AF, and it is not found in individuals from population databases. This case illustrates the importance of genetics in the management of sudden unexplained death in the young. In such patients genetic testing should be part of our diagnostic workup.

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### Acute myocarditis with prominent epsilon-waves on electrocardiogram

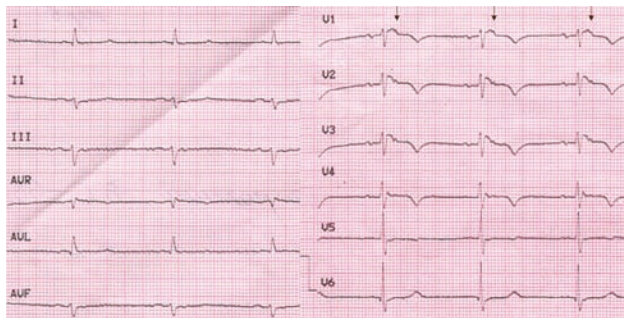
A Kulikov<sup>1</sup>; A Bobrov<sup>2</sup>; V Dvinyadinov<sup>2</sup>; S Rud<sup>2</sup>

<sup>1</sup>Saint Petersburg Pavlov State Medical University, Saint Petersburg, Russian Federation; <sup>2</sup>Military Medical Academy, Saint Petersburg, Russian Federation

A 66-year old male came to our emergency department with signs of arrhythmogenic shock caused by right ventricular tachycardia (190 bpm). Emergency defibrillation restored his sinus rhythm. From the age of 20 he had experienced a few episodes of paroxysmal palpitations. This episode of arrhythmia was accompanied by the loss of consciousness for the first time. After the cardioversion examination detected heart failure signs: acrocyanosis, peripheral oedema, jugular venous distention, mild hypotension (105/60 mm Hg) and hepatomegaly. Laboratory findings were slightly reduced haemoglobin level (120 g/l) and elevated brain natriuretic peptide (650 pg/ml). Sinus bradycardia (50 bpm) and high epsilon-waves in V1-3 leads were detected on ECG. 4 episodes of accelerated ventricular rhythm (up to 4 complex with 70-80 bpm) and frequent premature ventricular contractions (130 per hour) were found on Holter monitoring. Signal-averaged ECG detected late potentials (HF QRS



duration = 222 ms, RMS-40 = 27 mV, LAS40 = 105 ms). Echocardiography revealed enlarged right ventricle (RV) and right atrium (RV diastolic dimension - 45 mm, right atrium diastolic volume - 105 ml) with normal volumes of left chambers; RV wall thickening (up to 10 mm) and prominent trabeculations of middle and apex part of RV; impaired local and global RV contractility ( $S' = 6$  sm/c,  $FAC = 14\%$ ) with normal left ventricular systolic function ( $EF = 62\%$ ); signs of both ventricles diastolic dysfunction (left  $E/e' = 10$ , right  $E/e' = 9$ ). With magnetic resonance imaging of the heart we found thickening of the RV wall up to 8 mm, extensive subtotal wall fibrosis in apical and middle RV segments with small separate areas of fatty wall infiltration in some basal and apical segments. The kinetics of the RV walls was sharply decreased. RV diastolic volume was 190 ml, ejection fraction - 16%. Right ventriculography showed RV enlargement and high cavity trabeculation. Preliminary diagnosis of arrhythmogenic right ventricular dysplasia was made on the basis of 3 major and 3 minor modified McKenna criteria (2010). Meanwhile endomyocardial biopsy discovered degenerative changes of RV cardiomyocytes (vacuole dystrophia) with perivascular lymphocytic infiltration and small areas of granular tissue. The proportion of residual cardiomyocytes was 72%. Thus, we were unable to identify morphological features of arrhythmogenic right ventricular dysplasia. Analysis of biopsy samples showed that the patient has signs of acute healing myocarditis. As a result, possible relationships between myocarditis and arrhythmogenic right ventricular dysplasia are being discussed.



ECG epsilon-waves in V1-3 leads

### 637

#### A challenging case of infiltrative cardiomyopathy in a young man with syncope

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<sup>1</sup>Hospital of Santa Maria Nuova, Cardiology and Electrophysiology Unit, Florence, Italy; <sup>2</sup>University Hospital Careggi, Radiology Department, Firenze, Italy; <sup>3</sup>Gabriele Monasterio Foundation, Pisa, Italy

We report the case of a 43 years old man that was admitted to our Cardiac Care Unit - CCU because of syncope. Mild smoker with a family history of myocardial infarction and sudden death in young age. He reported that during the last month when performing moderate-to-intense sport activity his heart rate suddenly halved (he was used to wear a heart rate belt), a finding that he never observed before. The echocardiogram showed an increased thickness of the interventricular septum - IVS (15 mm) and a preserved left ventricular contractility (left ventricular ejection fraction - EF: 0.55). The patient underwent an electrophysiological study - EPS that showed normal intra-cardiac delays and no induction of ventricular arrhythmias. The coronary angiography was normal. An intra-cardiac loop-recorder - ILR was implanted and the patient was discharged. The day after the patient presented palpitations and a non-sustained ventricular tachycardia - NSVT was documented during the device interrogation; a therapy with beta-blocker was started. After few days the patient suffered exertional syncope; the recording from the ILR showed a complete atrioventricular block with 9 seconds of asystole. The patient was admitted to our CCU, underwent cardiac magnetic resonance - CMR and then was implanted with a dual chamber pacemaker-defibrillator - ICD. The CMR showed a late gadolinium enhancement - LGE of the right ventricle and a spotted LGE of the left ventricle. One month later the patient came to our Heart Failure Clinic for clinical follow-up. While he was waiting to be called in the doctor's office he suddenly lost consciousness. The ICD interrogation showed a ventricular fibrillation correctly recognized and treated by a 11 J shock. Amiodarone 200 mg was added to the betablocker. In the suspicion of an infiltrative cardiomyopathy the patient underwent chest computed tomography (CT) and positron emission tomography (PET) that placed the diagnosis of cardiac sarcoidosis. A myocardial biopsy guided by electroanatomical mapping system and targeted on low voltage right ventricular free wall areas showed a histological pattern of cardiac sarcoidosis. A therapy with prednisone was started and the patient rapidly recovered. After a two months follow-up no arrhythmia recurrence was detected by the ICD remote monitoring.

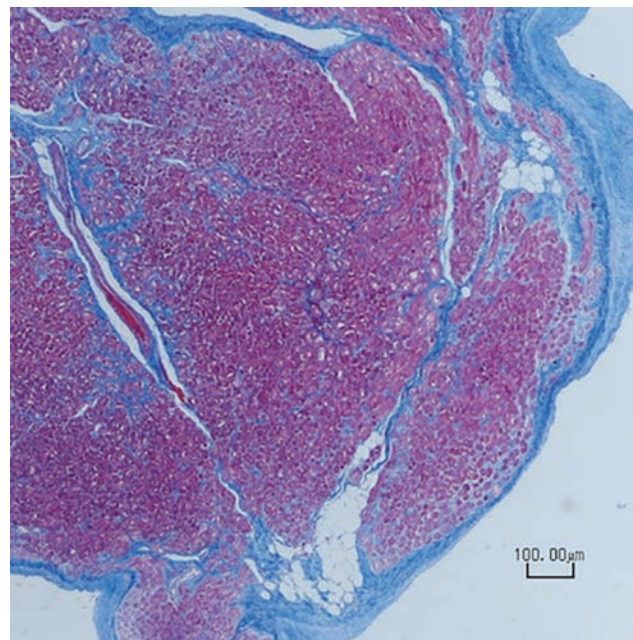
### 638

#### A rare acromegalic cardiomyopathy with malignant arrhythmogenic pattern

S Doimo<sup>1</sup>; D Miani<sup>2</sup>; C Nalli<sup>2</sup>; M Driussi<sup>2</sup>; N Finato<sup>3</sup>; G Sinagra<sup>1</sup>; U Livi<sup>2</sup>; A Proclemer<sup>2</sup>

<sup>1</sup>Postgraduate School in Cardiovascular Sciences, Cardiovascular Department, Trieste, Italy; <sup>2</sup>University Hospital Santa Maria della Misericordia, Department of Cardiothoracic Science and IRCAB foundation, Udine, Italy; <sup>3</sup>University Hospital Santa Maria della Misericordia, Laboratory Department of Medical and Biological Sciences, Udine, Italy

We report a case of 48 years old man, presented in emergency department in October 2011 for chest pain and dyspnea. Systemic examination revealed coarse facial features and signs of heart failure. The electrocardiogram showed sinus rhythm, left bundle branch block and ectopic ventricular beats. Echocardiographic evaluation was suggestive of dilated cardiomyopathy with left ventricular dilatation, posterior wall motion abnormalities, apical thrombosis, severe depressed ejection fraction (EF) and mild mitral regurgitation. Coronary angiography showed normal coronary arteries and cardiac magnetic resonance confirmed the severe left ventricular dilatation (indexed telediastolic volume: 195 ml/mq) and dysfunction (EF 22%), eccentric hypertrophy with apical thrombosis and transmural fibrosis. At the same time, the patient was evaluated for acromegaly. Elevated somatotropin levels (11.5 ng/ml) and cerebral magnetic resonance were compatible with pituitary adenoma. With tailored heart failure therapy, amiodarone, warfarin and somatostatin analog, the patient remained asymptomatic, with improved EF (35%) and only sporadic ventricular extrasystoles at Holter registration. Pituitary adenoma was removed by trans-sphenoidal surgical resection in 2013. Clinical stability was maintained until January 2014, when the patient was admitted to our hospital for sustained ventricular tachycardia (VT), 190 bpm, solved with 50 joule D.C. shock. A dual coil lead ICD defibrillator was implanted and amiodarone was interrupted for iatrogenic hyperthyroidism. After 6 months, the patient was readmitted for repeated ICD interventions due to VT episodes (190 bpm). With introduction of procainamide (1.5 gr/day per os) no recurrence of VT was documented and patient was successfully discharged. Unfortunately, in November the patient was readmitted for refractory VT and ventricular fibrillation storm, which required venous arteriosus ECMO, associated to intra-aortic balloon counterpulsation and urgent placement on the waiting list for heart transplantation. After 19 days, a compatible organ was available and heart transplantation with bicaval anastomoses was performed. At macroscopic analysis of the explanted heart, the severe dilatation and eccentric hypertrophy was confirmed. Histologically, we highlighted sporadic foci of fibro-adipose replacement, interstitial fibrosis and fibrous thickening of the endocardium without inflammation. **Conclusion:** acromegaly is a rare disease in which cardiovascular complication are common. Malignant ventricular tachyarrhythmias are a frequent manifestation of cardiac involvement and their severity correlates with increases in left ventricular mass. In most cases, cardiovascular complications might benefit from treatment directed towards the pituitary adenoma but in our case, despite the tumor removal, the sustained ventricular arrhythmias were uncontrollable due to the underlying end-stage acromegalic cardiomyopathy.



fibro-adipose foci, interstitial fibrosis

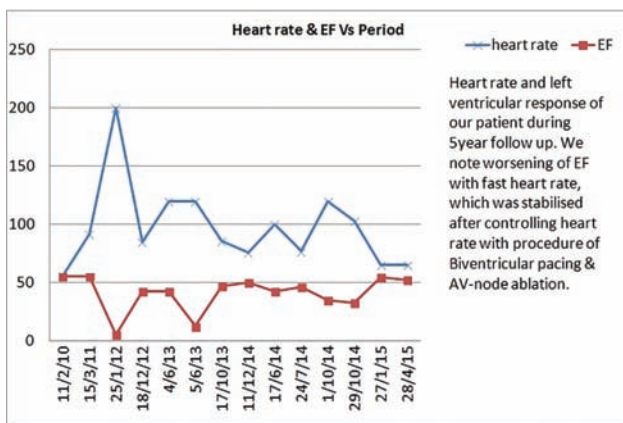


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**Unconventional approach to atrial fibrillation in friedreich's ataxia.**S Suhas Jadhav<sup>1</sup>; E Keelan<sup>2</sup>; D Ward<sup>1</sup><sup>1</sup>Adelaide & Meath Hospital, CRY-P, Dublin, Ireland; <sup>2</sup>Connolly Hospital Blanchardstown, Cardiology, Dublin, Ireland

**Background:** Friedreich's ataxia (FA) is an autosomal recessive, progressive, degenerative disorder. It causes neurological dysfunction & cardiomyopathy, with left ventricular hypertrophy. Cardiac arrhythmia & heart failure (HF) are the predominant cause of death & impaired quality of life (QOL) in FA. Management of atrial fibrillation (AF) in already fragile FA patient can be challenging. Case description: 32 year old male FA patient referred for cardiac assessment. He reported extreme fatigue since starting B-blocker (BB) for asymptomatic ectopic beats. At 1st consultation he was asymptomatic with stable mildly reduced ejection fraction EF ~48%. We stopped his BB & QOL improved. 2 years later he was hospitalised with 1st documented AF episode & decompensated HF. Initial attempt at rhythm control failed. After 5 days of amiodarone therapy he converted to sinus rhythm, EF returned to baseline & he was discharged on ramipril, amiodarone, aspirin, furosemide, digoxin, eplerenone. In next 28 months he was hospitalised on 3 occasions for paroxysmal AF related HF. We sought 2 separate electrophysiologist's (EP) opinion on each admission, were advised that AF-ablation was not indicated or likely to be successful & recommended medical therapy, including stopping amiodarone & uptitration of BB on 3rd admission. After stopping amiodarone, he went into permanent AF. In spite of optimization of medications, OPD review confirmed poor HR control, reduced EF & poor tolerance of BB as before. Possible options and our approach: 1) Continue BB (+/- increase dose) to improve rate control (side-effects likely to further impair QOL). 2) Stop BB (in the short term might improve QOL, but with frequent bursts of tachycardia would likely result in further reduction in EF and negatively impact on his morbidity & mortality). 3) AF-ablation (invasive with uncertain outcome in reduction in AF) 4) Biventricular pacing and AV-node ablation (on the positive side would remove the need for BB, but it has never been attempted in FA patients, to our knowledge, so outcome again uncertain).

**Discussion & Conclusion:** Use of rate control medications did not achieve the target & severely impaired QOL. While 2 experts EP agreed that ablation for AF was of doubtful assistance, a speculative staged biventricular pacing & AV-node ablation plan was agreed with 3rd EP. This allowed us to stop the BB amiodarone. Post ablation 3 months follow up confirms improved QOL & EF 55%. We suggest in complex patients that lack of evidence for a therapeutic approach could be interpreted as evidence of no benefit, but in a rare condition such as FA, randomised controlled trials to guide therapies will be difficult to achieve. Standard medications can be poorly tolerated in these patients. Although life expectancy is reduced in FA, aggressive intervention can be beneficial-immediately for QOL we hope longer term in increased longevity. We suggest invasive therapy on an individual basis & proactive advocacy by the treating Physician for their patient if warranted.



Heart rate and EF Vs Period

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**Management of an idiopathic left ventricular aneurysm presented with sustained ventricular tachycardia**D Menci<sup>1</sup>; FM Righini<sup>1</sup>; V Zaca<sup>1</sup>; M Cameli<sup>1</sup>; C Baiocchi<sup>1</sup>; S Mondillo<sup>1</sup>; R Favilli<sup>1</sup><sup>1</sup>University of Siena, Department of Cardiovascular Diseases, Siena, Italy

We report a case of a 67 year-old patient who displayed a monomorphic ventricular tachycardia with a finding of a left ventricle (LV) aneurysm of the basal segment of postero-lateral wall assessed by echocardiography. Coronary angiography ruled

out an ischemic cardiopathy and cardiac magnetic resonance (CMR) showed a non-ischemic pattern of fibrosis in the aneurysmal wall combined with adipose tissue replacement. An implantable cardioverter defibrillator (ICD) was implanted in secondary prevention and an antiarrhythmic therapy with amiodarone was started without recurrence of the ventricular arrhythmia in one year of follow-up. We also report some little evidence at our disposal about non-ischemic left ventricular aneurysms management.

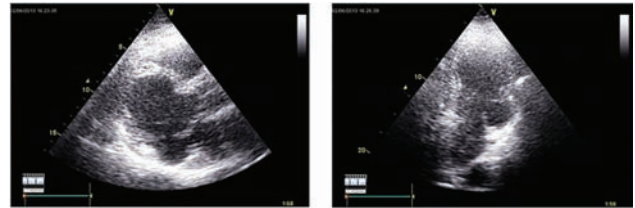


Figure 1

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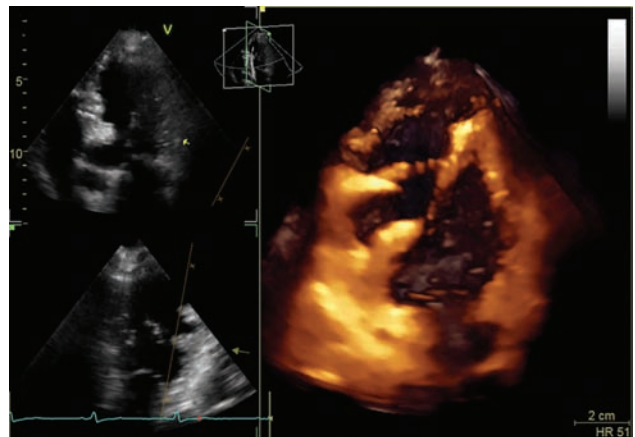
**A singular cardiac structure and morphology**C Catia Costa<sup>1</sup>; ML Pitta<sup>1</sup>; P Matos<sup>2</sup>; E Oliveira<sup>3</sup>; M Leal<sup>1</sup><sup>1</sup>Hospital of Santarem, Cardiology, Santarem, Portugal; <sup>2</sup>Hospital CUF Infante Santo, Lisbon, Portugal; <sup>3</sup>University Hospital De Santa Maria, Lisbon, Portugal

We report the case of an 85-year-old male, with type 2 diabetes and dyslipidaemia. He had no living ascendants or descendants. He was referred to Cardiology evaluation after documentation of a single cardiac morphology of unknown etiology. The patient was in NYHA class II and had frequent polymorphic ventricular extrasystole.

The 2D and 3D echocardiographic assessment revealed a dilated left ventricle, with mild systolic dysfunction, as well as multiple digitiform images at the inferior and posterolateral walls, as many bands and false tendons inside the cavity. Cardiac magnetic resonance confirmed the presence of numerous muscular digitiform images, with lesser sensitivity in detecting the bands and false tendons. It did not revealed changes in the late enhancement study or presented criteria for left ventricular non-compaction.

The myocardial perfusion scintigraphy documented the presence of myocardial ischemia, which has not translated into significant epicardial disease on coronary angiography.

The patient evolved to NYHA class I after beginning of beta-blocker therapy and suppressing therapy of the renin-angiotensin-aldosterone system, with better control of the arrhythmias. Although the optimized treatment, this patient had a relatively benign course of his cardiomyopathy with late detection and long survival. This is a rare case of muscular dysplasia not yet classified, designated by scarce reports as sawtooth cardiomyopathy, an unreliable designation after evaluation by 3D echocardiography that showed a more complex intracavitary structure, including not also multiple muscular digitiform images, as well as several bands and false tendons, presumably translating a deranged myofibril organization pattern.

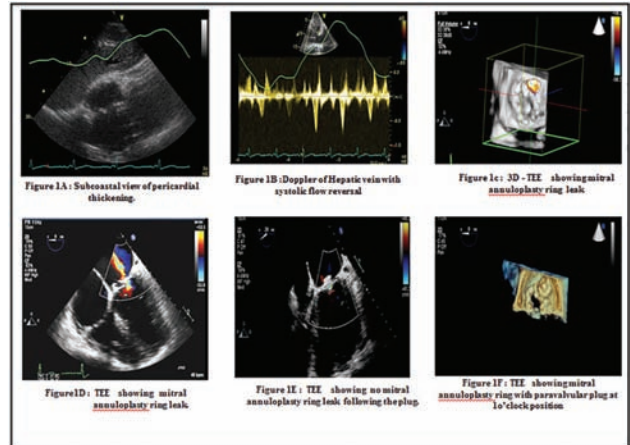


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**Rhyme and reason for a bad rhythm: triple ripple; 1. recurrent atrial fibrillation, 2. mitral periprosthetic leak, 3. constrictive pericarditis**VR Vinutha Rajesh<sup>1</sup>; N Ushler<sup>1</sup>; F Mookadam<sup>1</sup><sup>1</sup>Mayo Clinic, Arizona, Cardiology, Phoenix, United States of America

**Background:** Postoperative constrictive pericarditis is rare following open heart surgery. Patients presenting with heart failure (CHF) or arrhythmias late after cardiac surgery should have a complete investigation of the etiology of CHF. We describe a case post mitral valve annuloplasty repair for severe mitral regurgitation with recurrent atrial fibrillation and congestive heart symptoms. An unusual case with uncommon treatment strategies was successfully managed. Case: A 63-year-old man with recurrent atrial fibrillation and past medical history of mitral valve repair with annuloplasty ring, maze procedure, PFO closure, and single vein graft to the left anterior descending artery one year earlier. Following surgery, the patient had recurrent atrial fibrillation requiring three radiofrequency ablation procedures at an outside hospital was referred for repeat ablation with acute New York Heart Association (NYHA) Class II-III CHF symptoms. Physical exam was significant for distention of the neck veins to 25 cm of H<sub>2</sub>O, positive Kussmaul's sign, 3/6 holosystolic murmur, decreased breath sounds of the lower lungs bilaterally, with ascites and 3+ pitting pedal edema. Decision Making: Clinical examination was suspicious for CHF, recurrent periprosthetic mitral regurgitation and pericardial constriction. The transthoracic echocardiography showed constrictive pericarditis and a large periprosthetic mitral regurgitation as shown in Panel 1. Cardiac catheterization confirmed the constrictive physiology. Patient was recommended for re-do mitral valve surgery and pericardectomy. Patient declined surgery and preferred medical management. Constriction was treated with triple therapy including Colchicine, Non-Steroidal Anti-inflammatory Drugs (NSAIDs) and steroids for 2 months and followed by NSAIDs and Colchicine for 4 months. While the constrictive symptoms improved, persistent heart failure requiring diuretic for the management of NYHA class II symptoms secondary to periprosthetic mitral regurgitation. Patient was referred for percutaneous mitral valve periprosthetic leak closure. Post procedure echocardiography showed resting gradient of 5 mm of Hg after successful deployment of a single Amplatzer PDA closure device. Four years later patient remains in NYHA Class I.

**Conclusion:** This complex case demonstrates the importance of a good physical examination in the evaluation of the heart failure symptoms. A high index of suspicion is needed in the diagnosis of constrictive pericarditis and the severity of the periprosthetic mitral valve leak causing persistent CHF after the constriction has resolved. It is unusual for constriction beyond one year of surgery to respond to medical management. In the current era, where repeat open heart surgery is not an option because of patient preference or excessive surgical risk, alternative strategies for symptomatic periprosthetic leak can be successfully undertaken in expert hands.



Panel 1

# YOUNG INVESTIGATOR AWARD: CLINICAL

Sunday 22 May 2016 11:00–12:30

Location: Agora

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### Plasma fibroblast growth factor 23 is associated with poor outcome and unsuccessful uptitration of guideline-recommended pharmacotherapy in patients with worsening heart failure

This project was funded by a grant from the European Commission: FP7-242209-BIOSTAT-CHF

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<sup>1</sup>University Medical Center Groningen, Groningen, Netherlands; <sup>2</sup>University of Brescia, Brescia, Italy; <sup>3</sup>Stavanger University Hospital, Stavanger, Norway;

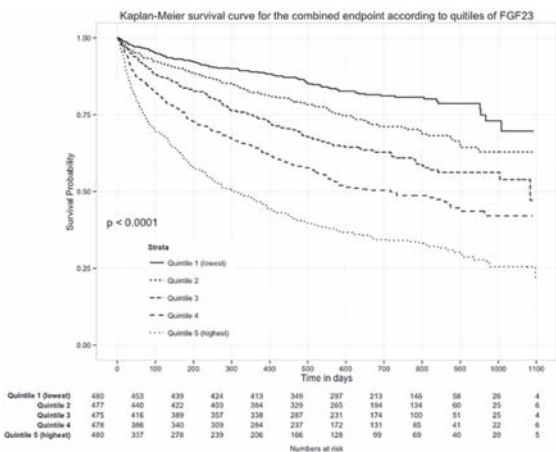
<sup>4</sup>University of Lorraine, Nancy, France; <sup>5</sup>Imperial College London, London, United Kingdom

**Background:** Recent studies suggest that fibroblast growth factor (FGF) 23 promotes sodium retention yet its potential value in worsening heart failure (WHF) has not been explored.

**Purpose:** To investigate the relation between FGF23 and clinical outcomes in patients with WHF.

**Methods:** We measured plasma C-terminal FGF23 levels in 2,399 of the 2,516 patients included in the BIOlogy Study to Tailored Treatment in Chronic Heart Failure (BIOSTAT-CHF) trial, in which patients with WHF were to be uptitrated to guideline recommended doses of angiotensin converting enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARB). The association between FGF23 and outcome was evaluated by Cox regression analysis adjusted for potential confounders, such as renal function. Results Median FGF23 was 218.0 [117.1-579.3] RU/ml, and patients with higher FGF23 levels had a worse NYHA class and more signs of congestion (all  $P < 0.005$ ). Patients with higher baseline FGF23 levels were less likely to use ACEi or ARB therapy at baseline and less likely to reach target dose after 3 months of uptitration. In multivariable Cox regression analysis, log transformed FGF23 was independently associated with all-cause mortality (1.25 (1.14-1.37) per log increase,  $P < 0.001$ ), and the combined endpoint of all-cause mortality and heart failure hospitalization (1.20 (1.11-1.29) per log increase,  $P < 0.001$ ). The predictive value of FGF23 for all-cause mortality was significantly greater than that for BNP (Univariable Harell's c-statistic: 0.689 vs. 0.649, respectively,  $P < .001$ ).

**Conclusion:** Higher plasma FGF23 levels are independently associated with less successful uptitration of guideline recommended therapies and an increased risk of all-cause mortality and heart failure hospitalization in patients with WHF.



Survival curve per quintiles of FGF23

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### Prognostic burden of heart failure diagnosed in primary care or secondary care: a population-based linked electronic health record cohort study in 2.1 million people

PLN foundation (hartspierziektepln.nl); Wellcome Trust (0938/30/Z/10/Z); DHF (Dekker 2014T001); UCL hospitals NIHR Biomedical Research Centre S Koudstaal<sup>1</sup>; M Pujades-Rodriguez<sup>2</sup>; S Denaxas<sup>2</sup>; JMIH Gho<sup>1</sup>; AD Shah<sup>2</sup>; CP Gale<sup>3</sup>; AW Hoes<sup>4</sup>; JG Cleland<sup>5</sup>; FW Asselbergs<sup>1</sup>; H Hemingway<sup>2</sup>

<sup>1</sup>University Medical Center Utrecht, Dept of Cardiology, Utrecht, Netherlands;

<sup>2</sup>University College London, Farr Institute of Health Informatics Research, London, United Kingdom; <sup>3</sup>Institute of Cardiovascular and Metabolic Medicine, Leeds, United Kingdom; <sup>4</sup>University Medical Center Utrecht, Julius Centre for Health Sciences and Primary Care, Utrecht, Netherlands; <sup>5</sup>Imperial College London, Dept of Cardiology, London, United Kingdom

**Background:** Heart failure (HF) is a heterogeneous disease and as such frequently encountered by caregivers across the entire health care system. No studies have evaluated prospectively collected information on distribution of HF and possible differences in HF prognosis based on level of care (i.e. primary care (PC) patients who are never hospitalised, PC patients who are also acutely hospitalised for HF, and patients hospitalised for HF but not known with HF in PC).

**Purpose:** To objective of this study was to assess the distribution of HF and compare its prognosis for patients seen in primary care, hospital admissions, both, or, have heart failure recorded as cause of death.

**Methods:** Linked electronic health record database of 2.13 million patients aged  $\geq 18$  years in England registered with a general practice contributing to CPRD between January 1997 and March 2010, linked with relevant hospital (HES) and mortality (ONS) registries. Patients aged 18 years or older with no prior history of HF who were diagnosed with HF throughout followup were included. Time to 90-day and 5-year all cause mortality and heart failure related mortality were modelled using Cox models.

**Results:** From a population of 2,134,615 people, we identified 89,554 patients with a diagnosis of heart failure, 23,547 (26%) in primary care who were never hospitalised for HF, 23,681 (26%) in primary care and hospitalised at least once for HF, 30,629 (34%) hospitalised for HF without ever receiving a PC diagnosis, and 11,697 (13%) with heart failure on their death record but no PC and/or hospital record (figure 1). The median age at diagnosis was 79.9 (interquartile range 71.9 to 86.3) years and 51.3%, 49.7%, 52.3%, and 53.3% were women in each of the above strata respectively. The 5-year survival was 88.1% (95%CI 87.9% - 88.3%) in the age and sex matched general population, compared to 43.9% (95%CI 43.2% - 44.6%) for HF patients in PC only, 39.8% (95%CI 39.2% - 40.5%) for PC with at least one hospital admission for HF, and 21.7% (95%CI 21.1% - 22.2%) for patients only hospitalised for HF without a PC record, respectively. Heart failure related mortality varied between groups and patients who were hospitalised for HF were more likely to die of HF compared to patients who were never hospitalised (hazard ratio, adjusted for age, sex and GP practice 1.71, 95% CI 1.63 - 1.78,  $P < 0.0001$ ). Furthermore, an acute hospital admission as the first presentation of the disease was associated with increased mortality, compared to HF diagnosed in PC (hazard ratio, adjusted for age, sex and GP practice 1.66, 95% CI 1.63 to 1.69,  $P < 0.0001$ ).

**Conclusions:** Important differences in terms of all-cause and HF related mortality exist depending on the level of care in which patients were diagnosed. Failure to address this heterogeneity in clinical practice or research may lead to biased estimates of the prognostic impact of a heart failure diagnosis.



Figure 1. Number and percentage of records in primary care (CPRD), hospital admissions (HES), and mortality registry (ONS) for heart failure across three national sources (n= 89 554 patients)

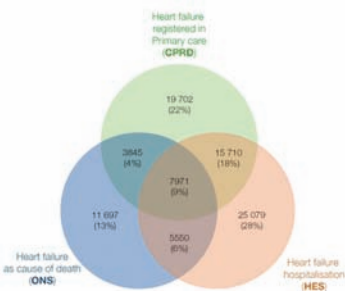


Figure 1. Distribution of Heart Failure

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**Treatment with insulin increases mortality in diabetic patients with chronic heart failure: data from the GISSI-HF Trial.**

D Cosmi<sup>1</sup>; S Barlera<sup>2</sup>; S Masson<sup>2</sup>; L Staszewsky<sup>2</sup>; A P Aldo Pietro Maggioni<sup>3</sup>; L Tavazzi<sup>4</sup>; G Tognoni<sup>2</sup>; F Cosmi<sup>1</sup>; R Latini<sup>2</sup>

<sup>1</sup>Valdichiana Cardiology, USL 8, Cardiovascular and Neurological Disease Department, Arezzo, Italy; <sup>2</sup>IRCCS - Istituto di Ricerche Farmacologiche Mario Negri, Department of Cardiovascular Research, Milan, Italy; <sup>3</sup>ANMCO Research Center, Florence, Italy; <sup>4</sup>Maria Cecilia Hospital, GVM Care & Research - ES Health Science Foundation, Cotignola, Italy

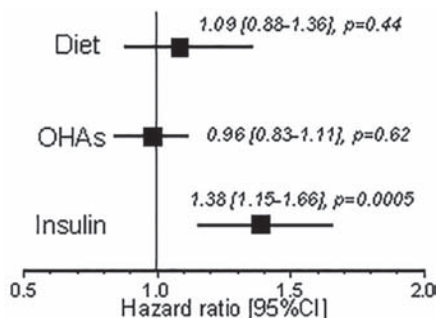
**Background:** Recent studies have found that insulin-treated diabetes (DM) is often associated with a significantly worse prognosis in patients with chronic heart failure (HF). However, the lack of general agreement on the detrimental effects of insulin in patients with HF and DM prompted this post-hoc analysis of the large database of the GISSI-HF trial.

**Purpose:** In patients with DM and chronic HF, we evaluated whether insulin treatment was independently associated with excess mortality compared to other anti-diabetic treatments. Methods. The association between anti-diabetic treatment and total mortality was evaluated with adjusted Cox proportional hazard models in the 6975 patients with chronic HF enrolled in the multicenter clinical trial GISSI-HF, of whom 1.974 (28.3%) had DM at entry. Of these, 313 were treated only with hypoglycemic diet, 1.119 only with oral hypoglycemic agents (OHAs), and 542 with insulin. Results were fully adjusted for demographic, clinical and laboratory covariates associated with mortality (p < 0.05).

**Results:** The median follow-time of the study was 3.9 years. All-cause mortality in DM patients was 675 (34.3%) versus 1294 (25.9%) in non-diabetics (p < 0.0001). The figure shows the adjusted risk of total mortality in patients with DM treated with diet, OHAs or insulin, compared to non-diabetic patients; there was a significant excess of risk only in the latter group.

**Conclusions:** In the GISSI-HF trial, DM patients treated with insulin showed a 38% higher mortality compared to those without DM. Prospective studies are warranted to confirm these results in a population commonly found in clinical practice, but orphan of hypoglycemic treatment with validated efficacy and safety.

**Conclusions:** In the GISSI-HF trial, DM patients treated with insulin showed a 38% higher mortality compared to those without DM. Prospective studies are warranted to confirm these results in a population commonly found in clinical practice, but orphan of hypoglycemic treatment with validated efficacy and safety.



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**Genetic screening in dilated and non-dilated cardiomyopathy: should we broaden our perspective?**

M R Mark Hazebroek<sup>1</sup>; J Verdonchot<sup>1</sup>; E Vanhoutte<sup>2</sup>; I Krapels<sup>2</sup>; M Hoos<sup>1</sup>; L Van Montfort<sup>1</sup>; A Van Den Wijngaard<sup>2</sup>; H Brunner<sup>2</sup>; S Heymans<sup>1</sup>

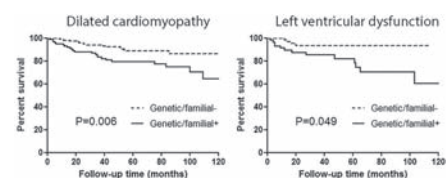
<sup>1</sup>Maastricht University Medical Center, Department of Cardiology, Maastricht, Netherlands; <sup>2</sup>Maastricht University Medical Centre (MUMC), Clinical Genetics, Maastricht, Netherlands

**Background:** The current ESC guidelines recommend genetic screening merely in patients with dilated cardiomyopathy (DCM). However, a significant subgroup presents with non-dilated cardiomyopathy also known as left ventricular (LV) dysfunction and recognized as a potential precursor of DCM. The presence of genetic or familial predisposition and the prognosis of patients with LV dysfunction versus DCM patients is currently unknown.

**Objectives:** To evaluate the diagnostic yield of next generation sequencing (NGS) gene testing, familial inheritance and prognosis in LV dysfunction patients versus DCM patients. **METHODS.** Within the Maastricht Cardiomyopathy registry 389 patients with initially unexplained CMP – excluding patients with ischemic, valvular, hypertensive, and congenital heart disease – were enrolled between January 2004 and September 2015. All patients underwent complete diagnostic evaluation including electrocardiography, echocardiography, 24h Holter registration and genetic screening. Genetic or familial predisposition is defined as familial inheritance pattern and/or the identification of a (likely) pathogenic mutation using next-generation sequencing (NGS). Familial inheritance is defined as the presence of ≥2 affected individuals in a single family or the presence of a 1st-degree relative with unexplained sudden cardiac death <60 years. Long-term outcome used a combined endpoint of life-threatening arrhythmia, heart transplantation, and all-cause death.

**Results:** A total of 262 consecutive DCM and 127 LV dysfunction patients were included. Baseline characteristics demonstrated no differences in the number of co-morbidities (P=0.81), but as expected a significant lower LVEF and higher age in DCM as compared to LV dysfunction (28 ± 11 vs 37 ± 10; P<0.001 and 58 ± 12 vs 55 ± 13; P<0.019, respectively). A genetic or familial predisposition was found to a similar extent in DCM as compared to LV dysfunction without dilatation (100 (38%) vs 57 (45%); P=0.21). As expected, a (likely) pathogenic mutation was more frequently found in patients with positive as compared to negative familial inheritance, irrespective of a DCM or LV dysfunction phenotype (20 (25%) vs 17 (9%); P=0.001 and 12 (27%) vs 11 (13%) P=0.049, respectively). After a median follow-up of 56 [31-82] months, long-term outcome did not differ between DCM and LV dysfunction (Log-rank P=0.671). However, outcome in patients with a genetic or familial predisposition was worse as compared to patients without a genetic or familial predisposition, in both the DCM and LV dysfunction phenotype (Figure 1, Log-rank P=0.006 and Log-rank P=0.049, respectively).

**Conclusion:** The diagnostic yield of NGS gene testing in DCM and LV dysfunction without dilatation is equally high. Moreover, the presence of genetic or familial predisposition exhibits a worse prognosis in both DCM and LV dysfunction patients. Therefore, genetic screening should not merely be restricted to patients with DCM.



Event-free survival

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**Renal venous pattern: a new parameter for predicting cardiorenal syndrome progression**

A Puzzo<sup>1</sup>; M Massimo Iacoviello<sup>2</sup>; F Monitillo<sup>3</sup>; M Leone<sup>3</sup>; C Rizzo<sup>3</sup>; MS Lattarulo<sup>3</sup>; D Grande<sup>3</sup>; P Terlizze<sup>3</sup>; F Massari<sup>1</sup>; MM Ciccone<sup>4</sup>

<sup>1</sup>Cardiology Unit, Murgia Hospital, Cardiovascular department of Bari, Altamura, Italy; <sup>2</sup>Institute of Cardiology - University of Bari, Bari, Italy; <sup>3</sup>University of Bari, School of Cardiology, Bari, Italy; <sup>4</sup>Polyclinic Hospital of Bari, Cardiology Unit, Cardiothoracic Department, Bari, Italy

**Background:** In chronic heart failure (CHF) patients, renal congestion plays a key role in determining the progression of renal dysfunction, that has been demonstrated to be associated with a worse prognosis.

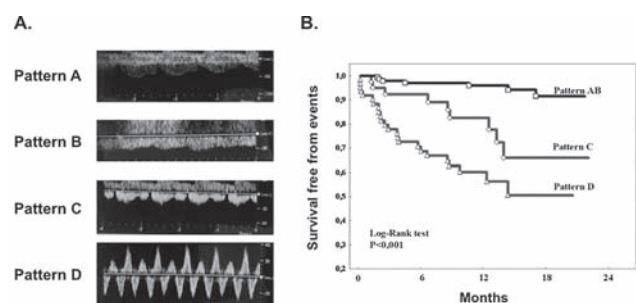
The aim of this study was to define whether Doppler venous patterns which reflect renal congestion, could play a role in predicting heart failure progression.

**Methods:** We enrolled 254 outpatients (76% males, 64 ± 14 years, NYHA class 2.2 ± 0.7, left ventricular ejection fraction, LVEF, 33 ± 9%) with CHF (ESC criteria), in stable clinical conditions (> 1 month) and in conventional therapy (86%

ACE-inhibitors and/or ARBs, 94% betablockers). All patients underwent a clinical evaluation, a routine chemistry, an echocardiogram and a renal echo-Doppler. Pulsed Doppler flow recording was performed, at the level of interlobular renal right veins in tele-expiratory phase. Inviting the patients to hold their breath. The venous flow patterns have been divided into 4 groups as shown in Figure A. Group A: flow patterns with normal decrease in flow velocity and biphasic pattern with no interruption of flow in tele-diastole; Group B: pattern of continuous flow with minimal fluctuations; Group C: Pattern monophasic or biphasic with interruption of the flow in tele-diastole; Group D: pattern of intermittent flow.

**Results:** During a median follow-up of 12 months (interquartile range 8-16 months), 40 patients experienced heart failure progression (hospitalization, heart transplantation or death due to heart failure worsening).

Venous patterns C (HR 6.01;95%CI:2.08-17.35; p:0.001) and D (HR 2.99;95%CI: 1.17-7.62; p:0.022) were associated with events at univariate Cox regression analysis. Moreover both pattern C (HR: 5.88; 95%CI:2.09-16.6; p: 0.001) and D (HR: 3.10; 95%CI: 1.28-7.50; p: 0.012) remained associated to events at multivariate Cox regression analysis after correction for the independent predictors of the reference model, with a high discrimination (correlation of 0.90 according to the C-statistic). Moreover, the addition of venous flow patterns to the reference model significantly improved reclassification according to both NRI 91% (0.58-1.25; p<0.001) and IDI (45% 95% CI: 0.01-0.08; p=0.012). Figure shows Kaplan Meier curves for pattern A-B, C and D. In conclusion, our findings demonstrate the independent and incremental role of Doppler venous patterns reflecting renal congestion in predicting HF progression among CHF patients, thus suggesting its possible utility in daily clinical practice in order to better characterize patients with cardio-renal syndrome.



Figure

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**The metabolic exercise cardiac and kidney indexes (mecki) score: a new prognostic tool in patients with heart failure. a multicenter comparison with seattle and hfss in a large cohort of patients**

M Massimo Mapelli<sup>1</sup>; RL La Gioia<sup>2</sup>; ME Emdin<sup>3</sup>; RR Raimondo<sup>4</sup>; GL Limongelli<sup>5</sup>; AS Scardovi<sup>6</sup>; CL Lombardi<sup>7</sup>; GS Sinagra<sup>8</sup>; UC Corra<sup>9</sup>; PA Agostoni<sup>1</sup>  
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**Background:** Heart failure (HF) prognostication is a challenging medical judgment, constrained by a magnitude of uncertainty. Cardiopulmonary exercise test (CPET)

is a well-recognized, valuable and accurate tool for risk stratification in HF. Peak oxygen uptake (VO2) and the relationship between ventilation and CO2 production (VE/VO2 slope) have been identified as robust predictors of HF prognosis. Risk stratification with CPET-derived parameters need to be integrated into clinical practice. MECKI score is a simple 6-variables (VO2, VE/VO2, Hemoglobin, Sodium, MDRD, left ventricle ejection fraction (LVEF)) score validated for systolic HF patients considering CPET data combined with clinical, laboratory and echocardiographic measurements.

**Purpose:** We evaluated the prognostic value of a new simple score (MECKI Score) in a large population of patients with systolic HF compared with two of the actually most-used and available scores Heart Failure Survival Score (HFSS) and Seattle Heart Failure (SHF).

**Methods:** We selected 4862 consecutive patients with systolic HF (LVEF <40%) clinically stable admitted in 21 cardiology departments. In every patient we collected clinical history, physical examination, blood sample, 12 derivations ECG, transthoracic echocardiogram, CPET. When all the data were available we calculated the MECKI, HFSS and Seattle Score and we calculated the Receiver Operating Characteristic (ROC) curves and the area under the ROC curve (AUC). We used the method proposed by DeLong to compare different AUCs.

**Results:** Study cohort consisted of 4862 (mean age 61.3±12.6 years) consecutive systolic HF patients, recruited and prospectively followed in 21 Italian HF centers (mean follow up 3.6±2.6 years). 998 patients died or underwent urgent transplantation during the follow-up period. Available data allowed calculation of MECKI score in 4139 patients, HFSS in 4007 and SHF in 2833. All the three scores were calculated in 2762 pts. At 1, 2 and 4 years AUC were 0,757, 0,742, 0,729 respectively. Including all the patients (by estimating the missing variables) AUC were 0.782, 0.767 and 0.756. In both cases MECKI's AUCs were significantly higher (p < 0.001 vs. HFSS and SHF) (Fig. 1).

**Conclusions:** MECKI score is a simple, reliable, easy to calculate, personalized heart failure prognostic tool. At present, MECKI is the most accurate prognostic score for systolic HF.

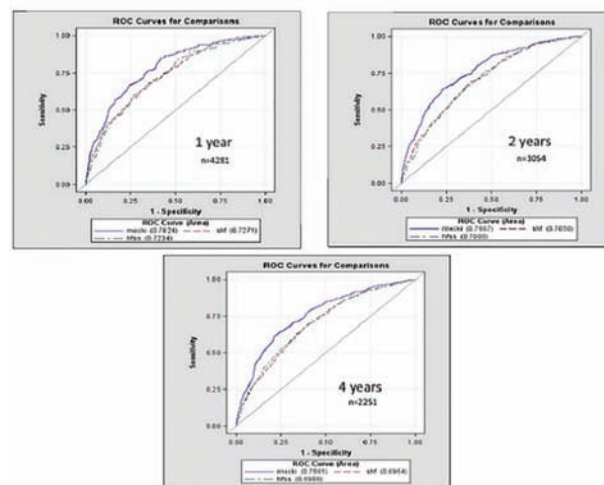


Fig.1 - Scores comparison

# YOUNG INVESTIGATOR AWARD: BASIC AND TRANSLATIONAL SCIENCE

Sunday 22 May 2016 14:15–15:45

Location: Agora

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## Endothelial deletion of protein tyrosine phosphatase-1B promotes angiogenesis and protects against pressure overload-induced heart failure in mice

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**Background:** Cardiac angiogenesis is an important determinant of heart failure, and previous studies underlined the essential role of vascular endothelial growth factor (VEGF) signalling during cardiac angiogenesis.

**Purpose:** To examine the hypothesis that protein tyrosine phosphatase (PTP)-1B, a negative regulator of VEGF receptor-2 activation, is causally involved in the cardiac microvasculature rarefaction during hypertrophy and that deletion of PTP1B in endothelial cells prevents the development of heart failure.

**Methods:** Cardiac hypertrophy was induced by transverse aortic constriction (TAC) in mice with inducible, endothelial cell-specific deletion of PTP1B (End.PTP1B-KO) and controls (End.PTP1B-WT).

**Results:** Survival was improved in End.PTP1B-KO mice up to 20 weeks after TAC. Serial echocardiography measurements revealed a better systolic pump function in End.PTP1B-KO vs. End.PTP1B-WT mice as well as a less pronounced cardiac hypertrophy (as determined by left ventricular [LV] mass and heart-to-body weight ratio) and LV dilation. Histologically, banded hearts from End.PTP1B-KO mice exhibited increased numbers of PCNA-positive, proliferating endothelial cells resulting in preserved cardiac capillary density and improved perfusion as well as reduced hypoxia, apoptotic cell death and fibrosis. Western blot analysis of banded heart protein lysates confirmed higher levels of phosphorylated VEGFR2 and p42/44 MAPK in End.PTP1B-KO vs. End.PTP1B-WT mice, which may have contributed to the observed changes. Absence of PTP1B in endothelial cells also promoted neovascularisation following peripheral ischaemia, and bone marrow transplantation experiments excluded a major contribution of Tie2-positive haematopoietic cells to the improved angiogenesis in End.PTP1B-KO mice. Increased expression of caveolin-1 as well as reduced NADPH oxidase-4 expression, ROS generation and TGF $\beta$  signalling were observed and may have mediated the cardioprotective effects of endothelial PTP1B deletion.

**Conclusions:** Endothelial PTP1B deletion improves cardiac VEGF signalling and angiogenesis and protects against chronic afterload-induced heart failure and mortality. PTP1B may thus represent a useful target to preserve cardiac function during hypertrophy.

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## The microRNA-146a - DLST axis: a new therapeutic target in heart failure.

This work was supported by grants from the Scientific Research Fund of Flanders (FWO) to WH (1183211N, 1183213N) and SH and AP (G074009N).

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**Introduction:** Cardiovascular diseases remain the predominant cause of death worldwide, with the prevalence of heart failure continuing to increase. Despite increased knowledge of the metabolic alterations that occur in heart failure, novel therapies to treat the observed metabolic disturbances are still lacking. The present study investigated the involvement of microRNA-146a and its downstream metabolic target dihydrolipoyl succinyltransferase (DLST) in cardiac hypertrophy and failure.

**Methods:** In our study, we show that microRNA-146a is critically involved in the development of pressure overload-induced cardiac hypertrophy and heart failure. We used a conventional model of murine heart failure by the administration of angiotensin-II in an osmotic minipump during four weeks.

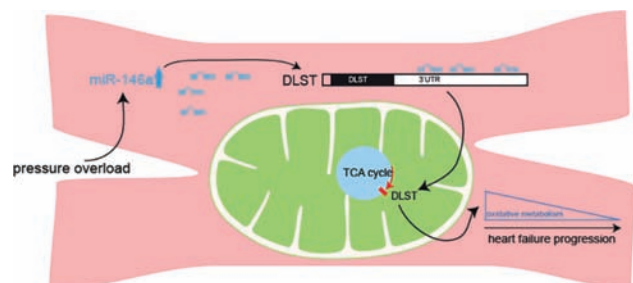
**Results:** \* While overexpression of microRNA-146a in cardiomyocytes provoked cardiac hypertrophy and heart failure in vivo, genetic knockdown or pharmacological blockade of microRNA-146a with antimiR blunted the hypertrophic response and prevented cardiac dysfunction at 4 weeks.

\* We found that the metabolic profile of microRNA-146a knockout cardiomyocytes was different compared to that of wild type cells: there was partial preservation of oxidative metabolism and the energetic efficiency of the mitochondria was higher in the absence of microRNA-146a. Mechanistically, we discovered that microRNA-146a targets dihydrolipoyl succinyltransferase (DLST) – the E2 sub-component of ketoglutarate dehydrogenase complex (KGDHC), a rate-limiting tricarboxylic acid (TCA) cycle enzyme.

\* While DLST levels significantly decrease upon pressure overload in wild type mice – paralleling a decreased oxidative metabolism – DLST protein levels and hence oxidative metabolism are maintained in microRNA-146a knockout mice. Subsequently, oxidative metabolism through TCA cycle flux is more preserved in angiotensin-II-exposed microRNA-146a knockout mice compared to their wild type littermates.

\* Moreover, overexpression of DLST in wild type mice with AAV9-vector technology significantly decreased cardiac hypertrophy in vivo. The same protection was observed in wild type mice to which dichloroacetate (DCA) was administered, a stimulator of oxidative phosphorylation through increased flux in the TCA cycle, confirming a critical role for oxidative metabolism in cardiac hypertrophy and failure.

**Conclusions:** The up-regulation of microRNA-146a in pressure-overloaded hearts is detrimental for heart failure progression. MicroRNA-146a decreases DLST causing an impaired oxidative metabolism in cardiomyocytes. Overexpression of DLST in cardiomyocytes protects against hypertrophy development. Altogether we show that the microRNA-146a – DLST axis is a crucial metabolic pathway in heart failure, with therapeutic potential.



Graphical Abstract

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## Implications of mitochondrial dysfunction in heart failure with preserved ejection fraction

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**Introduction:** Heart failure with preserved ejection fraction (HFpEF) represents 50% of patients with heart failure and its prevalence is associated with metabolic syndrome (MetS). The mechanisms underlying cardiovascular disease in MetS are complex and include, among others, metabolic and mitochondrial alterations, which culminate with increased oxidative stress. Thus, we intend to evaluate mitochondrial function and oxidative stress in an animal model of HFpEF triggered by MetS.

**Methods:** Lean ZSF1 (ZSF1Ln, n=7) and obese ZSF1 (ZSF1Ob, n=7) rats were submitted an effort testing to determine the maximal O<sub>2</sub> consumption (VO<sub>2</sub>max) and echocardiographically evaluated, at 20-25 weeks. Left ventricular (LV) samples were collected for mitochondrial functional studies, protein expression by immunoblotting and for in situ detection of myocardial oxidative stress by immunofluorescence.

**Results:** ZSF1Ob rats have a lower tolerance to VO<sub>2</sub>max effort and an aerobic threshold, despite the increased cardiac output. Echocardiographically, the ZSF1Ob group showed increased LV mass, which was accompanied by preserved ejection fraction and LV diastolic dysfunction. Mitochondrial functional studies showed that ZSF1Ob group presents significant dysfunction of complex 1 and a trend in complex 2, alterations in the permeability of the mitochondrial pore and an increase in the time for the repolarization of the membrane potential, evidences further supporting mitochondrial deterioration. Protein studies revealed a significant increase in the expression of NADPH oxidase 2 and a significant decrease in NADPH oxidase 4 in ZSF1Ob rats, enzymes responsible for regulating the formation of reactive oxygen species (ROS). In situ detection of superoxide anion was significantly higher in ZSF1Ob rats, which proves the formation of ROS. Additionally, ZSF1Ob group presented a decrease in eNOS phosphorylation revealing an impairment in nitric oxide production.

**Conclusion:** Mitochondrial dysfunction induced by oxidative stress in rats with MetS is an important pathophysiological mechanism in HFpEF.

Parameters	ZSF1Ln	ZSF1Ob	p
VO <sub>2</sub> max (mL/Kg/min)	27.79 ± 1.81	16.68 ± 0.99	<0.01
Cardiac output (mL/s)	97.4 ± 3.5	149.0 ± 25.8	<0.01
Ejection Fraction (%)	69.77 ± 2.94	69.67 ± 12.3	n.s.
E/E'	12.00 ± 0.08	14.27 ± 2.43	<0.05
E/A	1.52 ± 0.06	1.30 ± 0.21	<0.05
Lungs/TL (mg/cm)	376.49 ± 45.66	532.06 ± 36.01	<0.05
Swelling Mitochondrial (AU)	0.167 ± 0.002	0.204 ± 0.010	<0.05
NOX2 (AU)	0.20 ± 0.04	0.37 ± 0.04	<0.05
NOX4 (AU)	0.27 ± 0.97	0.08 ± 0.02	<0.05

Data are mean ± SEM. TL, Tibia length; NOX2, NADPH oxidase 2; NOX4, NADPH oxidase 4; AU, Arbitrary units; n.s., non-significant.

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#### Maturation assessment of recellularized human cardiac tissue by means of simultaneous voltage and calcium mapping

Supported in part by grants from the Spanish Ministry of Science and Innovation (PLE2009-0152), the Instituto de Salud Carlos III (Ministry of Economy AM Andreu Ciiment<sup>1</sup>; E Garreta<sup>2</sup>; ME Fernandez-Santos<sup>1</sup>; R Sanz<sup>1</sup>; MS Guillem<sup>3</sup>; JC Izpisua Belmonte<sup>4</sup>; N Montserrat<sup>2</sup>; F Fernandez-Aviles<sup>1</sup>

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**Background:** Human cardiomyocytes differentiated from induced pluripotent stem cells (CM-hiPS) represent a powerful tool to investigate and treat cardiac dysfunctions. However, technology used for their characterization is mainly limited to single cell analysis (e.g. patch-clamp).

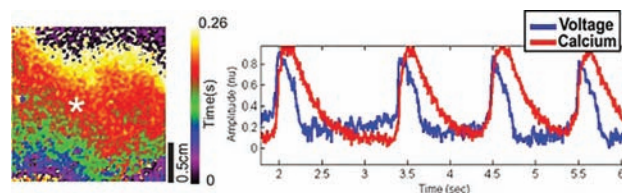
**Purpose:** In the present study we evaluate the possibility to use simultaneous voltage and calcium mapping to characterize CM-hiPS cultures.

**Methods:** hiPSC cells were differentiated into cardiomyocytes and cultured on two different substrates (i.e. matrigel and decellularized extracellular cardiac matrices dECM). Electrophysiological properties of cardiac cultures were evaluated 30 days after culturing by simultaneously recording transmembrane voltage and intracellular

calcium levels in a tissue of 2x2cm (i.e. di-4-ANBDQPPQ voltage sensitive dye and rhod-2(AM) as Ca<sup>2+</sup> sensitive probe). Main tissue electrophysiological properties were compared (i.e. wavefront propagation conduction velocity (CV) and upstroke time of the calcium transient).

**Results:** After 30 days of culture, cardiac structures presented electrically and mechanically connected functional activity (see figure). Our results demonstrated a dramatic increase in the mean conduction velocity from 2.54 ± 0.75 cm/s in matrigel coated wells to 7.45 ± 0.94 cm/s in ventricular dECMs. This increase in the conduction velocity in dECMs cultures was associated with a higher maturation in the kinetics of Ca<sup>2+</sup> that produced an increase in the upstroke velocity of the calcium transient (44.82 ± 0.13ms in the dECM vs. 85.75 ± 0.15ms in petri dishes).

**Conclusion:** Culture of hiPSC-derived cardiomyocytes in decellularized extracellular cardiac matrices has demonstrated to favor tissue maturation.



Optical Mapping

### 739

#### FOXO1A regulates arterial and venous identity in human pluripotent stem cells-derived endothelial cells

Hungarian Scientific Research Fund OTKA 10555

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**Background: and Purpose:** Endothelial derivatives of human pluripotent stem cells may offer regenerative treatments in ischemic cardiovascular diseases. We aimed to investigate the regulatory role of PI3K/FOXO1A signalling pathway on arterial and venous identity of endothelial subpopulations as well as the fate of generated cells in 3D cultures.

**Methods and Results:** To optimize endothelial differentiation, human embryonic stem cells (hESC) were differentiated via either embryoid body (EB) or monolayer method under normoxic 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 mature endothelial phenotype in vitro, including cobblestone pattern, ac-LDL uptake and tube formation. Proteome profiling revealed high abundance of angiogenesis-related proteins both in cell lysates and supernatant. Expressions of arterial (EphrinB2, Notch1-2) and venous (EphB4) endothelial markers were increased during differentiation, suggesting the presence of mixed endothelial population in culture. Transfection of hESC-EC/hiPSC-EC with plasmids encoding FOXO1A-eGFP or pmaxGFP was carried out by electroporation. Human ESC-EC and hiPSC-EC with high FOXO1A showed downregulated expressions of universal (CD31, angiopoietin-2 and ve-cadherin) as well as arterial and venous markers. Indeed, arterial index (EphrinB2/EphB4 mRNA ratio) decreased in response to FOXO1A overexpression (hESC-EC 8.16 ± 3.22 vs. 2.24 ± 0.49, p < 0.01; hiPSC-EC 6.46 ± 2.75 vs. 1.67 ± 0.72, p < 0.05; n = 3 biological replicates). This suggests a key role of PI3K/FOXO1A signalling pathway in the modulation of arterial and venous phenotype. For engineering 3D vascular constructs decellularised human aortic slices (300µm) were repopulated with hESC-EC and hiPSC-EC. Cells remained viable on engineered matrices. Imaging with Calcein AM live staining and 3DHistech analysis proved recellularisation with CD31-positive, viable endothelial cells.

**Conclusions:** We found that PI3K/FOXO1A signalling pathway has strong effects on arterial and venous endothelial identity. Human ESC-EC and hiPSC-EC remained viable on 3D vascular matrices. In-depth analyses of phenotype and functional characteristics of hESC-EC and hiPSC-EC may enhance their application for vascular tissue engineering.

# MODERATED POSTER SESSION 3 - TOP NEWS ON BIOMARKERS

Sunday 22 May 2016 15:45–16:30

Location: Poster Area

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### Clinical and prognostic value of pro-enkephalin in acute and chronic heart failure

Alere, Singulex, and Sphingotec kindly provided assays and performed biomarker measurements.

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<sup>1</sup>University of Groningen, Department of Cardiology, Groningen, Netherlands; <sup>2</sup>Sphingotec, Hennigsdorf, Germany; <sup>3</sup>University of Brescia, Brescia, Italy; <sup>4</sup>Duke University Medical Center, Durham, United States of America; <sup>5</sup>University of California San Francisco, San Francisco, United States of America

**Background:** Proenkephalin (pro-ENK) has emerged as a novel biomarker associated with both renal function and cardiac function, but its significance in heart failure patients is not so far evaluated.

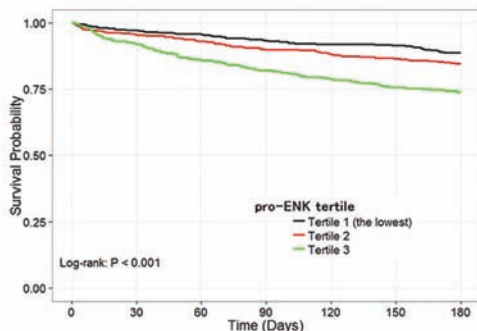
**Purpose:** To evaluate the association between pro-ENK and indices of glomerular and tubular function and clinical outcome in patients with acute and chronic heart failure.

**Methods:** The association between pro-ENK and markers of renal function was evaluated in 120 chronic heart failure patients who underwent renal hemodynamic measurements including renal blood flow (RBF) and glomerular filtration rate (GFR) using 131I-Hippuran and 125I-iothalamate clearances, respectively. The association between pro-ENK and clinical outcome in acute heart failure was assessed in another 2033 patients.

**Results:** Pro-ENK was strongly correlated with both RBF ( $r = -0.66$ ,  $P < 0.001$ ) and GFR ( $r = -0.71$ ,  $P < 0.001$ ), but not with renal tubular markers. Blood urea nitrogen and brain natriuretic peptide were also determinants of pro-ENK. In the acute heart failure cohort, pro-ENK was a predictor of death through 180 days, heart failure rehospitalization through 60 days, and death or cardiovascular or renal rehospitalization through day 60 in univariable analyses, but its predictive value was lost in a multivariable model, when other renal markers were entered in the model. Changes in pro-ENK from baseline (day 1) to day 2 and from baseline to day 7, did not associate to prognosis.

**Conclusions:** In patients with chronic and acute heart failure, pro-ENK is strongly associated with glomerular function, but not with tubular damage. Pro-ENK provides limited prognostic information in heart failure patients on top of established renal markers.

Kaplan-Meier curves of each tertile of pro-ENK in acute heart failure cohort



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### Diagnostic performance and reference values of novel biomarkers of heart failure in children and adolescents

Research grant of the Austrian Society of Cardiology; EU-research grant (MD-PAEDIGREE)

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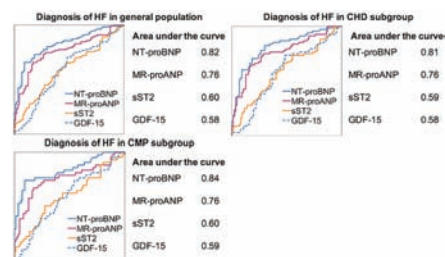
**Background:** Biomarkers play a pivotal role in the management of heart failure (HF). In adults, several parameters are known to provide accurate information on diagnosis, prognosis and treatment response. However, reference values and insights from validation studies in adults cannot be extrapolated to the paediatric age group as it differs substantially from the adult population in pathophysiology, comorbidity and compensatory reserve.

**Purpose:** Our aim was to assess the diagnostic performance of 3 novel biomarkers in paediatric HF and to elucidate their accuracy differentially in patients with cardiomyopathy (CMP) and congenital heart disease (CHD), respectively. Reference data from healthy children are presented.

**Methods:** Mid-regional pro-Atrial Natriuretic Peptide (MR-proANP), sST2 and Growth Differentiating Factor 15 (GDF-15) were measured cross-sectionally in 111 HF patients and 87 controls (mean age  $7.9 \pm 5.9$  years; range 5 days to 24 years). N-terminal pro-B Natriuretic Peptide (NT-proBNP) was used as a reference standard. A receiver-operating characteristic (ROC) was plotted to assess the diagnostic performance of the novel biomarkers alone or in combination with NT-proBNP. This was performed in all patients and, separately, for subgroups of patients with CHD ( $n = 68$ ) and CMP ( $n = 43$ ). In 38 patients with dilated CMP, left ventricular ejection fraction (LVEF) and diastolic volume were measured by echocardiography or magnetic resonance imaging. Associations with biomarker levels were assessed by logistic regression analysis.

**Results:** MR-proANP and NT-proBNP showed good diagnostic accuracy in the general population as well as in the CMP and CHD subgroups (Graph). By contrast, GDF-15 and sST2 did not perform sufficiently. None of the novel parameters improved the accuracy of NT-proBNP alone when combined with it. In the subgroup with dilated CMP, only NT-proBNP was associated with an impaired LVEF. Moreover, NT-proBNP and sST2 were predictive of left ventricular dilatation.

**Conclusion:** This is the first comprehensive assessment of novel biomarkers of HF in children and adolescents. MR-proANP can detect HF with accuracy comparable to that of the reference standard, NT-proBNP. This was the case in, both, CHD and CMP as the causal diagnosis. By contrast, neither sST2 nor GDF-15 were of any diagnostic usefulness, alone or in combination with NT-proBNP. Further research is needed to evaluate the prognostic significance of novel biomarkers in specific paediatric cardiac diseases.



Receiver-operating characteristics

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**Circulating relaxin as a biomarker of pulmonary hypertension and right heart overload in acute heart failure**M Pintahao<sup>1</sup>; P Castro-Chaves<sup>1</sup>; F Vasques-Novoa<sup>1</sup>; F Goncalves<sup>1</sup>; L Mendonca<sup>1</sup>; R Fontes-Carvalho<sup>1</sup>; P Lourenco<sup>2</sup>; P Almeida<sup>2</sup>; A Leite-Moreira<sup>1</sup>; P Bettencourt<sup>2</sup><sup>1</sup>Faculty of Medicine University of Porto, Department of Physiology and Cardiothoracic Surgery, Porto, Portugal; <sup>2</sup>Sao Joao Hospital, Department of Internal Medicine, Porto, Portugal**Background/Introduction:** Serelaxin has recently shown promising results as a new potential acute heart failure (HF) therapy. Yet, its clinical use preceded the understanding of the role of the endogenous relaxin system in HF.**Purpose:** We aimed to evaluate relaxin serum levels in a population of acute HF patients and their association with clinical and echocardiographic parameters of right and left heart overload.**Methods:** We studied patients from a registry of acute HF patients. Admission serum relaxin levels were measured using an ELISA kit (Immunodiagnostik, Germany, detection limit 0,5pg/ml). Relaxin was dichotomized according to the median value of its distribution. Clinical, analytical and echocardiographic parameters of right and left heart overload were compared between relaxin groups.**Results:** Relaxin serum levels were evaluated in 117 acute HF patients. Median age was 82 years (IQR 72-87), 41% of the patients were male and 63% had systolic dysfunction. Median serum relaxin was 31.4 pg/mL (range <0.5-1689.2). Patients with relaxin levels above the median had more clinical signs of right heart overload and significantly higher sodium retention score (mean 4.80 ± 1.53 vs. 3.60 ± 1.96, p < 0.001). These findings were supported by the echocardiography data. Patients with higher relaxin levels had a significantly higher systolic pulmonary arterial pressure [median 47.0 (IQR36.0-61.0) vs. 34.5 (IQR25.0-51.0) mmHg, p = 0.02], a higher risk of right ventricle (RV) systolic dysfunction (OR 3.38 95%CI 1.21-9.41), a higher prevalence of RV dilation (31.0% vs. 5.3%, p < 0.001) and right atrial dilation (66.1% vs. 36.5%, p = 0.002) and less inferior vena cava diameter variability with inspiration (41% vs. 60%, p = 0.01), suggesting an association between relaxin circulating levels and right heart overload. BNP admission levels were also positively associated with RV dysfunction. However, relaxin was able to predict RV dysfunction independently of BNP (adjusted OR 4.10; 95%CI 1.35-12.44; p = 0.01). No differences were noted regarding admission blood pressure, lung congestion, left chambers dimensions or parameters of left ventricle systolic and diastolic function.**Conclusion:** In our population of acute HF patients, admission serum levels of relaxin were associated with clinical and echocardiographic markers of pulmonary hypertension and RV dysfunction and overload, suggesting a role for circulating relaxin as a biomarker in this setting.**Methods:** From 43 biomarkers measured in 2033 serum samples of patients hospitalized for acute heart failure, 16 biomarkers predictive for 180 day mortality were selected. Biomarker values were compared with the levels of 12 acute heart failure specific miRNAs in a subset of 100 patients, at baseline and 48 hours. Patients were divided in 4 pre-defined groups, based on clinical parameters during hospitalization. Correlation analyses between miRNAs and biomarkers were performed and complemented by miRNA target prediction and pathway analysis.**Results:** No significant correlations were found at hospital admission. However, after 48 hours of hospitalization, 7 miRNAs were significantly negatively correlated to biomarkers indicative for a worse clinical outcome in the patient group with the most unfavorable in-hospital course (n=21); miR-16-5p was correlated to C-reactive protein (R=-0.66, p-value=0.003), miR-106a-5p to creatinine (R=-0.68, p-value=0.002), miR-223-3p to growth differentiation factor 15 (R=-0.69, p-value=0.001), miR-652-3p to soluble ST-2 (R=-0.77, p-value < 0.001), miR-199a-3p to procalcitonin (R=-0.72, p-value < 0.001) and galectin-3 (R=-0.73, p-value < 0.001) and miR-18a-5p to procalcitonin (R=-0.68, p-value = 0.002). MiRNA target prediction and pathway analysis identified several pathways related to cardiac diseases, which could be linked to some of the miRNA-biomarker correlations.**Conclusions:** The majority of correlations between circulating acute heart failure specific miRNAs were related to biomarkers predictive for a worse clinical outcome in a subgroup of worsening heart failure patients at 48 hours of hospitalization. These findings suggest a time-dependent effect of circulating miRNAs and highlight the susceptibility to individual patient characteristics influencing potential relations between miRNAs and biomarkers.

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**The prognostic effect of serum magnesium concentration in patients with heart failure**T Angkananard<sup>1</sup>; T Anothaisintawee<sup>1</sup>; S Eursirwan<sup>1</sup>; M Mcevoy<sup>2</sup>; J Attia<sup>2</sup>; A Thakkestian<sup>1</sup><sup>1</sup>Ramathibodi Hospital, Section for Clinical Epidemiology and Biostatistics, Faculty of Medicine, Bangkok, Thailand; <sup>2</sup>University of Newcastle, Center for Clinical Epidemiology and Biostatistics, Newcastle, Australia**Background:** Previous studies have demonstrated an inverse association between serum and dietary magnesium (Mg) intake and total cardiovascular (CV) disease risk. However data on this association in the setting of heart failure (HF) is conflicting.**Purpose:** To estimate effects of hypomagnesemia and hypermagnesemia on CV mortality and all-cause mortality (ACM) of HF patients when compared with normomagnesemia. Method: Medline and Scopus databases were used for identifying relevant studies published from inception until June, 2015. The selection was based

60724 Characteristics of included studies

Author	N	Type of heart failure	Mean Age (y)	% Men	Outcome	% DM	% HT	% CKD	Mean LVEF (%)	% NYHA ≥ III	Normal Mg concentration
Gottlieb (1990)	199	Chronic	64 (28-90)	72.4	ACM, CV mortality (SD)				19 (2-39)	81.4	1.6-2.1 mEq/L
Eichhorn (1993)	1068	Chronic	63.3	22.0	ACM, CV mortality (SD, PF)				21	100.0	1.6-1.8 mEq/L
Madsen (1997)	190	Chronic	66 (median) (42-75)	72.0	CV mortality (SD, PF)		17.9	23.2 <sup>+</sup>	6-74	45.8	0.81-0.89 mmol/L
Cohen (2003)	404	Chronic	74.3	56.4	ACM	43.6		40.3 <sup>#</sup>	36	39.1	0.77-1.08 mmol/L
Corbi (2008)	209	Chronic	77.14 +6.92 (65-93)	54.3	ACM, CV mortality (SD, PF, MI)	28.1			34.3+4		1.4-2.1 mEq/L
Adamopoulos (2009)	1120	Chronic	63.5 +10.6	74.8	ACM, CV mortality (PF)	46.4	47.5	46.4	32+12	30.1	> 2 mEq/L
Vaduganathan (2013)	1982	Acute	65.6	75.3	ACM, CV mortality (SD, PF, MI, Stroke)	37.5	71.4	27.1		39.9	1.9-2.2 mg/dL

Table 1. Characteristics of included studies

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**Use of biomarkers to establish potential role and function of circulating microRNAs in acute heart failure**

This study was supported by the Dutch Heart Foundation (CVON 2011-11). The PROTECT trial was supported by NovaCardia, a subsidiary of Merck.

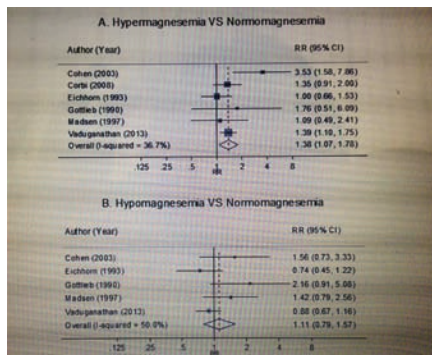
E L Vegter<sup>1</sup>; D Schmitter<sup>2</sup>; Y Hagemeijer<sup>1</sup>; E S Ovchinnikova<sup>1</sup>; P Van Der Harst<sup>1</sup>; D J Van Veldhuisen<sup>1</sup>; P Van Der Meer<sup>1</sup>; E Berezikov<sup>3</sup>; A A Voors<sup>1</sup>; M A F Khan<sup>1</sup><sup>1</sup>University Medical Center Groningen, Department of Cardiology, Groningen, Netherlands; <sup>2</sup>Momentum Research, Inc., Allschwil, Switzerland; <sup>3</sup>European Research Institute for the Biology of Ageing, Groningen, Netherlands**Background:** Circulating microRNAs (miRNAs) emerge as potential heart failure biomarkers. In the present study, we aimed to identify associations between acute heart failure specific circulating miRNAs and well-known heart failure biomarkers.

on original prospective studies that examined serum Mg concentration and the outcome of CV and all-cause mortality in heart failure patients. The risk ratio (RR) was estimated using Poisson regression and then a multivariate meta-analysis was applied for pooling RRs across studies. Source of heterogeneity was explored by performing a meta-regression and subgroup analysis with possible confounders.

**Results:** Seven prospective studies, including a total of 5,172 HF patients with 913 and 1,438 patients die from cardiovascular and all causes, respectively, were eligible for the meta-analysis. Those patients with baseline hypermagnesemia had a significantly higher risk of CV mortality (RR:1.38; 95% CI: 1.07, 1.78) and significantly higher risk of ACM (RR:1.35; 95% CI: 1.18, 1.54) than those with baseline normomagnesemia. In contrast, HF patients with hypomagnesemia did not have an elevated risk of cardiovascular and all-cause mortality (RR:1.11; 95% CI: 0.79, 1.57 and RR: 1.11; 95% CI: 0.87, 1.41, respectively).



**Conclusions:** The present systematic review and meta-analysis suggests that HF patients with hypermagnesemia associated with increased risk of CV mortality and ACM but this was not observed for those with hypomagnesemia. This finding is limited to the elderly patients who have reduced LV systolic function. Systematic review registration: The review protocol has been registered at PROSPERO



Association between abnormal serum magne

#### 745

##### Hyperparathyroidism and its prognostic role in men with chronic heart failure

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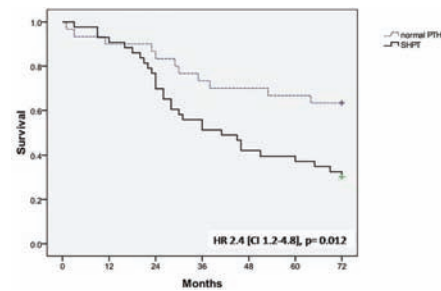
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**Aims:** To evaluate parathyroid hormone (PTH) levels in elderly men with stable chronic heart failure (CHF), and to investigate its relationship with all-cause mortality.

**Methods:** This prospective study included 73 men (mean age  $67 \pm 7$  years) with systolic CHF (NYHA class II/III) with 6-years follow-up for all-cause mortality. Baseline PTH, 25-hydroxyvitamin D (25-OHD), and N-terminal pro-brain natriuretic peptide (NT-proBNP) were measured. Echocardiography, 6-minute walk test, Minnesota-Living with Heart Failure Questionnaire, and osteodensitometry were performed according to the standard protocol. Patients were grouped according to PTH cut-off levels of 65 pg/ml [ $> 65$ pg/ml =secondary hyperparathyroidism (SHPT) vs. normal PTH].

**Results:** 43 (59%) patients presented with SHPT. A total of 65 (89%) of patients were vitamin D insufficient. Patients with SHPT vs. normal PTH group were of similar age but with higher levels of PTH ( $98 \pm 27$  vs.  $47 \pm 10$  pg/ml,  $p < 0.0001$ ), NT-proBNP [ $2452(3399)$  vs.  $918(1372)$ pg/ml,  $p < 0.0001$ ], while 25-OHD ( $29 \pm 15$  vs.  $35 \pm 14$  nmol/l), and creatinine clearance ( $60 \pm 22$  vs.  $69 \pm 21$  ml/min) were similar between studied groups. SHPT patients had more severe CHF compared to the patients with normal PTH regarding NYHA functional class ( $2.4 \pm 0.5$  vs.  $2.1 \pm 0.2$ ,  $p = 0.001$ ), quality of life score ( $34 \pm 14$  vs.  $24 \pm 12$ ,  $p = 0.005$ ), 6-minute walking distance ( $378 \pm 79$  vs.  $446 \pm 73$ m,  $p < 0.0001$ ), total hip bone mineral density ( $0.90 \pm 0.16$  vs.  $1.01 \pm 0.13$ g/cm<sup>2</sup>), and left ventricular ejection fraction ( $27 \pm 8$  vs.  $31 \pm 7$  %,  $p = 0.019$ ). A total of 41 (56%) patients died within 6 years of follow-up. ROC curve analysis showed that both PTH and NT-proBNP, but not 25-OHD, had the ability to detect patients at risk of death (AUC 0.683,  $p = 0.008$  vs. AUC 0.746,  $p < 0.0001$ , respectively). The patients with SHPT had worse survival, with a hazard ratio for death of 2.4 [CI 1.2-4.8] ( $p = 0.012$ ) in univariate analysis. Further, age, log-transformed NT-proBNP, left ventricular ejection fraction, and creatinine clearance were associated with impaired survival ( $p < 0.05$  for all). In multivariate analysis, only log-transformed NT-proBNP remained significantly related to impaired survival [HR 3.7 (CI 1.9-7.1),  $p < 0.0001$ ].

**Conclusion:** SHPT was highly prevalent in stable elderly men with CHF along with vitamin D insufficiency. Patients with SHPT had more impaired status compared to the patients with normal PTH levels. Unlike to vitamin D status, SHPT was associated with increased risk of death. Further studies are warranted to evaluate beneficial potential of PTH suppression in CHF patients.



KM survival analysis

#### 746

##### Determinants of temporal changes in galectin-3 level in the general population: data of PREVEND

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**Purpose:** High galectin-3 levels are associated with increased risk for adverse outcome. However, determinants of increasing galectin-3 level have not been established. Therefore, we aimed to identify baseline determinants of (temporal) change in galectin-3 level.

**Methods:** Galectin-3 plasma levels were studied in the PREVEND study, a cohort derived from the general population. Galectin-3 was measured at 3 different time points: at baseline and after ~4 and ~9 years. The association of baseline risk factors and (temporal) change in galectin-3 level was assessed using multivariable mixed-effects regression analysis.

**Results:** In 4,355 subjects, galectin-3 plasma levels were available at all time points (mean age:  $48 \pm 12$  years; 50% female). 324 (7%) of these subjects had increasing galectin-3 levels over time across the general accepted threshold for heart failure of 17.8 ng/mL. We found that urinary albumin excretion (chi square ( $\chi^2$ ): 34.03,  $p$ -value:  $< 0.0001$ ) and systolic blood pressure ( $\chi^2$ : 16.81,  $p = 0.002$ ) were independent determinants of temporal change of galectin-3. Furthermore, eGFR ( $\chi^2$ : 210.27,  $p < 0.0001$ ), gender ( $\chi^2$ : 43.85;  $p < 0.0001$ ), BMI ( $\chi^2$ : 19.68,  $p = 0.0001$ ), NT-proBNP ( $\chi^2$ : 18.76,  $p = 0.0001$ ) and total cholesterol ( $\chi^2$ : 8.63,  $p = 0.01$ ) were independent determinants of galectin-3 level.

**Conclusion:** In the general population, urinary albumin excretion  $> 30$  mg/24h and systolic blood pressure  $> 170$  mmHg are important determinants of increasing galectin-3 levels over time. Furthermore, we confirmed that impaired renal function is a very strong determinant of elevated galectin-3 levels. These results implicate that treatment of high blood pressure might be important to prevent increasing galectin-3 levels.

#### 747

##### Different clinical profile of patients with heart failure with reduced ejection fraction with low hepcidin versus high soluble transferrin receptor

Supported by the National Science Centre (Poland) grant allocated on the basis of the decision number DEC-2012/05/E/NZ5/00590

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**Background:** Recently, we have proposed a new definition of iron deficiency (ID) based on serum hepcidin and soluble transferrin receptor (sTfR), beyond traditionally used serum ferritin and transferrin saturation (Tsat). Pathophysiologically, low hepcidin reflects depleted iron stores, while high sTfR indicates augmented iron requirement for intracellular metabolism. We compared the clinical profile of patients with heart failure with reduced ejection fraction (HFrEF) based on aforementioned biomarkers of iron status.

**Methods:** We analyzed data of 291 patients with stable HFrEF (85% men, mean age:  $61 \pm 11$  years, NYHA III-IV: 34%, LVEF:  $26 \pm 7$ %). Abnormal values of iron biomarkers were derived as the 5th percentile of hepcidin ( $< 14.5$  ng/mL) and the 95th percentile of sTfR ( $\geq 1.59$  mg/L) from a control group of healthy subjects, published previously.

**Results:** We identified 4 groups of patients with HFrEF with: (A) both low hepcidin and high sTfR (n = 15, 5%); (B) isolated high sTfR (n = 76, 26%); (C) isolated low hepcidin (n = 11, 4%), and (D) preserved iron status (n = 189, 65%). Serum ferritin was slightly reduced in patients with isolated high sTfR ( $p < 0.05$ ), and was markedly diminished in those with low hepcidin (both with and without high sTfR) as compared to those with preserved iron status ( $p < 0.01$ ). T<sub>sat</sub> was reduced in patients with either isolated low hepcidin or isolated high sTfR, and was markedly reduced in patients with abnormal values of these 2 biomarkers (additive associations with both biomarkers, both  $p < 0.001$ ). There were no differences in haemoglobin level between analyzed groups, however low hepcidin and high sTfR were independently associated with reduced red cell indices (MCH, MCHC) (all  $p < 0.05$ ). As compared

to patients with preserved iron status, those with either isolated low hepcidin and isolated high sTfR had more severe HF (reflected by higher NT-proBNP, advanced NYHA class and higher daily dose of loop diuretics) with the most advanced HF in those with both high sTfR and low hepcidin (additive relationships with both iron status biomarkers, all  $p < 0.05$ ). Low hepcidin ( $p < 0.05$ ), but not high sTfR ( $p > 0.2$ ), was associated with impaired renal function (low GFR).

**Conclusions:** Although both low hepcidin and high sTfR reflect systemic iron deficiency, some patients with HFrEF develop abnormalities only within one biomarker. There are some clinical differences between patients with HFrEF, varying of serum hepcidin and sTfR, which may preclude diverse pathophysiological importance of these 2 biomarkers.

## CLINICAL CASE CORNER 3: CATCH ME, IF YOU CAN: CASES OF VERY FAST (OR SLOW) HEART - PART II

Sunday 22 May 2016 15:45–16:30

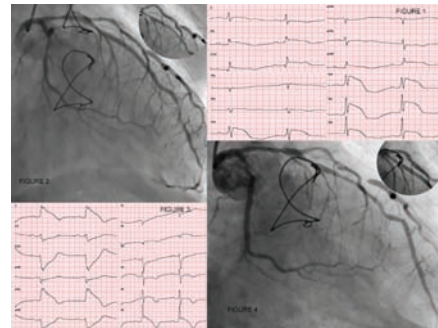
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748

### Coronary artery vasospasm in cardiac allograft presenting with malignant arrhythmia and left bundle branch block pattern in early post-transplantation period.

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Coronary vasospasm is a rare incidence in cardiac allograft (CA) and it's been reported mainly in late CA vasculopathy or rejection. There is limited data referring to it in early post-transplantation period. We report the case of 64-year old man with a history of cardiac transplantation 4 weeks before who had syncope related to wide complex ventricular tachycardia (VT) recorded on hospital ECG monitoring. Post-operative cardiac performance was stable with good ventricular function. On week 4 patient developed recurring, asymptomatic, self-limiting bouts of monomorphic nonsustained VT one of which degenerated into 60 second sustained VT with transient loss of consciousness. Palpitations, chest pain, dyspnea were negated. The results of physical examination were unremarkable. ECG showed sinus rhythm, with no conduction disturbances, nor ST-segment modification. Transthoracic echocardiogram (TTE) revealed normal biventricular function. Immunosuppressive agents blood concentrations were within therapeutic range. CA rejection was excluded already by endomyocardial biopsy. On the following day when patient was at rest sudden heart rate drop from 75to60 bpm ensued with significant QRS complex widening captured on continuous ECG tracking. ECG showed prominent ST-segment elevation(Fig.1). Serial ECG recordings in the complete absence of symptoms demonstrated dynamic changes in ECG waveform leading to complete resolution of ST segment elevation with lateral T-wave inversion in 7 minutes. The hypothesis of a possible vasospastic component of lumen narrowing was advanced. TTE showed normal regional kinesis. As a rise of troponin T to 354 ng/(ULN-14) and CK-MB to 9,37 ng/ml(ULN-6,73) were detected angiography was performed which showed myocardial bridging over the left anterior descending artery(LAD) followed by long significant stenosis, furthermore another significant focal stenosis in the left circumflex artery (LCx)(Fig.2). Successful stenting of LCx and LAD was performed. Recurrent asymptomatic QRS complex widening the same evening linked to new LBBB pattern in ECG(Fig.3) prompted repeat catheterization that revealed severe coronary spasm involving first diagonal branch, fully relieved by intracoronary isosorbide dinitrate(Fig.4). Diagnosis of CA multivesel disease with a significant vasospastic component was established. Treatment with calcium channel blockers and nitrate was started. Pharmacotherapy along with precedent successful angioplasty resulted in cessation of VT episodes and conduction disturbances at 4-week follow up period. As cardiac catheterization of donor heart is not routinely performed there are concerns regarding transmission of coronary artery disease to recipient. As a result of cardiac denervation patients very rarely present with typical syndromes of ischemia. It's worth considering as noninvasive diagnostic tool routine 24-h 12-lead Holter monitoring for an assessment of ST-segment modification or presence of arrhythmia.



749

### Prosthetic valve dysfunction, acute myocardial infarction, and cardiogenic shock following an uncomplicated pregnancy: what else could have been done?

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**Case:** A 18-year old female with history of VSD closure and AVR was found to be pregnant at her routine clinical evaluation. An echocardiogram showed normal post-thetic valve function. Five months after pregnancy termination she presented to the ED with chest pain and dyspnoea. PE revealed severe aortic stenosis and signs of congestive heart failure. The EKG showed LVH and diffuse ST-segment depression. Laboratory tests were remarkable for troponin I (12.74 ng/ml) and NT-ProBNP (24,225 pg/ml). Initial treatment included mechanical ventilation, inotropic support and anticoagulation. Echocardiographic evaluation showed a dilated left ventricle, severe systolic dysfunction (LVEF 22%) and severe aortic stenosis (mean gradient 72 mmHg). Coronary angiography showed normal coronary arteries. Percutaneous aortic balloon valvuloplasty was performed as a bridge to AVR. After the procedure the patient presented clinical deterioration with progressive troponin elevation and refractory shock. The patient developed ventricular tachycardia and died. Autopsy revealed a bioprosthetic aortic valve with heavy calcification, a hypertrophic LV and evidence of pulmonary oedema. Histopathologic findings were relevant for micro calcifications within the lumen of coronary arterioles and multiple myocardial infarctions.

**Discussion:** There are 3 main problems to analyze in this case: prosthetic valve dysfunction (PVD), the acute event, and the role of aortic balloon valvuloplasty (ABV). The mechanism of PVD was obstruction and central regurgitation. In the setting of calcified cusps, the presumed aetiology is primary structural failure, which usually occurs after 10 years of valve implantation. Pregnancy related early valve failure has been previously reported.

The initial clinical picture was one of an acute myocardial infarction. Microembolism could have been the most likely cause since the EKG showed diffuse



ischemic changes and coronary angiography showed a diminished TMP grade probably related to microvascular obstruction. Spontaneous calcium embolization is extremely rare and it has been previously reported in the literature. In this case it is difficult to conclude whether it occurred before and/or after ABV. Severe aortic stenosis itself produces diffuse subendocardial ischemia and it can rarely mimic acute myocardial infarction, but it might have contributed to the clinical presentation. ABV is a procedure associated with multiple complications. It is reserved as bridge to AVR in high risk patients. The clinical decompensation after the procedure suggests an ABV-related myocardial infarction secondary to coronary calcium micro embolization, which was confirmed in the autopsy.

**Conclusions:** Pregnancy related early PVD and a salvage treatment contributed to death of this patient. The use of a LVAD and/or heart transplantation could've changed the patient's prognosis, nevertheless limited access to such therapies is a reality in developing countries.

## 750

### Look carefully: acute heart failure after pregnancy

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The presentation of acute heart failure in the puerperium period is unusual and requires a careful evaluation to rule out differential diagnoses. Description of the problem: a 32 year-old woman presented to the emergency room with sudden shortness of breath and chest pain. Three months prior, she delivered a healthy baby without any complications. Her past medical history was negative for cardiovascular diseases, preeclampsia, or hypertension. The physical examination revealed BP 100/70, HR 90 BPM, and multiple signs of pulmonary congestion and acute heart failure. An EKG showed signs of an anterior STEMI. An emergency coronary angiography was performed, revealing a diffuse lesion of LAD and CX of 70% with a lot of thrombotic material. An infusion of tirofiban was started, and she was admitted to the ICU. 24 hours later, she started to have episodes of NSVT with hypotension and pulmonary edema. The echocardiogram showed an EF of 30% with hypokinesia of apical segments. A new coronary angiography with showed a dissection of the left main those extents to the LAD and CX that were treated with DES. Afterwards, she required IABP implantation and inotropic support for 48 hours. Her clinical condition improved, and 7 days later, she was discharged home with optimal medical therapy that included carvedilol, enalapril, eplerenone ivabradine, aspirin, and clopidogrel. She was followed-up in a heart failure clinic where optimization of the medical therapy was performed. After 2 months, a new echocardiogram showed an EF of 35%, and an ICD was implanted for primary prevention. Currently, the patient is in NYHA class II and returned to her work and normal life. Questions and problems: the main differential diagnoses of chest pain and acute heart failure in the puerperium period are acute pulmonary embolism, acute myocardial infarction, and aortic dissection. Answers and discussion: in this case, the evaluation of signs and symptoms and the EKG were the clues for the diagnosis. The initial coronary angiography did not show the dissection. The clinical evolution of the patient to cardiogenic shock suggested that the cause was not identified and treated.

**Conclusions:** acute myocardial infarction in women during childbearing age is rare. However, it is related to a high maternal mortality and morbidity, such as ventricular dysfunction and heart failure. This entity must be suspected in pregnant or post-partum woman with chest pain and acute heart failure.

## 751

### Tachycardia-induced cardiomyopathy after 16 years of incessant PJRT

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We present a case of exceptionally longstanding incessant supraventricular tachycardia that resulted in tachycardia-induced cardiomyopathy. The patient was 39 years old woman who presented to the emergency department with complaints of fatigue, shortness of breath and increasing exercise intolerance. On admission she was noted to have a tachycardia 100 bpm and her echocardiography revealed cardiomegaly with severely depressed LV EF (18%) and marked dilatation of all four chambers of the heart. Her ECG showed wide-complex tachycardia with LBBB-like morphology, QRS duration of 130 msec and 1:1 AV-relationship with negative P waves in leads II, III and aVF and positive P waves in lead V1. The patient stated that she had this tachycardia constantly for about 16 years already and it was always attributed to her emotional stress and dysautonomia. Multiple drugs were not successful in controlling her heart rate. The patient was sent to the arrhythmia specialist for electrophysiologic evaluation. The EP study was performed and the tachycardia was identified to be an orthodromic circus movement tachycardia utilizing slowly conducting concealed posteroseptal accessory pathway (PJRT) which was successfully ablated from within the coronary sinus.

The patient was started on ACE inhibitors, aldosterone antagonists and carvedilol

and her heart failure status markedly improved. After 1 year of treatment and already on full dose carvedilol she did not have an arrhythmia recurrence and her LV EF increased to 40% and she has no symptoms related to heart failure.

To our knowledge this is the first case of incessant tachycardia lasting 16 years. The relatively slow heart rate during tachycardia, patient's young age and the lack of comorbidities must have prevented earlier development of tachycardia-induced cardiomyopathy.



Tachycardia

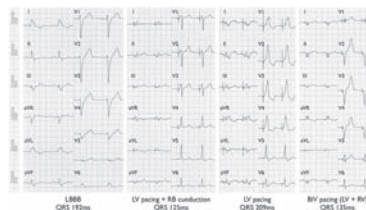
## 587

### Acute exacerbation of heart failure attributed to complete atrioventricular block in a patient with left univentricular pacing by cardiac resynchronization therapy

N Nobuhiro Nishiyama<sup>1</sup>; S Takatsuki<sup>1</sup>; K Nakajima<sup>1</sup>; S Kashimura<sup>1</sup>; Y Katsumata<sup>1</sup>; T Nishiyama<sup>1</sup>; T Kimura<sup>1</sup>; Y Aizawa<sup>1</sup>; K Fukumoto<sup>1</sup>; K Fukuda<sup>1</sup>

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A 77-year-old man with combined cardiac resynchronization therapy-defibrillator (CRTD) for dilated cardiomyopathy (DCM), ventricular tachycardia (VT), reduced ejection fraction (EF), complete left bundle branch block (LBBB), and New York Heart Association (NYHA) Class III underwent the 3rd replacement of the generator (Guidant COGNIS, 100-D) 1 year previously. The generator had been implanted under the skin of the chest wall with a screw-in right ventricular (RV) lead (Guidant 0154) placed in the septum of the right ventricle, a left ventricular (LV) lead (Guidant 4542) placed in the posterolateral branch of the coronary sinus, and a right atrial lead (Guidant 4472) in the right atrial appendage. At the time, it appeared that LV-only pacing mode with paced AV delay of 110 ms and sensed AV delay of 70 ms was the most effective mode for obtaining the narrowest QRS width. The QRS morphology of the electrocardiogram (ECG) was fusion beat of LV pacing and intrinsic right bundle branch conduction. Both the echocardiographic (UCG) parameters and the SmartDelay algorithm (which is available on Cognis P107) confirmed this result. During follow-up, the patient was well after the operation and less symptomatic (NYHA Class II), the atrial, ventricular and shock lead parameters were functioning normally, no shock and no necessary hospital admission during the previous year. He visited the out-patient clinic with complaints of breath shortness (NYHA class IV), the presence of weight gain and pitting edema. The cardiothoracic ratio (CTR) increased from 49.0% to 58.8% on chest X-ray, plasma brain natriuretic peptide (BNP) level rose from 256 pg/ml to 420 pg/ml on a blood test. The QRS morphology of the ECG was LV only pacing. He developed complete atrioventricular block (CAVB). As a relapse of ventricular dyssynchrony could cause acute exacerbation of heart failure, changing the mode to biventricular pacing and optimization of pacing intervals were performed using ECG and UCG parameters. Biventricular pacing mode with paced AV delay of 110 ms, sensed AV delay of 70 ms and VV (LV-RV) delay of 40ms was the most effective mode for obtaining the best ECG and UCG parameters. He had improvement of symptoms from NYHA class IV to NYHA class II without any change of oral medications. In conclusion, when programming the LV-only pacing mode in particular, it is important to be aware that the likelihood of developing CAVB can have some clinical implications. We report a rare case of acute exacerbation of heart failure which was attributed to CAVB in a patient with left univentricular pacing by CRTD.



Electrocardiograms

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### Recurrent episodes of life-threatening vasodilatory shock following unintentional intoxication with calcium channel blocker, amlodipine

C Chris Kapelios<sup>1</sup>; G Karamanakos<sup>1</sup>; S Liatis<sup>1</sup>; M Polizois<sup>1</sup>; M Sarafadi<sup>1</sup>; D Basoulis<sup>1</sup>; D Tsilingiris<sup>1</sup>; C Fytli<sup>1</sup>; I Papoutsis<sup>2</sup>; A Kokkinos<sup>1</sup>  
<sup>1</sup>Laiko University General Hospital, Athens, Greece; <sup>2</sup>National & Kapodistrian University of Athens, Athens, Greece

Calcium channel blockers (CCBs) overdose is associated with sustained hypotension and non-cardiogenic pulmonary edema. Importantly, in all cases reported, the intoxication was known at the time of patients' presentation. We present the case of a 72-year-old man with a history of hypertension who presented to the emergency department with sustained hypotension refractory to infusions of crystalloids and vasoconstrictors. His history started 2 months prior when he was admitted to the hospital for syncope, which was attributed to amiodarone overdosing. Two more hospitalizations with symptoms of shock followed; in the first one, due to refractory hypotension (SAP < 40 mmHg), severely hypokinetic and dilated right ventricle and elevated d-dimers he was treated with thrombolysis, based on the perceived diagnosis of pulmonary embolism (PE). His condition did not improve and he remained on hemodynamic support, while his renal function declined and was treated with hemodialysis. The patient's perfusion scintigram was negative for PE or chronic thromboembolic disease. After improvement, he was discharged on day 17 in good clinical status and having discontinued his anti-hypertensive medication. After a few days, he was admitted to our hospital due to a new episode of hypotension refractory to intravenous fluids and mineralocorticoids. He was started on intravenous antibiotics and noradrenaline under the presumptive diagnosis of septic shock. Detailed evaluation did not identify a cause for the shock. Due to anuria and dyspnea he was treated with hemodialysis, to which the patient responded and was finally discharged asymptomatic on day 20. He was transferred back to the clinic 16 hours later due to a new episode of sustained hypotension (SAP:65mmHg). Apart from hypotension, his physical examination was unremarkable. His laboratory results were notable for anemia, hyperglycemia and elevated creatinine. The patient was oliguric. Serum values for troponine, thyroid stimulating hormone, cortisol, adrenocorticotropic hormone and tryptase were normal. Multiple urine and blood cultures were negative. Prolonged pharmacologic support and intermittent hemofiltration induced stabilization and recovery. An extensive diagnostic workup to elucidate the cause of his condition was unfruitful, posing a conundrum for our team. The recurrent nature of presentation along with its incidence after the patient's leaving the protected setting of the hospital suggested the effect of an environmental factor. For this reason, a urine sample obtained on admission, was sent to the toxicology department for examination. The results, available ten days later, revealed high levels of amlodipine in the urine. The patient had discontinued the medication 40 days earlier; however, it was still available at his residence. CCB overdose should always be suspected in patients with sustained, refractory hypotension, who have no other apparent cause of shock and have access to the medication.

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### An unusual high risk pregnancy: severe preeclampsia, cardiac tamponade and previously undiagnosed left ventricular non-compaction with severe systolic dysfunction

O Calvillo Arguelles<sup>1</sup>; JC Perez Gamez<sup>1</sup>; G Melendez Ramirez<sup>2</sup>; H Rodriguez-Zanella<sup>3</sup>; BE Dominguez Mendez<sup>3</sup>; R Vera Urquiza<sup>2</sup>; LL Rodriguez Chavez<sup>1</sup>; LA Gonzalez Tapia<sup>1</sup>; CR Sierra Fernandez<sup>4</sup>  
<sup>1</sup>National Institute of Cardiology Ignacio Chavez, Clinical Cardiology, Mexico City, Mexico; <sup>2</sup>National Institute of Cardiology Ignacio Chavez, Cardiovascular Imaging, Mexico City, Mexico; <sup>3</sup>National Institute of Cardiology Ignacio Chavez, Echocardiography Laboratory, Mexico City, Mexico; <sup>4</sup>National Institute of Cardiology Ignacio Chavez, Coronary Care Unit, Mexico City, Mexico

**Case Description:** A 18 year-old female presented to a general hospital with progressive shortness of breath and peripheral oedema. Her past medical history was relevant for a twin pregnancy interrupted two months earlier because of severe preeclampsia. She was found with signs of heart failure and initial management included diuretic and vasodilator therapy with subsequent worsening hypotension and dyspnoea. She was referred to our institution on inotropic support. Initial PE revealed hypotension, tachycardia, hypoxemia, JVD, bilateral rales and peripheral oedema. EKG showed low voltage in the limb leads and NT-ProBNP was elevated (9,989 pg/ml). Echocardiographic evaluation was remarkable for a large pericardial effusion with signs of hemodynamic compromise, biventricular enlargement, reduced LVEF and NC/C myocardium ratio of 3.12 to 1. After initial stabilization, 400 ml of clear pericardial fluid were surgically drained. Pericardial biopsy and pericardial fluid analysis were non-diagnostic. Inotropic support was continued and 1 week later she was discharged on medical therapy. A cardiac MR confirmed the presence of LVNC with a NC/C ratio of 6:1, trabeculated LV mass of 36%, and biventricular systolic dysfunction (LVEF 12.7%, RVEF 18.2%).

**Discussion:** The patient presented 3 different cardiovascular conditions that complicated the last stage of her pregnancy and post-partum period. Nulliparity and twin pregnancy are risk factors for preeclampsia, but the relationship of severe preeclampsia and cardiac tamponade is not well established and its diagnosis requires a high index of suspicion. Aggressive diuretic and vasodilator therapy for HF might have triggered the hemodynamic decompensation in the presence of pericardial effusion. LVNC is a relatively rare inherited cardiomyopathy with a wide range of clinical presentations. Since diagnostic criteria are morphological, their diagnostic accuracy remains uncertain. Some patients with LVNC may exhibit morphologic features of other cardiomyopathies. The clinical picture of this case mimics a peripartum cardiomyopathy, with preeclampsia and multifetal pregnancy as risk factors. Whether this case represents a previously asymptomatic patient with LVNC and ADHF secondary to a pregnancy complicated by severe preeclampsia, or a peripartum cardiomyopathy with overlapping morphological LVNC features is hard to tell. In either case, the presence of severe biventricular dysfunction represents a poor prognostic sign and the relationship with cardiac tamponade is not clear.

**Conclusions:** Physiologic changes that occur during pregnancy in patients with previously undiagnosed cardiovascular disease may predispose to a more complicated pregnancy course. Different conditions such as pericardial effusion and systolic dysfunction may coexist and require a high index of suspicion since therapy for the more obvious HF syndrome may be followed by hemodynamic decompensation.

## CLINICAL CASE 2: WHAT A MASS! CASES OF CARDIAC MASSES AND OTHER STRUCTURAL ABNORMALITIES

Sunday 22 May 2016 16:30–18:00

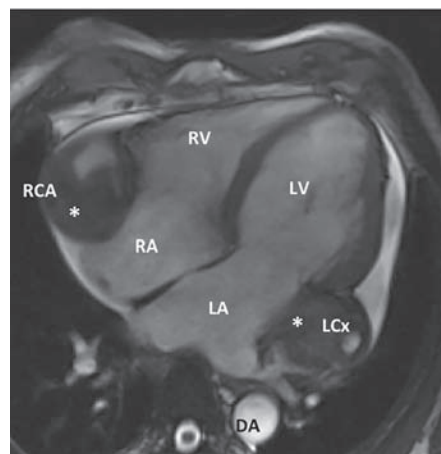
Location: Agora

786

### Giant coronary aneurysms as cause of heart failure

E Ammirati<sup>1</sup>; L Brevetti<sup>1</sup>; A Moreo<sup>1</sup>; L Scudiero<sup>1</sup>; D Artioli<sup>1</sup>; M Frigerio<sup>1</sup>; F Oliva<sup>1</sup>  
<sup>1</sup>Niguarda Ca' Granda Hospital, Milan, Italy

A 59-year-old Filipino man without previous illness presented to the emergency department with a recent history of worsening dyspnea. On arrival he was afebrile with stable hemodynamic parameters and diminished breath sounds bilaterally. Laboratory tests revealed increased high sensitivity troponin T level 860ng/L, proBNP 3850ng/L, C-reactive protein 3mg/dL. ECG showed sinus rhythm with diffuse flattened T waves. Echocardiography detected dilated cardiomyopathy with decreased left ventricular ejection fraction (LVEF 30%). Three large cystic aneurysmal structures were noted, one located at the level of the atrioventricular groove partially protruding inside the right atrium. The other two cystic structures that were in connection with the left main stem were located between the aorta and the pulmonary trunk. A contrast-enhanced cardiac magnetic resonance showed large circular masses compatible with giant coronary artery aneurysms (GCAAs) of all three coronary arteries with a maximum diameter of 63 mm in each vessel. The figure shows massive organized thrombosis inside the right coronary artery (RCA) and the left circumflex artery (LCx) with sluggish blood flow inside. No areas of myocardial oedema were observed. Coronary angiogram confirmed the diagnosis of GCAAs. A FDG-PET/CT of the chest and abdomen excluded an active vasculitis. A coronary angio-CT allowed to characterize the coronary aneurysms: the left anterior descending and RCA were characterized by 2 sequential fusiform aneurysms in the proximal and middle segments of the vessel, with calcified non-stenotic coronary tracts interspersed between the aneurysmal tracts. The presence of proximal coronary aneurysms with coronary calcifications, Asian origin, in the absence coronary stenosis and without probable alternative diagnosis made the clinical picture attributable to presumed late sequelae of antecedent Kawasaki disease (KD). As KD, a self-limiting vasculitis, mainly affects children younger than 5 years, the patient was not be able to recall details of his childhood illness. The patient presented an AHA risk level IV for KD, due to the presence of GCAAs with indication for long-term antiplatelet therapy and warfarin. Also heart failure (HF) medications were started. During hospitalization the patient experienced 2 episodes of symptomatic ventricular tachycardia that required DC shock to restore sinus rhythm, thus implantable cardioverter defibrillator was implanted as secondary prevention. Cardiac surgery to exclude the aneurysms was deemed unfeasible. The patient was considered to be at an unpredictable risk of sudden cardiac death by coronary rupture or total occlusion of the aneurysmal coronaries, and for this reason a screening for heart transplantation was commenced. After 5 months of follow up LVEF improved to 38% and he was asymptomatic. As our case shows, the severe sequelae of prior missed KD must be considered in the differential diagnosis of ischaemic cardiomyopathy with GCAA.



Cardiac magnetic resonance imaging

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### Hybrid treatment approach of right atrial angiosarcoma

J C Joana Catarina Duarte Rodrigues<sup>1</sup>; RC Rui Cerqueira<sup>2</sup>; JCS Joao Carlos Silva<sup>1</sup>; RAR Rui Andre Rodrigues<sup>1</sup>; RA Rui Almeida<sup>1</sup>; PBA Pedro Bernardo Almeida<sup>1</sup>; JC Jorge Casanova<sup>2</sup>; MC Manuel Campelo<sup>1</sup>; PP Paulo Pinho<sup>2</sup>; MJM Maria Julia Maciel<sup>1</sup>

<sup>1</sup>Sao Joao Hospital, Department of Cardiology, Porto, Portugal; <sup>2</sup>Sao Joao Hospital, Department of Cardiothoracic Surgery, Porto, Portugal

A 58-year-old male patient presented to our hospital with complaints of shortness of breath on exertion and generalized weakness and fatigue for several weeks. The chest X-ray showed an cardiothoracic ratio. Further evaluation with transthoracic and transesophageal echocardiogram revealed a large mass occupying almost the entire and severely dilated right atrium (RA), associated with a large pericardial effusion. Cardiac computed tomography (CT) angiogram confirmed the presence of a vascularized intramural mass originating from the RA free wall that widely invaded superior vena cava and pericardium. Pericardiocentesis was inconclusive. Coronary angiography showed a large area of hypervascularized myocardium near the right ventricle projection that was supplied by the acute marginal branches of the right coronary artery. In order to minimize the blood loss caused by surgical trauma, we opted to perform embolization of the heart tumor, which was successfully performed using polyvinyl alcohol, platinum coils and a covered stent. Cardiac surgery included the excision of the mass, RA, superior vena cava (SVC) and inferior vena cava (IVC). The RA, SVC, and IVC were further reconstructed using bovine pericardium and a cardiovascular patch. The RA mass proved to be an angiosarcoma with resection margin clear on permanent pathology. The patient has been doing well five months after being discharged from the hospital and is currently undergoing adjuvant chemotherapy. Although primary cardiac tumors, namely angiosarcomas, are rare, complete surgical resection of the tumor is the most successful treatment for improving patients survival rate. In our patient, preoperative embolization of the tumor helped to control blood loss during tumor resection. To the best of our knowledge, this is the first reported case of a hybrid approach involving an endovascular treatment of a cardiac tumor followed by surgical tumor excision.



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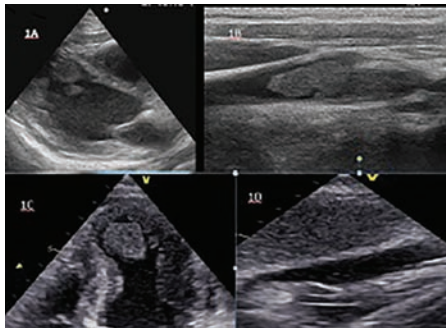
**Transitory thrombotic storm associated with myocardial infarction and dramatic systemic impact**C Stan<sup>1</sup>; N Natalia Patrascu<sup>2</sup>; DJ Mihalcea<sup>2</sup>; VD Vintila<sup>2</sup>; A Nicolescu<sup>1</sup>; AM Vladareanu<sup>2</sup>; D Vinereanu<sup>2</sup><sup>1</sup>University Emergency Hospital of Bucharest, Cardiology, Bucharest, Romania;<sup>2</sup>University of Bucharest Carol Davila, Bucharest, Romania

**Introduction:** Arterial thrombosis is mainly related to complicated atherosclerotic plaques. Nevertheless, proinflammatory and also hereditary prothrombotic disorders are other causes. Alternatively, venous thrombosis is due to pro-coagulant settings, hereditary or acquired and to the risk factors, the most significant being primary or secondary cancers (with a combined hazard of the presence of the tumor, patient's characteristics and the hemostatic system).

**Case presentation:** Female, 56 years old, no cardiovascular history, followed up in the Haematology department with paroxysmal nocturnal haemoglobinuria (PHN), was admitted for acute coronary syndrome with anterior ST-segment elevation, echocardiographic image of severe left ventricle systolic dysfunction and pericardial effusion. Angiography showed coronary thrombosis of LAD without evidence of underlying atherosclerosis requiring thrombus aspiration without stenting, with optimal flow regaining. In the follow-up we recorded worsening of clinical status along with increased pericardial effusion, acute peripheral ischemia syndrome with radial artery thrombosis and transient language disturbances, then fully developed ischaemic stroke, in context of acute massive thrombosis in the left common carotid artery and also new ventricular apical thrombosis at the echographic review.

Questions, problems, differential diagnosis: Given the context of multiple arterial thrombosis, apparently without a unique proven cause, an abdominal-pelvic CT scan was performed, showing expansive tumoral mass originating from the descendent colon. At colonoscopy, the biopsy showed vilous adenoma with high grade intraepithelial neoplasia. We also note the tomographic images of suprahepatic, common iliac veins and right external iliac vein thrombosis. After discharge, we recommended a surgical opinion in order to treat the malignant disease. Surgery was performed in a curative manner with an immediate favorable outcome, improvement of LV ejection fraction and no residual thrombosis recorded at 1-year follow up. Answers and discussion: This complex case is particular by the thrombotic "storm" in the context of PHN, usually associated with haemolytic anemia but also with thrombosis, predominantly venous and seldom arterial, with no clinical manifestations so far for this patient. This fact drove to investigation of other possible causes, namely a source of superimposed malignancy. The vital double major risk, pro-thrombotic and haemorrhagic, dictated the difficulty of therapeutic management.

**Conclusions/implications:** We present the case of a young patient with STEMI of non-atherosclerotic etiology (in situ thrombosis), as the first event in a fulminant process of multiple thrombosis (arterial, venous, intracardiac), triggered not by the haematologic disease but as a systemic hypercoagulant response of a potentially curable malignancy.



789

**Dilated cardiomyopathy due to pheochromocytoma: a review of one case**C D'amore<sup>1</sup>; P Perrone Filardi<sup>1</sup><sup>1</sup>Federico II University Hospital, Department of Advanced Biomedical Sciences, Naples, Italy

Dilated cardiomyopathy (DCM) is a rare cardiovascular expression of pheochromocytoma (PHEO). Usually, the coexistence of other cardiovascular risk factors makes difficult the diagnosis of PHEO. We describe the case of a patient with DCM and paroxysmal atrial fibrillation (AF) due to PHEO. A 60-year old man with history of hypertension (HYP) for 4 years (treated by furosemide, ramipril, nifedipine) was admitted at our hospital due to progressive dyspnoea and palpitation. The patient

reported history of cocaine abuse for 3 years (interrupted 5 years before) and frequent paroxysmal AF events treated with catheter ablation. He had no history of ischaemic heart disease, infective disease or other cases of cardiovascular disease. There were blood pressure of 150/90 mmHg at both upper limbs, mitral systolic murmur and lung cracklings. ECG revealed AF with ventricular rates of 120 beats/min. The laboratory exams showed sideropenic anemia, hyperglycemia, increased NT-proBNP, hypokalaemia and normal cardiac necrosis markers. No evidence of viral infection, thyrotoxicosis, impaired urinary electrolyte and alcohol abuse was found. The echocardiography revealed dilated left ventricle (LV) with uniform reduction of ejection fraction (40%) and severe mitral regurgitation. Patient underwent coronarography that showed normal major epicardial vessels. 24-h urinary cortisol excretion, urinary and serum fractionated metanephrines, aldosterone-renin ratio under standardized conditions were analysed and resulted normal. In addition, there were no alterations of parenchyma and of artery at renal ultrasound examination. The colonoscopy showed left colonic angioectasia. Despite the normal laboratory parameters values, abdomen computed tomography (TC) was performed and showed a solid mass of both adrenal glands. Then, 123I-labelled meta-iodobenzyl-guanidine (MIBG) scanning reported a marked uptake of the left adrenal gland (PHEO). He refused adrenalectomy and was discharged with the diagnoses of HYP secondary to PHEO determining DCM and HF complicated by AF and therapy with dose-adjusted vitamin K antagonist, beta-blockers, diuretics, calcium antagonist, aldosterone antagonist and angiotensin-converting enzyme inhibitors. In this case report PHEO coexisted with several important causes of DCM. Coronarography excluded an ischemic aetiology. The patient had limited cocaine abuse history that was not sufficient to explain LV dysfunction. Tachycardiomyopathy was excluded because our patients showed a recent onset of AF and previous efficacy catheter ablation. The laboratory values, ultrasound and TC findings excluded secondary form of HYP of renovascular hypertension, Chushing's syndrome and Conn syndrome. The clinical evidence suggested performing an imaging test to reach PHEO diagnosis. The reported case shows that in the management of patients is necessary a holistic approach. In the patient described dyspnoea could have had cardiac or extracardiac causes (anemia).



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**From shock to shunt - from bench to bedside**PHT Timmermans<sup>1</sup>; T Adriaenssens<sup>2</sup>; PJ Palmers<sup>3</sup>; F Rega<sup>4</sup>; E Troost<sup>5</sup>; S Janssens<sup>3</sup>

<sup>1</sup>Gasthuisberg University Hospital, Heart Failure and transplantation, Leuven, Belgium; <sup>2</sup>Gasthuisberg University Hospital, Cardiology; interventional cardiology, Leuven, Belgium; <sup>3</sup>Gasthuisberg University Hospital, Cardiology, Leuven, Belgium; <sup>4</sup>Gasthuisberg University Hospital, Cardiac surgery, Leuven, Belgium; <sup>5</sup>Gasthuisberg University Hospital, Adult congenital cardiology, Leuven, Belgium

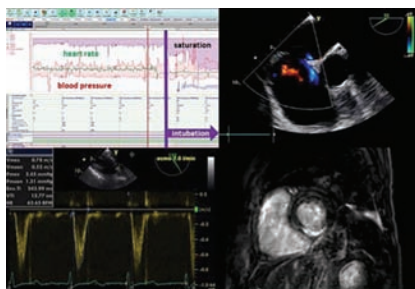
**Introduction:** A man of 78y was admitted because of chest pain. ECG showed an inferior STEMI. Occlusion of the proximal RAC was seen on angiography. Primary PCI was performed. .

**Course during hospitalization:** He developed cardiogenic shock with low blood pressures and refractory hypoxemia. Tracheal intubation was performed a few hours after admission. The patient now developed intractable hypoxemia (top left).

**Differential diagnosis:** The combination of an inferior STEMI with hypoxemia should raise the suspicion of an RV infarction with a PFO, resulting in right-to-left shunting. This was confirmed by urgent TEE (top right). The hypoxemia deteriorated right after intubation because in contrast to the effect on the LV, positive pressure ventilation increases RV afterload, resulting in an increased shunt flow in this case.

**Discussion:** Because of shock and hypoxemia, bedside percutaneous VA-ECMO was implanted. Systemic desaturation persisted because of the shunt and varied between 90 and 98%. On d3, contractile reserve was noted by TEE (bottom left). On d4, the patient was successfully weaned from the ECMO and a few hours later also from the ventilator. He had a smooth recovery both on the ICU and ward. Saturation remained around 92%. TEE and CMR showed a small persistent shunt and severe RV dysfunction due to infarction of the free wall (bottom right). After discussion with the adult congenital cardiology specialists, we decided not to close this PFO. First, saturations in rest as well as during exercise were above 90%. Second, the RV dysfunction could be aggravated by closing the "pressure valve". The patient was discharged from the hospital 2 weeks after admission, and is still in ambulatory FU>1 year after admission.

**Conclusion:** RAC infarction can be complicated by cardiogenic shock, and in combination with a PFO, also refractory hypoxemia. VA-ECMO can treat both the failing RV and the systemic desaturation. It is not mandatory to close the PFO in the acute nor in the recovery phase of heart failure. By converting our "text-book" knowledge on LV and RV physiology and their responses on positive pressure ventilation + VA-ECMO therapy, it is not only possible to understand what is going wrong with the patient bedside, but also to treat him adequately.



from shock to shunt.

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**A rare case of left atrial myxoma and disseminated tuberculosis in a patient with a history of peripartum cardiomyopathy**

D Dharmaraj Karthikesan<sup>1</sup>; AS Saad<sup>1</sup>; KS Liew<sup>1</sup>; NUH Adznan<sup>1</sup>; WF Wan Rahimi Shah<sup>1</sup>; GJ Mathews<sup>1</sup>; AF Mohd Ezanee<sup>1</sup>; AY Khamis<sup>2</sup>; S Krishnan<sup>1</sup>; O Ismail<sup>1</sup>  
<sup>1</sup>Hospital Sultanah Bahiyah, Department of Cardiology, Alor Setar, Malaysia; <sup>2</sup>Penang Hospital, Department of Cardiothoracic, Penang, Malaysia

**Introduction:** The management of cardiomyopathy is a challenge for most clinicians. A methodical approach is paramount when multiple etiologies are concerned. Case report: A 31-year-old lady presented with heart failure symptoms for 1-week duration postpartum. Clinical features and transthoracic echocardiogram (TTE) suggested peripartum cardiomyopathy. After 6 months of treatment, she defaulted follow up. She was seen again 4 years later during subsequent pregnancy and TTE revealed good left ventricular ejection fraction (LVEF). However, bilateral atrial enlargement was noted which was similar to the previous TTE. Assessment 6-weeks postpartum showed reduced LVEF with new onset of regional wall hypokinesia. Before further evaluation could be instituted, she once again defaulted follow up. She presented to the emergency department 2 months later with anasarca, worsening failure symptoms, productive cough, and significant weight loss for a 1-month duration. She had gross proteinuria and hypoalbuminemia with normal renal function. Chest radiograph, sputum smears for acid-fast bacilli and cultures confirmed pulmonary tuberculosis. Antituberculosis treatment was commenced. The computed tomography (CT) scan showed evidence of pulmonary and renal tuberculosis. Cardiac magnetic resonance imaging (MRI) revealed a mass in the left atrium with features suggestive of previous peripartum cardiomyopathy or myocarditis. TTE showed impaired LVEF, pulmonary hypertension and the presence of a left atrial mass. In view of the chronically dilated left atrium, we suspected left atrial thrombus with underlying disseminated tuberculosis. Proteinuria was attributed to renal tuberculosis or secondary amyloidosis precipitated by tuberculous infection. Anticoagulation with warfarin was commenced. Repeated TTE showed increasing size of left atrial mass despite optimal anticoagulation. The diagnosis was revised to left atrial myxoma. She underwent surgical excision of the left atrial mass. Histopathological studies confirmed atrial myxoma. Antituberculosis regime was completed uneventfully. Recent TTE showed marked improvement of LVEF with no recurrence of left atrial mass and there was complete resolution of proteinuria.

**Discussion:** This case raises several important questions. What was the primary cause of heart failure in this patient? What is the association between peripartum cardiomyopathy, left atrial myxoma and tuberculosis? Did secondary amyloidosis occur from tuberculous infection resulting in the nephrotic syndrome? It is clear that successful treatment of peripartum cardiomyopathy and disseminated tuberculosis with surgical excision of left atrial myxoma resulted in improvement of cardiac function.

**Conclusion:** To the best of our knowledge, this is the first reported case of peripartum cardiomyopathy, atrial myxoma and disseminated tuberculosis occurring in a single patient. A comprehensive guideline for management is currently unavailable.

## POSTER SESSION 2

Sunday 22 May 2016 08:30–18:00

Location: Poster Area

### ACUTE HEART FAILURE

#### P803

##### The frequency and causes of acute heart failure in women middle aged and elderly with acute myocardial infarction

I Irina Zheltova<sup>1</sup>; IA Sukmanova<sup>1</sup>

<sup>1</sup>Altay Regional Cardiology Centre, Cardiology department for patients with acute myocardial infarction, Barnaul, Russian Federation

**Introduction:** The most common complication of acute myocardial infarction (AMI) is the development of acute heart failure (AHF). The absence of infarct artery revascularization (IRA), as well as the nature of multivessel coronary lesions contributes to poor clinical and hemodynamic parameters, development of AHF and cardiac arrhythmias in patients with AMI.

**Purpose:** To evaluate the frequency and the factors that contribute to the development of acute heart failure (AHF) in women with acute myocardial infarction (AMI) of middle and old age.

**Methods:** The study involved 76 women of middle and advanced age with AMI (32 (42.1%) patients of middle age and 44 (57.9%) older), the average age of them was  $62.3 \pm 0.8$  years. In addition to laboratory tests evaluate the level of NT-PROBNP, conducted Holter (ECG) monitoring, echocardiogram and coronary angiography (CAG).

**Results:** In 54 (71.1%) patients with AMI showed no signs of AHF (Killip I), 11 (14.5%) - diagnosed with stage II for Killip, pulmonary edema (Killip III) was detected in 5 (6.6%), cardiogenic shock (Killip IV) - 5 (6.6%). Left ventricular (LV) systolic dysfunction was detected in 41 (53.9%) women. Average level NTPROBNP in the group of patients with AHF was  $1085 \pm 231.6$  pg/ml in group without signs AHF -  $590.3 \pm 62.4$  pg/ml ( $p = 0.0001$ ). Recanalization IRA with stenting were 36 (47.4%) women, 10 (13.2%) held thrombolytic therapy (TLT), 36 (47.4%) patients had not been carried out coronary revascularization. Arrhythmias were detected in 24 (31.6%) women. In the group of patients with TLT Killip I diagnosed in 8 (80%), Killip II - y 1 (10%) patients, Killip IV - y 1 (10%). The average level of LV ejection fraction in this group was  $55.8 \pm 1.6\%$ . Arrhythmias in patients with TLT were found in 4 (40%). In the group of patients with PCI, AHF has not been revealed in 29 (80.5%), Killip II - in 5 (13.8%), cardiogenic shock was diagnosed in 3 (8.3%). The level of the average LV ejection fraction in patients with PCI was  $56.9 \pm 1.6\%$ . Arrhythmias in this group were found in 14 (38.8%) patients. In 36 (47.4%) patients had not been carried out revascularization IRA. In this group, Killip I was detected in 29 (80.5%), Killip II in 4 (11.1%), Killip IV - 3 (8.3%). The average level of LV ejection fraction in this group was  $57.8 \pm 1.5\%$ , and arrhythmias - in 21 (58.3%).

**Conclusions:** The incidence of AHF in women with AMI middle aged and older was 27.6%, with stage II for Killip - 14.5%, Killip III - 6.6%, Killip IV - 6.6%. The primary cause of AHF in patients with AMI is no revascularization IRA. Level NTPRO-BNP is associated with the degree of LV dysfunction is an important predictor of the development of AHF in patients with AMI.

#### P804

##### Repetitive decompensation of heart failure leads truly to deterioration of organ function

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**Backgrounds:** Heart failure is an increased burden all over the world due to the frequent hospitalization. The post-discharge mortality and re-hospitalization rate are unacceptably high despite the advances in management of chronic heart failure (HF), such as evidence-based medication and mechanical device, including implantable cardioverter-defibrillator or cardiac resynchronization therapy. It is believed that repetitive decompensation of HF may be associated with progressive deterioration

of cardiac and/or non-cardiac function, however, it has not been well confirmed in real world.

**Methods:** We enrolled 250 consecutive acute decompensated HF patients who were hospitalized in our institute from January 2014 to December 2015. Among those patients, 45 patients experienced repetitive decompensation of HF (2 times: 28 patients, 3 times: 17 patients) after discharge and we evaluated the changes in hemodynamic and laboratory data.

**Results:** Mean age was 78.8 years old and ejection fraction was 43.4 % who experienced repetitive decompensated HF. Repetitive decompensation resulted in decreases in systolic blood pressure (SBP) 152.9 mmHg, 132.5 mmHg and 129 mmHg and heart rate 93 bpm, 86 bpm and 77 bpm ( $p = 0.03$  and  $0.07$ , respectively). Blood urea nitrogen increased 26.9 mg/dl, 29.5 mg/dl and 42.5mg/dl, serum creatinine increased 1.22 mg/dl, 1.38 mg/dl and 1.73 mg/dl, N-terminal pro B-type natriuretic peptide increased 7494 pg/ml, 11046 pg/ml and 15995 pg/ml ( $p < 0.001$ , 0.03, 0.13, respectively). The percentages of guideline-based treatments at admission were also increased in renin angiotensin inhibitors 42.2 %, 75.6 % and 82.4%, beta blockers 35.6%, 57.8% and 64.7%, anti-aldosterone blockers 17.8%, 42.2% and 70.6% ( $p < 0.01$ ,  $< 0.01$ , and  $0.04$ , respectively).

**Conclusions:** Despite the fact that guideline-based medications were performed better, prognostic factors including SBP, renal function and natriuretic peptides were deteriorated more over times.

#### P805

##### Contemporary assessment of lung ultrasound, BNP and echocardiography for outcome prediction in patients with decompensated heart failure

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**Background:** Pulmonary and systemic congestion at discharge remain strong predictors for poor prognosis in patients with Decompensated Heart Failure (DHF). Lung ultrasound (LUS) has been proposed as a simple, accurate, fast and economic tool to assess pulmonary congestion by imaging 'comets' or B-lines. Measurement of LUS, B-type natriuretic peptide (BNP) and echocardiographic variables could improve diagnosis and prediction of outcome.

**Purpose:** 1) To investigate the relation amongst B-lines, BNP, and echo measurements (E/e', systolic pulmonary arterial pressure [PAPs], restrictive left ventricular (LV) filling pattern E/A>1 and left ventricular ejection fraction [LVEF]) at admission. 2) To evaluate the prognostic power of admission compared to pre-discharge B-lines. 3) To explore potential differences in patients with DHF and LVEF below or above 50%.

**Methods:** We performed LUS, echocardiographic and BNP assessment in patients with DHF within 12h of admission. B-lines and BNP values were also evaluated at discharge. Patients were followed for 6 months for HF events. Data are shown as median and quartile (Q) range.

**Results:** Of 140 patients enrolled, 95 had HFrEF and 45 had HFpEF. For patients with HFrEF, the median number of B-lines at admission was 28 (IQR 22 to 36) and on discharge 20 (15 to 26) with a BNP of 1220 pg/mL (838 to 1810) and 725 pg/mL (406 to 1247) respectively. For patients with HFpEF, the median number of B-lines at admission was 31 (26 to 37) and on discharge 20 (15 to 25) with a BNP of 837 pg/mL (669 to 1083) and 512 pg/mL (316 to 864) respectively. In the overall population, the number of B-lines at admission correlated with BNP ( $r = 0.54$ ;  $p < 0.001$ ), E/E' ( $r = 0.29$ ;  $p = 0.001$ ) E/A ( $r = 0.45$ ;  $p < 0.001$ ) and PAPs ( $r = 0.09$ ;  $p = 0.289$ ). In the overall population, neither B-lines nor BNP at admission predicted HF events but either measured at discharge predicted 6 month outcome (AUC:0.72 [0.63-0.80], AUC:0.70 [0.60-0.79] respectively  $p < 0.001$ ; 6 month HF event rate for Q1 v Q4 was 17% vs 62% [ $p < 0.001$ ] and Q1 v Q4 was 16 vs 61% [ $p < 0.001$ ] respectively). There was a strong relationship between  $\Delta$ B-lines from admission to discharge (AUC: 0.83; CI: 0.75-0.91;  $p < 0.001$ ). In patients with HFrEF, there was a strong relationship between both B-lines and BNP levels at discharge (AUC:0.72 [0.62-0.83], AUC:0.71



[0.57-0.75] respectively  $p < 0.001$ ). However for HFpEF, only B-lines predicted outcome (AUC 0,74 CI 0,58-0,89  $p < 0,01$ ) Conclusions- LUS may be a useful tool to assess and monitor pulmonary congestion to identify patients at high risk of HF events. Pulmonary congestion at discharge evaluated by LUS was the strongest predictor of outcome in this study of patients with DHF. The power prediction of LUS is similar in both HFREF and HFpEF patients.

#### P806

##### Influence losartan and lisinopril indicators for exercise tolerance and quality of life parameters in patients with chronic heart failure

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**Purpose:** To study the effect of lisinopril and losartan on the exercise capacity and quality of life parameters (QL) in patients with chronic heart failure (CHF) I-III functional class (FC).

**Research methods:** The subjects were 120 patients with ischemic heart disease (IHD) I-III FC CHF (mean age  $53,3 \pm 5,8$  years). The first group (I) accounted for 60 patients with FC I (18), II FC (22) and FC III CHF (20 patients), took over 6 months with standard therapy (spiranolakton, beta-blockers, antiplatelet agents) - losartan; the second group (II) - 60 patients with FC I (19), II FC (21) and FC III CHF (20) - lisinopril (mean dose of losartan was  $66,3 \pm 25,6$ , lisinopril -  $6,8 \pm 2,6$  mg / day). The average age of patients was  $62,3 \pm 5,6$  years. The control group consisted of 20 healthy individuals. All patients underwent a six-minute walk test (SWT) study of QL of patients with the help of "Minnesota questionnaire" on the total index (TI QL), the clinical condition was evaluated on a scale of assessment of the clinical status of patients with chronic heart failure (SACS). The results showed that patients with Group I and II to FC II of CHF was observed a decrease in the distance SWT 17.1% and 15.4% ( $p < 0.01$ ) and III CHF FC 48% and 47.7% ( $p < 0.001$ ), respectively, compared with patients with SWT I FC CHF. Indicators SACS were significantly higher in patients with FC II and III heart failure compared with patients with FC I ( $p < 0.001$ ). Analysis of QL assessment on the results of the Minnesota questionnaire showed a significant increase in quality of life by increasing the TI QL. Against the background of 6 months of treatment with the inclusion of losartan or lisinopril it noted: patients with CHF FC I the first group during treatment TI QL score on a scale SACS increased by 32.4%, 50.7% ( $p < 0.001$ ), and Group II patients is 25% and 42.6% ( $p < 0.001$ ); with CHF FC II patients of the first group by 23.8% and 29.2% ( $p < 0.001$ ), while the second group by 12.8% and 41.8% ( $p < 0.001$ ); with FC III patients in the losartan group by 13.9%, 22.5% ( $p < 0.001$ ), in the lisinopril group by 8.5% ( $p < 0.005$ ), 18.2% ( $p < 0.001$ ), respectively, compared from baseline that was accompanied by an increase in the distance SWT patients I, II and III FC in the first group by 13.1%, 14.5% and 16.6% ( $p < 0.001$ ), and the second group by 16.3%, 9.4% and 13% ( $p < 0.005$ ).

**Conclusions:** Thus, in patients with CHF was observed significant improvement in quality of life and increase exercise tolerance with increasing six-minute walk distance and decrease on the total index of "Minnesota questionnaire", the amount of points on the scale SACS in the dynamics of the six-month treatment in both groups with misleading advantage in the losartan group.

#### P807

##### Prevalence, risk factors and prognostic impact of bleeding complications in patients in cardiogenic shock in intensive care unit

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**Introduction:** Cardiogenic shock occurs in 7-8% of patients with acute myocardial infarction (AMI) and is associated with a higher morbidity and a worse prognosis, with a hospital mortality rate of 50%.

The progress in antithrombotic therapy and revascularization has reduced mortality in patients (pts) with acute coronary syndrome (ACS), but these therapeutic advances are associated with an increased risk of bleeding. The prevention of major bleeding has an important role in the prognosis impact of pts with ACS.

**Aim:** To evaluate the prevalence, risk factors and prognostic impact of bleeding complications in pts admitted for cardiogenic shock in the context of AMI in a polyvalent intensive care unit (ICU).

**Methods:** We evaluated consecutive pts admitted with cardiogenic shock in the context of AMI in a polyvalent intensive care unit, over a period of 5 years. The population was characterized according to baseline characteristics, type of MI, in-hospital complications (death and bleeding - defined in moderate or severe according to the GUSTO classification) and death, reinfarction, or readmission in the ICU at follow-up.

**Results:** We studied 42 pts (64.3% male sex, mean age  $69 \pm 15$  years). Thirty-six percent ( $n = 15$ ) had bleeding complications.

Age, gender, cardiovascular risk factors, antiplatelet or anticoagulant therapy and invasive procedures were not associated with a higher bleeding risk.

The intra-aortic balloon has been used in the majority of patients, 64% ( $n = 27$ ), without a negative impact at short and long term.

In terms of prognostic impact, bleeding complications were associated with a longer hospital stay ( $10 \pm 8$  vs  $5 \pm 6$  days,  $p = 0.027$ ), but without statistical significance in terms of mortality, reinfarction, or readmission in the ICU.

**Conclusion:** In this population, hemorrhagic complications in context of cardiogenic shock were frequent and associated with prolonged hospitalization. Identification and correction of predisposing factors may be useful to minimize the risk of bleeding in these pts.

#### P808

##### Higher brachial-ankle pulse wave velocity is closely associated with lower functional capacity in especially heart failure patients

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**Background:** Previous studies demonstrated that brachial-ankle pulse wave velocity (baPWV) was associated with cardio vascular disease, but clinical characteristics and functional capacity in cardiopulmonary exercise testing (CPX) have not been well documented.

**Purpose:** The purpose of this study is to identify the association of baPWV with functional capacity in acute heart failure (AHF) and acute myocardial infarction (AMI) patients.

**Methods:** We have enrolled 146 patients (pts) doing cardiac rehabilitation with CPX in pts with AHF and AMI discharged from March 2014 to February 2015. We compared the baseline clinical characteristics, CPX variable and functional capacity between pts with baPWV  $\geq 1800$ cm/s ( $n = 44$ ; high baPWV) and the other pts ( $n = 102$ ; normal baPWV). We excluded the pts with ankle brachial index  $< 0.9$ .

**Results:** The pts with high baPWV were older, and had lower body mass index than those with normal baPWV ( $74.5 \pm 7.6$  vs.  $65.8 \pm 10.9$  years of age;  $p < 0.01$ ;  $22.5$  vs.  $24.3$ ;  $p < 0.01$ , respectively). They were more likely to have diabetes or chronic obstructive pulmonary disease ( $40.9\%$  vs.  $22.6\%$ ;  $p = 0.03$ ;  $13.6\%$  vs.  $2.0\%$ ;  $p < 0.01$ , respectively). There was no significant difference in other co-morbidities. In pts with high baPWV, peak VO<sub>2</sub> and VO<sub>2</sub>/pulse were significantly lower ( $15.5 \pm 4.5$  vs.  $18.4 \pm 4.6$  ml/kg/min;  $p < 0.01$ ,  $8.1 \pm 2.5$  vs.  $9.6 \pm 3.3$ ;  $p < 0.01$ , respectively) at baseline. In AMI pts, there was no difference in peak VO<sub>2</sub> or VO<sub>2</sub>/HR between high baPWV and normal baPWV. ( $17.5 \pm 5.5$  vs.  $18.8 \pm 4.8$  ml/kg/min;  $p = 0.35$ ,  $8.4 \pm 2.5$  vs.  $10.2 \pm 4.0$ ;  $p = 0.07$ , respectively) However, in AHF pts, high baPWV was associated with lower peak VO<sub>2</sub> and VO<sub>2</sub>/pulse ( $14.2 \pm 3.4$  vs.  $16.8 \pm 4.0$  ml/kg/min;  $p < 0.01$ ,  $7.8 \pm 2.0$  vs.  $9.1 \pm 2.8$ ;  $p = 0.04$ , respectively). Hand grip strength, Isokinetic knee extension muscle strength and calf circumference were lower in pts with high baPWV than those with normal baPWV ( $23.3 \pm 8.0$  vs.  $30.6 \pm 9.0$  kg;  $p < 0.01$ ,  $21.5 \pm 5.4$  vs.  $32.4 \pm 11.0$ ;  $p < 0.01$ ,  $31.7 \pm 3.3$  vs.  $34.0 \pm 3.5$  cm;  $p = 0.02$  respectively).

**Conclusion:** In AHF pts, higher baPWV was closely associated with lower functional capacity; peak VO<sub>2</sub>, VO<sub>2</sub>/HR, muscle strength and calf circumference.

#### P809

##### Continuous infusion versus bolus administration of intravenous furosemide in acute heart failure patients

Novartis - educational grant

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**Background:** Data on optimal diuretic treatment in patients (pts) with congestive heart failure (HF) remain scarce. Aim: To compare characteristics and prognosis of acute HF (AHF) pts treated with intravenous (IV) furosemide in a continuous infusion (CI) versus bolus administration (BA).

**Methods:** We used the data from SLOVASEZ II, nationwide multicenter AHF survey with 592 consecutive pts enrolled between 1 April and 31 June 2014. We analysed 77 variables in relation to clinical manifestation, management and outcome of AHF in univariate analysis, significant of them ( $p < 0.05$ ) were used for multivariate analysis.

**Results:** 368 (82.5%) pts were enrolled into CI group (CIG) and 78 (17.5%) in BA group (BAG). Pts in CIG were younger ( $65 \pm 14$  vs  $73 \pm 11$  years), severely symptomatic (NYHA class 3.6 vs 3.3) and frequently hospitalized due to AHF in last year (56 vs 32%; all  $p < 0.001$ ). CIG pts were more admitted for acute decompensation of chronic HF (74 vs 45%), with dilative cardiomyopathy and arterial hypertension as more frequent primary etiology (22 vs 12 and 24 vs 17% resp., both  $p < 0.05$ ), as well as with higher incidence of renal failure (60 vs 39 %,  $p < 0.001$ ; mean serum creatinine and estimated glomerular filtration - eGFR were  $156$  vs  $126$   $\mu$ mol/L and  $0.8$  vs  $0.9$  ml/s resp.; both  $p < 0.05$ ). Pts in CIG had lower systolic blood pressure (mean  $124$  vs  $142$  mmHg,  $p < 0.001$ ), but more often signs of congestion as S3 gallop or jugular vein distension (23 vs 11 or 60 vs 39 % resp.; both  $p < 0.005$ ). They were more treated with digoxin and furosemide (41 vs 20 and 85 vs 70 % resp., both  $p < 0.005$ ) as well as eplerenone and warfarin (24 vs 13 and 31 vs 18 % resp., both  $p < 0.01$ ) before admission. Pts in

CIG had more dilated left ventricle with lower ejection fraction (median 62vs54 mm and 34vs42 % resp., both  $p < 0.01$ ). The number of pts with implanted defibrillators/resynchronisation therapy or administered inotropes was higher in CIG (26vs7 % and 17vs2%, resp., both  $p < 0.001$ ). The in-hospital mortality was high (14vs10 % in CIGvsBAG,  $p=ns$ ), with longer hospitalization in CIG (11vs9 days,  $p < 0.05$ ). There was symptomatic improvement in both groups (NYHA class 2.5vs2.4 in CIGvsBAG) without detected worsening in renal function (eGFR 0.8vs0.9 ml/s in CIGvsBAG) at discharge. Parameters independently associated with CI administration of IV furosemide were age, history of HF and renal failure (all  $p < 0.01$ ).

**Conclusion:** Administration of IV furosemide in continuous infusion is often, effective and safe therapeutic strategy in AHF pts which should be considered even more in high-risk subgroups, especially older pts with history of HF and renal failure.

#### P810

##### Body mass index and gender-specific clinical outcome measures of congestive heart failure with reduced ejection fraction: a Middle Eastern population study

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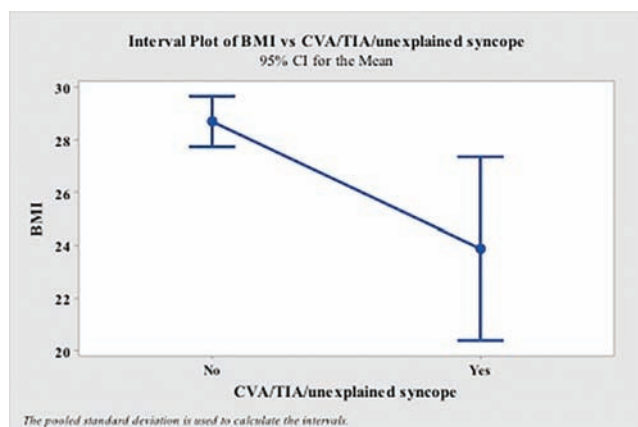
**Background:** Low body mass index (BMI) has been linked with congestive heart failure mortality. However, gender-specific BMI-related clinical outcome measures are not well defined.

**Aim:** We examined the correlation between BMI gender variability and clinical mortality, cerebrovascular accident (CVA), transient ischaemic attack (TIA), composite outcome of myocardial infarction (MI), unexplained syncope, infection and bleeding outcome measures of heart failure in patients with reduced ejection fraction (HFrEF).

**Methods:** A group of 166 consecutive HFrEF patients, 37 females and 129 males, were enrolled in a prospective HFrEF single-centre registry from December 2014 to December 2015.

**Results:** Males with lower BMI had higher composite MI/CVA/mortality, (42% vs. 25%,  $P=0.05$ ) for BMI of  $25.9 \pm 5.3$  vs.  $29.8 \pm 7.2$  kg/m<sup>2</sup>,  $P=0.08$ . They also showed higher rates of CVA/TIA/unexplained syncope than the high-BMI males (23% vs. 4.1%,  $P=0.01$  for BMI of  $23.9 \pm 5.4$  vs.  $28.4 \pm 6.1$  kg/m<sup>2</sup>,  $P=0.018$ ). However, length of stay (LOS) at the hospital was shorter for low-BMI females ( $3.6 \pm 2.4$  vs.  $9.7 \pm 8.15$ ,  $P=0.024$  for BMI  $29.7 \pm 6.2$  vs.  $35.8 \pm 7.2$  kg/m<sup>2</sup>,  $P=0.01$ ). Low-BMI females had lower rates of infection/bleeding (26% vs. 0%,  $p=0.001$  for BMI of  $35.8 \pm 7.2$  vs.  $27.8 \pm 4.9$  kg/m<sup>2</sup>).

**Conclusion:** Among the examined HFrEF patients, low BMI in males was associated with high incidence of MI/CVA/mortality and composite rates of CVA/TIA/unexplained syncope. Low BMI in females was associated with low all-cause infection/bleeding rate and short LOS.



Low BMI and CVA/TIA/syncope outcome

#### P811

##### Non invasive evaluation of hemodynamic effects of continuous positive airway pressure in acute heart failure with right ventricular dysfunction.

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**Background:** beneficial effects of continuous positive airway pressure (CPAP) in patients (pts) with acute pulmonary edema (APE) have been already demonstrated.

However, few it is known regarding the effects of CPAP on pts with acute heart failure (AHF) and contemporary right ventricular dysfunction. This lack of data is mainly due to concerns about possible harmful hemodynamic effects on right function in this subgroup of pts. The purpose of our study is to evaluate the hemodynamic effects of CPAP, measured by echocardiography, in pts with acute HF and right ventricular dysfunction.

**Methods:** we evaluated 30 pts with acute HF referring to our ICU department of which 11 (37%) had right ventricular dysfunction. Acute HF was defined as a left ventricular ejection fraction  $< 0.45$  associated with at least one criteria between dyspnea at rest, pulmonary rales or radiological signs of pulmonary congestion. Right ventricular dysfunction was defined as a reduction of tricuspid annular plane systolic excursion (TAPSE)  $\leq 16$  mm evaluated by transthoracic echocardiography. Echocardiographic hemodynamic assessment was performed at presentation (T0) and at 30 minutes (T1), 24 h (T2) and 48 h (T3) after C-PAP beginning. Patients were treated with a different level of positive end expiratory pressure (PEEP 5-7,5-10 mmHg) chosen according to clinical needs.

**Results:** mean cardiac output (CO) significantly increased during CPAP therapy (3.7 l/min at T0 vs. 4.2 l/min at T2;  $p=0.03$ ) as well as mean cardiac index (CI) (1.9 l/min/m<sup>2</sup> at T0 vs. 2.2 l/min/m<sup>2</sup> at T2;  $p=0.04$ ). There were no significant variations of systolic, diastolic and mean systemic blood pressure during the two days of treatment while mean ejection fraction improved at 48 h (31.7 % vs. 35.7%,  $p=0.04$ ). Right ventricular function did not deteriorate after application of PEEP (mean TAPSE of 14.5 compared to 14.5 at T0 to T1) and central venous pressure (CVP) has increased but not significantly (mean 9.3 at T0 vs. 9.8 at T1). Systolic pulmonary pressure did not vary significantly after C-PAP ( $38,72 \pm 13,66$  vs  $37,31 \pm 13,15$   $p:0.8$ ). We have not had adverse cardiovascular events. All patients were discharged alive.

**Conclusion:** C-pap is safe in patients with right ventricular dysfunction and provides significant hemodynamic support even in this subgroup of patients. The beneficial effects of C-PAP could be explained mainly by the reduction of pulmonary vascular resistances due to correction of hypoxia levels compare to the decrease of venous return which is not significant in euvolemic patients. These encouraging results should be confirmed with larger numbers or maybe dedicated trials

#### P812

##### Treatment of acute myocardial infarction in shock with ECMO: beyond the intraaortic balloon pump

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**Background:** Cardiogenic shock is a well known complication of acute myocardial infarction (AMI). At this moment there is controversy about the utility of intraaortic balloon pump in this context, and different devices are being used to support the patients. One option is the use of venoarterial extracorporeal membrane oxygenation (VA-ECMO), that can be implanted percutaneously in the catheterization laboratory.

**Methods:** We analyzed our experience in the treatment of AMI complicated with refractory shock with percutaneous VA-ECMO since July 2013, when our program started, to December 2015. ECMO Cardiohelp (Maquet AG) was percutaneously implanted in the Cath Lab by interventional cardiologists in all cases, using femoral approach.

**Results:** During the period of study 11 patients with AMI in refractory shock were treated with VA-ECMO. Eight patients were men, with a median age of 52.4 (range [42.5-63.1]). Mean LVEF was 0.13, lactic acid  $9.14 \pm 3.27$  mmol/L, time of cannulation  $21.6 \pm 9.4$  min, time of support  $4 \pm 2.5$  days. During the ECMO therapy 4 patients presented major bleeding (36%), 2 patients presented limb ischemia (18%), 1 patient required venovenous hemofiltration (9%). Weaning from ECMO was achieved in 7 of the 11 cases (63.6%), 2 patients required implantation of a ventricular assist device as bridge to heart transplantation (18.2%). One patient died after weaning due to electrical storm and 2 patients died during the therapy. Global survival to discharge was 72.7%.

**Conclusion:** Our experience with percutaneous VA-ECMO in the treatment of AMI complicated with cardiogenic shock is favourable, with a high survival in a scenario of bad prognosis with conventional treatment. We think it is a useful tool to take into account in the catheterization laboratory.

#### P813

##### Venoarterial extracorporeal membrane oxygenation in adults: clinical experience in heart failure and cardiac arrest.

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**Background:** Venoarterial extracorporeal membrane oxygenation (VA-ECMO) is an established treatment for severe heart failure not responding to conventional

therapy, for failed weaning from cardiopulmonary by-pass in post-cardiotomy and post-transplantation patients, to facilitate specific intervention (i.e. coronary angiography or percutaneous coronary intervention) and in cardiac arrest when initial cardiopulmonary resuscitation (CPR) is unsuccessful.

**Purpose:** This report reviews our experience with VA-ECMO in adult in-patients of a Cardiovascular Science Department of a University hospital.

**Methods** From October 2012 to December 2015, 12 adult patients affected by acute severe cardiac failure or cardiac arrest with potentially reversible cause, were placed on VA-ECMO using heparin-coated circuits. In cardiac arrest, the indications were no-flow time <5 minutes, low-flow time between 10 and 60 minutes, age <65 years, and absence of other contraindications.

Data were obtained from patient records. Continuous variables were presented as mean  $\pm$  SD whereas discrete variables were presented as frequencies. Differences were compared with unpaired student t test.

**Results:** VA-ECMO was utilized in 12 patients, aged  $52.4 \pm 14.7$  years (range 29 – 73), seven males and five females. ECMO was instituted during CPR in six patients (50%), in the operating room because of inability of weaning from cardiopulmonary bypass in three patients (25%), and for acute heart failure in three patients (25%) (one for valvular disease, one during a percutaneous coronary intervention and one for a catastrophic antiphospholipid syndrome). Nine patients were successfully weaned from AV-ECMO (75%); three of them died in the hospital (30%) and six (50%) were alive three months later. The peak value of serum LDH during ECMO was significantly lower in survivors than in non-survivors ( $637.8 \pm 110.4$  vs.  $1536.6 \pm 910.1$  IU/L;  $p=0.03$ ). Also plasma lactate was significantly lower in survivors than in non-survivors after 3 hours ( $6.3 \pm 2.8$  in vs.  $10.3 \pm 3$  mmol/L;  $p=0.05$ ) and 24 hours ( $2.8 \pm 2$  vs.  $6.7 \pm 3.7$ ;  $p=0.05$ ) the beginning of ECMO support.

**Conclusions:** In our series of patients treated with AV-ECMO, three month survival was 50% and eCPR was characterized by the highest mortality (66%). These results are consistent with the literature (3). Survivors presented lower levels of plasma lactate in the first 24 hours after starting ECMO. Higher values of serum LDH during support may be associated with poor outcome.

**P814**

**Clinical characteristics and social backgrounds in super elderly patients of acute congestive heart failure in community-based registry; kickoff registry**

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**Background:** Heart failure (HF) is frequent in the elderly. HF in the elderly patients (pts) was closely associated with social backgrounds, but in a suburb of city, social backgrounds of HF have not been well documented. Very few trials have reported participants about home living situation, social support and social backgrounds in the Asia Pacific region, Japan.

**Purpose:** This study aimed to identify the association of super elderly and social backgrounds, home living situation, social support and so on, in acute heart failure (AHF) patients (pts).

**Methods:** We have enrolled 374 inpatients with AHF in the KICKOFF Registry (13 hospitals in Kitakawachi, Osaka, Japan). The KICKOFF Registry is a community-based survey of HF pts in Kitakawachi which is located at the eastern end of the city of Osaka, Japan. The age distribution of the population in Kitakawachi is similar to that in the city of Osaka, as well as that in Japan. We compared the clinical characteristics and social backgrounds between HF pts  $\geq 80$  years (elderly pts;  $n=190$ ) and the other pts (control;  $n=184$ ).

**Results:** We had 50.8% of super elderly pts. The elderly pts were more in female, had lower body mass index, and longer mean length of hospitalization than control (64.2% vs. 36.4%;  $p < 0.01$ ,  $20.3 \pm 3.7$  vs.  $23.0 \pm 4.2$ ;  $p < 0.01$ ,  $29.2 \pm 26.8$  vs.  $22.6 \pm 19.9$  days;  $p = 0.02$ , respectively). They had more valvular disease and chronic kidney disease (40.2% vs. 27.0%;  $p = 0.01$ , 63.9% vs. 46.7%;  $p < 0.01$ , respectively). There was no significant difference in other co-morbidities between them, history of heart failure, ischemic heart disease, hypertension, diabetes and atrial fibrillation. Elderly pts were more likely to need support by others; less by living alone, own drug therapy monitoring or own dietary manager than control (16.7% vs. 40.9%;  $p < 0.01$ , 45.1% vs. 86.1%;  $p < 0.01$ , 22.2% vs. 42.3%;  $p < 0.01$ , respectively). In elderly pts, there were more of downgrade ADL, long-term care insurance available, dementia and limb motion disorder (33.3% vs. 16.1%;  $p < 0.01$ , 73.6% vs. 19.0%;  $p < 0.01$ , 45.1% vs. 11.7%;  $p < 0.01$ , 40.3% vs. 13.9%;  $p < 0.01$ , respectively).

**Conclusion:** There was 50.8% of super elderly pts in our study. The elderly pts with HF need more support by other person, and they had lower ADL, dementia and limb motion disorder. Therefore, more strict social supporting systems of elderly pts should be constructed in the Asia Pacific region, Japan.

**P815**

**Effect of ivabradine on the infarct size and remodeling in patients with STEMI**

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**Objective:** To assess the effect of ivabradine on LV function and remodeling in patients with STEMI immediately after primary PCI (PPCI).

**Methods:** Fifty seven patients who presented with STEMI within the time window of reperfusion (12hrs) were included in our study. These patients were divided into two groups: Group 1: optimal medical treatment (OMT) including beta-blockers + Ivabradine; Group 2: OMT including beta-blockers without Ivabradine. within 24 hours of PPCI all the patients did baseline echocardiography (LVEF, LVEDD, LVESD) and SPECT (LVEF, LVEDV, LVESV,17-segment score). After 21 days, echocardiography and SPECT study were repeated.

**Results:** our patients were predominantly males (84.2%) with mean age of  $48.8 \pm 10.53$  yrs. All the patients underwent PPCI and the most revascularized vessel was LAD (93%). Admission HR was  $95.71 \pm 12$  bpm. Both groups revealed no significant difference after 21 days of treatment apart from significant HR reduction to 68 bpm with Ivabradine (group I) ( $P < 0.001$ ). Subgroup analysis of Group I diabetic patients with HR  $> 100$ bpm showed significant reduction of echocardiographic LVESD by  $-4.80 \pm 2.09$  mm; ( $P = 0.015$ ) and significant improvement of SPECT LVEF to  $+14.10 \pm 7.06$  % ( $P = 0.03$ ).

**Conclusion:** In the setting of STEMI treated with PPCI, Ivabradine significantly reduced the HR. In a subgroup of Diabetic patients with HR  $> 100$ bpm, Ivabradine significantly reduced the echocardiographic LVESD and improve the SPECT LVEF.

Diabetic patients with HR>100			
	Diabetic patients with HR > 100 bpm on Ivabradine + BB (n = 10)	Diabetic patients with HR > 100bpm on BB (n = 6)	P.Value
	Mean $\pm$ SD	Mean $\pm$ SD	
HR on admission	106.50 $\pm$ 5.79	107.00 $\pm$ 3.89	0.855
% of HR reduction	38.00 $\pm$ 7.22	24.66 $\pm$ 3.93	0.001
Echo changes	EFe %	7.40 $\pm$ 2.17	6.00 $\pm$ 2.36 0.247
EDDe mm	-2.30 $\pm$ 2.21	-2.16 $\pm$ 1.94	0.905
ESDe mm	-4.80 $\pm$ 2.09	-2.00 $\pm$ 1.67	0.015
SPECT changes	EFSp ml	14.10 $\pm$ 7.06	5.83 $\pm$ 5.98 0.031*
EDVSp ml	-14.30 $\pm$ 16.55	-16.50 $\pm$ 11.16	0.779
ESVSp ml	-22.40 $\pm$ 12.54	-15.50 $\pm$ 12.19	0.300
17-Segment score	-7.40 $\pm$ 2.87	-7.83 $\pm$ 5.03	0.828

**P816**

**What makes inter-hospital mortality difference in acute heart failure: a study from the KorAHF registry**

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**Background:** Inter-hospital mortality difference in acute heart failure (HF) still exists despite emphasis on standardized evidence-based guidelines. Previous research for acute HF lacks comparison of inter-hospital difference.

**Purpose:** We aimed to investigate treatment factors affecting different outcomes of acute HF between hospitals.

**Methods:** We used data from a multi-center national registry for acute HF patients registered between May 2011 and March 2014. We chose two biggest university hospitals in the registry, which are in the same urban area, with similar scale. We assessed data for 1,511 patients, 690 in hospital A and 821 in hospital B. We compared in-hospital mortality, baseline characteristics, HF severity and treatment factors between the two hospitals.

**Results:** In-hospital mortality rate was significantly higher in hospital A than B (8.4% vs. 3.7%,  $p$ -value  $< 0.001$ ). It remained statistically significant even after adjusting for possible confounders including age, hypertension, diabetes, obesity, renal failure, acute myocardial infarction, left ventricular (LV) function, hypotension and hyponatremia (adjusted OR 2.1,  $p$ -value = 0.002). The mortality difference remained significant in various subgroups defined by factors such as age, gender, LV function, de novo or not, and blood pressure. There was significant difference in prescription of beta-blockers and ACEI/ARBs between the hospitals. Beta-blockers were less frequently prescribed in hospital A than B not only before admission (30.4% vs. 37.5%,  $p$ -value 0.004) but also during the hospitalization (48.7% vs. 66.0%,  $p$ -value  $< 0.001$ ). ACEI/ARBs were used similarly before admission but less used for HF with reduced ejection fraction (HFREF) during the hospitalization in hospital A (75.1 vs. 85.9%,  $p$ -value  $< 0.001$ ). ACEI/ARBs were less frequently prescribed in hospital A regardless of blood pressure. Use of parenteral inotropes was more frequent in hospital A in all subgroups, especially in patients with blood



pressure over 100mmHg (53.8% vs. 27.0%,  $p < 0.001$ ). Following adjustment of the prescription of ACEI/ARBs, beta-blockers and parenteral inotropes, inter-hospital mortality difference was disappeared (adjusted OR 1.2,  $p$ -value = 0.544).

**Conclusion:** Though it is hard to clarify the causal relationship in this analysis, the difference in medical care between the hospitals could result in different mortality. Inter-hospital comparison study might contribute to upward standardization of medical treatment of acute HF.

#### P817

##### Hemodynamic effects of continuous positive airway pressure in patients with acute heart failure

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**Background:** Continuous positive airway pressure (CPAP) reduces the need for invasive mechanical ventilation and has been associated, in some reports on patients with acute pulmonary edema (APE) with a reduction of mortality. In current guidelines its use is recommended only in patients with acute heart failure (AHF) and APE unless systemic hypotension is present (SBP < 85 mmHg). However, in clinical practice, the rate of CPAP utilization is very low, varying from 2.3% up to 13.9% (data from registers).

**Aim:** the aim of the present study is to evaluate the hemodynamic effects of CPAP, measured by echocardiography, in patients with AHF.

**Methods:** 30 patients (median age 71 years) with AHF referring to our ICU department, have been enrolled. Of those, 25 (83%) had a first diagnosis of HF, while 5 (17%) presented an AHF decompensation. AHF was defined as a left ventricular ejection fraction (LVEF) < 0.45 associated with at least one criteria among dyspnea at rest, pulmonary rales, radiological signs of pulmonary congestion and/or respiratory distress. Five patients (17%) presented with APE, 12 (40%) with acute HF with normal blood pressure, 2 (6.6%) with AHF with low blood pressure (SBP < 90 mmHg) and 9 (30%) with cardiogenic shock. 93% of patients had an acute coronary syndrome. Echocardiographic hemodynamic assessment was performed at presentation (T0), then at predefined time points after CPAP beginning: 30 min (T1), 24 h (T2) and 48 h (T3).

**Results:** Mean cardiac output (CO) significantly increased during CPAP therapy (3.9 l/min at T0 vs. 4.4 l/min at T3;  $p = 0.01$ ). Mean cardiac index (CI) significantly increased too (2.1 l/min/m<sup>2</sup> at T0 vs. 2.4 l/min/m<sup>2</sup> at T3;  $p = 0.01$ ) as well as mean stroke volume index (28 ml/m<sup>2</sup> at T0 compared to 33 ml/m<sup>2</sup> at T3,  $p = 0.001$ ). There were no significant variation of systolic, diastolic and mean systemic blood pressure during the three days of treatment while LVEF improved at 48 h (33% vs. 36%,  $p = 0.02$ ). Despite a significant increase of the mean central venous pressure (9.23 mmHg vs. 9.83 mmHg,  $p = 0.04$ ), there was no worsening of right ventricular function (TAPSE from 17.6 mm to 17.9 mm) and mean pulmonary systolic pressure significantly decreased (37.1 mmHg at T0 vs. 32.7 mmHg at T4,  $p = 0.03$ ). We have not had MACE.

**Conclusion:** CPAP provides significant hemodynamic support in patients with AHF. This is due to the reduced left ventricle afterload which can increase stroke volume and systemic perfusion. Furthermore in euvoletic patients, CPAP did not worsen right ventricular function. CPAP is safe in this setting of patients and therefore should always be considered as a treatment urgent and indispensable in view of its beneficial effects respiratory and hemodynamic.

#### P818

##### Medium-term outcomes in patients post va-ecmo

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**Purpose:** Venous-Arterial Extracorporeal Membrane Oxygenation (VA-ECMO) has been shown to improve short-term outcomes in patients with refractory cardiogenic shock (RCS). However the medium-term outcomes are unclear. We aim to examine the course of those patients surviving their initial admission requiring VA-ECMO.

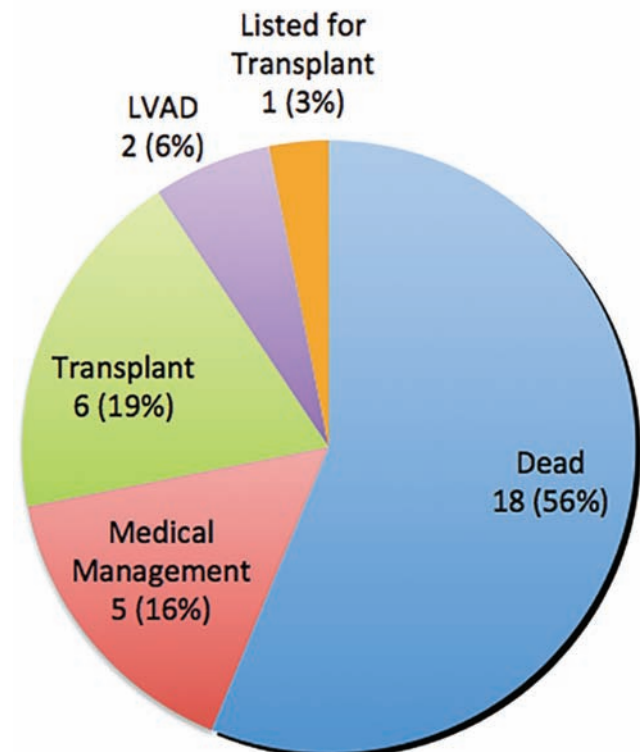
**Methods:** This study was a retrospective, single-centre review of patients who received VA-ECMO for RCS. Baseline patient characteristics, aetiology of RCS, survival as well as cardiovascular and neurological outcomes both at hospital discharge and at 1 year were collected by review of medical records.

**Results:** From 2008 to 2014, 34 patients received VA-ECMO for RCS. Mean age was 43 years (+ 19), 65% were male and total time on VA-ECMO was 6 days (+ 4.3). The aetiology of RCS was acute myocarditis in 9 (25%), post-cardiac surgery in 6 (18%), post heart/lung transplant in 5 (15%), acute myocardial infarction in 4 (12%), decompensated cardiomyopathy in 4 (12%), right heart failure in 3 (9%) and other in 3 (9%). 18 (53%) patients survived to hospital discharge, of whom 14 (41%) made a full neurological recovery. 8 (24%) patients were medically managed without advanced therapy, 6 (18%) required heart transplantation, 3 (9%) required left ventricular assist devices (LVAD) and 1 patient (3%) was listed for

heart transplantation. At 1 year, 14 patients (44%) were still alive. 5 (16%) patients were medically managed. 6 (19%) patients had required heart transplantation. 2 (6%) patients required LVAD support and 1 (3%) was listed for transplant. During this time, 1 patient was newly listed for transplant, 1 patient had progressed from medical therapy to LVAD and 1 patient progressed from LVAD to transplant.

**Conclusion:** Patients receiving VA-ECMO for RCS who survive to discharge have a favourable medium-term prognosis however a significant proportion will require LVAD support or transplantation. A minority of patients survive to 1 year without advanced therapy highlighting the need for all ECMO survivors to have close follow-up by a heart failure/transplant unit

## 1 Year Outcomes



Outcomes Chart

#### P819

##### Trauma-induced cardiomyopathy requiring emergency extracorporeal life support.

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**Introduction:** The sequelae of severe poly-trauma may include myocardial dysfunction followed by acute heart failure and death. Trauma-induced cardiomyopathy or Inverted-Takotsubo Cardiomyopathy (ITC) is a variant of stress cardiomyopathy, characterized by a contractile abnormality with extensive left ventricular circumferential dyskinesia or akinesia with a hyperkinetic apex. We report our experience with refractory cardiogenic shock and/or cardiac arrest, treated with extracorporeal life support.

**Methods:** From June 2008 to December 2015, we treated 6 adult poly-trauma patients (5 men, 1 woman, mean age:  $28.4 \pm 15.4$  years, mean ISS score  $52.5 \pm 17.2$ ) with veno-arterial (V-A) extracorporeal life support for cardiopulmonary failure/cardiac arrest refractory to conventional treatment, due to inverted-Takotsubo cardiomyopathy. We used a miniaturized extracorporeal life support (ECLS) device. **RESULTS.** ITC myocardial dysfunction appeared  $14.6 \pm 12.4$  h after intensive care unit admission and rapidly evolved to refractory cardiopulmonary failure and cardiac arrest (within  $3.4 \pm 3.2$  h of the onset). At ECLS, initiation median pH was  $7.11 \pm 0.15$  ( $6.91$ - $7.25$ ), median lactate was  $6.9 \pm 3.1$  ( $4$ - $10$ ) mmol/l and median vasoactive-inotropic score was  $184.4 \pm 51.4$   $\mu$ g/kg/min. Tissue perfusion

improved significantly within 4 h on ECLS. Cardiac function improved gradually but consistently. Initial median ejection fraction was  $12.8 \pm 5.1\%$  and median global longitudinal strain test was  $-7.1 \pm 4.8$ . At complete cardiac recovery, they were  $60.51 \pm 8.1$  and  $-17.83 \pm 3.2\%$ , respectively. After that, 2 patients survived and were sent to neurological rehabilitation before hospital discharge. In the other 2 cases, post-traumatic cerebral death occurred and they underwent organ explantation.

**Conclusions:** Rapid heparin-free ECLS may improve outcome in the most severe cases of poly-traumatized patients demonstrating refractory trauma-induced cardiomyopathy.

**P820**

**Prognostic value of decreased peripheral congestion detected by Bioelectrical Impedance Vector Analysis (BIVA) in patients hospitalized for acute heart failure.**

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**Background:** Acute heart failure (AHF) is a frequent reason for patients to be admitted. 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 these patients. Bioelectrical Impedance Vector Analysis (BIVA) is a validated technique able to quantify fluid overload.

**Purpose:** To investigate the prognostic role of quantitative reduction of congestion during hospitalization assessed by BIVA serial evaluations in patients admitted for AHF.

**Methods:** a prospective, multicenter, observational study in AHF and no AHF patients in 3 Emergency Departments centres in Italy. Clinical data and BIVA evaluations were performed at admission (t0), and discharge (tdis). A follow-up phone call was carried out at 90-days.

**Results:** 336 patients were enrolled (221 AHF and 115 no AHF patients). We found that clinical signs showed the most powerful prognostic relevance. In particular the presence of rales and lower limb edema at tdis, were linked with events relapse at 90 days. At t0, congestion detected by BIVA was observed only in AHF group, and significantly decreased at tdis. An increase of Resistance variation (dR/H) > 11 Ohm/m during hospitalization, was associated with survival. BIVA showed significant results in predicting total events, both at T0 (AUC 0.56, p < 0.04) and at Tdis (AUC 0.57, p < 0.03). When combined with clinical signs, BIVA showed a very good predictive value for cardiovascular events at 90 days (AUC 0.97, p < 0.0001).

**Conclusions:** In AHF patients, an accurate physical examination evaluating the presence of rales and lower limbs edema, remains the cornerstone in the management of patients with AHF. A congestion reduction, obtained as a consequence of therapies and detected through BIVA analysis, with an increase of dR/H > 11 Ohm/m during hospitalization seems to be associated with increased 90 day survival in patients admitted for AHF.

**P821**

**Clinical characteristics of patients with moderate to severe mitral regurgitation admitted for an episode of acute heart failure**

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**Objective:** To determine the clinical characteristics of patients with moderate to severe mitral regurgitation, admitted for acute heart failure.

**Methods:** It is a limited clinical observational study on one year period-01 October 2014 to 01 October 2015, on patients presenting with moderate to severe mitral regurgitation and an episode of acute heart failure.

**Results:** We study 78 patients, 55 female (70%) and 23 male (30%), with mean age of all patients' group 69,7 years of age. The study shows that more than two thirds of the selected patients were with acute ischaemic attack-n 68, 87%, related to left main or multivessel disease-n 59, 75%. Only two patients, 2%, had prolapse or flail mitral valve. Patients with moderate to severe functional mitral regurgitation due to primary dilated cardiomyopathy, were 8, 10%. Trough the study we registered 14 % in hospital death and one patient died one month after discharge.

**Conclusion:** Ischaemic heart disease and associated risk factors-arterial hypertension, diabetes, atrial fibrillation, chronic renal disease, linked to acute ischaemic attack are the prevalent causes for acute heart failure in patients with moderate to severe mitral regurgitation.

**P822**

**Acute heart failure and infections**

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**Objective:** Acute heart failure (AHF) can be triggered by "some" risk factors. We looked at infection as a trigger of AHF.

**Patients and methods:** From 1.st June to 31.st December 778 patients (pts) were admitted to Internal Department, 140 with AHF (71 ys old, 47% men), diagnosed clinically (NTproBNP, ECG, echocardiography included). Infection was diagnosed clinically (CRP, leukocytes, FW, X-ray included).

**Results:** \* infections deteriorated chronic HF in 36 pts (26% of AHF admissions), uncontrolled hypertension 25 pts (18%), diabetes 24 pts (17 %) \*\* infections: pneumonia/acute bronchitis (17 from 36 pts, 47%), uroinfections (10/36 pts, 28%), other (9/36 pts, 25%). \*\*\* Characteristics of AHF pts (infections/noninfections): women (53%/55%), age (72ys/69ys), smokers (39%/32%), less mobility of pts (22%/16%), comorbidities: diabetes (35%/28%), renal insufficiency (45%/36%), anemia (15%/12%), NYHA III (40%/26%), NYHA IV (12%/8%).

**Conclusion:** AHF patients admitted due to infection are: more women, elderly, smokers, weaker pts with more comorbidities (diabetes, renal insufficiency, anemia) and higher NYHA classes.

**P823**

**Descriptiveness predictor of acute heart failure development in patients with acute myocardial infarction and obesity.**

N Ryndina<sup>1</sup>; G Ganna Tytova<sup>1</sup>; A Yermak<sup>1</sup>; T Soe<sup>1</sup>; PG Kravchun<sup>1</sup>; <sup>1</sup>Kharkiv National Medical University, Kharkiv, Ukraine; **Purpose:** To investigate predictor informativeness of copeptin, MRproADM and troponin I in the development of acute heart failure in patients with acute myocardial infarction and obesity

**Material and methods:** 75 patients with acute myocardial infarction and obesity were examined. All patients were divided into 2 groups according to presence or absence of acute heart failure (AHF). 1st group consisted of 39 patients who had a complicated AMI by acute heart failure: Killip class 1 was found in 23% of patients, Killip class 2- in 27% and 50% of patients had Killip class 3. 1Ind group - 36 obese patients with acute myocardial infarction without acute heart failure.

Table 1. Data results

Data, units	Patients with AMI and obesity		
I group	II group		
Copeptin ng/ml	179,29 ± 13,04	149,59 ± 13,85	0,05
MRproADM ng/ml	649,21 ± 26,38	559,77 ± 24,49	<0,01
Troponin I ng/ml	5,42 ± 1,35	7,06 ± 1,13	> 0,05

**Results:** Results are shown in the Table 1. Patients of the 1st group found significantly higher levels of MRproADM - 19.85% (p < 0.01) compared with patients of the 2nd group. Concentration of copeptine revealed a tendency (p = 0.05) to increase the chance of appearance of AHF in patients with AMI and obesity, which did not reach the level of probability when compared with patients of second group. Troponin I level did not differ significantly in both groups (>0,05).

**Conclusion:** The results indicate that the presence of AHF in patients with AMI and obesity is associated with increased activity of MRproADM, which makes it possible to use it as a marker of prognosis.

Abstract 60801 Table

AH	AF	Diabetes	Chronic renal disease	Acute ischaemic attack	EF<35%	LM or multivessel disease	Mechanical moderate to severe MR (prolapse or flail mitral valve)	Functional MR
n 70, 89%	n 60, 76%	n 44, 56%	n 66, 84%	n 68, 87%	n 31, 39%	n 59, 75%	n 2, 2%	n 8, 10%

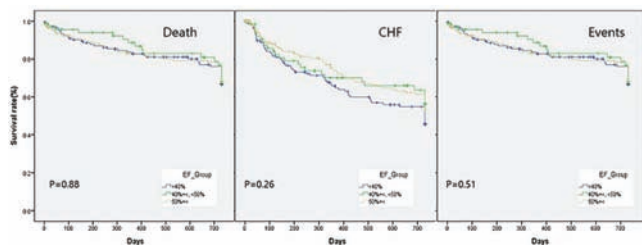
## P824

## Mid-term outcomes of acute heart failure with preserved left ventricular ejection fraction

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**Purpose:** Approximately 40~50% of patients with acute heart failure (AHF) have preserved left ventricular ejection fraction (LV EF). They are known to have different clinical characteristics, but similar prognosis compared with those with decreased LVEF. However, long-term outcomes of acute heart failure with preserved EF (HFpEF) were rarely investigated in Korea, especially in one community.

**Method:** We enrolled 405 patients with AHF from Jan. 2005 to July 2013. They were divided into three groups according to LV ejection fraction; reduced EF (Group 1, EF < 40%, n = 142), mild LV dysfunction (Group 2, 40 ≤ EF < 50, n = 72) and normal EF group (Group 3, EF ≥ 50, n = 191). Clinical characteristics and laboratory findings were reviewed from medical records. They were followed at least 2 yrs. Clinical end-points were death or readmission due to congestive HF (CHF). Results; Total 191 patients (47.2%) had normal EF. They were older (69.82 ± 14.4, 71.85 ± 14.3 vs. 75.77 ± 11.4 years, p < 0.001) and female predominant (40%, 52.8% vs 70.2%, p < 0.001). Among the three groups, Gr 3 showed the least peak proBNP level (8717.89 ± 8789.2, 6226.40 ± 7871.5 vs. 5068.37 ± 6157.9, p < 0.001) and better CKMB and troponin level. 1-year and 2-year survival rates were not different in three groups (84.5% : 73.2%, 90.2% : 76.4% and 84.2% : 74.2%, p = 0.876). 2-year CHF-free survival rates were low in all groups but not different (57.7%, 66.7% vs. 65.3%, p = 0.260). These findings consisted with age and gender subgroups. Conclusions; LVEF was preserved in 47% of patients with acute decompensated heart failure. Their mid-term prognosis was as poor as those with reduced LVEF.



2 years cumulative survival curve

## P825

## Reversible acute heart failure in young females

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**Background:** There is an increased awareness and interest in young females who present with acute heart failure (AHF) or cardiogenic shock following physical or emotional discomfort. These physical stimuli can be time of ovulation, pre-menstrual discomfort, any forms of anaesthesia, abdominal surgery or caesarean section. Purpose. The purpose of this study is to report demographics of acute heart failure or cardiogenic shock in young females, their clinical and echocardiographic features, management and follow-up Methods: Eight young females (age range 19-38 years) who presented with acute heart failure with subsequent complete recovery of systolic and diastolic function over one week and without any known cause of AHF are reported.

**Results:** Four patients presented with acute pulmonary oedema, three had cardiogenic shock and one patient developed rash followed by syncope and persistent hypotension. Initiating events were caesarean section in two, acute on chronic cholecystitis in two, puncture for cardiac catheterisation, premedication before general anaesthesia and ovulation in one each and no identifiable initiating event in the remaining one. All the patients had evidence of global or segmental left ventricular systolic dysfunction, rise in BNP and troponins. None had associated right ventricular dysfunction or arrhythmias. Recovery was complete in all. One patient required Intra-aortic balloon pump insertion for four days. The patients in shock were managed with fluids and those in pulmonary oedema with diuretics and oxygen therapy. Ivabradine was used to control sinus tachycardia in five patients.

**Conclusion:** Transient global or segmental left ventricular systolic dysfunction leading to AHF or cardiogenic shock is rare in young females. Possibly, it is a variant of Takotsubo cardiomyopathy.

## P826

## Clinical characteristics and outcomes of elderly patients with acute heart failure: a secondary analysis of the ALARM-HF registry

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**Introduction:** Clinical characteristics and outcomes of elderly patients with acute heart failure (AHF) differ from younger patients according to previous European and American registries.

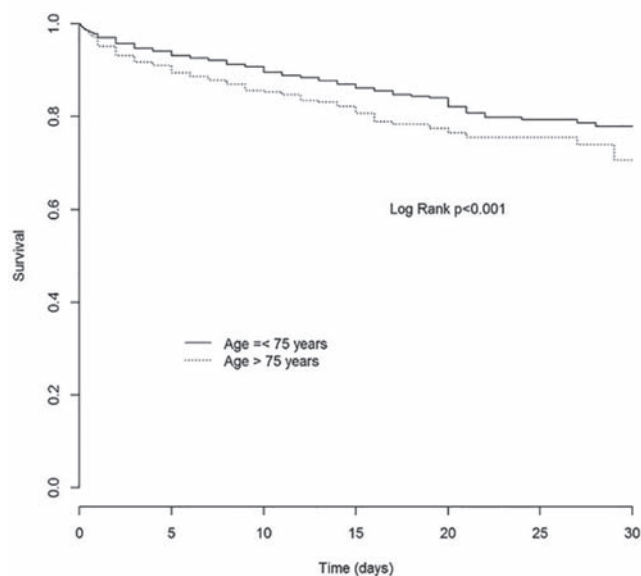
**Aim:** To compare the clinical characteristics and in-hospital outcomes between elderly and younger patients with AHF who were enrolled in the global survey Acute Heart Failure Global Survey of Standard Treatment (ALARM-HF).

**Methods:** We performed a secondary analysis of the ALARM-HF, a retrospective survey via questionnaire that included 4953 AHF patients from 9 countries. Patients were divided to 2 age groups using a cut-off age of 75 years (elderly > 75, younger ≤ 75). Age groups were compared regarding their clinical characteristics and mortality up to either hospital discharge or 30 days of hospitalization.

**Results:** The group of elderly patients comprised 29% of the study population, and compared to the younger age group, included a higher percentage of female patients (49.4% vs 32.7% in the younger group, p < 0.001), and had more frequently a history of arterial hypertension (74.8% vs 68.3%, p < 0.001), coronary artery disease (36.6% vs 28.3%, p < 0.001), chronic HF (38.6% vs 35.4%, p = 0.033), atrial fibrillation (33.2% vs 20.9%, p < 0.001), and chronic renal dysfunction (28.9% vs 18.3%, p < 0.001); more frequently had as underlying cause of AHF arrhythmias (29.1% vs 26%, p = 0.029), infections (18.3% vs 15.5%, p = 0.017) and valvular heart diseases (15% vs 12.7%, p = 0.035); and more often presented with pulmonary edema (39.6% vs 35.6%, p = 0.008), with preserved systolic arterial pressure (> 110 mmHg: 69.8% vs 59.3%, p < 0.001), and preserved left ventricular ejection fraction (LVEF) (26.4% vs 21.8%, p = 0.004). Younger patients were more frequently than their elderly counterparts obese (28.3% vs 22.1% in elderly, p < 0.001) and current smokers (29.8% vs 8.5%, p < 0.001); more often had acute coronary syndrome as underlying cause (40.4% vs 28.4%, p < 0.001) and presented with cardiogenic shock (12.6% vs 9.6%, p = 0.003) with reduced LVEF (78.2% vs 73.6%, p = 0.004). In-hospital mortality of elderly patients was higher than their younger counterparts (13.5% vs 9%; median survival 24.7 ± 0.4 vs 26 ± 0.3 days, p < 0.001).

**Conclusions:** Elderly as compared to younger patients with AHF have more comorbidities and higher in-hospital mortality.

## Kaplan-Meier Curves by age category



In-hospital survival by age category



**P827**  
**Acute heart failure in patients with acute coronary syndrome: a retrospective analysis**

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**Relevance:** Acute heart failure (AHF) is a frequent complication of acute coronary syndrome (ACS) with ST-segment elevation. Presence of AHF is associated with a 3-4-fold increase in hospital mortality, in particular the incidence of cardiogenic shock ranges from 7% to 15%, and hospital mortality reaches 78%. Objective. The objective of our work was to assess the prevalence of AHF in patients with ACS, features of the sex-age structure and prognosis for such patients based on a retrospective analysis. **Methods and materials.** We conducted a retrospective analysis of the prevalence of AHF in patients with ACS (class III-IV) for 2010-2014 at the Cardiology Department of the city hospital. A total of 2167 patients were on treatment. 1938 patients were discharged from the hospital, 229 patients died. **Results.** It was established that the signs of AHF were diagnosed in 317 patients (14.63%). The sex structure of patients with AHF was distributed as follows: 185 were men (58.36%) with the average age of 64.8±6.9 years, 132 were women (41.64%) with the average age of 76.8±3.5. The age characteristic of patients with AHF differs slightly among men and women, thus in the group aged 40 and under and in the age group aged 40-49 there were only men, and in the group aged 50-59 men dominated over women with 46 men (24.86%) and 8 women (6.06%) respectively, p=0.05; there was no significant difference between men and women in the group aged 60-69 with 28.65% and 28.03% respectively, whereas among patients older than 70 years AHF was found significantly more often among women than men: 36.22% and 65.91%, p=0.05. In 237 patients (75%) AHF was diagnosed with the first heart attack. Mortality after myocardial infarction is 229 people (10.57%). AHF has made significant contribution to the causes of death in patients with ACS: in particular, there were 114 deaths (49.78%). However, among the discharged patients there were 203 patients with early diagnosed AHF (10.47%).

**Conclusions:** Therefore, we found that the prevalence of AHF is quite substantial (14.63%) among patients who died, the share of people with AHF is 47.78%, there was no significant difference between men and women but AHF was diagnosed in men at a young age while in women at the age of over 70.

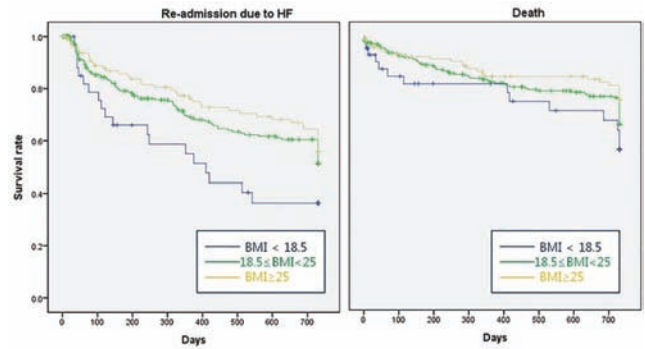
**P828**  
**Body mass index and prognosis in acute decompensated heart failure**

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**Purpose:** In patients with chronic heart failure (CHF), previous studies have reported reduced mortality rates in patients with increased body mass index (BMI). The aim of this study was to determine whether BMI influences the mortality risk in acute decompensated HF.

**Method:** We enrolled 419 patients with AHF from Jan. 2005 to July 2013. They were divided into three groups; underweight group (Group 1, BMI < 18.5, n=43), normal (Group 2, 18.5≤BMI<25, n=253) and overweight to obese group (Group 3, BMI≥25, n=123). Clinical characteristics and laboratory findings were reviewed from medical records. They were followed at least 2 yrs. Clinical end-points were death or readmission due to congestive HF (CHF). **Results;** Patients of higher BMI group were younger (73.22±12.7 vs. 70.82±14.2, p=0.003), less female portion (74% vs. 55%, p=0.036) and had more diabetes (23%, 20.5% vs. 39%, p=0.001). Among the three groups, Gr 3 showed the least peak proBNP level (10745.29±1894.6, 8329.83±557.8 vs. 3951.61±376.8, p<0.001) and better echocardiographic parameters, such as LV EF and E/E'. By BMI category, patients who were normal and overweight had mortality risks that were 27.7% and 20.3%, respectively, lower as compared with the mortality risk of healthy weight patients with HF, whereas patients who were underweight had a 32.6%. 2-year heart failure rate and 2 year mortality were the highest in underweight group. (Cox hazard ratio 1.987, 95% CI; 1.15-3.43; p=0.014 and Cox hazard ratio 2.034, 95% CI; 1.06-3.92; p=0.034) **Conclusions;** In this single center cohort of hospitalized patients with acute decompensated HF, higher BMI was associated with a significantly lower mortality and readmission risk independent of other prognostic variables.



2 years cumulative survival curve

**P829**  
**Chitotriosidase enzyme can be a negative acute phase protein in acute heart failure unlike coronary artery diseases**

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**Introduction:** Heart Failure (HF) is a complex, neurohumoral and inflammatory syndrome. Recent studies show that proinflammatory cytokines contribute heart's systolic or diastolic dysfunction causing cardiac depression. Chitotriosidase (CHIT), an enzyme released from active macrophages, plays a role in many diseases involving inflammation. Therewithal, it has been observed that CHIT activity in plasma is significantly high in ischemic heart diseases with arterial inflammation. This thesis aims to figure out the role of CHIT in HF and the relationship between other cytokines.

**Method:** 43 Newyork Heart Association (NYHA) class III/IV acute heart failure (AHF) patients who were hospitalized in the coronary intensive care unit (CICU), 48 chronic heart failure (CHF) patients and 45 healthy controls included in the study. All participants' detailed echocardiography, doppler and tissue doppler measurements were performed and left ventricular ejection fractions (LVEF) were calculated by Simpson method. All participants' plasma CHIT IL-1β, TNF-α, IL-6, Hs-CRP and NT-proBNP levels were determined by ELISA method.

**Results:** The lowest CHIT activity in plasma (527,876±323,04 ng/ml) is detected in AHF patients. It was observed that when LVEF of acute heart failure patients decrease their CHIT activity levels decrease as well. Also a negative correlation (p=0,038 and r=-0,32) occurred between CHIT activity levels and NYHA class levels in AHF patients.

**Conclusion:** CHIT enzyme may play a role as a negative acute phase protein in AHF. Plasma CHIT value of AHF patients decreases when left ventricular systolic dysfunction increases and it is negatively correlated with NYHA values.

**P830**  
**Clinical characteristics, management and outcomes of very elderly patients hospitalized with heart failure in internal medicine units of Tuscany**

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**Introduction:** In Italy most of very elderly patients (pts), defined as age 85 years and older, with Heart Failure (HF) are admitted in Internal Medicine Units (IMU). In these pts HF is a major cause of morbidity and mortality and the prevalence

Abstract	60069		Correlation		Analyse		in		AHF		patients	
	NT-proBNP		hs-CRP		IL-6		IL-1		CHIT		TNF-α	
p	r	p	r	p	r	p	r	p	r	p	r	p
NYHA	0,683	0,06	0,433	0,12	0,665	0,07	0,359	0,14	0,038	-0,32	0,102	0,25
sPAP	0,226	0,19	0,090	-0,26	0,320	-0,15	0,087	-0,26	0,705	-0,06	0,707	0,06
LVEF	0,246	-0,18	0,678	-0,07	0,912	-0,02	0,064	-0,28	0,022	0,35	0,136	-0,23
RVEF	0,835	-0,03	0,035	-0,32	0,171	-0,21	0,546	-0,10	0,974	-0,01	0,938	-0,01

is expected to increase in the future. However these pts are under-represented in randomized clinical trials. The objective of the present study was to evaluate clinical characteristics, management and outcomes of unselected very elderly pts hospitalized with HF in IMU of Tuscany (Italian region with 3.7 million inhabitants). Methods. A multicenter observational study on pts consecutively hospitalized for HF between January 30th and February 28th 2014 in most of Tuscany IMU (32 of 35) was performed. There are not exclusion criteria. Clinical and echocardiographic data was collected; the degree of disability was calculated by Barthel Index. The pooled population (770 pts) was divided into two age groups:  $\geq 85$  years (groupA: n=365, age  $89.3 \pm 3.4$  years) and  $< 85$  years (groupB: n=405,  $76.3 \pm 7.6$  years) for comparison. Results. Female gender was more common among the very elderly (64.9 vs 47.4%,  $p < 0.0001$ ). In the groupA a lower prevalence for diabetes (27.7 vs 41.5%,  $p = 0.001$ ), but an higher prevalence of chronic kidney disease (96.7 vs 90.4%,  $p = 0.006$ ), dementia (46 vs 17.3%,  $p < 0.0001$ ) and of three or more co-morbidities (78.3 vs 65.4%,  $p = 0.001$ ) was evident. The echocardiogram was performed in 204 (55.9%) pts of groupA and in 287 (70.9%) pts of groupB ( $p < 0.001$ ); a preserved ejection fraction was revealed in 45.6% of pts in the groupA and in 37.6% of groupB ( $p = 0.989$ ). The mean length of hospital stay was comparable (groupA:  $7.6 \pm 4.3$  days, groupB:  $8.2 \pm 5.3$  days,  $p = 0.098$ ). Overall in-hospital death occurred in 27 (7.4%) pts of groupA and in 19 (4.7%) of groupB ( $p = 0.475$ ). At discharge in the very elderly a lower prescription of  $\beta$ -blockers, aldosterone antagonists, statins and warfarin ( $p < 0.01$  for all), a greater disability (61.6% of pts with Barthel Index score  $\leq 40$ ,  $p < 0.0001$ ), a greater number of transfer in a nursing home or geriatric wards ( $p = 0.02$ ) than groupB were observed; a follow-up program (home care or in-hospital program) was performed less frequently in older patients ( $p = 0.02$  vs groupB).

**Conclusions:** This study revealed that in the real world of Tuscany IMU the very elderly constitute 47% of pts hospitalized with HF and that in these pts diagnostic and therapeutic approach is different from HF guidelines. The HF very elderly, compared with younger pts, are undertreated and the echocardiogram and follow-up program were carried out less frequently.

### P831

#### Iron deficiency and anemia in acute heart failure: a problem?

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**Introduction:** Anemia is a frequent comorbidity in heart failure and further worsens prognosis and disability. Regardless of anemia status, iron deficiency (ID) is a common and usually unidentified problem in patients with heart failure.

**Purposes:** To evaluate the prognostic impact of ID, with or without the presence of anemia, in patients (P) with acute heart failure (AHF).

**Methods:** Retrospective study with 201 P, admitted in a cardiac intensive care unit, between February 2010 and September 2015. The selected patients (n = 104) had a iron study done. Anemia has been defined with hemoglobin  $< 13$  g/dL in men and  $< 12$  g/dL in women. IF was classified according to the ferritin value: absolute IF – ferritin  $< 100$  ng/ml; relative IF – ferritin between 100-300 ng/mL and transferrin saturation  $< 20\%$ . After the two variable association, the sample was divided into 3 groups: group 1 (G1: without anemia and without IF, n = 35), group 2 (G2: without anemia but with IF, n = 22) and group 3 (G3: with anemia and with IF, n = 27). Clinical follow-up (24 months) was performed targeting for readmission with AHF.

**Results:** The sample had an average age of  $68 \pm 14$  years old with a majority of male (78%). In 28% P the etiology was ischemic. The average FEVE was of  $33 \pm 12\%$ . Readmission with AHF occurred in 38% and mortality was of 40%. Anemia has been identified in 51% of P. In what concerns to IF: 68% didn't have IF, 16% had absolute IF and 16% had relative IF. The groups presented similar clinical and analytical characteristics: congestive HF (G1 100% vs G2 91% vs G3 100%), ischemic etiology (G1 28%, G2 4.1% and G3 22%) and NT-proBNP values (G1  $13270 \pm 10513$  pg/nL vs G2  $13895 \pm 16897$  pg/nL vs G3  $13895 \pm 16897$  pg/nL). Regarding therapeutics, most had intravenous diuretic (G1 72% vs G2 62% vs G3 63%). Inotropic support with dobutamine was used in all the groups (G1 24% vs G2 14% vs G3 26%) and levosimendan was predominantly used in G1 (G1 76% vs G2 32% vs G3 37%). Noninvasive ventilation was used in 52% of G1, 41% of G2 and 56% of G3. The survival rate was statistically similar for the 3 groups at 12 and 24 months (79% vs 63% vs 54% e 72% vs 51% vs 29%; Log rank  $P = 0.089$ ).

The multivariate analysis showed that IF was not a predictor of follow-up events, even if there is an higher risk trend in this P (HZ = 2.3, HF 95%=[0.8-6.7],  $P = 0.13$ ). Patients with both anemia and IF had a 3 times superior mortality risk (HZ=2.8, HF 95%=[1.1-7.5],  $P = 0.04$ ).

**Conclusions:** According to our data, the IF has an impact in the prognosis when associated with anemia, in patients with HF.

### P832

#### Adrenaline use is related to prominent deterioration in cardiac and renal biomarker profiles in cardiogenic shock

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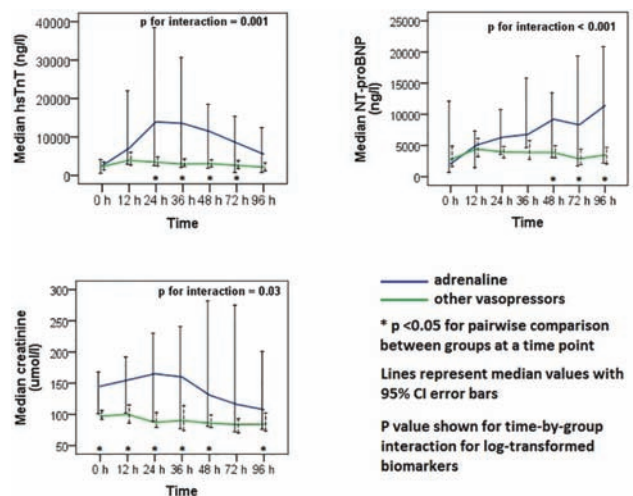
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**Purpose:** Use of adrenaline has been proposed to be harmful in cardiogenic shock (CS) due to, for example, an increase in oxygen consumption and myocardial ischemia. We are, to our knowledge, the first to assess serial measurements of cardiac and renal biomarkers in patients with CS in order to detect patterns in injury and function of these organs over time in relation to adrenaline use.

**Methods:** The CardShock study is a European multicenter study including 219 patients with CS. Serial plasma samples were collected in 178 patients, of which 95 had samples taken until 96 hours from the study baseline. The samples were immediately frozen at  $-80^{\circ}\text{C}$ . Creatinine, high-sensitivity troponin T (hsTnT) and NT-proBNP were analysed centrally. Use of vasoactive medications was registered until 96 hours from baseline. Survival analyses were performed with X2-test and propensity score adjustment. Differences in biomarkers at each time point between groups were analyzed with Mann-Whitney U test. Linear mixed modeling was used to analyse differences in changes of biomarkers between groups over time.

**Results:** Of the patients with baseline plasma samples, 146 received vasopressors. In this cohort, mean age was 66 (SD 12) years, 74% were men and 82% had acute coronary syndrome as CS etiology. Adrenaline was used in 29 (20%) patients whereas other vasopressors (noradrenaline, dopamine) were used in 117 (80%) patients. Overall 90-day mortality was 46% and significantly higher in adrenaline group vs other vasopressors: 90% vs 35%,  $p < 0.001$ . The strong association of adrenaline with increased mortality remained even after propensity score adjustment. Evolution of cardiac and renal biomarker levels were much worse in adrenaline patients over the first 96 hours (figure). Especially NT-proBNP levels persistently increased over time in adrenaline patients.

**Conclusions:** Compared with use of other vasopressors, adrenaline use was associated with markedly worse evolution of cardiac and renal biomarker profiles over the initial 96 hours in CS. This may, in part, explain significantly higher mortality among patients receiving adrenaline.



figure

**P833**

**Optimisation of decongestion in acute decompensated heart failure: role of tolvaptan and aquapheresis.**

Otsuka  
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**Background:** Symptom relief for acute decompensated heart failure (ADHF) requires decongestive therapies. Standard of care is based on loop diuresis, but vasopressin inhibition and aquapheresis offer additional options. We performed a single center pilot study in ADHF patients to compare these three approaches.

**Methods:** We enrolled 45 patients with ADHF with evidence of volume overload, BNP > 300, serum Na < 145, and serum creatinine < 3. They were randomized within 12 hours of admission to either 1) standard of care (SC) - continuous drip furosemide, 2) tolvaptan (Tol), SC plus daily dose of tolvaptan, or 3) aquapheresis (Aq). Data were collected at baseline, and daily until end of treatment or 4 days. Results Baseline characteristics were similar between the three groups. Volume loss in SC and Aq groups were similar, while greater in the Tol group. Dyspnea was similarly improved in all 3 groups. Effect of treatment on BUN, creatinine, and urinary nGAL suggest a neutral effect of SC and Tol on renal function, while Aq may lead to early renal injury. Conclusions In this pilot trial comparing three approaches to decongestion, the addition of tolvaptan to loop diuretic appeared to achieve the best balance between volume removal and renal injury. In contrast, aquapheresis did not remove more volume and was associated with worse quality of life and a rise in uNGAL.

Table

	Standard care (SC, n = 15)	Tolvaptan (Tol, n = 15)	Aquapheresis (Aq, n = 15)
Serum Na	139	139	140
Creatinine	1.5	1.69	1.63
uNGAL	17.13	4.27	18.68
BNP	638	825	1265
I/O (liters)	-5.7	-8.9*	-5.8†
ΔMLWHF	-2.5	-2	+ 8.5
ΔDyspnea score	-30	-28	-31
LOS	6.5	7	5
30 day readmissions	0	4	5*
30 day death	3	1	1
Δcreatinine	0.13	0.12	-0.02
ΔBNP	-252	-313	-234
ΔuNGAL	-2.18	0.46	8.65*

All values medians. \* p < 0.05 vs SC, † p < 0.05 vs. Tol. MLWHF - Minnesota Living with Heart Failure quality of life score, LOS - length of stay.

**CHRONIC HEART FAILURE**

**P834**

**Telephone intervention in chronic heart failure**

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**Background:** Heart failure (HF) remains a serious global health problem associated with poor quality of life, diminished functional class and frequent hospital admissions which leads to heavy personal, social, and economic burdens. Nurse-based telephone interventions have been associated with clear clinical benefits for patients with HF, in the West; however, their effectiveness is unknown in this region. Objective The purpose of this study was to assess the effectiveness of a telephone intervention in patients with heart failure (HF) attending a nurse-led HF clinic in King Abdulaziz cardiac Center (KACC). Method Quality initiative project which assigned the first 50 consecutive HF patients to standard care in the nurse-led HF out-patient clinic (control group) and the second 50 consecutive patients to standard care in addition to a telephone intervention (Intervention group) Patient's symptoms, quality of life, risk factor control was followed over 3 months. Analysis was performed using SPSS Advanced Statistics for Windows, version 18. Result A total of 100 patients (75%

Male, mean age 62 years) were included in this study. The patients who received telephone calls showed improvement in blood sugar control and LDL control. Significant Improvement in medication adherence in the intervention group compared to the control group using Morisky Medication Adherence Scale (MMAS-8-Item) Conclusion Out comes Improves in the cardiac patient who received a Telephone follow on addition to regular care

**P835**

**Is undiagnosed heart failure common on orthopaedic wards?**

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**Introduction:** Approximately 1–2% of the adult population in the United Kingdom has heart failure (HF), with the prevalence rising to ≥10% among people aged 70 years or older. Osteoarthritis, rheumatoid arthritis and orthopaedic fractures share both risk factors for HF and potentially a common pathophysiology.

**Purpose:** To discover whether undiagnosed heart failure was common in patients on orthopaedic wards and to explore diagnostic strategies.

**Methods:** The study was conducted on 2 orthopaedic wards, one receiving elective admissions (group A) and the other receiving patients admitted following fragility fractures (group B). Between 20th January 2014 and 5th April 2015, 419 patients over the age of 65 were screened. After exclusion of patients with known heart failure, 100 consecutive new patients in each group consented to participate. Serum BNP was measured and if >35 ng/l (pg/ml), transthoracic echocardiography was performed using British Society of Echocardiography accredited physiologists. Diagnosis of heart failure was based on the European Society of Cardiology definition, sub-classified in to HF with preserved (HFpEF) or reduced (HFrEF) ejection fraction (EF).

**Results:** Of the 156 patients admitted for elective orthopaedic surgery, 10 (6%) were known to have heart failure. In the remaining group of 146, 100 patients agreed to participate in the study (mean age 74 years, female 57%, hypertension 35%, ischaemic heart disease (IHD) 4%, AF 3%, Diabetes 6%). 65% had possible heart failure symptoms and 6% had heart failure related signs. Their mean haemoglobin (Hb) was 133, creatinine 76, TSH 2.1, PT 11. ECG abnormalities were identified in 50% and chest X rays were suggestive of heart failure were 24%. The BNP level was above 35 pg/ml in 52% (maximum 677 pg/ml) of which 3 had HFpEF and 3 had asymptomatic low EF (6% undiagnosed HF). In the 263 patients with fragility fractures, 39 (15%) had known HF, and a further 14 (5%) were diagnosed with heart failure by the clinical team following admission. Of the remaining 210, 100 consented to participate (mean age 82 years, female 83%, hypertension 31%, IHD 7%, AF 8%, Diabetes 8%). 57% had heart failure related symptoms and signs. Their mean Hb was 108 (post fracture), creatinine 78, TSH 2.1, PT 12.8 (within normal range). ECG abnormalities were found in 58% and the CXR was suggestive of heart failure in 23%. BNP level was above 35 pg/ml in 84% (maximum 759 pg/ml) and 3 proved to have HFrEF, 10 had HFpEF and 1 has asymptomatic low EF (14% undiagnosed HF).

**Conclusion:** Patients with fragility fractures were older and had more risk factors for HF. 84% had a serum BNP above the threshold of which 17% had heart failure. Screening for undiagnosed heart failure identified a significant number of new cases, particularly in the fragility fracture population. Screening for HF should be considered in orthogeriatric units.

**P836**

**Cardiac tumor mimicking heart failure**

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**Introduction:** Cardiac tumors (CT) are extremely rare and may be asymptomatic or have symptoms that mimic heart failure (HF). We studied the cases simulating HF in order to recognize the different pathophysiologies than can cause these symptoms. Method: We retrospectively reviewed patients with a diagnosis of CT from 1979 to 2015 and analyzed the most outstanding of these epidemiological characteristics. Our sample was selected from a surgical serie so that data may differ from other series.

**Results:** We found 55 cases of which 30 CT simulated HF symptoms. Average age was 55 ± 17 years, with a 57% of women. The diagnosis was achieved by transthoracic echocardiography in 83% of cases. With regard to histopathological diagnosis, 20 were benign tumors (66.7%), being mostly of them myxomas and only one hamartoma. Of the remaining 10 CT, two patients were cardiac angiosarcomas and 8 were secondary tumors. The most common symptoms were dyspnoea (100% of patients), congestive heart failure (33%), palpitations or oedema (16%) and constitutional syndrome (13%). Regarding the pathophysiology of the symptoms, fourteen (46.7%) cases were due to valvular obstruction in the outflow tract, seven (23%) to direct invasion of the myocardium or pericardium; among other causes, there were two (6.7%) cases of pulmonary embolism, two (6.7%) adjacent lung invasion or



metastasis, one (3.3%) case of valvular regurgitation, three (10%) cases of constitutional syndrome and five (16%) cases from unknown causes. No patient died during surgery and mortality directly related to the tumor during follow-up was 23.3%, in all cases they were malignant neoplasms.

**Conclusions:** Cardiac tumors can mimic symptoms of HF through different mechanisms. Despite they are an unfrequent etiology of heart failure or dyspnoea, it's adequate diagnosis is mandatory because they are in most cases treatable causes.

### P837

#### Prognostic value of hyponatremia among patients with chronic 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 (CHF). It is an established predictor of adverse outcomes in hospitalized patients with reduced ejection fraction (EF).

**Aim:** 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 results:** We examined the prevalence, risk factors, and long-term outcomes of hyponatremia (serum sodium  $\leq$ 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.

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 hyponatremia showed a higher risk of long-term morbidity than patients without.

### P838

#### Risk stratification for heart failure: comparison between the new proposed HLM classification and the classic NYHA

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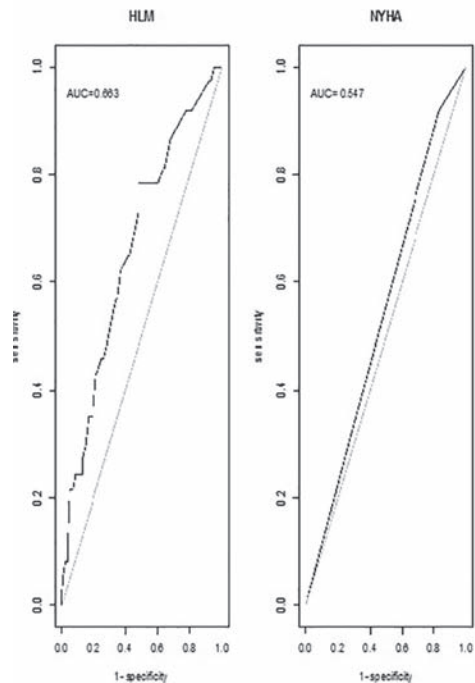
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**Purpose:** Among all HF classifications, NYHA is the most commonly used. However, it doesn't include a global clinical evaluation of patients, nor the assessment of other organs involvement. We proposed HLM classification, a new staging system for HF, similar 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 of this study was a preliminary comparison between HLM and NYHA in HF patients, to work out the most accurate prognosis in term of rehospitalization and mortality.

**Methods:** We performed a prospective and observational registry of 500 consecutive patients. 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. Four stages were determined by the sum of H, L and M values (i.e. score): stage 1 (score of 1 or 2); stage 2 (score 3-4); stage 3 (score 5-6); stage 4 (score >6). Each patient was also classified according to the NYHA system.

**Results:** Among 500 patients, regarding to the "H" parameter, left ventricular (LV) systolic dysfunction rate was 8.45%, right ventricle systolic dysfunction rate was 12.42%, LV diastolic dysfunction was 19.22%. Regarding to the "L" parameter, 70% of patients showed a pulmonary involvement. Regarding to the malfunction of other organs, kidney was involved in 8.45% of patients, liver in 37.1%, brain in 9.7%, blood in 21.33%. According to HLM, patients were classified as follows: 13.4% in stage 1; 36.77% in stage 2; 44.2% in stage 3 and 5.76% in stage 4. Considering the NYHA classification, 7% was in class I, 45% in class II, 41.27% in class III and 5.81% in class IV. The mortality rate for each stage of HLM and NYHA, the mortality rate was: 0% in HLM 1 vs 0% in NYHA I ( $p=1.000$ ); 2.6% in HLM 2 vs 4.4% in NYHA II ( $p=0.559$ ); 10.7% in HLM 3 vs 13.2% 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 ( $p=0.633$ ); 14.2% in HLM 3 vs 16.1% in NYHA III ( $p=0.55$ ); 60.6% in HLM 4 vs 26.2% in NYHA IV ( $p=0.037$ ). ROC curve analysis shows a  $AUC=0.663$  for HLM versus a  $AUC=0.547$  for the NYHA classification (Figure 1).

**Conclusions:** HLM classification seems to be more accurate than NYHA to stratify risk for HF patients in term of rehospitalization and mortality, mostly in advanced stages. According to our preliminary data, HLM can be useful for the physician in the patient management and to perform the best patient-centered therapy. Differently from NYHA, HLM includes the evaluation of objective parameters of cardiac, pulmonary and multi-organ involvement.



### P839

#### Altered left ventricular diastolic function in subjects with spinal cord injury

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**Purpose:** Subjects with spinal cord injury (SCI) have increased cardiovascular risk in comparison to able-bodied ones. This study investigated the cardiac structure and function of SCI individuals and the impact of metabolic, hemodynamic and inflammatory factors in this regard.

**Methods:** We evaluated 65 nondiabetic, nonhypertensive, nonsmoker men (34 with SCI and 31 healthy subjects) by medical history, blood pressure measurement, hemodynamic parameters, anthropometry, routine laboratory tests, echocardiography and tissue doppler imaging. Serum levels of C-reactive protein (CRP), TNF-Receptors I and II, ICAM-1, VCAM-1, E-selectin and TGF-beta were also assessed. Data are given as mean  $\pm$  standard error.

**Results:** SCI (18 quadriplegic and 16 paraplegic) subjects had similar age, body mass index, cardiac output, glucose and lipid levels, but lower systolic blood pressure ( $109 \pm 3$  vs  $120 \pm 2$  mmHg;  $p=0.09$ ) in comparison to controls. Injured individuals exhibited higher levels of CRP ( $6.2 \pm 1.7$  vs  $1.1 \pm 0.3$  mg/mL;  $p=0.001$ ), TNF-Receptor I ( $1.81 \pm 0.13$  vs  $1.48 \pm 0.14$  ng/mL;  $p<0.05$ ) and TNF-Receptor II ( $3.14 \pm 0.05$  vs  $2.93 \pm 0.07$  ng/mL;  $p<0.05$ ) than able-bodied ones. SCI group presented similar left ventricular (LV) structural and systolic parameters, but lower Em ( $9.2 \pm 0.5$  vs  $12.3 \pm 0.5$  cm/s;  $p<0.0001$ ) and higher E/Em ratio ( $7.7 \pm 0.5$  vs  $6.1 \pm 0.3$ ;  $p<0.01$ ) compared to controls, even after adjustment for CRP. Conversely, we found that SCI subjects with  $E/Em > 8$  ( $n=13$ ) had lower Sm, cardiac output and higher relative wall thickness than SCI individuals with  $E/Em < 8$  ( $n=24$ ) but similar age, body mass index, blood pressure, injury level, metabolic parameters and inflammatory markers.

**Conclusion:** Subjects with SCI presented impaired LV diastolic function in comparison to able-bodied ones. In addition, worse left ventricular diastolic function was paralleled by signs of reduced volemia, a pattern of LV concentric remodeling and decreased systolic function among subjects with SCI. These findings might contribute to explain the increased cardiovascular risk reported for SCI individuals.

### P840

#### Metabolic effects of betablockers, assessed by cardiac magnetic spectroscopy, in patients with systolic heart failure

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**Background:** The addition of Betablockers to standard treatment has been shown to improve left ventricular (LV) function in patients with systolic heart failure. The aim of this study is to non-invasively assess, by means of in vivo <sup>31</sup>P-magnetic resonance spectroscopy (<sup>31</sup>P-MRS), the effects of betablockers on LV cardiac phosphocreatine and adenosine triphosphate (PCr/ATP) ratio in patients with systolic heart failure.

**Methods and Results:** Ten heart failure patients (pts) on full medical therapy were beta-blocked by either carvedilol (6 pts) or bisoprolol (4 pts). Before and after three months of treatment, exercise testing, 2D echocardiography, MRS, New York Heart Association (NYHA) class, ejection fraction (EF), maximal rate–pressure product and exercise metabolic equivalent system (METS) and NT-pro BNP analysis were evaluated. Relative concentrations of PCr and ATP were determined by cardiac <sup>31</sup>P-MRS. After beta-blockade, NYHA class decreased (from 2.2 ± 0.54 to 1.9 ± 0.52, p = 0.05), whereas EF (from 33 ± 7 to 44 ± 6%, p = 0.0009) and METS (from 6.74 ± 2.12 to 8.03 ± 2.39, p = 0.01) increased. Accordingly, the mean cardiac PCr/ATP ratio increased by 33% (from 1.48 ± 0.22 to 1.81 ± 0.48, p = 0.03). Serum NT-pro BNP improved (from 1831 ± 1360 to 1023 ± 641 pg/ml; p = 0.04).

**Conclusions:** Beta-blockade induced symptomatic and functional improvement in patients with systolic heart failure is associated to increased PCr/ATP ratio, indicating preservation of myocardial high-energy phosphate levels.

#### P841

##### Multi-biomarker strategy improves prediction of mortality in heart failure and aortic stenosis

R&D Grant

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**Background:** There is an increasing number of serum biomarkers that are validated in studies to assess prognosis in patients with a variety of cardiovascular disease. However, many of these studies involving heart failure do not standardise optimal medical management and even fewer studies have investigated the role of biomarkers in severe aortic stenosis.

**Purpose:** We intended to investigate how novel and traditional biomarkers predicted outcome in patients with severe non-valvular heart failure (EF < 40%) who were on optimal medical and device therapy according to latest ESC guidelines or severe aortic stenosis who were undergoing transcatheter aortic valve implantation (TAVI) to assess how individual or panel of markers could add to the clinical assessment of these patients.

**Methods:** We studied 140 patients and obtained baseline biomarkers including NT-pro BNP, ST2, Galectin3, Osteopontin, PIIINP, TIMP1 and cardiostrophin. Patients were followed up for up to 2 years. Statistical analysis was performed on SPSS 22, outcome was analysed by Kaplan Meier curves and the receiver operating characteristics were analysed as a continuous variable per individual biomarker and as a panel, this was added as a total area under the curve.

**Results:** Area under the curve for ST2 at baseline appeared to be the most promising of all the biomarkers (0.612) compared with NT-pro BNP (0.610), TIMP1 (0.610), Cardiostrophin (0.602) Osteopontin (0.601), PIIINP (0.353), Galectin 3 (0.370) for 1 year mortality; 2 year mortality was similar. However, when novel biomarkers were combined (cardiostrophin, osteopontin and TIMP1), this improved the AUC (0.690). Adding ST2 and BNP gave AUC of 0.721.

**Conclusions:** A multi-biomarker adds to the assessment of high risk patients in both severe aortic stenosis and heart failure, and larger trials should be performed to validate their use in prognostic scoring.

#### P842

##### Clinical-pharmacist intervention reduces clinically relevant drug-drug interactions in patients with heart failure: a randomized, double-blind, controlled trial

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**Background:** Incidence of drug–drug interactions (DDIs) increases with the complexity of treatment regimens and comorbidities, as observed in heart failure (HF). Clinically relevant DDIs need to be identified and managed accordingly. This randomized, double-blind study evaluated the intervention of the pharmacist on the prevalence of clinically relevant DDIs (NCT01855165).

**Methods:** Patients admitted with acute HF were screened for clinically relevant DDIs, and randomized into the control or intervention group. The attending physician in the control group received standard advice about pharmacological therapy. In the intervention group, the attending physician received written alerts about clinically relevant DDIs. The primary endpoint was prevalence of clinically relevant DDIs on admission and at discharge.

**Results:** Of 213 screened patients, 51 (mean age, 79 ± 6 years; male, 47%; eGFR, 49 ± 22 mL/min/1.73 m<sup>2</sup>) had a total of 66 clinically relevant DDIs and were randomized. The most common DDIs were between angiotensin-converting enzyme inhibitors or angiotensin receptor blockers and spironolactone (14% of all DDIs). In the intervention group (n = 26), compared to the control group (n = 25), significantly fewer patients had clinically relevant DDIs at discharge (8 vs. 18; p = 0.003). Similarly, the total number of clinically relevant DDIs at discharge was significantly lower in the intervention group than in control group (10 vs. 31; p = 0.0049). From admission to discharge, in the control group, the number of clinically relevant DDIs was reduced (46 vs. 31; p = 0.018), and further in the intervention group (40 vs. 10; p = 2.08 × 10<sup>-6</sup>). During the 6-month follow-up, 11 patients in the control group and 9 in the intervention group were re-hospitalized or died. No significant differences were seen between the control and intervention groups for the group of patients (78%) with eGFR < 60 mL/min/1.73 m<sup>2</sup>, in terms of the composite of death or re-hospitalizations (10 vs 7; p = 0.74).

**Conclusions:** The pharmacist intervention significantly reduced the number of patients with clinically relevant DDIs and the number of clinically relevant DDIs. However, this did not reduce the clinical endpoints 6 months after discharge.

#### P843

##### Persistent referral of stable heart failure patients to primary care using a seamless heart failure care program

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**Purpose:** Since 2013 a seamless heart failure program has been applied in the region Alphen a/d Rijn in the Netherlands. Purpose of the program has been to share care for heart failure patients across all lines of care as a method to cope with the rise in number of heart failure patients. As has already been shown in 2015 there has been a marked increase in number of stable patient being referred to primary care compared to previous years. As the program itself has been expanded including more primary care facilities additional numbers have been collected in 2015 about this referral to primary care including reasons for referral.

**Methods:** Data have been collected about all heart failure patients being referred to primary care for their HF care in the region around Alphen a/d Rijn. Numbers collected from 2000 until 2013 have been compared to numbers from 2014-2015 during those years that the seamless heart failure program has been conducted.

**Results:** For 100 patients in this region, total heart failure care responsibility has been taken by the general practitioners in the years from 2000 until 2013. In this same region from 2014 until the end of 2015 74 patients in total have been discharged from the heart failure outpatient cardiology clinic to primary care. Five patients because of complete recovery of left myocardial function, 22 because of stable heart failure, 3 because of endstage heart failure and 22 patients because of frailty. Twelve patients were discharged because of other reasons. After referral to primary care 16 of the 74 patients have deceased. Three out of these 74 patients were rehospitalized, all 3 previously been discharged because of endstage heart failure or frailty. None of the remaining 55 patients have been referred back to the heart failure outpatient clinic.

**Conclusion:** A seamless heart failure care program as has been started several years ago results in progressive referral of a large group of HF patients to primary care. Majority because of stable heart failure or frail patients. As the numbers show, it appears safe to do as it does not result in large numbers of rehospitalized patients or patients being referred to the outpatients heart failure clinic. This referral can be an important method to be able to cope with the growing number of heart failure patients in the future. As number of patients included in this heart failure program will grow in the near future prospective data will be collected about the future follow-up of these patients.

#### P844

##### Comparison of the effects of two training modalities on chronic heart failure patients.

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**Introduction:** Chronic Heart Failure (CHF) as the common final stage of all heart diseases is associated with significant mortality and morbidity. Clinical characteristics of CHF include dyspnoea, fatigue and exercise intolerance. Current evidence has recommended exercise-based cardiac rehabilitation (CR) programs as a key component in the management of CHF patients aiming to the reduction of symptoms and the improvement of clinically relevant outcome parameters. The best established training modalities in CHF are Moderate Intensity Continuous Exercise (MICE) and High Intensity Interval Training (HIIT). However, the optimum exercise modality remains unclear. **PURPOSE:** The objective of this study was the comparison of the two prevalent training programs (MICE vs HIIT) in CHF patients.

**Methods:** 15 haemodynamically stable patients with CHF (NYHA II, III) were divided into 2 groups and followed a 3 months supervised exercise program (3 times per week). Group A (n = 8, mean aged 75.25 y., SD ± 5.6) followed MICE program on

treadmill (60-80% of Heart Rate Reserve) and group B (n=7 mean aged 59,3 y., SD $\pm$ 11,4) followed HIIT program on cycle ergometer (30/60 s). Additionally, both groups performed functional resistant lower limbs exercise program (squat, toe standing, step ups). Blood pressure, oxygen saturation and heart rate were monitored at each session using the Cardiowise software. All patients were assessed prior to and after the 3 months CR program with the six minute walking test (6MWT). **Results:** T-test was used for the statistical analysis and p-value level was set at 0.05. Group A showed statistically significant increase at mean walking distance from 387,25 m (SD: $\pm$ 78,5m) to 461,6m(SD: $\pm$ 70,4m) (p<0.05). Respectively, group B increased the mean walking distance from 494 m(SD: $\pm$ 135,8) to 559m(SD: $\pm$ 154,5)(p<0.05). However, comparing the improvement to mean walking distance of group A (MO:73,8,SD: $\pm$ 23,8) with that of group B (MO:64,7, SD: $\pm$ 9,6), there was no statistically significant difference(p=0.3). **Conclusions:** Supervised exercise-based CR programs improve exercise intolerance in CHF patients regardless of the training modality used.

#### P845

##### Rivaroxaban in resolution of thrombus in the left ventricle

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Treatment efficacy of new oral anticoagulants (NOACs) for prevention of thromboembolism in patients with thrombus in the left ventricle (LV) was not determined. The authors (AA) intended to demonstrate the efficacy and safety of Rivaroxaban in patients with thrombus in LV.

**Material and Methods:** The AA present a case series of patients with thrombus in the left ventricle in whom was used Rivaroxaban as anticoagulant.

**Resultados:** 4 patients were included: 3 men, mean age 65.5 $\pm$ 17.5 years. 50% of patients were hospitalized for decompensated heart failure, 25% for myocardial infarction and 25% for left hemiparesis. All patients had LV systolic dysfunction with a mean ejection fraction of 37%. The most sensitive method for visualization of thrombi was MRI. 1 patient initially started anticoagulation with warfarin, while one with enoxaparin. 50% of patients started immediately anticoagulation with Rivaroxaban. The doses used were 15 mg and 20 mg 50% to 50%. 75% of patients had thrombus resolution. There were no complications with anticoagulant treatment. A patient is waiting for an echocardiogram to confirm the disappearance of thrombus **Conclusion:** The Rivaroxaban showed to be an effective and safe therapeutic treatment of patients with a thrombus in the left ventricle. Larger scale studies should be conducted to verify the results.

#### P846

##### Do oral nitrates affect all-cause mortality and hospitalization in systolic heart failure?

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**Background and Purpose:** Hydralazine-nitrates combination is a recommended therapy for systolic heart failure (HFrEF) patients who are symptomatic despite optimal medical therapy. However, use of nitrates alone on top optimal therapy is controversial. They are effective for relieving angina in associated coronary artery disease; but, are not shown to affect clinical endpoints. This study aims to evaluate the association of oral nitrates usage with all-cause mortality and hospitalization risk in HFrEF patients.

**Methods and Results:** This study was a retrospective propensity-matched analysis of HFrEF patients attending a HF clinic between years 2003 and 2014. Nitrates use at baseline and its association with all-cause mortality and HF hospitalization was examined in median 56 months (range 6-132 months) follow-up. Of 648 patients (mean age 65 $\pm$ 12 years; 65% men), 216 (33%) were prescribed oral nitrates. After propensity-matching, 212 couples were established according to presence and absence of baseline nitrates usage. During the follow-up period, 269 (42%) patients died. In Cox regression analysis, oral nitrates use was associated with a slightly increased mortality risk compared to not using nitrates (HR=1.29; 95% CI 1.01-1.65; p=0.040), but this was not statistically confirmed by the propensity-matched analysis (HR=1.26; 95% CI 0.95-1.68; p=0.102). In both prematch and propensity matched analysis, nitrates use was not associated with risk of hospitalization. Evaluation of the effects according to presence or absence of coronary artery disease did not change these findings. **Conclusions—**In this study, oral nitrates therapy in HFrEF patients did not affect all-cause mortality and hospitalization risk during long-term follow-up.

#### P847

##### Aldactone in Patients with Heart failure: Friend or Foe?

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**Background:** The guidelines recommend using spironolactone in moderate to severe heart failure (HF) and reduced left ventricular systolic function, if there is no contraindication. Spironolactone was shown to have a significant mortality and morbidity benefit in the placebo-controlled trials. **Objective:** To study the frequency and causes of discontinuing spironolactone in Saudi HF patients in HF nurse-led clinic at King Abdulaziz medical city (KAMC) cardiac center. **Method:** A Retrospective observational study which included all patients with HF enrolled from 2000 -2010 who were prescribed spironolactone at any period and had at least one follow-up visit. **Result:** A total of 565 patients (49 % Male, mean age 55.6 years) were included in this study. Spironolactone was discontinued in 277/565 patients (49 %); 187/565 patients (33 %) were discontinued secondary to improved ejection fraction (EF) and/or functional class; 83/565 patients (14.3 %) were stopped due to worsening renal function and/or hyperkalemia ; other side effects such as hypotension, gynecomastia affected the remaining <1 %.

**Conclusion:** Nearly half of Saudi HF patient discontinue Spironolactone within 2 years ;the majority of the discontinuation is due to improved EF or/and functional class.

#### P848

##### The magnitude and management of chronic heart failure in the netherlands

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**Purpose:** To understand the magnitude and management of patients with chronic heart failure (CHF) in the Netherlands (NL) in order to identify possible opportunities to improve medical care.

**Methods:** A survey of cardiologists in NL utilizing a structured iPad-based questionnaire with the following items: number of patients CHF per hospital; most valued diagnostic tool in CHF; use of biomarkers in CHF; therapeutic decisions based upon biomarkers; first line treatment for CHF; conditions for a change in CHF therapy; preferred change in CHF therapy; follow-up in outpatient setting; involvement and tasks of heart failure nurses.

**Results:** A total of 31 cardiologists, representing 34% of hospitals in NL, took part in this survey conducted from Sept 2015 to April 2016. Preliminary data based on 12 hospitals are presented. On average 1095 patients with CHF per hospital are managed in an out-patient setting. Echocardiography (100%) was valued most when confirming the diagnosis of CHF, followed by physical exam (67%), ECG (50%), cardiac biomarkers (50%) and chest X-ray (25%). The use of (NT-pro)BNP in the management of CHF was reported by 83% of the respondents. Therapeutic decisions based on fluctuations in biomarkers were made: up-/down titration of the existing CHF therapy (92%), followed by the addition of a new therapy (33%). Preferred first line treatment for new CHF patients consisted of an ACE- inhibitor and a beta blocker with (57%) or without (21%) a diuretic. A change in CHF therapy was considered when signs and symptoms worsened (92%), a rise in biomarkers (42%), pre-discharge (50%) or post-discharge (17%) following an acute event. 91% of respondents would prefer up- or down titration of the existing CHF therapy when considering a change in therapy. A patient would visit the outpatient between 2 to 8 times depending on the stability of their CHF. 92% of hospitals have dedicated heart failure nurses, who provide patient education (100%) , up titrate existing CHF therapy (100%), initiate new medical therapy on request of the physician (58%) and perform in-practice monitoring (50%).

**Conclusions:** Extrapolating the results of this survey to all cardiology outpatient clinics in the NL 84% of CHF patients in the NL would be under supervision in an outpatient setting, assuming a prevalence of 130.000 CHF patients (Dutch Heart Foundation, 2012). Guideline recommended therapy for new CHF patients is strictly adhered. Biomarker guided management of CHF is not well-embedded into daily practice yet. Dedicated heart failure nurses continue to play a profound role in the management of CHF in the NL.

#### P849

##### Risk predictors of heart failure in STEMI patients on mid-term follow-up

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**Purpose:** The present study aims to identify in-hospital risk predictors to develop heart failure in ST-elevation myocardial infarction (STEMI) patients

**Methods:** A questionnaire based study analysed a total of 493 consecutive STEMI patients treated by primary PCI in a single centre, with a follow up period for over 3 years. The main question was addressing heart failure symptoms - evaluates the exertion capacity using as a parameter the number of floors the patients were able to climb without experiencing heart failure symptoms. Thus the exertion capacity was quantified in 4 levels (similar to NYHA classes). **Results :** The mean age of the study group was 64,56 years (IQR: 27 - 89), there were more men (351; 71,1%) and the mean follow-up time was 3,29 years. The prevalence of smoking in study population was 37,7 % and 68,8% were hypertensives. 23,1% of patients were diabetes mellitus and 54% had dislipidemia. The discharge mean LV (left ventricle)



ejection fraction was 42,87% (IQR: 10 – 60). 96.3% were in sinus rhythm, 3.3% of patients were in atrial fibrillation and 0.4% were in rhythm of pacemaker. Follow up treatment in STEMI patients was with beta-blocker in 86,9%, with renin-angiotensin aldosterone system (RAAS) inhibitor in 73,6%, with diuretic in 35% and with statin in 84%. The significant correlations were found between exertion capacity and ejection fraction (p=0,014), but also with age (p < 0,01), gender (p < 0,01), hypertensive (p < 0,01), smoking (p < 0,01) and cardiac rhythm (p=0,011). Patients being treated with RAAS inhibitors had a better exercise capacity, while those with diuretic treatment was poorer.

**Conclusions:** It is well known as the LV ejection fraction is an independent predictor of evolution after myocardial infarction. Our study showed that in STEMI patients the appearance of heart failure symptoms is also associated with older age, female gender, smoking, hypertension and non-sinusal rhythm. The beta-blocker therapy did not influence their exertion capacity, but the patients with RAAS inhibitors appear to have a better quality of life, and those requiring diuretic treatment have a reduced exercise capacity.

**P850**  
**Flu vaccine reduces recurrent hospitalizations in heart failure outpatients**

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**Purpose:** to evaluate the influence of regular annual flu vaccination onto cardiovascular(CV) death and HF-related hospitalization in chronic stable HF outpatients

**Methods:** Turkish Research Team-HF (TREAT-HF) network has been testing a questionnaire to investigate several aspects of HF outpatients. TREAT-HF 1 and 2 cohorts were recorded in the last month of 2013 and 2014 overall reaching 1003 HF outpatients out of 16 HF centers. Follow up data were available for 657 patients for hospitalizations.

**Results:** Mean EF was 32 ± 8% with a mean follow up of 15 ± 6 months. Other baseline characteristics ,which were significantly different between vaccinated and not vaccinated patients , were presented in Table 1. At the end of follow up; 113 (18%) patients experienced CV death with no significant difference in between those who had flu vaccine versus who did not (16% vs 19%, p=0.377). 303 (46%) patients experienced recurrent HF-related hospitalization. Rate of recurrent HF-related hospitalization was lower in patients who had flu vaccine regularly than those who did not have flu vaccine (16% vs 66%, p < 0.001). In multivariate Cox proportional-hazards model , vaccination status remained to be independently associated with risk of recurrent HF-related hospitalization.

**Conclusion:** It seems that regular vaccination against flu does not influence the rate of CV deaths, however, decrease recurrent HF-related hospitalizations in HF outpatients.

Table 1

Characteristic	Vaccinated (n = 265)	Not Vaccinated (n = 391)	p
Age (years)	60 ± 14	63 ± 13	0.026
Graduated from University (%)	32 (12%)	20 (5%)	0.002
Income level > 750\$ (%) (n = 457)	38 (18%)	30 (12%)	0.069
NYHA III-IV (%)	103 (39%)	206 (53%)	0.001
Creatinin (mg/dl)	1.1 (0.4-4.8)	1.2 (0.6-4.8)	< 0.001
Hemoglobin(g/dl)	13 ± 2	12 ± 2	< 0.001
LA diameter (mm)	46 ± 9	44 ± 7	0.001
Variables	HR	(95% CI)	P
Vaccinated against flu	0.303	0.206-0.448	< 0.001
Age(years)	1.017	1.007-1.029	0.002
Graduated from University	0.963	0.947-0.979	< 0.001
Hemoglobin(g/dl)	0.914	0.846-0.987	0.022
Creatine (mg/dl)	1.240	1.053-1.459	0.010

Baseline characteristics and multivariate cox regression analyses for predicting recurrent HF –related hospitalizations

**P851**  
**Systolic heart failure outpatients on ACEi/ARB+b-Blocker low dose (< 50%), ivabradine addition improves survival**

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**Introduction:** Systolic heart failure (SHF) medical therapy optimization algorithm includes the prescription and up-titration of ACEi/ARB, b-blocker and spironolactone. After this optimization, those in sinus rhythm and heart rate > 70/min should receive ivabradine.

**Objective:** Evaluate in SHF outpatients, already on optimized therapy, the effect on survival of ivabradine according to the dose level of the ACEi/ARB plus b-blocker combination.

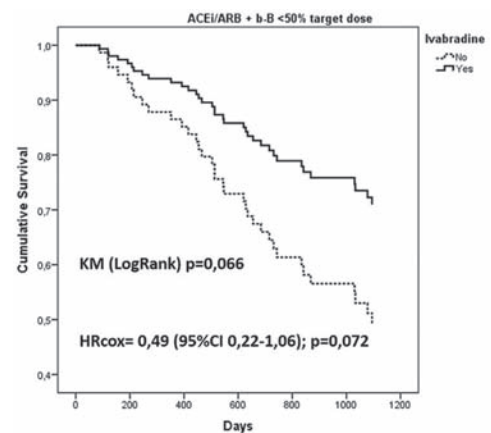
**Methods:** 159 patients with SHF (LVEF<40%) from one Heart Failure Clinic, all in sinus rhythm, all on ACEi/ARB+b-blocker therapy, and with optimal heart failure therapy according to the ESC guidelines and confirmed by 2 senior HF specialists of the clinic were included in the study. ACEi/ARB+b-blocker combination was categorized according to the percent dose in relation to target dose of both drugs: 1-49%; 50-99% and target dose (TD). Follow-up time was 3 years and the outcome all cause death.

**Statistics:** The hazard risk was calculated with Cox Regression for each ACEi/ARB+BB dose level according to ivabradine (No/yes) therapy.

**Results:** (1) Forty-three (27%) patients died. (2) Of the 160 patients 55 (34.6%) received ivabradine; ACEi/ARB-BB therapy- 1-49% TD in 57.2%, 50-99% 33.3 and TD of both drugs 9.4%. (3) The heart rate was similar for each ACEi/ARB+BB dose level by the ivabradine therapy. (4) Patients receiving ACEi/ARB+BB <50% target dose the ivabradine addition improved the survival curve (KM Log-Rank p = 0.066) and decreased the risk of death (HRcox 0.49 95% CI 0.22-1.06; p = 0.072).

**Conclusion:** SHF patients on optimized therapy, for similar heart rate values, ivabradine had an important impact in the survival of those receiving <50% target dose of both ACEi/ARB and b-blocker.

ACEi / ARB + BB	n	Ivabradine	KM (Log-rank)	HRcox (95% CI);p	Heart Rate	p
1-50%	91	No	0.066	Ref	70.1+13	0.687
		Yes	0.49 (0.22-1.06); 0.072	69.9+9.0		
>=50%	53	No	0.114	Ref	70.4+12.5	0.264
		Yes	4.9(0.5-44); 0.154	74.4+12.0		
Target dose	15	No	0.948	Ref	72.0+10	0.353
		Yes	0.52 (0.07-10.7); 0.92	79+16		



**P852**  
**Objectives, activities, organization of a nurse-led heart failure outpatient clinics: data from a community-based cardiovascular observatory**

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**Background:** Cardiovascular (CV) diseases are the first cause of death in the world population. To preserve the effectiveness of cardiological therapeutic interventions,

the elderly patient with chronic heart diseases (CHD), heart failure (HF) or atrial fibrillation (AF) need a global taking care, carried out by a multi-professional team. The aim of this study is to describe the organization, purposes and preliminary results of a nurse-led cardiology outpatient clinic with particular focus on heart failure (HF) patients.

**Methods:** Between November 1st, 2009 and October 31st, 2014, the Nurse-led Cardiological Outpatient Clinic provided care to 2,081 patients. 1,875 of these patients received nurse-led interventions in HF care (n=402, 19.3%), in CHD care (n=451, 21.7%) and in AF care (n=1022, 49.1%), while 206 patients, 9.9%, underwent Nursing Triage. Clinical multidimensional analysis, with identification of relevant health issues and planning of a nursing intervention (education, intensified monitoring, support to therapy) was shared with the cardiologist in a joint report. Data were derived from the E-data chart for Outpatient Clinic collected in the community-based population of Cardiovascular Observatory.

**Results:** The clinical characteristics and the social care needs of the patients who received nurse-led care were extremely heterogeneous. Patients with HF were the oldest (79 years), most severe (57.7% hospitalized last year), more prescribed drugs (72.4%  $\geq 7$  drugs daily), more frequent comorbidities (Charlson Index  $\geq 3\%$  82.8%). The majority of them had medium-to-low education levels and more frequently lived alone, with disabilities and inadequate self-monitoring and self-care behaviors. The patients of HF nurse-led clinics were those who came most frequently after hospital discharge, presented mainly clinical instability and problems of adherence to the therapeutic programs, and needed in most cases a therapeutic intervention associated with an intensification of clinical/behavioral monitoring. These patients showed the most severe prognosis with 1-year death in 19.6% of patients, CV hospitalization in 45.1%, non CV hospitalization in 46.6%, all-cause hospitalization in 58.2%.

**Conclusion:** Patients cared by Nurse-led Outpatient Clinic are very different from those enrolled in multicenter trials on which guidelines rely. Nursing assessment in HF patients effectively supports the specialist's intervention by intensifying clinical surveillance and therapeutic intervention and providing multidimensional information, essential to better understand patients' health and social care needs and to suggest and coordinate a tailor-made plan.

### P853

#### Treatment patterns in patients with chronic heart failure in Germany: a retrospective study of the health risk institute healthcare claims database

This research was funded by Novartis Pharma AG, Basel, Switzerland S Hupfer<sup>1</sup>; F Calado<sup>2</sup>; D Souto<sup>2</sup>; R Handrock<sup>1</sup>; J Jacob<sup>3</sup>; J Walker<sup>3</sup>; S Klebs<sup>1</sup>  
<sup>1</sup>Novartis Pharma GmbH, Nuernberg, Germany; <sup>2</sup>Novartis Pharma AG, Basel, Switzerland; <sup>3</sup>Elsevier, Berlin, Germany

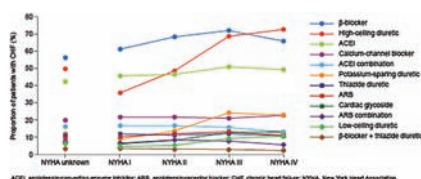
**Background:** Data are limited regarding pharmacological treatment of patients with chronic heart failure (CHF) in clinical practice in Germany. Therefore, a retrospective study of anonymized healthcare claims data from the Health Risk Institute database was conducted.

**Purpose:** The objective was to investigate how patients with CHF are treated in Germany.

**Methods:** Data from patients with at least two recorded CHF-related diagnoses based on ICD-10 German Modification codes for CHF in a hospital or ambulatory setting in 2011 were analysed. A subgroup of patients with new CHF diagnoses was identified based on the absence of a CHF diagnosis in the year before first diagnosis in 2011. Prescription data for CHF medication were retrieved; single and combination agents were analysed separately.

**Results:**  $\beta$ -blockers (58.4%), high-ceiling diuretics (50.6%) and ACEIs (43.1%) were the most frequently prescribed agents in the 123 925 patients identified. Prescription frequency of diuretics (high-ceiling, low-ceiling or potassium-sparing),  $\beta$ -blockers and ACEIs generally rose with disease progression (Figure). Patients received CHF medication as monotherapy (24.4%), or dual (30.3%), triple (21.3%) or quadruple therapy (7.6%), more than four agents (0.9%) or no CHF drug therapy (15.4%). Among 26 368 patients with new diagnoses,  $\beta$ -blockers (63.2%), high-ceiling diuretics (52.3%) and ACEIs (45.5%) were the most frequently prescribed agents. Prescription of diuretics and ACEIs declined in this group over the 2 years after first CHF diagnosis (relative decrease from Q1 to Q8: high-ceiling, 10.9%; low-ceiling, 14.9%; potassium-sparing, 15.3%; ACEIs, 9.1%), whereas prescription of ARBs increased by 18.8%.

**Conclusions:** Prescription rates of ACEIs decline over the 2 years after first diagnosis of CHF, whereas prescriptions of ARBs increase in this period.



Drug prescriptions in patients with CHF

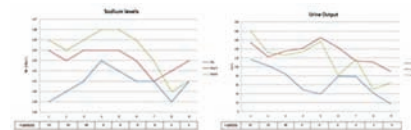
### P854

#### Dose response to Tolvaptan in repetitive admission for heart failure

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**Purpose:** Tolvaptan, a vasopressin receptor antagonist, is a safe and effective therapeutic alternative for refractory hyponatremia (plasma sodium (Na)  $\leq 135$  mEq/L despite fluid restriction and/or administration of hypertonic saline). The aim of this study was to assess the response to Tolvaptan in patients with hyponatremia and repetitive heart failure (HF) admissions. Methods. A retrospective study of patients with several admissions for HF and refractory hyponatremia treated with Tolvaptan was made. Evaluation of Na, potassium (K) (mEq/L), creatinine (Cr) (mg/dL) and glomerular filtration rate by MDRD ( $< 60$  mL/min/1.73m<sup>2</sup>) in plasma, rate of diuresis (mL/h), blood pressure (mmHg) and weight (kg) when Tolvaptan administered, and 24 and 48 hours later, was made. Results. 15 patients were included (nine (60%) women) with an average age of  $70 \pm 17$  years. Nine (60%) had renal impairment with baseline Cr and MDRD levels of  $1, 4 \pm 0,1$  mg/dL and  $45 \pm 10$  mL/min/1.73m<sup>2</sup> respectively. Most common cardiomyopathies were ischemic (26%) and valvular disease (26%). Four (27%) patients had severe ventricular dysfunction. NYHA functional status was III in 60%. All carried optimal treatment for HF and 100% standard diuretic therapy at home. Median number of admissions was 3 (range of 2-9). In the first 5 hospitalizations, 15mg of Tolvaptan was the dose of choice. Na levels increased in 3 mEq/L at 24 hours (0-5) and in 4 mEq/L by 48 hours (0-6). Urine output increased in all of the hospitalizations, with an increase of 64 ml/h (20-126) at 24 hours and 42 ml/h (3-117) at 48. Clinically no relevant changes were detected in levels of K, Cr, MDRD and blood pressure.

**Conclusions:** Our study shows that Tolvaptan is an effective and safe treatment for patients with multiple admissions for HF, increasing plasma sodium levels and improving urine output.



Sodium and urine output

### P855

#### Heart Failure Management Programme improves prognosis and reduces costing

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**Background:** We evaluated whether multidisciplinary disease management programme developed with collaboration of physicians and nurses inside and outside general district hospital settings can affect clinical outcomes in heart failure population over a 12-month period.

**Methods:** 571 patients hospitalised with CHF were referred to our unit and 509 patients agreed to participation. The intervention team included physicians and nurses from Internal Medicine and Cardiac Dept., and the patient's general practitioners. Contacts were on a pre-specified schedule, included a computerised programme of hospital visits and phone calls; in case of NYHA functional class III and IV patients, home visits were also planned.

**Results:** The median age of patients was  $77.7 \pm 9$  years (43.3% women). At baseline the percentage of patients with NYHA class III and IV was 56.0% vs. 26.0% after 12 months ( $P < 0.05$ ). Programme enrolment reduced total hospital admissions (82 vs. 190, -56%,  $P < 0.05$ ), number of patients hospitalised (62 vs. 146, 57%,  $P < 0.05$ ). All NYHA functional class benefited (class I=75%, class IV=67%), with reduction in the costing (-48%,  $P < 0.05$ ). Improvement in symptoms ( $-9.0 \pm -3.2$ ) and signs ( $-5.2 \pm -3.1$ ) scores was measured ( $P < 0.01$ ). Therapy optimisation was obtained by 20.5% increase in patients taking betablockade and 21.0% increase in those on anti-aldosterone drugs.

**Conclusions:** Multidisciplinary approach to CHF management can improve clinical management, reducing hospitalisation rate and costing.

### P856

#### Effect of CPAP therapy in obese patients with chronic heart failure with preserved ejection fraction and severe obstructive sleep apnea

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**Purpose:** To assess efficacy of CPAP therapy in obese patients with chronic heart failure with preserved ejection fraction and severe obstructive sleep apnea

**Methods:** We conducted a study of 18 men aged 62 - 75 years with CHF (II-III classes according to NYHA functional classification system). All patients had severe

obstructive sleep apnea. Performed blood tests besides routine biochemical parameters also included N-terminal pro-BNP (NT proBNP). Echocardiography parameters of systolic and diastolic LV function, dimensions of heart chambers, tissue Doppler parameters were assessed prospectively at baseline and after 6 month after the onset of study. CPAP therapy was added to evidence-based therapy of chronic heart failure.

**Results:** After 6 months of the beginning of CPAP therapy levels of NT proBNP decreased from  $769,3 \pm 102,4$  pg/mL (at baseline) to  $585,3 \pm 38,2$  pg/mL (at 6-month follow up) ( $p < 0,05$ ). Diameter of left atrium decreased by 9%, parameters of diastolic function determined by tissue Doppler improved, exercise tolerance increased, mean NYHA functional class decreased from  $2,75 \pm 0,79$  to  $2,47 \pm 0,86$ . CPAP therapy also relieved symptoms and improved quality of life and function in these patients.

**Conclusions:** CPAP therapy in obese patients with chronic heart failure with preserved ejection fraction and severe obstructive sleep apnea was accompanied with improvement of diastolic function of left ventricle, clinical symptoms, exercise capacity and quality of life.

## P857

### Implementation of European guidelines in real practice of congestive heart failure treatment in Russia 2002 - 2012

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It is proved that neurohormonal modulators (Renin angiotensin system blockers = RASB, beta-adrenergic receptor blockers = BAB and mineralocorticoid receptor antagonists = MRA) can improve survival and reduce risk of worsening of CHF. In modern European guidelines administration of these three classes of drugs in optimal doses seems the cornerstones of successful treatment.

Aim of the study was to analyze implementation of European guidelines for treatment of CHF in real clinical practice in Russia during decade 2002-2012.

Results received from three databases: EPOCH-O-CHF trial 2002 (n=1051), EPOCH-CHF trial 2007 (n=897) and National heart failure registry 2012 (n=1176) conducted in 36 sites across Russia. All three registries included pts with clinically relevant CHF (NYHA II-IV) hospitalized due worsening of CHF. Treatment regimens studied twice: in time of discharge from the hospital and on outpatient basis 6-9 months after discharge.

In 2002 in hospital 81,2% received RASB, 51,5% BAB and only 7,7% MRA. On outpatient basis this figures dramatically decreased to 45,5% for RASB ( $\Delta=35,7\%$ ), to 13,7% for BAB ( $\Delta=37,8\%$ ) and to 1,1% for MRA ( $\Delta=6,6\%$ ). Five years later (2007) hospital treatment of CHF pts improved: RASB have been prescribed to 87,7% pts, BAB to 80,1% and MRA to 49,2% of pts. After discharge on outpatients basis administration of RASB slightly decreased to 78,9% ( $\Delta=8,8\%$ ), BAB decreased to 58,7% ( $\Delta=21,4\%$ ) and MRA drop to 11,4% ( $\Delta=35,2\%$ ). Ten years later (2012) already 95,0% of pts in hospital have been treated with RASB (+13,8% compare with 2002), 91,1% with BAB (+40,2% compare with 2002) and 56,4% with MRA (+48,7% compare with 2002). On outpatient basis the treatment was less effective: with 87,3% still on RASB ( $\Delta=7,7\%$ ), 75,6% on BAB ( $\Delta=15,5\%$ ) and 31,6% still on MRA ( $\Delta=24,9\%$ ), but for all three drugs difference in administration between hospital and ambulatory treatment diminished. During ten years frequency of prescribing RASB in ambulatory practice increased by 42,1%, BAB by 61,9% and MRA by 31,5%, respectively, but still the gap between guidelines and real practice remains.

Moreover pts with CHF in real ambulatory practice received 46% (mean) of recommended doses of ACEI and 37% (mean) doses of BAB

**Conclusion:** During the 10-year period from 2002 to 2012 implementation of European guidelines for treatment of CHF in real practice in Russia significantly increased. However, in outpatient, the usage of basic therapy and doses of RASB and BAB remains insufficient.

## P858

### Therapeutic effects of metabolic therapy with a modified release trimetazidine in patients with chronic stable heart failure and angina (Russian study PERSPECTIVE)

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**Introduction:** Cardiac energy metabolism is altered in heart failure (HF) and can contribute to the progression of myocardial dysfunction in HF.

**Purpose:** Investigate clinical efficacy the long-term addition of modified release trimetazidine (TMZ MR) to standard current treatment of patients (pts) with stable ischemic HF and angina (SA) in real practice settings in 40 Russian cities.

**Methods:** 806 pts with HF I-III functional class (FC) NYHA and with (NYHA functional class II-III) and SA (II-III CCS), aged 35-65 years were randomized into two groups (gr): 1 gr receiving TMZ MR at a dose of 35 mg twice daily on top of standard therapy, n = 691) and 2 gr - control (the standard therapy, n = 115). The mean weekly number of angina attacks (AA) and nitroglycerine consumption (NC), the standard

ECG corrected QT dispersion (QTdc), left ventricular ejection fraction (LVEF), LV end-systolic volume, level of high sensitivity C-reactive protein (hsCRP), leukocytes, sum of cardiac hospitalizations were evaluated during 12 months follow-up.

**Results:** TMZ MR reduced AA by 62,8% ( $p < 0.0001$ ) and NC by 67,7% ( $p < 0.0001$ ) per week after 12 month, but not in control gr. LVEF increased significantly by 8,7% ( $p < 0.001$ ) and LV end-systolic volume decreased by 10,3% ( $p < 0.05$ ) after 12 months in pts receiving TMZ MR. No significant change was observed in the control gr. The addition of TMZ MR reduced QTdc by 10,5% ( $p < 0.05$ ) after 12 months. The 12-month TMZ MR treatment was associated with a reduction in serum hsCRP level by 17,4% ( $p < 0.05$ ) and leukocytes by 4,2% ( $p < 0.05$ ) vs a significant increase the inflammatory biomarkers in pts of control gr. We observed a new hospitalization for cardiovascular causes and heart failure in 7,1% pts in TMZ MR gr and 19,1% in control gr (- 62,8%,  $p < 0.001$ ) at 12 months.

**Conclusion:** The long-term addition of TMZ MR therapy for up to 12 months provides a reduce angina pain, improvement the left ventricular function and the remodeling process in HF pts with SA in primary care settings in various Russian regions. The results also suggest that TMZ MR may limit the inflammatory process and prevent of new hospitalization in pts with chronic ischemic HF and SA.

## P859

### Geographic variation in the access to heart transplantation in the

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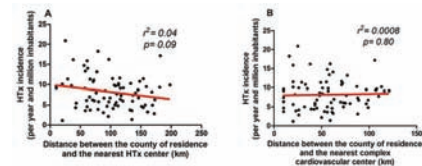
<sup>1</sup>IKEM, Prague, Czech Republic; <sup>2</sup>Center of cardiovascular surgery and transplantation, Brno, Czech Republic

**Background:** Heart transplantation (HTx) is the last resort therapeutic option in management of end-stage heart failure (HF). Geographic variation in incidence of HTx may disclose regional bias in the access to health care. The purpose of the study was to evaluate regional distribution of HTx in the Czech Republic.

**Methods:** We retrospectively analyzed data from all patients who underwent HTx in the Czech Republic between 1.1.2008 and 30.9.2013 and determined the incidence of HTx in all counties ("okresy") and higher administrative regions ("kraje"). In addition, we determined whether such regional incidence of HTx was related to geographical, demographic, socioeconomic factors or regional variation in coronary artery disease (CAD) or diabetes mellitus (DM) prevalence.

**Results:** Within the period above, 496 HTx were performed in the only two national transplant centers (8.211 per year and million inhabitants). Their regional incidence ranged between 4.4 and 12.2 per year and million inhabitants without a significant difference. On the level of counties, difference in HTx incidence was statistically significant ( $p < 0.0001$ ) with five counties out of seventy-seven being responsible for uneven distribution. The incidence of HTx was not related to the distance to the nearest HTx center ( $p = 0.09$  for counties, Fig. 1A,  $p = 0.28$  for regions) and was similar in regions with and without a complex cardiovascular center ( $7.77 \pm 2.17$  vs.  $7.94 \pm 1.56$ ,  $p = 0.87$  per year and million inhabitants). Similarly, there was no relationship between the distance of the county of residence to the nearest complex cardiovascular center and the HTx incidence in that county ( $r^2 = 0.0008$ ,  $p = 0.80$ , Fig. 1B). The incidence of HTx was unrelated to the number of hospitalizations for CAD in regions ( $p = 0.78$ ), number of patients with DM in regions ( $p = 0.10$ ), percentage of males both in regions ( $p = 0.32$ ) and counties ( $p = 0.76$ ) and age of population ( $r^2 = 0.006$ ,  $p = 0.79$  for regions,  $r^2 = 0.009$ ,  $p = 0.42$  for counties). HTx incidence also did not correlate with average salary in regions ( $p = 0.30$ ) and unemployment rate both in counties ( $p = 0.76$ ) and regions ( $p = 0.89$ ).

**Conclusion:** Regional incidence of HTx was found evenly spread throughout regions, indicating no geographic restrictions in access to this advanced therapy in the Czech Republic. The variation in regional HTx incidence was unrelated to average regional age, gender, incidence of CAD or DM, income or unemployment rate.



## P860

### Effects of febuxostat on cardiorenal function in patients with heart failure and hyperuricemia: effect study

Grant from Japan Promotion Society for Cardiovascular Diseases

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**Background:** It has been shown that serum uric acid (UA) level is an independent predictor of adverse clinical outcomes in patients with heart failure (HF). Actually allopurinol, a xanthine oxidase (XO) inhibitor, was shown to improve the prognosis of HF patients, whereas benzbromarone which promotes the excretion of UA showed no clinical benefit. These findings suggest that the suppression of reactive oxygen species production by XO inhibition might account for its beneficial effect. However, the clinical benefit of UA lowering agent for cardiorenal pathology in HF has yet to be fully determined.

**Purpose:** Effect study was a proof of concept study to examine the effect of a potent, specific XO inhibitor, febuxostat on cardiorenal function in patients with HF

**Methods:** The present study was conducted in an open-label, randomized manner. Thirty seven HF patients with New York Heart Association class II-IV symptom and hyperuricemia ( $\geq 7.0\text{mg/dl}$ ) were enrolled. Three patients were excluded since 1 patient died before the initiation of study drug and 2 patients withdrew consent. Thirty four patients were randomly assigned to febuxostat (10-40mg/day, F, n = 19) or conventional therapy (C, n=15). Cardiorenal function and other clinical parameters including biomarkers which represent inflammation or oxidative stress were examined at 12 and 48 week after the initiation of study drugs. Primary endpoint was defined as the change of estimated glomerular filtration rate (eGFR).

**Results:** There were no significant differences in baseline characteristics between F and C. UA decreased and significantly lower in F compared to C at 48 weeks (F,  $8.2 \pm 1.8$  to  $5.8 \pm 0.3\text{mg/dl}$ , C,  $8.0 \pm 1.5$  to  $7.7 \pm 0.3\text{mg/dl}$ ,  $P < 0.001$  at 48 week). eGFR did not change significantly in either group. E/E' tended to decrease in F compared to C (F,  $15.1 \pm 2.4$  to  $13.7 \pm 2.8$ , C,  $20.3 \pm 2.7$  to  $19.5 \pm 3.5$ ,  $P = 0.09$  by repeated measures ANOVA). Left atrial volume decreased and significantly lower in F compared to C (F,  $109 \pm 29$ , to  $92 \pm 30\text{ml}$ , C,  $161 \pm 128$  to  $145 \pm 76\text{ml}$ ,  $P < 0.001$  by repeated measures ANOVA). There were no significant differences in the time course of left ventricular volume, ejection fraction, N-terminal pro-brain natriuretic peptide level, C-reactive protein or biomarkers indicating oxidative stress. There were no significant differences in all cause death or hospitalization due to HF. The addition of HF medication tended to be more common in C than F ( $P = 0.06$ ).

**Conclusions:** Febuxostat safely decreased serum uric acid level in patients with HF. However, its effect on cardiorenal function was of borderline significance. Further investigation which includes more number of subjects will be warranted.

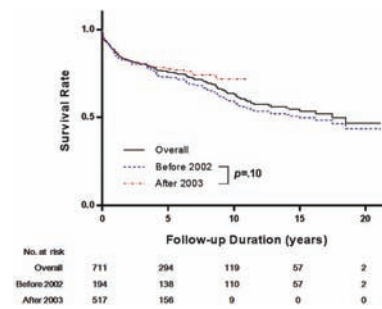
**P861 Heart transplantation in Korea: 20-years of experience**

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**Background:** Heart transplantation has become the gold standard treatment option for end-stage heart failure. We reports 20-years of experience in Korea. Methods. From January 1992 to December 2012, 742 patients were undergone heart transplantation. We excluded 27 patients with multi-organ transplantation and reviewed the medical records retrospectively. Results. Heart transplantation had been performed in 10 institutes. Mean age of recipients was  $42.9 \pm 16.8$  years and 72.6% were men. Gender-matched transplantation was preceded in 75.0%. Leading indication for transplantation was dilated cardiomyopathy (60.6%). Short-term mortality (within 1 month) was 4.5% (n = 32) and infection was the most common cause of death (50% of all-cause death, n = 16). After 1-, 5-, 10- years of follow-up, overall survival rates were 87.3%, 78.2%, and 74.8%, respectively. Rejection-free survival rates were 71.0%, 66.3%, and 65.2%, and malignancy-free survival rates were 99.1%, 97.7%, and 96.9%. Chronic allograft vasculopathy was occurred in 10 patients. After 2003, rejection rate was lower than that of before 2003 ( $p < .001$ ), but all-cause mortality ( $p = .10$ ) and malignancy-free survival rate ( $p = .58$ ) was not statistically remarkable. Conclusion. With upgrading of procedural techniques and postoperative care including immunosuppressant therapy, outcome of heart transplantation has been improving.

Variables	Total (n = 219)	1992-2002 (n = 103)	2003-2012 (n = 116)
Infection	66 (30.1)	33 (32.0)	33 (28.4)
Acute or technical graft failure	36 (16.4)	19 (18.4)	17 (14.7)
Cardiovascular	35 (16.0)	13 (12.6)	22 (19.0)
Organ failure	21 (9.6)	8 (7.8)	13 (11.2)
Chronic graft failure	15 (6.8)	8 (7.8)	7 (6.0)
Malignancy	14 (6.4)	10 (9.7)	4 (3.4)
Suicide	4 (1.8)	3 (2.9)	1 (0.9)
Others	28 (12.8)	9 (8.7)	19 (16.4)

All variables are expressed in number (% of all cause death). HT=heart transplantation.



All-cause Death Survival of HT Recipient

**P862 Return to work following first hospitalization for heart failure**

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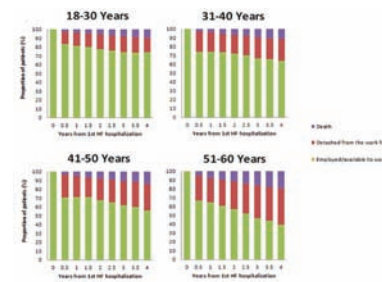
**Background:** Return to work is important financially, as a marker of functional status and for self esteem in patients suffering from chronic illness.

**Purpose:** We examined return to work after first heart failure (HF) hospitalization.

**Methods:** By individual-level linkage of nationwide Danish health and administrative registries, we identified 11880 patients of working age (18-60 years) who were employed prior to HF hospitalization. We estimated odds ratios (OR) for associations between patient age, length of hospital stay, sex, level of education, income, comorbidity and return to work one year after first HF hospitalization.

**Results:** One year after first HF hospitalization, 8040 (68%) returned to the work force, 2981 (25%) did not and 805 (7%) died, with return to work most likely among the youngest patients (81%) and highest 1-year mortality in the oldest age group (8%). Predictors of return to work included younger age (18-30 vs. 51-60 years, OR 3.28; 95% CI 2.53-4.26), male sex (OR 1.24 [1.13-1.36]), and higher levels of education (long-higher vs. basic school OR 2.07 (1.64-2.63)). Conversely, hospital stay > 7 days (OR 0.56 [0.51-0.62]) and comorbidity including history of stroke (OR 0.55 [0.44-0.69]), chronic kidney disease (OR 0.46 [0.36-0.59]), COPD (OR 0.62 [0.52-0.74]), diabetes (OR 0.75 [0.67-0.84]) and cancer (OR 0.49 [0.39-0.60]) were all significantly associated with lower chance of return to work.

**Conclusion:** Patients employed prior to HF hospitalization had low one-year mortality but high risk of detachment from the labour force. Young age, male sex, and higher level of education were predictors of return to work.



Return to work after HF hospitalization

**P863 Dyslipidemia as a factor of heart remodeling and failure processes**

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Cardiac remodeling is generally accepted as a determinant of the clinical course of heart failure (HF). The aim of our work is revealing the dyslipidemia parameters status in different types of heart remodeling in CHD patients with heart failure.

**Materials and methods:** 120 patients were investigated among them- 45 persons from control group. Patients with CHD and HF (75 pts) were divided in four group by Ganau classification: I group - patients with normal geometry (NG), II group

– concentric hypertrophy (CH), III group –eccentric hypertrophy (EH), IV group – concentric remodeling (CR) Blood for investigation was taken after 13 hours fasting. Lipid spectrum (TC, LDLC, HDLC, Triglycerides) was studied in blood serum using spectrophotometer by enzyme method. Ultrasonographic investigation of heart was performed by recommendations of the American Society of Echocardiography. Obtained data was statistically analyzed by Microsoft Office SPSS – 11.5 program. **Results and Conclusion:** lipid spectrum of NG group is characterized by comparative normal lipid spectrum in comparison with other groups, and its parameters did not differ from control group. The most changes in lipid spectrum was observed in CH groups confirmed by statistically differences in LDLC (elevation), TG (elevation), HDLC (decreases) with control and NG groups, while between NG and CR and EH groups differences were observed only in TG ( $p < 0.01$ ). The involvement of HDLC in remodeling processes indicates the negative correlation between mass of LV and HDLC in all groups of remodeling more expressed in CR group ( $r = -0.99$ ) and EH group ( $r = -0.64$ ) and in functions of compensatory mechanisms, reflected in positive correlation with EF in all groups. Atherogenic LDLC and TG play an important role in heart remodeling reflected by significant correlation (but less as with HDLC) between mass of LV, as well as with EF (one sides) and LDLC and TG (in other sides). Thus: Dyslipidemia is one of the important factor provoked heart remodeling, hemodynamic changes and heart failure by circulatory factors (atherosclerosis) and metabolism disturbance action. Especially HDLC levels correction have a significant role in prevention of heart failure.

#### P864

##### The relationship between clinical and echocardiographic characteristics and beta-blockers and antialdosterone treatment in patients with heart failure

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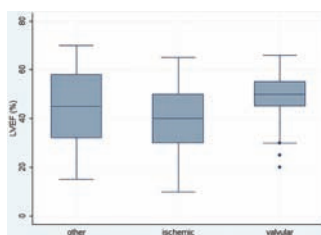
**Introduction:** The relation between the causes of heart failure (HF) and the election of the effective treatment has always been a challenge, in finding out an improvement in clinical or echocardiographic parameters in treated patients.

**Purpose:** To make a nowadays description of some clinical and echocardiographic parameters in patients with HF receiving beta-blockers or/and antialdosterone agents.

**Methods:** We included into a retrospective survey, 262 patients with HF, admitted between January 2014 to February 2015 in our hospital, found into NYHA III (82.9% patients) or IV. The statistical analysis was performed using StataSE 12 (significant  $p < 0.05$ ).

**Results:** 55.3% were men. The mean age was 64.9 years old. 74.8% patients received antialdosterone agents. 82.06% patients received beta-blockers. The main cause of HF was: 36.26% ischemic HF, 32.06% valvular HF, 31.68% other causes of HF. Those who received beta-blockers, 41.86% had ischemic HF, 31.6% had valvular HF, 26.51% had another cause of HF ( $p < 0.01$ ). The mean left ventricular ejection fraction (LVEF) was 48.53% in valvular HF, 39.22% in ischemic HF and 43.97% in other cause of HF ( $p < 0.01$ ). The mean systolic blood pressure was with 12.26 mmHg higher ( $p = 0.0004$ ) and the mean diastolic one with 5.74 mmHg higher in those without antialdosterone treatment ( $p = 0.0021$ ). The mean LVEF was with 9.2% lower ( $p < 0.01$ ) and the pulmonary artery pressure systolic was with 5.9 mmHg higher in those with antialdosterone treatment ( $p = 0.04$ ). The mean LVEF was with 7.5% lower in patients with beta-blockers ( $p = 0.0008$ ). The pulmonary artery pressure systolic was with 12.68 mmHg higher in those without beta-blockers ( $p = 0.0001$ ). In those who needed beta-blockers, the glomerular filtration rate estimated with MDRD Formula was with 14.6 ml/min/1.73 m<sup>2</sup> lower than in others ( $p = 0.0005$ ). In patients into sinus rhythm (52.2% of all patients) those with antialdosterone treatment had the mean LVEF with 12.34% lower than others ( $p < 0.01$ ) and those with beta-blockers had the mean LVEF with 14.38% lower than others ( $p < 0.01$ ). In patients with AF, those with antialdosterone treatment had a mean LVEF with 5.7% lower than others ( $p = 0.04$ ). There was no significant difference of the mean LVEF in patients with AF with beta-blockers.

**Conclusions:** Most of the patients who needed beta-blockers had an ischemic HF. The highest mean LVEF was found in patients with valvular HF, the lowest in those with ischemic HF. The pulmonary artery pressure systolic was higher in patients who received antialdosterone agents but was lower in patients who received beta-blockers.



The mean LVEF for different causes of HF

#### P865

##### Plasma testosterone levels in men with ischemic left ventricular dysfunction

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**Background:** High androgen levels have been linked with an increased cardiovascular risk. However, more recent data suggest that low androgens levels are associated with adverse cardiovascular outcomes. Aim of the present study was to evaluate the relationship between plasma sex hormone levels and presence and degree of CAD in patients with moderately reduced LV function (40-50%) or with ischemic left ventricular dysfunction (<40%) undergoing coronary angiography and in matched controls.

**Methods:** We studied 98 consecutive male patients (mean age 59±3 years, range 46-72) referred for diagnostic coronary angiography but without acute coronary syndromes or prior diagnosis of hypogonadism. Patients were matched with healthy volunteers.

**Results:** All pts, had proven coronary artery disease, more specifically 16 of them had one, 61 two and 22 three vessel disease respectively. Patients had significantly lower levels of testosterone than controls ( $2.6 \pm 1.6$  and  $3.5 \pm 1.3$  ng/dL;  $p < 0.01$ ). Also, both free and bioavailable testosterone, free androgen index and plasma estradiol levels were lower in patients as compared to controls. Patients had lower levels of estradiol-17b than control group ( $10.2 \pm 1.5$  and  $12.9 \pm 3.7$  ng/dl  $p < 0.04$ ). Hormone levels were compared in cases with 1, 2, or 3 vessel disease showing significant differences ( $p < 0.01$ ) associated with increasing severity of coronary disease and degree of left ventricular dysfunction. An inverse correlation between the degree of coronary artery disease and plasma testosterone levels was found.

**Conclusions:** In conclusion patients with ischaemic left ventricular dysfunction have lower testosterone and estradiol levels than healthy controls. These changes are inversely correlated to the degree of CAD and left ventricular dysfunction.

#### P866

##### Influence of levosimendan on a life quality of patients with severe chronic heart failure

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**Purpose of the research:** Studying of Levosimendan's influence on life quality of patients with Acute decompensation of Chronic Heart Failure in comparison with a standard therapy of Chronic Heart Failure.

**Material and methods:** 50 patients were involved in this research. 30 patients (14 men and 16 women) with Acute decompensation of CHF class IV by NYHA. The comparison group included 20 patients with decompensated CHF matched for sex and age, getting a standard therapy. The total duration of the research was 1 month. Results of the research. During the course of receiving levosimendan comparing with a standard therapy of CHF, it was noted a considerable improvement of life quality of the patients. The survey of the patients of both groups showed that the quality of life of patients treated with levosimendan after 48 hours increased by 40%, and by the end of the observation period was  $54.2 \pm 16.17$  points which is 43% over than the initiative indicators ( $p < 0.05$ ). In the comparison group by the end of the observation period the quality of life improved by 22.8%. A 6 minute walk test conducted by us showed the exercise tolerance increased by 60% after infusion of levosimendan within 48 hours, and by the end of the observation period increased by 63.5%. Whereas in the control group this indicator increased by 10% in 1 month. On a scale of assessment of clinical states an average number of points of the studying levosimendan patients really reduced by 50% (from  $13.1 \pm 3.04$  points to  $6.85 \pm 1.20$  points), and by the end of the observation period by 51.5%  $p < 0.05$ . In the control group this indicator decreased by 20%. This therapy helped to reduce the severity of Chronic Heart Failure and it facilitated to switch patients high functional class to lower one. The number of levosimendan group patients switched from class IV to class III were 64.3%, to class II were 35.7%. In the control group there were 21.1% of patients with class IV, 76.3% of them changed to class III and 2.6% to class II. Conclusion. Levosimendan significantly improves the quality of life of patients with Acute decompensation of Chronic Heart Failure.

#### P867

##### Heart failure increased due to poor hospital financial care

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**Abstract:** This article is focused around two important things in medicine: the lack of money in Europe and the quality of life. Europe is in crisis, but as always the best way to save money is in health for the citizen. We want to talk about crisis as the important cause of morbidity and mortality in our Hospitals, last 7 years, especially in cardiovascular surgery.

**Introduction:** There are currently very few articles discuss the effects that has brought the crisis in Europe on the quality of medicine and, above all, in cardiovascular surgery. This is an issue that affects millions of European citizens, because due to the crisis European hospitals have been forced to save a lot of money on materials: stents and prostheses and dismiss physicians. For primary angioplasty there is unanimous consent that a direct immediate mechanical opening of the occluded artery with angioplasty is preferable. Unlike in stable coronary syndromes there is no discussion whether patients should be better off in terms of prognosis and long term relief of symptoms after bypass surgery or coronary angioplasty or simply remaining on medical therapy, a difficult decision in individual cases that often leads to fierce discussions in our multidisciplinary meetings.

**Conclusions:** As we could see in our graphics and descriptions, the crisis in all European countries have an important considerations in global health for their citizens. As a conclusion we can say that 75% of European countries have difficult times and only Germany, France and United Kingdom can keep their status and give support to the health public system. Baltic countries have serious problems and will be very difficult to eradicate their economic problems is Hospitals, when many physicians are moving out to other EU countries and USA. Health system recovery in Greek will take more than 30 years. About Spain.

#### The risk of thrombosis after implantation

The risk of stent thrombosis, cobalt-chromium everolimus stent compared to some other types of stents

Stent	The ratio of opportunity (95% confidence interval)
Bare metal	0.23 (0.13-0.41)
Paclitaxel-eluting	0.28 (0.16-0.48)
Standing polymer-based sirolimus eluting	0.41 (0.24-0.70)
Phosphorylcholine-based zotarolimus-eluting	0.21 (0.10-0.44)
Resolute zotarolimus-eluting	0.14 (0.03-0.47)

The risk of thrombosis after implantation of metal stents.

#### P868

##### Arrhythmias and heart failure in patients with medial arterial calcification

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**Introduction:** Decreased ankle-brachial pressure index (ABI) is a well-known marker of increased cardiovascular mortality. However, also the values of ABI 1.3 and more, typical in medial arterial calcification (MAC), are associated with increased cardiovascular and all-cause mortality.

**Purpose:** To determine the prevalence of heart failure, cardiac arrhythmias and myocardial ischemia in a group of patients with type 2 diabetes mellitus and medial arterial calcification.

**Methods:** 41 patients with type 2 diabetes mellitus (25 male and 16 female), mean age 59 ± 8 years were investigated. MAC with ABI at least 1.3 was present in all members of our group. Arterial hypertension was present in 35 patients (85.3%), history of MI in 8 patients (19.5%) and history of stroke was present in 7 patients (17.1%). Holter ECG monitoring with an average recording duration of 22.36 hours was carried out by GE-Marquette MARS PC-ambulatory ECG Holter system (USA). MAC was detected by the BOSO ABI-system 100 (Germany). After physical examination blood samples with biochemical analysis, blood count and standard echocardiography was done.

**Results:** 12 patients (29.2%) had signs of heart failure (9 patients NYHA II and 3 patients NYHA III). Normal Holter ECG records without ischemia or arrhythmias were present only in 10 patients (24.4%). Complex forms of arrhythmias were in 18 patients (43.9%), Lown IIIB in 12 patients and Lown IVA in 6 patients. Myocardial ischemia was present in 6 patients (14.6%).

**Conclusion:** Patients with medial arterial calcification are threatened by serious cardiac complications such as cardiac arrhythmias and heart failure. We have detected high incidence of cardiac arrhythmias, including complex forms and myocardial ischemia on Holter ECG monitoring (75.6%). 12 patients (29.2%) had also signs of heart failure. Holter ECG monitoring in patients with MAC is highly recommended since subsequent cardiology management can improve their prognosis.

#### P869

##### Type D personality, negative emotions and quality of life in coronary artery disease patients with heart failure

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<sup>1</sup>Kazan State Medical University, Kazan, Russian Federation

**Introduction:** Type D personality, or distressed personality, refers to the joint tendency to experience negative emotions and to inhibit self-expression in social interactions. Type D personality has been associated with a variety of emotional and social difficulties as well as with poor prognosis in patients with established heart failure. But the relationship between type D, negative emotions and quality of life in heart failure patients was detected by some investigators, however, the factors that can explain this association remain unclear.

**Purpose:** To examine the effects of negative emotions, type D personality on the quality of life in coronary artery disease patients with heart failure.

**Methods:** We enrolled 80 HF patients (average age – 65,9 ± 8,4 years, left ventricular ejection fraction – 53,8 ± 11,4%, I-II FC – 45%, III-IV – 55%). Duration of heart failure did not exceed 6 years. In the study of emotional status for the diagnosis of type D personality used a DS-14 test, to determine the anxiety/depression – The Hospital Anxiety and Depression scale. Questionnaire Minnesota living with heart failure used in the study of quality of life.

**Results:** The prevalence of type D personality within the study population was 32,5% (30 patients). Type D personality patients had experienced negative emotions (anxiety and depression) in 83,4% cases, but the prevalence of negative emotions in non-type D personality patients was 50%. Distressed personality patients scored significantly lower on health status – 40,4 ± 9,6 than non-type D patients – 60,9 ± 8,8. Anxiety and depressive symptoms, type D personality were all found to be determinants of decreased quality of life (p < 0,05).

**Conclusion:** Type D personality and negative emotions were independent predictors of impaired quality of life in CHF.

#### P870

##### Estimating canadian heart failure prevalence using prescription treatment patterns

Novartis Pharmaceuticals Canada Inc.

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**Purpose:** It is currently estimated that over 600,000 Canadians have heart failure (HF). As diagnosis database coverage can be limited in Canada, we used IMS Health Brogan's (IMS) national patient-level longitudinal retail prescription database (LRx) to understand HF prevalence and its demographic variances. We therefore developed a prediction algorithm identifying Canadian HF patients using retail prescription patterns from a national database to understand and update HF prevalence estimates.

**Methods:** Patient data from IMS's E360 Canadian electronic medical record database were used to develop a decision tree prediction algorithm to identify treatment patterns in HF patients. The final study cohort was composed of 675 HF diagnosed (ICD-9 428) patients and 804 randomly sampled non-HF patients. All studied patients were aged ≥18 years, had ≥2 doctor visits between January 2006 - January 2015, and had been prescribed an ATC-1 cardiovascular product. The resulting algorithm was validated against a test dataset to evaluate the models prediction accuracy. To estimate age group, and gender prevalence, the algorithm was applied to IMS's LRx dataset to all patients with > 6 months follow-up.

**Results:** Age and standardized duration treated with beta-blockers, ACEs/ARBs, high ceiling diuretics, or vasodilators were strong indicators of a HF diagnosis, while physician referral and gender variables were not. When validated on a test dataset, the model demonstrated an 80.0% accuracy, 81.1% positive predictive value, and 79.5% negative predictive value. Overall, we estimated a 2014 national HF prevalence of 2.31%, or 657,902 patients aged ≥18 years. This estimate aligned well with literature population estimates - 590,416 and 626,199 patients. Elderly patients (aged ≥65 years) made up 76.08% of the 2014 HF patients with a prevalence of 8.97%, while those aged 18 to 64 years represent 23.92% of 2014 HF patients with a prevalence of 0.69%. Nationally, the 2014 prevalence was slightly higher in women (2.44%) compared to men (2.17%).

**Conclusion:** The prediction algorithm's overall HF prevalence estimates align well with literature prevalence estimates; overall, we estimate 657,902 Canadians are treated for HF. Prior cost studies demonstrated a substantial cost per HF hospitalization. As HF is associated with a high rate of mortality and hospitalization, treatments that reduce the number of patients requiring hospitalization events can materially lower the overall utilization and cost burden on the Canadian healthcare system.

#### P871

##### Sudden cardiac death in muscular dystrophy patients

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**Introduction:** Muscular dystrophy (MD) is a group of inherited diseases in which the muscles that control movement progressively weaken. In several forms of muscular dystrophy, cardiac dysfunction occurs, and cardiac disease may even be the predominant manifestation of the underlying genetic myopathy. Sudden cardiac death (SCD) is an unexpected death due to cardiac causes that occurs in a 1 hour of symptom onset.

**Methods:** The study was conducted in a Special hospital for treatment of progressive muscular and neuromuscular diseases in Serbia, from 2009 to 2014. The study included 70 patients with Duchenne, Becker, myotonic, limb girdle, Emery-Dreifuss and facioscapulohumeral muscular dystrophy. All of them had electrocardiograms (ECG). Results. Of the 70 patients with MD, 43 (61.4%) had SCD during the five years of our research. Diagnosis of SCD is based on the history, clinical findings, ECG findings and certain biochemical tests. Conclusion. The heart become necrotic in MD patients resulting in cardiorespiratory failure as the leading cause of death. Managing cardiac dysfunction, therefore, is the most important component of MD treatment. Cardiac screening has been recommended for MD mutation carriers, particularly beginning after the teenage years, as these individuals are known to be at risk for developing cardiomyopathy.

## P872

### Prognostic value of Minnesota index determined at discharge after acute decompensated congestive heart failure

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**Aim:** To study prognostic implications for rehospitalizations of the self reported global health status by Minnesota index (MS), correlated with left ventricular ejection fraction (LVEF) and NTproBNP values in patients (pts) discharged after acute decompensated congestive heart failure (HF)

**Method:** 100 pts hospitalized for decompensated HF were included in the study, mean age 72 +/- 10 years, 57% male. Echocardiographic determination of LVEF, NTproBNP (normally below 900 pg/mL) and MS were performed at discharge, after the compensation of HF. MS above 75 was considered high. History of hypertension, ischemic heart disease, myocardial infarction, diabetes mellitus, chronic kidney disease and also NYHA class at discharge were noted. After three months pts were contacted by phone and were interviewed about the rehospitalization for decompensated HF. Data were correlated with MS, LVEF and NTproBNP at discharge. Statistical analysis was performed using Statistica 8.

Results. 37% pts were in NYHA class II, 56% in NYHA III, 7% in NYHA IV, with no differences between men and women. Mean LVEF was 41 +/- 12%. Mean NTproBNP was 2547 +/- 1036 pg/ml, with no differences related to NYHA class, sex and etiology of HF. Mean MS was 66 +/- 20. MS above 75 was recorded in 53% of the pts in NYHA III, versus 21% pts with NYHA II (p = 0.002) and 57.14% pts with NYHA IV. MS above 75 was correlated with increased frequency of rehospitalization, regardless of NYHA class (r = 0.71). NTproBNP had higher mean values in pts with MS above 75 (2790 +/- 890 pg/ml), compared with those having MS below 75 (2304 +/- 912 pg/ml), without statistical significance (p = 0.08).

**Conclusions:** High Minnesota score value at discharge, comprising objective and subjective self-assessment data of patients with HF, correlates with rehospitalization rate, regardless of NYHA class and LVEF. NTproBNP was higher in the pts with high Minnesota score but without statistical significance.

## P873

### A description of unselected patients with heart failure: a swedish population-based study

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**Background:** The signs and symptoms of heart failure (HF) are non-specific, age- and gender-dependent; a better understanding of patient characteristics, especially amongst elderly patients, is needed.

**Purpose:** To characterize patients newly diagnosed with HF (main ICD-10 code I50) in Uppsala County, Sweden.

**Methods:** Patients were identified via electronic medical records from primary

(~90% coverage) and secondary (100% coverage) care and the local echocardiography registry. Patients aged ≥18 years with a first HF diagnosis from 1 January 2010 to 31 March 2015 were included. A 9-year look-back period to 1 January 2001 excluded prevalent HF cases. Echocardiography, electrocardiogram and natriuretic peptide testing were used to diagnose HF, assessed within 6 months after first diagnosis. Data were linked with the Swedish Prescribed Drug Register, Patient Registry and Cause of Death Registry. Co-medications used in the year before first diagnosis and comorbidities in the 5 years before first diagnosis were assessed.

**Results:** Of 8777 records, 4070 patients with newly diagnosed HF (47.1% women) were identified; 31.3% and 68.3% were diagnosed in primary care or secondary care, respectively. Mean (standard deviation [SD]) age at first diagnosis was 78 (13) years. The largest proportion of patients (33.6%) was aged ≥85 years; 32.1% were aged 75–84 years; 19.9% were aged 65–74 years; 8.2% were aged 55–64 years; and 6.2% were aged 18–54 years. The mean (SD) body mass index (BMI) was 27 (6) kg/m<sup>2</sup>. The commonest pre-diagnosis co-medications were antithrombotic agents (used by 71.8%), beta blocking agents (68.0%) and high-ceiling diuretics (47.9%). The commonest comorbidities were hypertension (56.0% of patients) and atrial fibrillation (36.4%). Overall, 1168 patients (28.7%) received echocardiography; 10.8% had HF with preserved ejection fraction (HF-pEF; left ventricular EF > 50%), 17.9% had HF with reduced EF (HF-rEF; left ventricular EF ≤50%); 71.3% were diagnosed with HF but echocardiography was not performed. Patients with HF-pEF had a mean (SD) age of 76 (12) years, mean (SD) BMI was 28 (6) kg/m<sup>2</sup> and 54.8% were women. Patients with HF-rEF were younger (mean [SD] age: 71 [15] years), had a mean (SD) BMI of 27 (5) kg/m<sup>2</sup> and the minority (33.1%) were women.

**Conclusions:** A large proportion of patients in this cohort were aged ≥85 years. The majority did not have an identified HF phenotype, which would delay appropriate treatment. This warrants targeted diagnostic and therapeutic strategies in primary and secondary care settings.

## P874

### Heart failure in cvdmp daily practice: characteristics, management and outcomes

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**Background:** The characteristics and outcomes of heart failure (HF) patients were described by numerous studies worldwide. However very limited information about Saudi HF patients is available. Aim: To determine the general characteristics, treatments and outcomes of Saudi patients with the diagnosis of HF who are followed up in a Nurse Led Cardiovascular Disease Management Program (CVDMP).

**Methods:** This is a retrospective chart review study, that included all HF patients who are followed up in King Abdul Aziz Cardiac Center (KACC) CVDMP over the time period from 2000-2015. Data extracted from the cardiac electronic data base (Apollo) for all patients who have at least 2 visits; enrollment (EV) and last follow up (LV).

**Results:** A Total of 2298 patients (72 % Male, mean age 58 STD 12.7 years) included in this study. Ischemic cardiomyopathy presented in 60% of patients, Diabetes mellitus in 66 %, Dyslipidemia in 76% and 64 % of patients were hypertensive. Majority of patients had both Systolic and Diastolic HF (70%), with stage C HF in EV and LV. Average EF Improved from 32 -38 % (P 0.0001). Over 90 % of the patients were on ACE, ARBs or the combination during EV and LV. Overall Mortality over 15 years follow up was 12.1%. (further analysis and results to follow)

**Conclusion:** Saudi heart failure patients are relatively younger with higher prevalence of cardiac risk factors. Nurse led CVDMP in KACC did improve survival in Saudi HF patients compared to international figures.

## P875

### Features of lesions of the coronary channel at coronary heart diseases patients with low ejection fraction

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**Objective:** to study features of lesion of coronary channel at CHD patients with low ejection fraction (EF) of left ventricle (LV) subjected to percutaneous coronary interventions (PCI).

**Material and methods:** From January 2013 to January 2015 y, selective coronary angiography has been executed at 1876 pts of cardiovascular diseases. Selective CAG at CHD pts with EF LV less than 45 % have been executed at 257 (14.1 %) pts. From them at 158 (62.4 %) pts have been executed PCI; 54 (20.7 %) are recommended to pnts carrying out CABG, at 45 (28.5 %) pts were therapy is continued: in 55.5 % (25) cases - coronary arteries were without changes, and in 45.5% (20) - were patients with various degree of lesion of coronary arteries. Criterion of an exception - echo-poor pts, pts in which anamnesis, were available

earlier transferred operations of myocardial revascularization (CABG and/or PCI) for more than 1 year.

**Results:** At carrying out diagnostic CAG at 144 CHD pts with low EF of the LV atherosclerotic lesions have been revealed in 352 arteries that has on the average made 2.44 arteries counting on 1 pt. According to selective CAG 29.9 % (43) pts had an one-vascular lesion, and for 70.1 % (101) – multivascular lesions. Most often lesions were localised (taking into account artery branches) in anterior descending branch of left coronary artery (LAD LCA) – 152 (43.2 %); in circumflex branch of LCA – 92 (26.1 %); in right coronary artery(RCA) – 92 (26.1 %); in a.intermedia-6 (1.7 %). Hemodynamic significant ( $\geq 50$  %) lesion of a trunk of the left coronary artery (LCA) has been revealed in 10 (2.9%) cases. By CAG results it has been revealed 402 hemodynamic significant lesions of coronary arteries: of 56.3 % (174) have made type stenoses of them “B”, stenoses of type “C” - 34.3 % (106) and stenoses of type “A” - 6.5 % (29) from total of the revealed narrowings. Among lesions of coronary arteries occlusion have made 23.1 % (93), from them in 76.4 % (71) cases are revealed chronic total occlusion.

**Conclusions:** the analysis of our experience shows that at pts with CHD (EF LV less than 45 %) most often meet multivascular lesions of a coronary channel – in 70.1 % (101) cases. As a whole lesions of coronary arteries of "high" risk (type "C" on morphology classification stenotic atherosclerotic defeat ACC/AHA) type have made 44.1 %.

**P876**

**Prevalence of P wave dispersion and interatrial block in patients with systolic heart failure and their relationship with functional status, hospitalisation and one year mortality.**

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**Background:** P wave dispersion (PWD) and Interatrial block (IAB) are common in heart failure (HF), and could be associated with cardiac events.

**Purpose:** To assess the prevalence of PWD and IAB and their relationship with functional status, hospitalization and mortality rate in patients with systolic HF.

**Methods:** We enrolled 110 HF patients in sinus rhythm & LVEF <50%. Patients had undergone clinical evaluation, 6 minutes walking test (6MWT), 12-lead electrocardiography (ECG), 24-hour Holter ECG & echocardiogram. PWD was defined as the difference between maximum & minimum P wave duration > 40 msec. IAB was defined as maximum P duration > 110 msec. Measurements were done by 2 blinded investigators using a caliper, a ruler and a magnifying lens.

**Results:** Mean age was 58.9 ± 9.7 years and 67.3% were males. Prevalence of PWD and IAB was 68.2% and 57.3%, respectively. Patients with PWD showed these features: 84% in NYHA class III or IV HF, 77.4% had LVEF <35%, 78.7% had paroxysmal Atrial Fibrillation (AF) and 89.4% couldn't complete > 200 meters (m) in 6MWT. Patients with PWD had more hospitalizations (72% vs 28.6%, P value < 0.02) and higher 1-year mortality rate (20% vs 8.6%, P value < 0.04) than patients without PWD. Likewise, patients with IAB had nearly similar clinical features, hospitalization and mortality as patients with PWD (refer to table).

**Conclusion:** PWD and IAB are prevalent in patients with systolic HF and they are significantly associated with low LVEF, paroxysmal AF, poor functional capacity, hospitalization and mortality rate.

Features of HF patients with PWD & IAB			
Parameter	PWD	No PWD	P value
NYHA class III or IV	84%	34.4%	0.01
Paroxysmal AF	78.7%	11.4%	0.001
LVEF <35%	77.4%	22.8%	0.001
6MWT <200 m	89.4%	45.7%	0.01
Hospitalization	72%	28.6%	0.02
1-year Mortality	20%	8.6%	0.04
	IAB	No IAB	
NYHA class III or IV	87.3%	42.6 %	0.01
Paroxysmal AF	77.8%	27.6%	0.001
LVEF <35%	79.4%	31.9%	0.01
6MWT <200 m	90.5%	55.3%	0.01
Hospitalization	61.9%	38.3%	0.019
1-year Mortality	22.3%	4.3%	0.012

Abbreviations are listed in the abstract text.

**P877**

**Duration of heart failure and outcomes in patients with heart failure and reduced ejection fraction**

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**Objective:** The pathophysiology of heart failure (HF) is believed to evolve with disease progression and the duration of HF may impact outcomes. In the current study, we examined the association of HF duration with outcomes in patients with HF and reduced ejection fraction (HFrEF).

**Methods:** The 2706 patients with advanced HF and EF <35% in the Beta-Blocker Evaluation of Survival Trial (BEST) were categorized into 4 groups based on their quartiles of HF duration: 26% had 1–12 months, 25% had 13–36 months, 26% had 37–72 months, and 23% had 73–456 months. Using multivariable-adjusted Cox regression models, we examined association of HF duration with outcomes during an average of 2 years of follow-up, using 1st quartile as reference.

**Results:** Patients had a mean age of 60 years, 22% were women and 23% African American. Association of HF duration with all-cause hospital admission and all-cause mortality are displayed in Table. Associations of longer HF duration with increased risk of HF hospitalization were similar to that with all-cause hospitalization.

**Conclusion:** In patients with advanced HFrEF, duration of HF appears to have

**61749 Outcomes in Heart Failure by Duration**

Table. Outcomes in heart failure by duration of heart failure

Outcome	Duration (months)	Unadjusted events % (n/N)	Hazard ratios (95% confidence intervals)		
	Age-sex-race-adjusted	Multivariable-adjusted*			
All-cause hospital admission	1-12	55% (395/714)	1 (Reference)	1 (Reference)	1 (Reference)
	13-36	64% (430/658)	1.24 (1.08-1.42)	1.22 (1.07-1.40)	1.24 (0.98-1.29)
	37-72	67% (472/704)	1.40 (1.23-1.60)	1.37 (1.19-1.56)	1.22 (1.06-1.40)
	73-456	66% (406/620)	1.14 (1.08-1.19)	1.12 (1.07-1.17)	1.09 (1.04-1.14)
All-cause mortality	1-12	25% (179/714)	1 (Reference)	1 (Reference)	1 (Reference)
	13-36	30% (200/658)	1.24 (1.02-1.52)	1.17 (0.96-1.44)	0.97 (0.78-1.19)
	37-72	35% (243/704)	1.50 (1.24-1.82)	1.42 (1.17-1.73)	1.13 (0.92-1.38)
	73-456	38% (237/620)	1.22 (1.14-1.30)	1.17 (1.10-1.25)	1.09 (1.02-1.17)

\*Adjusted for age, sex, race, smoking, coronary artery disease, chronic kidney disease, diabetes mellitus, atrial fibrillation, hypertension, hyperlipidemia, peripheral arterial disease, randomization to beta-blocker bucindolol, the use of ACEI or ARB, digitalis, diuretics, vasodilators, anticoagulants, NYHA class, cardiothoracic ration, pulmonary edema, heart rate, systolic and diastolic blood pressure, left and right ventricular ejection fraction, serum potassium and hemoglobin

stronger independent associations with all-cause and HF hospitalization than with all-cause mortality.

### P878

#### Incidence and predictors of stroke among patients with chronic heart failure

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**Background:** Stroke is associated with poor prognosis in patients with heart failure. This study investigated the incidence and predictors of stroke among this population.

**Methods and results:** We examined the prevalence, risk factors of stroke in ambulatory HF with reduced EF ;The cohort consisted on 3000 patients admitted in the therapeutic unit of heart failure (TUHF) between 2006 and 2015. During , the study period 3042 patients were diagnosed with heart failure with reduced ejection fraction < 0.50. Thirty-five per cent were women. Of these patients ,11% of them presented an ischemic stroke with a male predominance (12% versus 11% , sex ratio 2). Patients with HF with ejection fraction superior to 30% exhibited similar risk of stroke as those with reduced ejection fraction inferior to 30%: 13% versus 8% per 100. Eleven per cent of patients without atrial fibrillation presented a stroke. Among the studied population, 17,5% had a prior history of myocardial infarction ;When we compared the incidence of stroke among patients without atrial fibrillation in terms of medical treatment, there was 10% of stroke in the group taking vitamin K antagonist and 11% in the group taking antiplatelet therapy.

**Conclusion :** In our study, it seems that femal patients were at lower risk of stroke, in the other hand , prior history of myocardial fraction was predictor of stroke; however the severity of left ventricle systolic dysfunction did not influence the risk of embolic events.

### P879

#### Increased epicardial adipose tissue volume correlates with cardiac sympathetic denervation in patients with heart failure

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**Background:** It has been reported that epicardial adipose tissue (EAT) may affect myocardial autonomic function. Purpose. The aim of this study was to explore the relationship between EAT and cardiac sympathetic nerve activity in HF patients. **Methods.** We evaluated the correlation between echocardiographic EAT thickness and cardiac adrenergic nerve activity, assessed by 123I-metaiodobenzylguanidine (123I-MIBG), in 110 patients with systolic HF. Further, catecholamine levels, catecholamine biosynthetic enzymes, and sympathetic nerve fibers were measured in EAT and subcutaneous adipose tissue (SCAT) biopsies obtained from HF patients undergone cardiac surgery. **Results.** EAT thickness correlated with 123I-MIBG early and late H/M ( $r = -0.30$ ,  $p = 0.001$ ;  $r = -0.33$ ,  $p = 0.0001$ , respectively), and SPECT TDS ( $r = 0.70$ ,  $p = 0.0001$ ) but not with left ventricular ejection fraction (LVEF). EAT resulted an independent predictor of 123I-MIBG early and late H/M, and SPECT TDS and had significant additive predictive value ( $p < 0.05$ ) on 123I-MIBG planar and SPECT results over demographic and clinical data (age, gender, body mass index, NYHA class, heart failure of ischemic etiology, diabetes, hypertension and dyslipidemia). Although no differences were found in sympathetic innervation between EAT and SCAT, EAT presented an exalted sympathetic activity. In fact, EAT showed a 5.6 fold increase of norepinephrine levels compared to SCAT ( $0.168 \pm 0.026$  vs  $0.030 \pm 0.008$  ng/ml;  $p < 0.0001$ ) and a 2 fold increase compared to plasma ( $0.168 \pm 0.026$  vs  $0.085 \pm 0.014$  ng/ml;  $p = 0.017$ ). Epinephrine levels were significantly higher in EAT than in SCAT ( $0.016 \pm 0.001$  vs  $0.008 \pm 0.0005$  ng/ml;  $p < 0.0001$ ) but lower than in plasma ( $0.016 \pm 0.001$  vs  $0.06 \pm 0.008$  ng/ml;  $p < 0.0001$ ). mRNA levels of NE synthesizing enzymes, TH and DBH, were both significantly higher in EAT than in SCAT (8.6 fold and 6.5 fold increase, respectively), explaining the higher NE concentrations in EAT. We observed a robust increase of both TH and PNMT protein levels in EAT compared to SCAT ( $p = 0.002$ ;  $p < 0.001$ , respectively).

**Conclusions:** This study provides the first evidence of the correlation between EAT thickness and cardiac sympathetic denervation in HF

### P880

#### Association of left ventricular function parameters and maximal duration of apnea/hypopnea event in heart failure patients with central sleep apnea

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**Introduction:** Central sleep apnea (CSA) in heart failure with reduced ejection fraction (HFrEF) is highly prevalent and associated with more severe forms of heart dysfunction. The repetitive episodes of hypoxemia leading to oxidative stress and elevated levels of circulating catecholamines have detrimental effects on myocardial oxygen supply and ventricular performance. There is only few data concerning association between maximal duration of apnea/hypopnea event (Tmax A/H) and ventricular function in these patients.

**Methods:** 27 consecutive patients (20 males and 7 females,  $63.7 \pm 9.7$  years) with HFrEF (LVEF < 35%) were enrolled. In 17 cases HFrEF resulted from ischemic heart disease, and from non-ischemic cardiomyopathy- in 10. All patients underwent echocardiographic examination using standard protocol and polysomnography.

**Results:** The average left ventricular (LV) ejection fraction (EF) was  $25 \pm 3\%$  (Simpson EF) with mean end diastolic (EDD) and end systolic (ESD) diameters of  $69.2 \pm 2$  mm and  $58.6 \pm 2.5$  mm respectively and average LV diastolic and systolic volumes of  $278.3 \pm 63.5$  and  $209.6 \pm 33.5$  respectively. Sleep apnea with predominant CSA was diagnosed in 20 patients, in 3 patients CSA coexisted with obstructive apneic events and 4 patients had no sleep-breathing disorders. In subjects diagnosed with CSA mean apnea/hypopnea index (AHI) was  $23.98 \pm 13.05$ . In these patients Tmax A/H lasted between 52.5 and 339.5 s. EF exhibited statistically significant negative correlation to Tmax A/H;  $r = -0.51$ ,  $p = 0.0206$ . However no correlation was observed between Tmax A/H and LV diameters (EDD, ESD) as well as LV volumes (EDV, ESV).

**Conclusion:** The maximal duration of apnea/hypopnea event is significantly associated with deterioration of LV function in heart failure patients with central sleep apnea.

### P881

#### Hyponatremia increases significantly across worse NYHA functional class categories in chronic heart failure patients with reduced ejection fraction: results from TREAT HF

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**Purpose:** Hyponatremia has been established as a strong predictor for worse clinical outcomes for both in outpatients and hospitalized patients with heart failure (HF). NYHA functional class has also been known to be a strong marker of poor prognosis. TREAT HF (Turkish Research Team-HF) data were analyzed to evaluate any relation of blood sodium levels or hyponatremia with NYHA functional class categories in patients with chronic HF and reduced ejection fraction (HFrEF).

**Methods:** TREAT HF is a network which undertakes multicenter, national, observational studies designed to evaluate HF patient's clinical characteristics and current treatment modalities and enrolled ambulatory patients with the diagnosis of HFrEF and > 18 years of age. 908 patients who had blood sodium measurement and ECG-based heart rhythm were included in this analysis. Hyponatremia was defined as blood sodium level < 135 mEq/L. Patients with recent acute coronary syndromes, severe hepatic or renal dysfunction, severe chronic obstructive pulmonary disease, severe anemia, cancer, hyper-/hypothyroidism and pregnant women were excluded from the study.

**Results:** Mean blood sodium level was  $137.9 \pm 4.1$  mEq/L in overall study population. Among 908 patients, hyponatremia was found in 219 (24.1%) patients and 689 (75.9%) patients had normonatremia. Mean sodium level was  $138.5 \pm 3.4$  mEq/L in those with NYHA class I,  $138.2 \pm 3.9$  mEq/L in those with NYHA class II,  $137.7 \pm 4.3$  mEq/L in those with NYHA class III and  $135.9 \pm 4.4$  mEq/L in those with NYHA class IV and overall, sodium levels were found to significantly decrease across NYHA functional class categories ( $p = 0.001$ ). Hyponatremia was found in 17 patients (15.7%) in those with NYHA class I ( $n = 108$ ), 89 patients (22.1%) in those with NYHA class II ( $n = 403$ ), 94 (26.9%) in those with NYHA class III ( $n = 350$ ) and 19 patients (40.4%) in those with NYHA class IV ( $n = 47$ ) and overall, the prevalence of hyponatremia was also found to gradually and significantly increase across NYHA functional class categories ( $p = 0.004$ ). There found no significant difference in prevalence of hyponatremia between NYHA I and NYHA II ( $p = 0.181$ ), and also between NYHA II and NYHA III ( $p = 0.075$ ) while patients with NYHA IV showed significantly higher rate of hyponatremia when compared those with NYHA III, NYHA II or NYHA I ( $p = 0.042$ ,  $p = 0.006$  and  $p = 0.001$ , respectively), and also those with NYHA III had higher prevalence of hyponatremia when compared to those with NYHA I ( $p = 0.011$ ).

**Conclusions:** These results suggest that hyponatremia increases significantly across worse NYHA functional class categories in chronic HFrEF patients.

### P882

#### Pulmonary hypertension secondary to left heart disease: clinical characteristics and correlations between right heart catheterization and non-invasive parameters

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**Introduction:** Left heart disease is the main cause of pulmonary hypertension (PH). PH is considered a risk factor for worse outcomes in patients with heart failure. Initial evaluation of PH patients involves non-invasive methods including echocardiography and B-type natriuretic peptide tests (BNP); however, the final diagnosis requires right heart catheterization (RHC).

**Aim:** To characterize patients with heart failure with reduced ejection fraction (HFrEF) with and without PH, and to evaluate the role of echocardiography and BNP tests in diagnosis of PH in HFrEF patients.

**Methods:** This was a prospective analysis of 55 patients (both genders) with HFrEF (LVEF <40%) hospitalized at a tertiary health care center, undergoing qualification process for heart transplantation. The following were analyzed: medical history, epidemiological data, chosen laboratory test results (including BNP), and chosen parameters obtained in echocardiography and RHC (thermodilution method). PH was diagnosed according to the ESC guidelines. Correlation tests were performed for RHC parameters, BNP and chosen echocardiographic parameters. Analysis was performed using Statistica 10, Statsoft. Correlations were tested using the Spearman's test.  $P < 0.05$  was considered significant.

**Results:** Mean age was  $51.3 \pm 9$ . Most patients were men (91.5%). Mean NYHA class was 2.5. There were 37 patients with PH and 18 without. The patients with PH did not differ significantly from those without as to age (50.8 vs. 52.1 respectively), gender, cause for HF and NYHA class. Patients with PH showed significantly higher BNP test results (783.5 pg/mL vs. 269 pg/mL;  $p < 0.0001$ ), larger left ventricle (LV) in echocardiography (74.5 mm vs. 64.8 mm;  $p = 0.0039$ ), lower LVEF (20% vs. 25.4%;  $p = 0.0154$ ), and higher right ventricular systolic pressure (RVSP) (44.9 mm Hg vs. 34.9 mm Hg;  $p = 0.0017$ ). There were no significant differences as to size of right ventricle and left atrium. BNP test result showed a significant positive correlation with mean pulmonary arterial pressure (mPAP) ( $r = 0.58$ ), with mean right atrial pressure ( $r = 0.37$ ), with mean right ventricular pressure ( $r = 0.44$ ), with pulmonary capillary wedge pressure (PCWP) ( $r = 0.45$ ) and with pulmonary vascular resistance (PVR) ( $r = 0.37$ ). There was no significant correlation between BNP and transpulmonary gradient (TPG). Indirect evaluation of PH, i.e. RVSP measurement in echocardiography correlated significantly with mPAP measured in RHC ( $r = 0.57$ ). There were also significant correlations between RVSP and PCWP ( $r = 0.40$ ), TPG ( $r = 0.58$ ) and PVR ( $r = 0.44$ ).

**Conclusions:** Patients with PH secondary to HFrEF have lower EF, larger LV hypertrophy and higher BNP test results in spite of similar clinical profile. BNP test results and RVSP measured in echocardiography correlate with invasive RHC parameters.

### P883

#### Cardiac extracellular matrix accumulation is associated with adverse outcome in patients with chronic heart failure

Austrian fellowship grant, KLI 246, KLI 245 and the Austrian Society of Cardiology, the Österreichischer Herzfonds  
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**Background:** Accumulation of extracellular matrix (ECM) is known to play a crucial role in the pathophysiology of heart failure. However, its prognostic relevance is poorly investigated.

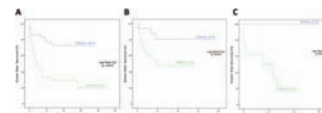
**Purpose:** We aimed to elucidate the influence of ECM area on outcome in non-ischemic heart failure (HF).

**Methods:** 73 HF patients who underwent left ventricular (LV) endomyocardial biopsy (EMB) were enrolled in our study. ECM area was quantified by TissueFAXS and ImageJ software. Patients were followed prospectively. The study endpoint was hospitalization for cardiac reason or cardiac death. Multivariable Cox regression analysis was used for survival analyses. Influence of ECM area on invasively assessed hemodynamic parameters was tested as well.

**Results:** During follow-up 34 patients reached the combined endpoint. Median ECM area was 30.5%. Patients with ECM area  $\geq 30.5\%$  experienced more events ( $p < 0.001$ ). ECM area was independently associated with outcome in the total HF cohort ( $p < 0.001$ ) as well as in HF patients with preserved (HFpEF,  $p = 0.014$ ) and HF patients with reduced ejection fraction (HFrEF,  $p = 0.011$ ). ECM area correlated with pulmonary artery wedge pressure ( $p = 0.042$ ,  $R = 0.249$ ), mean pulmonary arterial pressure ( $p = 0.258$ ,  $R = 0.035$ ), as well as right atrial pressure ( $p = 0.353$ ,  $R = 0.003$ ). Stroke volume index ( $p = 0.045$ ,  $R = -0.247$ ) was negatively correlated with ECM area. Conclusion. ECM area within the LV myocardium is a determinant of left and right heart hemodynamics and crucially impacts clinical course in various non-ischemic HF types.

Baseline Characteristics				
Clinical parameters	All Patients n = 73	ECM <30.5% n36	ECM $\geq 30.5\%$ n = 37	p-value
Age (years)	62.9 $\pm$ 14.5	59.6 $\pm$ 14.5	66.2 $\pm$ 13.9	0.037
Female, n (%)	30 (41.1)	14 (38.9)	16 (43.2)	0.705
BMI (kg/m <sup>2</sup> )	29.4 $\pm$ 6.4	30.6 $\pm$ 7.7	28.2 $\pm$ 4.7	0.253
ECM area (%)	34.2 $\pm$ 15.5	22.3 $\pm$ 5.8	45.8 $\pm$ 12.9	< 0.001
NYHA III-IV, n (%)	36 (49.3)	16 (44.4)	20 (62.5)	0.208
NT-proBNP (pg/ml)	3903 $\pm$ 6462	3396 $\pm$ 8248	4383 $\pm$ 4196	0.003
eGFR (ml/min/1.73m <sup>2</sup> )	65.6 $\pm$ 27.8	73.6 $\pm$ 36.2	58.4 $\pm$ 14.4	0.632
Follow-up (months)	14.0 $\pm$ 13.9	19.1 $\pm$ 13.7	9.1 $\pm$ 12.5	0.001
Cardiac Event, n (%)	34 (46.6)	9 (25.0)	25 (67.6)	< 0.001

BMI indicates body mass index; ECM, extracellular matrix; NYHA, New York Heart Association Class; NT-proBNP, N-terminal prohormone of brain natriuretic peptide; eGFR, estimated glomerular filtration rate; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; AL CA, light chain cardiac amyloidosis; WT-TTR CA, wild type transthyretin cardiac amyloidosis;



Kaplan Meier Analyses for HF Cohorts

## HEART FAILURE DIAGNOSIS

### P884

#### Diastolic wall strain and vortex formation time: new parameters in assessment of heart failure with preserved ejection fraction

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**Introduction:** Heart failure with preserved ejection fraction (HFpEF) is currently observed in 30-50% of all patients with chronic heart failure. Diagnosis of HFpEF is frequently challenging and relies upon careful clinical evaluation, echo-Doppler cardiography, and invasive hemodynamic assessment. However, a simple echocardiographic parameter has not been established so far. The aim of this work is to evaluate new indexes, that could be calculated from routine 2D echocardiography, to improve the current non-invasive diagnostics of HFpEF. Diastolic wall strain of posterior wall (DWS PW) has been proposed as a marker of left ventricular stiffness. Vortex formation time (VFT) is an index of the optimal conditions for vortex formation in early diastole.

**Methods:** Echocardiographic data from 111 subjects with exertional dyspnea having normal left ejection fraction (Group A) and 20 healthy volunteers (Group B) were retrospectively evaluated. In addition to the standard parameters used in the diagnosis of HFpEF, DWS PW and VFT were assessed in all patients. HFpEF has been proved in 38 patients with dyspnoea (Group A1). The remaining 73 patients have not met established criteria for positive diagnosis of HFpEF (Group A2).

**Results:** Patients with HFpEF (Group A1) were compared with other subjects with dyspnea (Group A2) and significantly different values were found: DWS PW (0.261  $\pm$  0.064 vs. 0.329  $\pm$  0.066,  $p < 0.001$ ), E/e' (11.00  $\pm$  2.61 vs. 8.2  $\pm$  1.95,  $p < 0.001$ ), e' (7.10  $\pm$  1.47 cm/sec vs. 9.10  $\pm$  1.89 cm/s,  $p < 0.001$ ), LV mass index (106.70  $\pm$  25.90 g/m<sup>2</sup> vs. 83.30  $\pm$  17.04 g/m<sup>2</sup>,  $p < 0.001$ ), NT-proBNP (326.60  $\pm$  280.41 pg/ml vs. 119.70  $\pm$  83.82 pg/ml), s' (peak mitral annular systolic velocity, 7.40  $\pm$  0.98 cm/sec vs. 8.80  $\pm$  1.49 cm/s,  $p < 0.001$ ) and VFT (3.00  $\pm$  1.14 vs. 4.1  $\pm$  1.50,  $p < 0.001$ ). No difference was observed between the group A2 and the control group B. Multivariate analysis, which includes standard parameters for the diagnosis of HFpEF as well as new parameters, revealed, that NT-proBNP (Odds Ratio 1.136, 95% CI 1.052 to 1.226), LV mass index (Odds Ratio 1.307, 95% CI 1.1055 to 1.620) and DWS PW (Odds Ratio 0.848, 95% CI 0.750 to 0.959) independently predict the presence of HFpEF.

**Conclusion:** The data indicates a potential role for DWS PW and VFT as a part of an integrated approach to the non-invasive assessment of diastolic function. Moreover DWS PW appears to be an independent predictor of HFpEF presence.

**P885****The severity of dyspnea predicts the final diagnosis of heart failure and is related to BNP level in patients admitted to the emergency department**

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**Background/Introduction:** Criteria of diagnosis and therapeutic strategies for heart failure (HF) patients still remain under discussion. Emergency departments became a major entry point for the initial management of acute heart failure (AHF) patients. Misdiagnosis, under or overtreatment, or inappropriate admission may place patients at increased risk for adverse events. The severity of dyspnea might be helpful for differentiating HF from other related clinical conditions. Purpose. The study evaluated whether the severity of dyspnea could be used as a prognostic marker of the final diagnosis of AHF and if it correlates with the degree of cardiomyocyte stress assessed with the use of biochemical parameter – BNP value. Methods. 151 consecutive patients admitted to the emergency department were enrolled in the study. Inclusion criteria were: dyspnea and suspected conditions of acute or recently decompensated HF, exacerbation of chronic obstructive pulmonary disease, pneumonia and pulmonary embolism. The exclusion criterion was acute coronary syndrome. Patients fulfilled the dyspnea test scale with marks from 1 to 10. Patient groups were defined based on the dyspnea test

**Results:** significant dyspnea group (SDG) – dyspnea test value  $\geq 6$  and moderate dyspnea group (MDG) – dyspnea test value  $< 6$ . Final HF diagnosis was independently adjudicated on the basis of electronic case records including a discharge letter by heart failure cardiologist. Data was analysed using SPSS v23 statistical package. Results. 83 (55%) patients were male and 68 (45%) female. SDG consisted of 91 (60,3%) patients and the MDG of 60 (39,7%). 96 (63,6%) patients with the final diagnosis of acutely decompensated HF or de novo HF demonstrated significantly higher dyspnea test grades ( $6,83 \pm 2,43$ ) compared to 55 (36,4%) patients who were not diagnosed with HF ( $5,85 \pm 2,36$ ) ( $p=0,018$ ). Mean concentration of BNP cardiac biomarker in the SDG patients' serum was  $944,81 \pm 1236,00$  pg/mL and  $667,67 \pm 780,87$  pg/mL in MDG ( $p > 0,05$ ). There was a statistically significant positive correlation between the severity of dyspnea and BNP concentration in patients' serum ( $G=0,334$ ,  $p=0,012$ ). All patients with three or more cardiovascular co-morbidities presented with significantly greater dyspnea than patients with less than three cardiovascular co-morbidities ( $p=0,025$ ). Binary logistic regression analysis revealed that patients with BNP serum concentration greater than 400 pg/mL were 4,92 times more likely to be diagnosed with acute, recently decompensated or de-novo HF ( $p=0,025$ ).

**Conclusions:** Dyspnea is a significant predictor of the final diagnosis of acute, recently decompensated or de-novo HF. Patients with AHF and de-novo HF have more severe clinical presentation of dyspnea compared to patients with other related clinical conditions. Serum concentration of BNP cardiac biomarker is significantly related to the severity of dyspnea.

**P886****Predictors of one year mortality in chronic systolic heart failure**

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**Introduction and problematic:** heart failure is a common pathology, with a heavy morbidity and mortality. Its prevalence in the world varies between 1 and 2% of the adult population and reaches 10% after 70 years. It represents the ultimate evolution of many cardiovascular diseases, especially ischemic and hypertensive. Heart failure is associated with high morbidity and mortality. A lot of progress where new techniques have emerged and made possible functional improvement and, especially a better survival, to certain category of patients. Therefore, the prognostic evaluation becomes a crucial step in the management of heart failure, to guide treatment decisions based on individual risk. Objective : identifying and measuring predictors of one-year mortality in newly diagnosed chronic systolic heart failure

**Methods:** we conducted a longitudinal prospective analytical bi – centric study, with one year follow-up.

**Results:** 206 patients were enrolled with a mean age of  $54,9 \pm 1,8$  years, a sex ratio of 1,9. The prevalence of diabetes mellitus was 39,8%, hypertension 30,1%. Coronary artery disease was present in 50,5%, dilated cardiomyopathy in 30,1% and toxic cardiomyopathy in 1,9%. The mortality rate was 12,7% (11,7% in men vs 14,2% in women,  $p$  not significant) and re-admission rate was 17,6% (23,1 % for men vs 6,6% in women,  $p=0.004$ ). Most clinical, echographic, biological and functional parameters cited in the literature have demonstrated prognostic predictive value with different rates of sensitivity and specificity. In multivariate analysis, pulmonary vascular resistance (new highly sensitive and specific parameter , RR 47 ), BNP , TAPSE , dP / dt, the distance travelled in six-minutes' walk test and serum sodium level were predictors of mortality in heart failure. The median survival by Kaplan- Meier was 24 months, with no gender difference. All parameters influencing mortality had an impact on survival. Improving the quality of life as measured by the six minutes' walk test and the questionnaire was significantly improved in patients

remained alive. Finally, the evaluation of drug prescriptions trends, according to new international guidelines, is quite reassuring in that the new molecules that allowed a significant reduction in morbidity and mortality in heart failure are widely prescribed in our patients.

**P887****In - hospital results of the percutaneous coronary interventions at coronary heart diseases pts with low ejection fraction**

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**The purpose:** the analysis of in hospital results of the percutaneous coronary interventions at coronary heart disease (CHD) pts with low ejection fraction (EF) of the left ventricle (LV).

**Materials and methods:** From January, 2013 year to December 2014 y PCI have been executed at 1266 pts with various forms of CHD. At CHD pts with low EF of the left ventricle PCI have been executed in 11.9 % (151) cases. 138 pts have been included in the research conducted by us with low EF of LV (less than 45 %) defined by method Teicholz by which in the subsequent it has been executed PCI. At 138 pts it has been spent 161 PCI. At 21 pts PCI it has been executed in 2 stages, and at one pt in 3 stages. Criterion of an exception - echo-poor pts, pts in which anamnesis, were available earlier transferred operations myocardial revascularization (CABG and/or PCI) for more than 1 year. Pts of a male have made - 80.4 % (111), and female - 19.6 % (27). The age of pts fluctuated from 35 till 78 years, and has on the average made  $58.9 \pm 8.6$  years. From the standard risk factors most often met an arterial hypertension - at 79.7 % (110) pts, hyperlipidemia - at 75.4% (104); a diabetes mellitus at 34.7 % (48) pts. The EF of the LV fluctuated from 18 % to 45 %, and has on the average made  $37.6 \pm 5.6$  %. In 42.9 % (69) cases PCI have been executed at pts with acute myocardial infarction; in 41.6 % (67) cases at a stable angina II-IV FC, and in 15.5 % (25) cases at an unstable angina. In total it has been implanted 259 stents (on the average 1.8 stents on one pt) from them of 85.3 % (221) drug eluting stents; 12 % (31) bare metal stents and 2.7 % (7) bioabsorbed vascular skeletons 'ABSORB'. Average diameter drug eluting stents  $3.4 \pm 1.56$  mm, and length  $26.4 \pm 7.8$  mm; diameter bare metal stents  $3.04 \pm 0.32$  mm, and length  $19.4 \pm 6.8$  mm.

**Results:** In our research frequency of angiographic success at implantation stents at CHD pts with low EF LV has made 89.4 % (144), the in-hospital success of procedure has made 85.7 % (138), and clinical success - 89.4 % (144). Frequency of complications has made 8.1 % (13) cases; from them in dissection a coronary artery has developed in 69.2 % (9) cases; occlusion a side branch - in 15.4 % (2) and in 15.4 % (2) cases has developed the phenomenon 'no-reflow'. Frequency of the major adverse cardiac events (an acute myocardial infarction, a lethal outcome, coronary artery bypass grafting) has made - 1.2 % (2); in both cases the non Q-wave acute myocardial infarction has developed. The reasons of development of not fatal acute myocardial infarction in 1 case was occlusion a side branch, and in 1 case – dissection a coronary artery.

**The conclusion:** Thus, the analysis of our experience shows that PCI at CHD pts with low ejection fraction of the left ventricle is an effective and safe method revascularization. Frequency of clinical success at a hospital stage of supervision has made 89.4 % (144) cases, and frequency of development major adverse cardiac events - 1.2 % (2).

**P888****Role of investigation of b-natriuretic peptide in chronic heart failure**

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**Purpose:** Study of the level of correlation - B - natriuretic peptide (BNP) in patients with CHF.

**Materials and methods:** The study tested 40 patients with CHD and heart failure, aged 45 to 68 years (mean age  $56.6 \pm 1.3$ ), including 15 women and 25 men admitted urgently with pain in the No.1 Republican Clinical Hospital over the 2015, at-echocardiography studied ejection fraction was over than 50%. All participants underwent an electrocardiogram, chest X-ray, general clinical and biochemical study: lipid profile, blood glucose, cardiac markers (troponin, myoglobin, BNP). Results and discussion. Recommendation to determine BNP levels at CHF questionable part of the modern clinical guidelines with the highest level of evidence A. Ejection fraction in our patients was  $51.8 \pm 1,6\%$  (for Simpson). According to clinical manifestations of heart failure, all patients distributed as follows: 18 patients-the first stage, and 22-the second stage. According to the results of our study, the level of BNP in our patients ranged from 80.0 to 375.0 and amounted to  $216.4 \pm 2.7$  pg /ml. At the same time, with first stage of CHF, it was significantly lower than with second stage ( $126.2 \pm 2.1$  in the first and  $233.8 \pm 3.3$  in the 2nd;  $P < 0.05$ ). In the treatment of 22 patients with CHF with second stage, 12 patients moved into the first. In the dynamic study of the content of BNP is equal to  $104.71 \pm 3.4$  in the first and  $181.6 \pm 2.7$  – in the 2nd stage. Conclusion. Thus, determination of BNP in CHF

helps to identify heart failure in the early stages, and can be recommended for monitoring the effectiveness of the treatment of CHF. BNP levels had a direct correlation with the stage of heart failure, and along the improvement patient's health, the level decreased respectively.

#### P889

##### Simplified ultrasound diagnosis of pulmonary oedema in heart failure.

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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 axilar line with IV and V intercostal spaces), which corresponded to the projection of lower, middle and upper lobes of right lung and upper and lower lobes of left lung.

**Results:** During ultrasound examination 94.5% of patients with HF had "Comet tail phenomenon" (CTPh), which was registered only in 35.5% patients without HF ( $p > 0.001$ ). In DHF group CTPH was registered in 90.5% and in systolic HF group in 95.9% patients. In 91% of patients with HF CTPH was registered from 3 and more registration points. In control group CTPH was registered from more than 3 points only in 2 (1.3%) patients. The best results in diagnosis of DHF can be achieved if we take "3 and more registration points" as a reference point for diagnosis of pulmonary congestion (sensitivity - 0,911, specificity - 0,942, positive predictive value 0,975). The time of examination by simplified method for evaluation of CTPH and pleural space took 3-4 minutes.

**Conclusion:** In patients with HF during pulmonary ultrasound examination significantly often was registered CTPH. The count of registration points from the thoracic wall of CTPH 3 and > is sensitive and specific sign of HF. The simplified thoracic ultrasound is highly effective in diagnosis of PE in patients with HF

#### P890

##### Raised red blood cell distribution width as a predictor of heart failure and mortality in patients with st-elevation myocardial infarction

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**Background:** Recent studies have reported increased red blood cell distribution width (RDW), a measure of red blood cell size heterogeneity, has been associated with adverse outcomes in heart failure and stable coronary disease. We investigated the association between RDW and risk of heart failure in patients with ST-elevation myocardial infarction (STEMI).

**Methods:** We prospectively enrolled 147 patients admitted for STEMI within 24 hours of symptom onset in our hospital from September 2012 to August 2013 (mean age  $63.1 \pm 11.6$  years; men 77.6%). According to the median RDW at baseline (13.5%) on admission, the patients were divided into two groups: a low-RDW group (RDW <13.5%,  $n = 77$ ) and a high-RDW group (RDW  $\geq 13.5\%$ ,  $n = 70$ ). The patients were followed up for clinical outcomes for up to 1 year after discharge.

**Results:** Patients in the highest RDW group (RDW  $\geq 13.5$ ) had higher risk of Heart failure during hospitalization (40% vs. 15.6%;  $p = 0.001$ ) compared to those in the lowest group (RDW <13.5). The value of RDW was correlated with the severity of heart failure according to KILLIP classification ( $p = 0.01$ ). High RDW remained significantly associated with increased risk for in-hospital mortality and left ventricular dysfunction (FE < 40%) (17.1% vs. 6.5%,  $P = 0.04$  and 39.1% vs 14, 3%  $p = 0.001$  respectively). Twenty-two patients (15%) died during follow-up. The cumulative incidence of all-cause death was significantly higher in the high-RDW group than in the low-RDW group (hazard ratio: 3.12; 95% confidence interval: 1.22-7.97;  $p = 0.018$ ). The area under the receiver-operating characteristic curve of the RDW was 0.678 (0.548-0.809,  $P = 0.008$ ).

**Conclusion:** RDW is an independent predictor of all-cause mid-term mortality in NSTEMI patients. It was associated with increased risk for heart failure during hospitalization. Further studies are needed to clarify the mechanisms of this association between RDW and adverse outcomes in patients with coronary artery disease.

#### P891

##### Non selective characterisation of heart failure with preserved ejection fraction in patients presenting to A and E

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**Background:** The incidence of Heart Failure with preserved Ejection Fraction (HFpEF) has been estimated to be approximately 50%, although more recent publications suggest that adherence to the ESC guidelines result in a smaller incidence of HFpEF patients.

**Purpose:** At our institution, all patients presenting with possible heart failure undergo NT -proBNP testing. Those with results above 400ng/l automatically receive an echocardiogram with a dedicated heart failure sonographer, if a study had not been done in the last 6 months, and a heart failure consultant review. We reviewed all the plasma NT-proBNP results in our institution over one year and characterised those in whom the heart failure consultant subsequently diagnosed HFPEF.

**Methods:** All consecutive patients who had plasma NTpro-BNP requested between 10/09/2014 and 09/09/2015 were included. Hospital databases and records were used to identify diagnoses, length of stay and inpatient mortality. Outpatient mortality was confirmed using Summary Care Records (follow up range 4 to 16 months). Data was collected as part of our Institution's approved Clinical Audit.

**Results:** In total, 2135 patients had plasma NTpro-BNP tested between 10/09/2014 and 09/09/2015. 1791 patients had NT-proBNP over 400ng/litre. Of these, 605 patients had heart failure - 138 patients were diagnosed with HFPEF (22.8%), 398 with Left Ventricular Systolic Dysfunction - LVSD (65.7%) and 69 patients with Right Heart Failure (11.4%). There was no difference in the average time to review between these patients (1.01 days, SD 0.51). The patients with HFPEF had lower plasma NTpro-BNP - 5342.7ng/litre (SD 6808) compared to the patients with LVSD 12,298.0ng/litre (SD 16613.9) and RHF 6633.1ng/litre (SD 8967.4). The length of stay was shorter 7.7 days (SD 39 days) compared to patients with LVSD (12 days, SD 9.8) and patients with RVF (11.3 days, SD 7.3). The mortality was reduced in patients with HFPEF (12.5%) compared to patients with LVSD (25.8%) and RVF (22%).

**Conclusions:** In our institution over one year, only 22.8% of the patients presenting acutely with heart failure symptoms were diagnosed with HFPEF. These patients had lower plasma NT-proBNP, duration of stay and mortality than patients with LVSD and RHF.

#### P892

##### Using intrinsic cardiac shear waves to measure myocardial stiffness: initial results on a patient cohort with heart failure with preserved ejection fraction and hypertrophic cardiomyopathy

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**Background:** Transient Magnetic Resonance Elastography (tMRE) has been shown to detect stiffness in many organs and so we have applied this concept in vivo to assess whether myocardial stiffness can be measured in patients with Heart Failure with preserved Ejection Fraction (HFpEF) and Hypertrophic Cardiomyopathy (HCM).

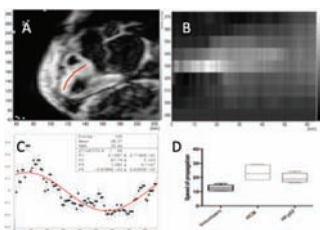
**Methods:** Aortic valve closure results in a shear wave that propagates through the myocardium. The speed of this wave can be measured if the sequence is timed to the exact valve closure time. Cardiac Magnetic Resonance (CMR) imaging individual sequences are ECG and navigator gated and take approximately 90 seconds; the complete scan including planning takes approximately 40 minutes. Increased myocardial stiffness results in increased speed of shear wave propagation.

In this study the speed of propagation was compared in normal volunteers, patients presenting acutely with HFpEF ( $n = 4$ ) and patients with HCM ( $n = 4$ ). All 8 patients had echocardiographic evidence of diastolic dysfunction. The speed of propagation was compared with age, echocardiographic measures of diastolic dysfunction and plasma NT-proBNP.

**Results:** Motion-encoded images (with a motion sensitized gradient at 165Hz) demonstrated myocardial wall shear waves associated with the aortic valve closure at 329ms (range 280-380ms) after the R wave (Figure 1 A B C). tMRE successfully showed a difference in speed of propagation between volunteers, patients with HFpEF and patients with HCM (speed volunteers  $12.6\text{m/s} \pm 2.0\text{m/s}$ , speed HFpEF  $19.5\text{m/s} \pm 3.5\text{m/s}$ , speed HCM  $23.3\text{m/s} \pm 5.8\text{m/s}$ ,  $p < 0.05$ , Figure 1D). One HFpEF patient who had invasive pressure volume loop studies was found to have increased left ventricular end diastolic pressure (LVEDP) and prolonged tau (represents the exponential decay of the ventricular pressure during isovolumic relaxation). There was no clear correlation shown between the speed of propagation in patients and age or the degree of diastolic dysfunction (measured by LVH, LA dilatation and E/E') but the Pearson coefficient with plasma NT-proBNP was 0.63 in patients presenting with acute heart failure.

**Conclusions:** The speed of propagation of the shear wave generated by the aortic valve was statistically higher in patients with Hypertrophic Cardiomyopathy, than patients with HFpEF than healthy volunteers. This suggests myocardial stiffness is increased more in HCM than in HFpEF, and in HFpEF more than in normal volunteers. tMRE has the potential to be an important diagnostic tool for the early detection of myocardial stiffness.





Transient Cardiac Elastography

**P893**

**Comparison of clinical presenting features of patients admitted with right versus left predominant heart failure. a single large tertiary referral centre retrospective study**

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**Background:** HF affects more than 10% of adults aged 70 years or older and is associated with significant morbidity, mortality and frequent hospital admissions. Research efforts mainly focus on left ventricular (LV) dysfunction, while the syndrome of right heart failure (RHF) is overlooked. The prevalence and significance of predominantly right versus left sided heart failure in a cohort admitted with decompensated symptoms remains poorly described. Objective: To describe the prevalence of predominantly RHF in a cohort admitted for decompensated symptoms, and to assess for differences in clinical characteristics and length of stay (LOS) in those with predominantly RHF vs. LHF. Methods/

**Results:** 442 patients hospitalized for decompensated HF between January 2010 and January 2011 were identified and the health records retrospectively analyzed as part of a larger ongoing study. Based on signs and symptoms, a diagnosis of predominantly RHF or LHF was determined by a panel of HF experts according to current guidelines. The prevalence of RHF was 22% and LHF was 78%. RHF was associated with fatigue ( $p < 0.0001$ ), pre-syncope/ syncope ( $P < 0.01$ ), loss of appetite ( $p = 0.01$ ), increased abdominal girth ( $p < 0.0001$ ) and abdominal discomfort ( $p < 0.001$ ). LHF was associated with orthopnea ( $P = 0.0003$ ), PND ( $p = 0.003$ ), and chest pain ( $p < 0.001$ ). RHF patients had more hepatomegaly ( $p = 0.0001$ ), ascites ( $p < 0.0001$ ) and anasarca ( $p = 0.0006$ ) while LHF patients more often had rales ( $p < 0.0001$ ) and pulmonary edema ( $p < 0.0001$ ). Both a longer mean duration of HF symptoms prior to admission ( $46.7 \pm 81.6$  vs.  $21.0 \pm 37.6$ ,  $p < 0.0001$ ) and a longer LOS ( $18.0 \pm 20.5$  vs.  $14.6 \pm 12.6$ ,  $p = 0.04$ ) was observed among those with RHF.

**Conclusions:** More than 1 in 5 patients admitted with decompensated symptoms had predominantly RHF. The clinical syndromes of predominantly right and left sided HF are associated with distinct sets of presenting features. Patients with RHF had a significantly longer LOS. In ongoing work, we are assessing for differences in the frequency of HF re-admissions and of time to re-admission among the two groups.

**P894**

**What is the role of strain analysis by speckle tracking on the evaluation of left ventricular systolic and diastolic function in patients with type 2 diabetes?**

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**Background:** Diabetic cardiomyopathy (DC) describes left ventricle (LV) dysfunction secondary to diabetes and not attributable to hypertension, coronary or valvular disease. Diastolic dysfunction is considered to be the earlier feature of DC. Few studies have evaluated systolic and diastolic function by strain analysis in diabetic patients.

**Objective:** Assess systolic and diastolic LV function in patients with type 2 diabetes with strain analysis by speckle-tracking.

**Methods:** Prospective study including 43 patients with type 2 diabetes and 20 healthy controls. All subjects were submitted to transthoracic echocardiogram with evaluation of LV systolic and diastolic function using conventional echocardiography, tissue Doppler imaging (TDI) and strain analysis by speckle tracking.

**Results:** Patients with type 2 diabetes were older than controls ( $59 \pm 12$  vs  $48 \pm 13$ ) and gender was not significantly different between groups (51% vs 35% males;  $p = 0.231$ ). Time since diagnosis of diabetes was  $12 \pm 8$  years, and the mean glycated hemoglobin was  $7.9 \pm 1.6\%$ . Hypertension was present in 63% of diabetic patients. Diabetic patients presented higher thickness of the interventricular septum ( $9.8 \pm 1.6$  vs  $8.2 \pm 1.2$ mm,  $p < 0.001$ ) and posterior wall ( $8.9 \pm 1.4$  vs  $7.8 \pm 0.9$ mm,  $p:0.002$ ) and higher LV mass ( $83 \pm 20$  vs  $71 \pm 12$ g/m<sup>2</sup>,  $p:0.025$ ). Diabetic patients and controls were similar regarding ejection fraction ( $65 \pm 5\%$  vs  $66 \pm 4\%$ ,  $p:0.347$ ) and TDI

systolic velocity ( $8.4 \pm 1.5$  vs  $8.7 \pm 1.5$ cm/s,  $p:0.367$ ). However, global longitudinal strain (GLS) was significantly worse in diabetic patients ( $-20.3 \pm 1.7$  vs  $-21.2 \pm 1.3\%$ ,  $p:0.046$ ). Diabetic patients presented significantly lower TDI early diastolic velocities ( $9.2 \pm 2.4$  vs  $11.8 \pm 2.3$ cm/s,  $p < 0.001$ ) and higher E/e' ratio ( $9.2 \pm 3.6$  vs  $6.6 \pm 1.7$ ,  $p:0.002$ ). Strain analysis revealed that diabetic patients also presented worse early diastolic strain rate (EDSR) ( $1.54 \pm 0.31$  vs  $1.95 \pm 0.19$ ,  $p:0.002$ ). No differences were found between hypertensive and non-hypertensive diabetic patients regarding GLS ( $-20.3 \pm 2.0$  vs  $-20.9 \pm 1.3\%$ ,  $p = 0.800$ ) and EDSR ( $1.51 \pm 0.26$  vs  $1.60 \pm 0.39$ ,  $p = 0.315$ ). Multivariate linear regression analysis revealed that diabetes mellitus was a predictor of GLS ( $p:0.049$ ) independent from age ( $p:0.839$ ).

**Conclusion:** In diabetic patients, both TDI analysis and strain analysis by speckle-tracking showed that diastolic dysfunction occurred earlier than systolic dysfunction. This suggests that strain analysis by speckle-tracking offers no incremental value over TDI regarding the detection of diastolic dysfunction. However, strain analysis by speckle-tracking played an important role in the evaluation of LV systolic function in diabetic patients, allowing an early diagnosis of systolic dysfunction while conventional and TDI parameters were still normal. Diabetes mellitus is a predictor of GLS, independent from age.

**P895**

**State-of-the art multilayer strain to study left ventricular contractility at rest and during exercise in patients with sickle cell anemia**

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**Background:** Left ventricular (LV) systolic dysfunction was reported in patients with sickle cell anemia (SCA) and is considered as the reflection of chronic sub-endocardial ischemia due to microcirculatory disorders. The contribution of LV systolic dysfunction to functional limitation of these patients has never been specifically investigated.

**Purpose :** Using multilayer strain technology, the aim of the study was to explore LV sub-endocardial layer function at rest and during exercise in SCA patients with chronic dyspnea. In addition we sought to investigate the contribution of LV systolic dysfunction to exercise functional limitation of these patients.

**Methods:** Echocardiography at rest and during maximal symptoms limited exercise was performed in 60 SCA patients referred for assessment of dyspnea and in 20 healthy controls matched for sex and age. The exercise capacity in metabolic equivalent (METs) was determined and the global longitudinal strain values of the three LV layers were measured. The results were compared between groups. Correlations between LV systolic parameters and exercise capacity were assessed in SCA patients.

**Results:** Compared with controls, patients had a severe impairment of exercise capacity ( $5.8 \pm 1.1$  vs.  $10.3 \pm 2.2$  METs;  $p < 0.001$ ). While epicardial and mid layers LV longitudinal strain were impaired in patients compared to controls ( $-16.3 \pm 2.2$  vs.  $-17.6 \pm 2.2$ ;  $p = 0.02$  and  $-18.6 \pm 2.3$  vs.  $-19.8 \pm 2.2$ ;  $p = 0.04$ ) sub endocardial strain was similar at rest ( $-21.2 \pm 2.5$  vs.  $-22.4 \pm 2.3$ ;  $p = 0.08$ ). During exercise, patients and controls had similar LV contractile reserve and multilayer LV strain values were similar. No correlation was found between myocardial contractility measures and patient exercise capacity (table 1).

**Conclusion:** Exercise LV contractility of SCA patients with dyspnea was similar to healthy controls and do not contribute to exercise functional limitation of these patients.

Table 1: Correlation between myocardial contractility measures and patient exercise capacity (n = 60)

Variable	r	P-value
LVEF at rest	0.06	0.66
LVEF at 20 Watts	-0.01	0.97
LVEF at peak	0.03	0.83
Endocardial GLS at rest	-0.22	0.10
Endocardial GLS at 20 Watts	-0.21	0.11
Endocardial GLS at peak	-0.18	0.18
LVEF : left ventricular ejection fraction.		

**P896**

**Reliability of diagnostic parameters from echocardiography and cardiopulmonary exercise testing in heart failure patients with preserved ejection fraction: results from Aldo-DHF trial**

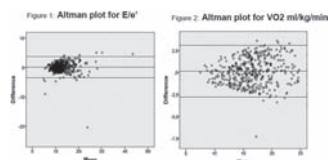
R Ruhdja Lindhorst<sup>1</sup>; A Bobenko<sup>1</sup>; T Trippel<sup>1</sup>; K Nolte<sup>2</sup>; G Hasenfuss<sup>2</sup>; HD Duengen<sup>1</sup>; G Gelbrich<sup>3</sup>; R Wachter<sup>2</sup>; B Pieske<sup>1</sup>; F Edelmann<sup>1</sup>

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**Aims:** Echocardiography (E/e') and cardiopulmonary exercise testing (peak VO<sub>2</sub>) are common tests for evaluation of diastolic dysfunction; however their reliability remains uncertain. The aim of this study was to investigate the reliability of E/e' and peak VO<sub>2</sub> in the Aldo-DHF cohort. Methods and

**Results:** Echocardiography and cardiopulmonary exercise testing (CPET) were performed on all 422 included patients of the Aldo-DHF trial twice, at baseline and repeated after a week ( $\pm 1$  day) under stable conditions without any changes in medication. All observed patients (mean age 67 years) presented with New York Heart Association class II or III heart failure, preserved left ventricular ejection fraction of  $\geq 50\%$ , diastolic dysfunction  $\geq I^\circ$ . To analyse reliability of the respective method, Bland Altman analysis were used. For E/e' mean difference was 0,1046. 95 % of variations in measurements were within the upper limit of 3,70 and the bottom limit of -3,49. We found a mean difference in peak VO<sub>2</sub> of 0,15 ml/kg/min with having an upper and bottom limit of 3,10/-2,81 ml/kg/min.

**Conclusion:** Taking in account that there was no clearance of outliers, the results from E/e' and peak VO<sub>2</sub> show a clinically high reliability for evaluating heart failure patients with preserved ejection fraction in recurrent examination. Although the Altman plot for peak VO<sub>2</sub> shows a crescendo for higher values, this effect was not clinically significant for the values of Aldo-DHF cohort with diastolic dysfunction but may have a different impact in testing a healthy, younger high performance population.



Altman plot for E/e' and peak VO<sub>2</sub>

## ADVANCED HEART FAILURE

### P897

#### Hemodynamic effects of ivabradine in patients with advanced heart failure

This research was sponsored by Servier the manufacturer of ivabradine. R Ramon Tschierschke<sup>1</sup>; A Ruhparwar<sup>2</sup>; P Ehlermann<sup>1</sup>; HA Katus<sup>1</sup>; PW Raake<sup>1</sup>  
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**Introduction:** The number of hospitalized patients with severe and advanced heart failure is continuously increasing. In very severe cases the heart rate in these patient is increased due to endogenous sympathetic drive or to necessary positive inotropic pharmacological support. This tachycardia unfavourably affects hemodynamics by shortening of diastole resulting in decreased cardiac output and additionally elevated heart rate is regarded as an independent risk factor. We analysed in a retrospective approach all patients being listed for heart transplantation at high-urgency status (HU) at heart centre Heidelberg in the time from 2004 to 2015 whether a selective heart rate reduction with ivabradine is safe and analysed its impact on hemodynamics.

**Methods:** This is a single-center, non-interventional, retrospective study. From 2004 to 2015 384 patients have been evaluated for heart transplantation at University-hospital Heidelberg and received an organ or deceased on waiting list. Of those 37 fulfilled patients fulfilled all inclusion criteria (HU heart transplant listing, stable sinus rhythm, heart rate  $> 70$ /min in non-ivabradine treated patients or ivabradine treatment, two invasive hemodynamic evaluations at least 8 weeks apart). 20 patients were pretreated with ivabradine at study inclusion and were continued on ivabradine over the 8 weeks observation period. 17 patients served as controls. Original data from the hospital archive were analysed in a retrospective fashion.

**Results:** In patients listed in HU status treatment with ivabradine was safe. No adverse events in context with ivabradine treatment occurred during the study period. At first evaluation hemodynamics were favourably affected by ivabradine, as despite lower ejection fraction in the ivabradine treated group cardiac output was similar in both groups at study inclusion. In addition, after 8 weeks ejection fraction worsened in controls compared to study inclusion, whereas a trend towards improvement in the ivabradine treated group was observed. A tendency towards use of ivabradine in sicker patients with regard to ejection fraction was perceived.

**Conclusion:** Use of ivabradine in advanced heart failure patients appears safe and a tendency towards improved hemodynamics in ivabradine treated patients was observed.

Conflicts of interests

This research was sponsored by Servier the manufacturer of ivabradine.

### P898

#### Anti-HLA antibodies prevalence in an advanced heart failure population

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**Introduction:** Anti-HLA antibodies detection is a mandatory test before including a patient in heart transplantation waiting list and can preclude this therapy. The presence of these antibodies has been traditionally related with several risk factors: female sex, transfusions, previous pregnancies, previous cardiac surgery, congenital heart condition, previous circulatory assist device. Nowadays, demographic and clinical characteristics of candidates to cardiac transplantation have changed. In the other hand, newer and more precisely techniques are being used for anti-HLA antibodies detection. Our objective has been to evaluate the prevalence and risk factors associated with anti-HLA antibodies presence.

**Material and methods:** We included patients with advanced heart failure evaluated for heart transplantation in our centre between June 2010 until April 2015. Basal characteristics, anti-HLA antibodies test results and risk factors were collected. We performed a description of the data and risk factors analysis by logistic regression.

**Results:** 134 patients were evaluated during the study period. Mean age was 54.43  $\pm$  11.12 years-old, 67.91% were male, 11.45% were smokers, 44.19% suffered from hypertension, 32.06% from diabetes and 38.93% were dyslipemic. According to traditional risk factors, 47.37% had previously received a transfusion, 33.33% had been operated from heart condition, 67.44% had been pregnant, 7.87% had had a circulatory assist device and 5.97% suffered from a congenital heart disease. 11.94% patients had developed HLA antibodies. 68.75% were type I (90.9% PRA  $> 10\%$ ) and 50% were type II (100% PRA  $> 10\%$ ). 2 patients had developed antibodies without any traditional risk factors. Simple logistic regression analysis related antibodies presence with female sex ( $p=0.002$ ; OR 5.91; CI 95% 1.91- 18.35), previous pregnancy ( $p=0.002$ ; OR 5.57; CI95% 1.86- 16.67) and previous cardiac surgery ( $p=0.044$ ; OR 2.99; CI95% 1.03- 8.68). We did not find statistical relation in patients who had had a circulatory assist device ( $p=0.797$ ), had received previous transfusions ( $p=0.064$ ) nor patients suffering from a congenital heart disease ( $p=0.256$ ). Multivariate logistic regression analysis showed that sex was a confusion variable due to pregnancies and was discarded in the final model: Previous pregnancies (OR 4.302; CI 95% 1.29- 14.42) and previous cardiac surgery (OR 4.005; CI95% 1.19- 13.51) were the variables finally significantly associated with anti-HLA presence.

**Conclusion:** In our experience, HLA antibodies prevalence in an advanced heart failure population was 11.94%. Its presence was related with previous pregnancies and cardiac surgery.

### P899

#### Genetic variations in end-stage dilated cardiomyopathy patients

PTDC/BIM-MEC/0650/2012

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**Introduction:** Dilated cardiomyopathy (DCM) is a major cause of heart transplantation. One of the hypotheses to explain disease progression, despite optimal medical therapy or device implantation, may be the presence of a particular genetic background. Currently, molecular diagnosis of cardiomyopathies, which are characterized by a great clinical heterogeneity, has been facilitated by the accessibility to next generation sequencing (NGS) technology.

**Purpose:** In this work we aimed to assess genetic background of adult patients with end-stage DCM.

**Methods:** Adult patients ( $> 18$  years old) that undergone or were in active list for heart transplantation, because of idiopathic or familial DCM, were evaluated. Molecular analysis included the search of mutations in LMNA/C, MYH7, MYBPC3, TNNT2, ACTC1, TPM1, CSRP3, TCAP, SGCD, PLN, MYL2, MYL3, TNNI3, TAZ and LBD3 genes, using PCR technique with direct-sequencing (NGS with at least a 30- fold coverage combined with Sanger sequencing). Pathogenicity was assessed by comparisons with mutations previously described, functional tests and segregations studies.

**Results:** We included 14 patients, 9 (64%) with criteria of familial DCM; 11 (78%) males, mean age 46  $\pm$  11 years, with mean age at diagnosis of 32  $\pm$  14 years. Mean left ventricle ejection fraction was 20  $\pm$  8% and mean end-diastolic left ventricular diameter 68  $\pm$  10 mm. Four patients presented left bundle branch block, 7 had an ICD and 3 a CRT device. We identified nine genetic variants in 6 (43%) different patients: 5 in lamina A/C gene, 2 in LBD3 gene, one in TNNT2 gene and one in TCAP gene. New mutations were found in the majority (5/6) of the patients. Two of

the patients with LMNA mutations had also subclinical skeletal myopathy and one evolved to atrial paralysis. Based on family studies, we conclude that one of the variants (TCAP, c.313G > C in exon2, p.Glu105Gln) did not explain familial segregation of the disease.

**Conclusion:** In our restrict sample of end-stage DCM patients, the identification of genetic variants was not uncommon and allowed genetic screening in some families. The exploration of genes and genes/ambience interactions in larger series will certainly contribute for understanding the dismal heart remodeling process that occurs in a subgroup of DCM patients.

**P900**

**Transition between early and late experience with continuous intravenous morphine for relief of dyspnea in patients with advanced heart failure**

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**Background:** Palliative care for advanced heart failure is commonly recommended. However, we could not fulfill a demand because of limited evidence and experience.

**Objectives:** We have experienced continuous intravenous infusion of morphine for relief of dyspnea. We divided years into separate terms, early and late, and compared patients characteristics, dosage of morphine, sedative agents, inotropic agents and others, and effect of morphine among those phase.

**Results:** Morphine was administered for 42 patients for palliation of dyspnea from 2011 to 2015. Twenty-one patients were divided into two groups each according to the date. In late phase, patients were older than in early phase, however other characteristics of patients were not different between groups. In late phase, respiratory rate was further ameliorated (p = 0.013) and symptom was similarly relieved. Sedative agents in addition to morphine for overwhelmingly-stressful general malaise were administered more frequently in late phase (p = 0.0063). No patients discontinued morphine due to adverse events.

**Conclusion:** Low dose morphine was safe and effective. We have to continue evaluating how to use morphine and other drugs in order to appropriately provide palliative care for distressed patients.

	Early	Late	p value
Number	21	21	
Age (years)	76.5 ± 2.4	84.0 ± 2.4	0.0328
Etiology:ischemic (%)	8 (38.1)	13 (61.9)	0.30
LVEF (%)	34.4 ± 15.5	36.1 ± 12.0	0.41
Estimated GFR (ml/min/1.73m2)	42.2 ± 53.4	25.9 ± 19.5	0.36
BNP (pg/ml)	1941 ± 1937	1559 ± 1036	0.97
Dosage at maintenance of morphine	13.6 ± 9.2	8.6 ± 4.3	0.11
Δ Respiratory rate at 24hr	-5.5 ± 6.2	-11.3 ± 7.9	0.013
Symptom relief at 24hr (Visual Analogue Scale)	3.3 ± 3.4	5.0 ± 1.7	0.28
Inotropic agents (%)	15 (76.2)	20 (95.2)	0.55
Sedative agents (%)	2 (9.5)	10 (47.6)	0.0063

Transition between Early and Late Experience

**P901**

**Effect of angiotensin converting enzyme inhibitors and angiotensin II receptor blockers on cardiovascular deaths in patients with and without diabetes mellitus in advanced chronic heart failure**

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**Background:** Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin II receptor blockers (ARBs) may have different effects on cardiovascular deaths in patients with and without diabetes mellitus (DM) in advanced chronic heart failure.

**Purpose:** To compare the effect of ACEIs and ARBs on cardiovascular mortality in advanced systolic heart failure in patients with and without DM.

**Methods and Results:** We analysed the data of 630 patients (mean age: 66 ± 12 years, 231 female, mean ejection fraction (EF): 25 ± 10%) with advanced systolic heart failure. 250 patients (40%) had diabetes mellitus in the study group. 313 patients (49.7%) of the cohort died during a median follow-up duration of 54 months. While 48% of the patients with diabetes died, 44% of patients without diabetes died during the follow-up period (p = 0.27). 460 patients were receiving ACEIs and 121 patients were on ARBs therapy. 49 patients did not take either ACEIs or ARBs. 43% of patients with diabetes who were on ACEIs therapy, 65% of patients with

diabetes who were on ARBs therapy and 48% of patients with diabetes who did not take either ACEIs or ARBs therapy died. There was only statistically significant difference between patients with diabetes who were on ACEIs therapy and patients with diabetes who were on ARBs therapy among patients who died during follow-up (p = 0.005). There was no impact on survival of taking ACEIs or ARBs in patients without diabetes in advanced chronic heart failure.

**Conclusion:** Angiotensin-converting enzyme inhibitors reduced the cardiovascular deaths in patients with diabetes in advanced chronic heart failure, whereas ARBs had no benefit on this outcome. Thus, ACEIs should be considered as first-line therapy to limit cardiovascular deaths in this population.

**P902**

**Endomyocardial biopsy through a brachial venous approach.**

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**Introduction:** recipients of a heart transplant need to undergo serial procedures of endomyocardial biopsy to rule out rejection. This requires the repeated puncture of central veins, usually the internal jugular or the femoral, which is not completely free of risks, pain and discomfort for the patient. So far, the brachial venous approach has not been considered a routine alternative for endomyocardial biopsy. In our center, we have developed a technique for brachial venous endomyocardial biopsy, which we have implemented as the preferred route. In this article, we describe the technique and the initial clinical experience.

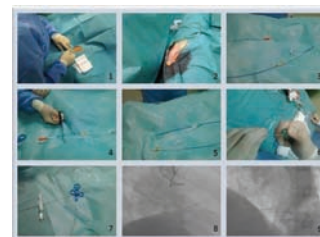
**Methods:** Between February and October 2015, we developed and implemented the brachial venous approach technique. We registered prospectively the main clinical and procedural variables. Furthermore, we retrospectively recorded all the biopsy procedures performed in our center since 2010. We compared the characteristics of the procedures performed through different routes.

**Results:** the brachial route was attempted in 63 procedures, and achieved successfully in 62 (98,4%). No complications occurred. Between 2010 and 2015, 322 biopsy procedures were performed in 65 patients. Of them, 56,5% were through the jugular vein, 24,2% through the femoral and 19,3% through the brachial. The jugular procedures needed less fluoroscopy time and dose than the femoral and brachial procedures (fluoro time 2,4 / 5,3 / 6,2 min, p < 0,01; fluoroscopy dose 700 / 1473 / 2049 µg\*m2, p < 0,01). The femoral procedures were longer than the rest (40 vs 30 min, p < 0,01). Brachial procedures were recalled as less painful than jugular or femoral ones (2 / 8 / 9 score on a scale of 1-10; p=0,001). All patients who underwent procedures through two different paths preferred the brachial access.

**Conclusion:** the venous brachial route is a good alternative to central venous route for endomyocardial biopsy, with high feasibility and safety, and additional patient comfort.

	Brachial	Femoral	Jugular	p
Procedure time (min)	30 (19-35)	40 (32-51)	30 (21-40)	<0,001
Fluoroscopy time (min)	6,2 (4,1-8,0)	5,3 (3,0-7,4)	2,4 (1,5-3,5)	<0,001
Fluoroscopy dose (uGy m2)	2049 (1400-3281)	1473 (796-3065)	700 (400-1084)	<0,001

Total procedure time, fluoroscopy time and fluoroscopy dose according to the different access routes.



Steps of the brachial biopsy procedure

**P903**

**Actual condition survey of terminal illness in the advanced heart failure: symptoms and drug utilization during the last two weeks of life**

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**Background:** Management and therapy have improved the survival of heart failure (HF) patients. However, many patients progress to advanced chronic HF and death



with variety of symptoms. Recently, palliative and supportive care intervention in advanced heart failure has referred in guidelines for heart failure. On the other hand, reports referred for characteristics and symptoms of the patients which should be intervened during the last few weeks.

**Subjects and Methods:** We retrospectively investigated the characteristics, symptoms, and drug usage during the last 2 weeks of patients with hospital admission for heart failure and die between November 2012 and October 2014.

**Results:** We investigated 40 patients (aged  $79 \pm 11$ , 38% males, 33% ischemic etiology) with cardiac death (sudden cardiac deaths: 4 patients) among 841 patients with hospital admission for heart failure. Their last hospital length of stay was  $32 \pm 28$  days and 73% of patients had a history of hospitalization within a year. Noninvasive positive pressure ventilation (NPPV) was used for 5 (13%) patients and endotracheal intubation was performed for 7 (18%) patients during two weeks. Left ventricular ejection fraction (LVEF) was  $33 \pm 18\%$ , plasma brain natriuretic peptide (BNP) level was  $1709 \pm 1890$  pg/ml, and estimated glomerular filtration rate (eGFR) was  $31.0 \pm 20.4$  mL/min/1.73 m<sup>2</sup>. They complained of breathlessness (55%), fatigue (60%), pain (28%), nausea and vomiting (25%), anxiety (23%), and depression (10%) during last two weeks, respectively. Intravenous inotropic agents were continuously administered for 70% of patients until the last breath, and intravenous morphine was administered for 23% of patients for palliation of breathlessness and pain.

**Conclusion:** In this study the current situation of terminal phase of advanced heart failure became clinically evident. Appropriate palliative and supportive care was provided for patients based on right assessment of symptoms. Anxiety and depression were possibly underestimated because they tended to be missed without careful observation. Accurate evaluation and treatment including palliative and supportive care were required for the improvement in quality of life of advanced heart failure patients.

#### P904

##### Left atrial strain and capillary wedge pressure in patients candidate to heart transplantation

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**Background:** Left atrial (LA) deformation analysis by speckle tracking echocardiography (STE) was recently proposed as an alternative approach to estimate LV filling pressures. This study aimed at exploring the correlation of LA longitudinal function by STE and Doppler measurements with direct measurements of LV filling pressures in patients candidate for heart transplantation at baseline and after nitroprusside challenge test.

**Methods:** 75 hemodynamically stable, end stage heart failure patients who were undergoing right heart catheterization (RHC) were included. Doppler echocardiography and RHC catheterization were simultaneously performed. Echocardiographic measures and STE were obtained as LA peak atrial longitudinal strain (PALS).

**Results:** LA PALS was inversely correlated with invasively assessed pulmonary capillary wedge pressure ( $r = -0.83$ ;  $P < 0.0001$ ). LA PALS retained this correlation even after nitroprusside challenge test ( $r = -0.88$ ;  $P < 0.0001$ ), indicating patients responder to preload decrease. E/E' showed poor correlation with wedge pressure at baseline and after nitroprusside infusion ( $r = 0.24$ ,  $p = ns$ ; and  $r = 0.22$ ,  $P = ns$ ). Area under the curve optimal cut offs for predicting the wedge pressure  $> 18$  mmHg were for LA PALS 15.0% (AUC:0.91, sensitivity: 97%, specificity: 83%).

**Conclusion:** LA strain significantly correlate with pulmonary capillary wedge pressure and its changes after nitroprusside challenge test in patients candidate for LV filling pressures.

## ATRIAL FIBRILLATION

#### P905

##### Characteristics of heart failure decompensation on atrial fibrillation and on sinus rhythm.

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**Aim:** to reveal some peculiarities of CHF decompensation course and unfavorable exits risk depending on cardiac rhythm on moment of hospitalization. Methods and materials: 60 patients who had been hospitalized due to CHF decompensation (average age  $71.6 \pm 11.5$  yrs) were examined. They were divided into 2 groups depending on cardiac rhythm on moment of admission. The 1st group consisted of 30 patients with sinus rhythm, and the 2nd group – 30 patients with atrial fibrillation (AF) (12 patients with paroxysmal or persistent form, and 18 with permanent form). All the patients underwent standard clinical examination and observation for 3 months after discharge.

**Results:** groups were not different in sex, age, comorbidities, main biochemistry, doses of intravenous diuretics and inotropes, RAAS blockers and mineralocorticoid

blockers. Regimens of both anticoagulants and digoxin administration were different with prevalence in 2nd group ( $=0.073$  and  $=0.026$ , respectively). There was significant disparity in LV EF affected by evident decrease:  $35.8 \pm 2.7\%$  on sinus rhythm vs  $33.9 \pm 3.1\%$  on AF ( $=0.014$ ). Also, stands out the difference in hemoglobin level, which is low in both groups:  $106.6 \pm 7.7$  g/L vs  $101.7 \pm 6.1$  g/L ( $=0.011$ ). Next hospitalizations after 3 months occurred reliably more frequently in the 2nd group: 3.3% vs 30.0% ( $=0.044$ ). Correlation analysis showed that low hemoglobin has influenced on followed hospitalizations for CHF decompensation more than LV EF value ( $r = -0.41$ ,  $p = 0.045$  vs  $r = -0.60$ ,  $p = 0.102$ , respectively).

**Conclusion:** CHF decompensation with atrial fibrillation proceeds with more evident systolic dysfunction, and anemia as the sign of system impairment, as well as it deteriorates prognosis in term of repeat episodes of CHF decompensation.

#### P906

##### Central blood pressure at different pulse wave velocity and atrial fibrillation recurrence in heart failure patients with preserved ejection fraction

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**Objective:** Atrial fibrillation (AF) is common in heart failure (HF), but few data regarding relationship between arterial stiffness and AF recurrence are available in HF patients with preserved left ventricular ejection fraction (HF-P EF).

**Aim:** the purpose of this study was to compare AF recurrence rate in patients with HF-P EF and different PWVcf.

**Methods:** The study included 55 patients (40% men) aged 66 (62; 73) years with mild-to-moderate AH, one year anamnesis of recurrent AF and HF-P EF (>50%). All patients were performed applanation tonometry. Patients were divided into 3 groups: with increased arterial stiffness ( $PWV \geq 10$  m/s) and AF recurrence ( $n = 9$ ), with normal arterial stiffness and AF recurrence ( $n = 18$ ) and normal arterial stiffness and without recurrence of arrhythmia during 3 months follow-up ( $n = 18$ ).

**Results:** Groups were significantly different by age ( $p < 0.001$ ), the risk of thromboembolic events according to CHA2-DS2-VASc ( $p = 0.002$ ), these rates were highest in the group with  $PWV \geq 10$  m/s and AF recurrence. Patients with increased arterial stiffness had the highest heart rate (HR,  $p = 0.009$ ), shorter time to return of reflected wave (Tr,  $p < 0.001$ ) and a greater augmentation index (AIx-HR75,  $p = 0.02$ ) with comparable values of both brachial and central SBP and DBP. Peripheral and central pulse pressure (PP and cPP) had significantly lower ranges in patients with normal arterial stiffness and without recurrence of arrhythmia ( $p < 0.001$  and  $p = 0.006$ , respectively). Regression analysis showed positive correlations of AF recurrence with age ( $\beta = 0.65$ ,  $p < 0.001$ ), HR ( $\beta = 0.54$ ,  $p < 0.001$ ), cPP ( $\beta = 0.60$ ,  $p < 0.001$ ), AIx-HR75 ( $\beta = 0.66$ ,  $p < 0.001$ ) and negative relations with Tr ( $\beta = -0.48$ ,  $p = 0.001$ ).

**Conclusion:** AF recurrence in patients with increased PWV was associated with higher pulse pressure and worse parameters of reflected wave. Reflected wave could have a role in modification of arterial stiffness in patients with  $PWV \geq 10$  m/s.

#### P907

##### Optimization of warfarin dosing for patients with chronic kidney disease

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**Materials and Methods:** The study included 238 patients with paroxysmal and persistent atrial fibrillation receiving anticoagulation therapy (warfarin) for at least 1 year before to inclusion in the study. All patients assessed the risk of thromboembolic complications - on a scale CHA2DS2VASS, the risk of bleeding - on a scale HAS-BLED, and TTR. All patients (100%) had at least two points on the scale CHA2DS2VASS. 93 patients (39%) have a high risk of thromboembolic complications on a scale CHA2DS2VASS, and 105 patients (44%) have the average risk on a scale of HAS-BLED. TTR during the year before the study was 38%. According to MDRD glomerular filtration rate (GFR) was calculated for all patients. GFR of 107 patients (45%) is 60-45 ml / min, GFR of 99 patients (42%) is 44-30 ml / min, GFR of 32 patients (13%) is of less than 30 ml / min. Considering the clinical experience of our clinic, patients with a GFR less than 30 ml / min have been proposed a new algorithm of warfarin dosing, in compare with the classic, which is used in warfarin-dosing.org and other resources. Patients with GFR less than 30 mL / min were considered as patients at high risk of bleeding, and therefore, they held control of the international normalized ratio (INR) 1 every 3 days, but it was recommended to increase the dose of warfarin 1 time in 7 days, despite the low or high INR. At a high INR - cessation of the drug with a further decrease in dose. INR control is carried out every 4-5 days, as the reduction in the INR is slow in this group of patients. Recommended level of INR in this group of patients is in the range from 2 to 2.7. It was estimated large and small bleeding, thromboembolic complications and TTR index. Retrospective data during 1 year and data during research also 1 year were compared.

**Results:** The amount of bleeding was significantly ( $p = 0.019$ ) prevailed in the group of retrospective analysis. In applying the new algorithm it was mentioned 1 big bleeding (3%) and 4 small bleedings (12%), but in group of retrospective analysis it was

mentioned 5 big bleedings (16%) and 24 small bleedings (75%). Significant difference in the number of thromboembolic complications were not found ( $p=0.547$ ). Statistically significantly TTR was different ( $p=0.044$ ). In the group of retrospective analysis TTR is 32%, in the study group TTR is 51%.

**Conclusions:** in the application of the recommended warfarin dosing algorithm, patients with chronic kidney disease (GFR less than 30 / min) have statistically significant reduction in both large and small hemorrhages. However, no statistically significant correlation between thromboembolic complications investigated groups. TTR remains within the therapeutic range greater amount of time when using the new algorithm.

#### P908

##### Do patients under non-vitamin K oral anticoagulants need to switch to parenteral anticoagulation when admitted for acute decompensated heart failure?

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**Background:** Patients with both atrial fibrillation (AF) and hospitalization for acute decompensated heart failure (ADHF) often have transient renal function impairment. This may lead to a temporary contraindication to NOAC therapy.

**Purpose:** We aimed to evaluate the need for NOAC cessation due to renal function impairment in patients admitted for ADHF with non-valvular AF in order to help define a standard approach.

**Methods:** 2181 consecutive patients with AF who were evaluated in our Emergency Department (ED) in a 12 month period. All patients underwent routine clinical and laboratory exams. We evaluated the degree of renal impairment (peak estimated glomerular filtration rate, eGFR) during hospital stay using Cockcroft-Gault (CG), simplified Modification of Diet in Renal Disease (MDRD), and Chronic Kidney Disease Epidemiology Collaborative (CKD-EPI) equations. An eGFR  $\leq 15\text{mL/min/1.73m}^2$  was used in order to determine the proportion of patients hypothetically requiring NOAC cessation. Additionally we determined the need for dose adjustment for each NOAC (dabigatran, rivaroxaban and apixaban) according to FDA prescribing guidance.

**Results:** 96 patients were admitted with both non-valvular AF and ADHF (mean age of  $77.1 \pm$  standard deviation 9.7 years, 40.6% males). CKD-EPI identified a greater proportion of patients requiring NOAC cessation (12.5%), followed by MDRD (10.4%) and CG (8.0%). Among patients who would discontinue NOAC, 33.3% would experience renal recovery (eGFR  $>15\text{mL/min/1.73m}^2$ ) according to CKD-EPI, 20.0% using MDRD equation and 14.3% patients according to CG. Dose adjustment would be needed in 65.5% of patients for rivaroxaban, in 40.6% for apixaban and in 33.3% for dabigatran.

**Conclusion:** Only 1 in 10 patients admitted for ADHF under NOAC therapy for non-valvular AF would have to discontinue NOAC and initiate parenteral anticoagulation, although dose adjustments would be frequently necessary. In patients with 'de novo' severe renal impairment, up to one third would need to switch to vitamin K antagonists at discharge.

#### P909

##### Risk of recurrent atrial fibrillation after pulmonary vein isolation- a gender specific approach.

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**Purpose:** Pulmonary vein isolation (PVI) is a standard treatment option in chronic atrial fibrillation (AF). Recurrence of AF (recAF) is an issue, however. Prediction of recAF in patients with paroxysmal AF was related to atrial reservoir function, whereas atrial size has been demonstrated to be a risk factor in permanent atrial fibrillation. We hypothesized that risk of recAF ( $\geq 3$  months after PVI) should be assessed by a stratified approach and investigated the impact of gender on risk prediction.

**Methods:** We evaluated data sets from 154 consecutive patients (age  $61 \pm 12$  years, 50 females, 69 paroxysmal AF) prior to pulmonary vein isolation (PVI). Transthoracic (transmitral and tissue Doppler, linear parameters and area and volume measurements) and transoesophageal echocardiography (pulmonary vein Doppler) were performed. Data were evaluated for correlation with recAF by Kendall's-tau. Parameters with significant correlation were further evaluated in logistic regression analysis. This was performed by either treating gender as variable or analysis in gender subgroups. Partial validation was performed by bootstrap.

**Results:** Treating gender as a variable in regression analysis yielded a 62% correct prediction of recAF. If regression modeling was performed in subgroups separately, 70% of recurrences were predicted correctly in either group. This improvement was significant. Moreover, interestingly in females recAF was associated with lower systolic pulmonary vein velocities (PVsys) and smaller end-diastolic diameters (LVEDD), whereas there was no significant difference in 4-chamber end-systolic area (LA-area) and no significant constant in a significant logistic regression model

(-2 Log-Likelihood 43). Model coefficients B (no bootstrap because of limited sample size):

PVsys:  $-0.130 (-0.027-0.233)$ ,  $p=0.013$ ; LVEDD:  $0.069 (0.0139-0.123)$ ,  $p=0.013$ .

On the contrary in males pulmonary vein velocities did not correlate with recAF and LVEDD. In males LA-area and E/E' (E-wave divided by averaged tissue Doppler E-wave) were the best predicting variables in a significant logistic model (-2 Log-Likelihood: 113) including a significant constant. Model coefficients B (bias corrected/bootstrap):

E/E':  $0.231 (0.03-0.524)$ ,  $p=0.032$ ; LA-area:  $0.112 (0.027-2.18)$ ,  $p=0.002$ ; constant:  $-4.832 (-7.603-3.009)$ ,  $p=0.001$ .

**Conclusion:** Subgroup specific modeling may help to improve risk prediction for recurrence of AF after pulmonary vein isolation. Our results remains to be corroborated by further validation studies. Variations in causal pathology may be reflected by differing associations of outcome with distinct measurement variables. These associations may cancel or be smoothed in aggregated samples. Stratified analysis, although limited by sample size, may provide interesting insights.

#### P910

##### Predicting atrial fibrillation in critically ill patients admitted in a general intensive care unit: is BNP really helpful?

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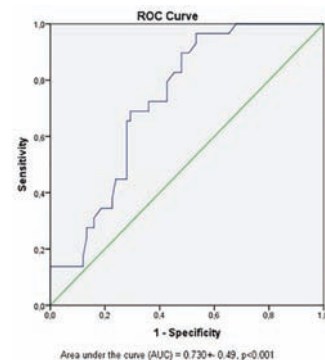
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**Introduction and objective:** In a general intensive care unit (GICU), newly-diagnosed atrial fibrillation (AF) has many different etiologies, and has been associated with a worse prognosis. The correlation between B-type natriuretic peptide (BNP) and AF has been evidenced by some large scale studies, but many questions still remain, especially in regard to such a particular population as the GICU patients. The potential role of BNP as a predictor of AF in this population was investigated.

**Methods:** The authors (AA) analyzed a consecutive group of 104 patients admitted in a GICU with BNP assessed within the first 48 hours and compared two groups: the group that developed newly-diagnosed AF (wAF,  $n=29$ ) and the group with no AF (noAF,  $n=75$ ). Statistical comparison and binary regression was done to search for differences and predictors of AF.

**Results:** Mean age was  $65.4 \pm 16.0$  years, with 61.5% of males and a mean APACHE score of  $22.8 \pm 6.6$ . Overall mean BNP was  $412.3 \pm 663.1$  pg/mL. In-hospital mortality was 17.3% ( $n=18$ ). Twenty patients (19.2%) developed signs of heart failure. Mean BNP value was significantly different between the groups: wAF ( $737.4 \pm 197.2$  pg/mL) vs. noAF ( $286.5 \pm 41.3$ );  $p=0.033$ . After statistical adjustment for age, gender, APACHE score and HF diagnosis, a BNP value  $>300$  pg/mL was an independent predictor for atrial fibrillation (OR = 4.46, IC95: 1.58-12.58,  $p=0.005$ ), with ROC-curve analysis showing a 70.7% specificity and 69.0% sensibility for this cut-off.

**Conclusion:** Based on the current data BNP seems to be a prognostic marker to predict AF occurrence in critically ill patients admitted in a GICU. More studies with larger populations are needed.



ROC Curve

#### P911

##### Cardio-vascular interconnection in patients with decompensated CHF depending on cardiac rhythm.

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**Aim:** to reveal some peculiarities of cardio-vascular interconnections in patients with decompensated ischemic CHF in the context of different cardiac rhythms. Methods and materials: 92 patients with decompensated ischemic CHF and decreased LV

EF were examined. Patients were divided into 2 groups depending on cardiac rhythm. The 1st group consisted of 60 patients with atrial fibrillation (AF), and the 2nd group – 60 patients with sinus rhythm. All the patients underwent Echo, biochemistry (NT-proBNP and TIMP-1), and sphygmopletismography (VaSera1000, Japan), which showed pulse wave velocities (PWV) in several segments of central and peripheral flow (carotid-femoral PWVcf, aortal PWVao, carotids PWVc). Both groups were equal in swx, age, comorbidities.

**Results:** severity of CHF symptoms did not differ: CHF functional class was  $2,68 \pm 0,49$  in the 1st group,  $2,59 \pm 0,40$  in the 2nd group ( $=0,375$ ). Decrease of LV EF was indicated in the both groups, but they differed reliably between the groups:  $44,71 \pm 11,06\%$  vs  $51,3 \pm 2,6\%$  ( $=0,001$ ). Myocardial stress severity (evaluated by NT-proBNP), was harder in patients with AF:  $618,4 \pm 106,6$  pg/mL vs  $305,0 \pm 151,5$  pg/mL,  $<0,001$ . Myocardial collagenolysis activity was also lower in patients with AF:  $932,7 \pm 15,1$  vs  $653,5 \pm 10,8$ ,  $<0,001$ . Sphygmopletismography showed significant prevalence of vascular remodeling in patients with CHF and AF, what appeared in decrease of both flow velocity and elasticity, and in increase of arterial stiffness in central and peripheral segments. PWVcf:  $11,9 \pm 1,7$  m/sec vs  $10,3 \pm 3,02$  m/sec ( $=0,002$ ); PWVao:  $11,36 \pm 5,24$  m/sec vs  $8,90 \pm 3,3$  m/sec ( $=0,018$ ); PWVcarotid:  $1,19 \pm 1,23$  m/sec vs  $1,68 \pm 0,03$  m/sec ( $=0,003$ ); CAVI-1:  $9,49 \pm 1,53$  vs  $8,47 \pm 1,86$  ( $p=0,006$ ).

**Conclusions:** permanent AF in patients with decompensated CHF aggravates arterial remodeling by decrease of collagenolysis activity and by rate- and rhythm-dependent unfavorable ventricular-arterial interaction.

### P912

#### Difference in mortality among digoxin users treated for non-valvular atrial fibrillation with different stages of chronic kidney disease: a nationwide register-based cohort study.

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**Introduction:** Changes in renal function due to chronic kidney disease could change digoxin serum concentration. It is well accepted that digoxin benefit/risk ratio is highly related to the dosage and consequently to the serum concentration. Digoxin has a narrow therapeutic window and even small change in dosage could affect the risk of toxicity. Despite the well-known effect of renal function on risk of digoxin toxicity, there is a lack of knowledge regarding the impact of different stages of chronic kidney disease on several clinical outcome (including mortality) in patients with atrial fibrillation treated with digoxin.

**Purpose:** Considering is not rare to see patients with both conditions as previous studies have found a higher prevalence of patients with both atrial fibrillation and chronic kidney disease compared to the general population, the objective of this study was to investigate the impact of different stages of chronic kidney disease on mortality across non-valvular atrial fibrillation patients treatment-naïve with digoxin.

**Methods:** All patients with non-valvular atrial fibrillation or atrial flutter as hospitalization diagnosis from January 1, 1997 to December 31, 2012 were extracted through Danish nationwide administrative registries. From this preliminary population were extracted only digoxin treatment-naïve users that have started pharmacological treatment for non-valvular atrial fibrillation in the period. Patients were excluded if they started digoxin in co-administration with other antiarrhythmic drugs. All patients should be diagnosed with non-valvular atrial fibrillation before first digoxin prescription. Using creatinine measurement within 180 days from the first digoxin prescription, the estimated glomerular filtration rate (eGFR) was established for each patient which had creatinine measurement. Based on the results of eGFR, patients were divided into two cohorts, those with eGFR  $<30$  and those with eGFR  $\geq 30$  ml/min/1.73m<sup>2</sup>. Propensity score was used to match patient with eGFR  $<30$  with 4 patients with eGFR  $\geq 30$  ml/min/1.73m<sup>2</sup> for the main confounders and co-administrated drugs. A total of 2740 patients was used; 548 patients with eGFR  $<30$  ml/min/1.73m<sup>2</sup>. Cox proportional hazard analysis was performed to assess differences in all-causes and cardiovascular mortality between the two cohorts. Results. Cox regression analysis showed no statistically significant differences in all-causes and cardiovascular mortality among patients with eGFR  $<30$  compared to those with eGFR  $\geq 30$  ml/min/1.73m<sup>2</sup> within both 180 days and 2 years from index date.

**Conclusions:** The results suggested that eGFR is not a predictor for all-causes and cardiovascular mortality across non-valvular atrial fibrillation patients treatment-naïve with digoxin.

### P913

#### Is body mass index a risk factor for new onset atrial fibrillation in patients with acute coronary syndrome

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**Purpose:** Atrial fibrillation (AF) is a common complication of acute coronary syndrome (ACS) and usually it is associated with an increase in mortality and adverse events. The aim of the study was to evaluate the incidence of AF in patients with ACS and to evaluate if body mass index (BMI) is a risk factor for new-onset AF in patients with ACS.

**Methods:** We enrolled 600 patients with ACS, 290 patients with STEMI and 310 patients with NSTEMI. At entry, all patients were in sinus rhythm. The AF group included patients with ACS and new onset AF during the hospital course and control group included patients with ACS without AF during the hospital course.

**Results:** Mean age of patients was  $63.6 \pm 10.6$  years, between them 425 were men and 275 women, mean BMI was  $26.8 \pm 2.6$  kg/m<sup>2</sup>. The incidence of new-onset AF was 8% in the patients with ACS during the hospital course. In AF group there were 48 patients and in control group were 552 patients. We analyzed risk factors for coronary artery disease (CAD) and incidence of AF and found that the patients in AF group were older  $69.9 \pm 9.4$  years versus  $63.1 \pm 11.4$  in control group and with higher BMI ( $28.0 \pm 2.6$  kg/m<sup>2</sup> in AF group versus  $26.7 \pm 2.6$  kg/m<sup>2</sup> in control group),  $p < 0.01$ . There was not difference in gender distribution, frequency of smokers, arterial hypertension, hyperlipidemia, diabetes mellitus and family history for CAD between the groups,  $p > 0.05$ . Multivariable logistic regression analyses showed that from risk factors for CAD older age, OR (95% CI) is  $2.37$  ( $1.23-4.58$ ),  $p = 0.01$  and increased BMI, OR (95% CI) is  $1.17$  ( $1.04-1.33$ ),  $p = 0.012$  were independent predictors of new onset AF in the patients with ACS.

**Conclusions:** The incidence of new-onset AF was 8% in the patients with ACS during the hospital course. The independent predictors of new-onset AF from risk factors for CAD in the patients with ACS were older age and increased BMI.

### P914

#### Efficacy and safety of novel oral anticoagulants in patients with atrial fibrillation and heart failure: a meta-analysis

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**Background:** Symptomatic heart failure (HF) has a prevalence of 30% in patients with atrial fibrillation (AF). Patients with HF are older and frailer, have more comorbidity and are at higher risk of both stroke and bleeding, compared with younger patients.

**Purpose:** To investigate the efficacy and safety of novel oral anticoagulants (NOAC) in patients with AF and HF, in a meta-analysis of all the recent phase III warfarin comparison trials.

**Methods:** The 4 major clinical trials (ARISTOTLE, ENGAGE AF, RE-LY, ROCKET AF) comparing NOACs to warfarin in patients with non-valvular AF were included. Pre-specified outcomes were the composite of stroke and systemic embolism (SSE), major, intracranial and any bleeding, cardiovascular (CV) and all-cause death.

**Results:** 55,011 patients were enrolled in 4 trials, 26,384 (48%) with HF and 28,627 (52%) without HF, 27,518 receiving NOACs and 27,493 warfarin [median age 70 years, 36% females, follow-up range: 1.5-2.8 years]. Rates of SSE (RR:0.98 [95% CI:0.90-1.07],  $p = 0.68$ ) and major bleeding (RR:0.95 [0.88-1.03],  $p = 0.21$ ) were comparable in patients with and without HF. HF patients had reduced rates of any (RR:0.86 [0.81-0.91],  $p < 0.01$ ) and intracranial (RR:0.74 [0.63-0.88],  $p < 0.01$ ) bleeding, but increased rates of all-cause (RR:1.70 [1.31-2.19],  $p < 0.01$ ) and CV death (RR:2.05 [1.66-2.55],  $p < 0.01$ ). In HF patients, NOACs, as compared to warfarin, significantly reduced the risk of SSE (RR:0.86 [0.76-0.97],  $p = 0.01$ ), major (RR:0.77 [0.68-0.87],  $p < 0.01$ ), intracranial (RR:0.43 [0.33-0.56],  $p < 0.01$ ) and any (RR:0.88 [0.80-0.98],  $p = 0.02$ ) bleeding, without any significant effect on all-cause (RR:0.94 [0.88-1.01],  $p = 0.08$ ) and CV (RR:0.92 [0.84-1.01],  $p = 0.11$ ) mortality. In patients without HF, NOACs, as compared to warfarin, significantly reduced the risk of SSE (RR:0.77 [0.68-0.87],  $p < 0.01$ ), major (RR:0.88 [0.79-0.97],  $p = 0.01$ ) and intracranial (RR:0.51 [0.41-0.64],  $p < 0.01$ ) bleeding, as well as all-cause (RR:0.85 [0.77-0.95],  $p = 0.04$ ) and CV (RR:0.81 [0.71-0.93],  $p = 0.02$ ) mortality. Rates of any bleeding were numerically lower with NOACs, but this did not meet statistical significance (RR:0.90 [0.80-1.00],  $p = 0.054$ ). Consequently, no difference in the efficacy and safety of NOACs, as compared to warfarin, was detected between patients with and without HF (Pinteraction  $> 0.05$  for each).

**Conclusions:** Patients with AF and HF had increased mortality, but reduced rates of intracranial and any bleeding compared to no-HF patients, with no difference in rates of SSE and major bleeding. NOACs significantly reduced SSE, major bleeding and intracranial haemorrhage in HF patients. No interaction in efficacy and safety of NOACs was observed between AF patients with and without HF.



## CARDIOMYOPATHY

## P915

**Right ventricular function and the evolution of echocardiographic parameters in patients with inflammatory cardiomyopathy**

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**Introduction:** The right ventricle (RV) function is considered as an important prognostic predictor in patients with heart failure. According to an earlier study, impaired RV function is negative prognostic marker also in inflammatory cardiomyopathy (ICM).

**Objective:** Evaluation of the significance of RV function at the time of diagnosis for prediction of echocardiographic parameters evolution in patients with biopsy proven ICM in the 6-month follow-up.

**Patients and methods:** 64 patients with left ventricular ejection fraction (LVEF)  $\leq 40\%$  with bioptic findings of  $>7$  CD3+ cells / mm<sup>2</sup> and / or  $>14$  CD45+ cells / mm<sup>2</sup>. They were divided into two groups: 1 / patients with initially preserved RV systolic function and 2/ patients with RV dysfunction. RV dysfunction was defined as the presence of at least two of the three following parameters: RV diameter  $\geq 31$  mm, s'tri  $\leq 10$  cm/s and TAPSE  $\leq 16$  mm. Changes in echocardiographic parameters in 6-month follow-up in both groups were assessed and compared.

**Results:** In the group 2 (with RV dysfunction, n = 37) LVEF at baseline was lower than in the group 1 (with preserved RV function, n = 27):  $21 \pm 7\%$  vs.  $29 \pm 7\%$  ( $p < 0.001$ ). Conversely, improvement in LVEF in the group 2 ( $21 \pm 15\%$ ) was more significant than in the group 1 ( $12 \pm 13\%$ );  $p < 0.05$ . Improvement in diastolic LV function expressed by the ratio E/e' was more pronounced in the group with RV dysfunction ( $-6.7 \pm 6.6$  vs  $-1.0 \pm 4.8$ ;  $p < 0.001$ ). Similarly, more significant improvement in other parameters was observed in the group 2: s' and e' mitral annular velocities, LV end-systolic volume, TAPSE, s'tri and RV diameter.

**Conclusion:** The RV dysfunction at baseline was associated with more significant improvement in majority of evaluated echocardiographic parameters in a group of patients with biopsy-proven ICM.

## P916

**Septic myocarditis is mainly due to cardiac failure without significant myocardial necrosis**

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**Background:** Only few studies incorporating electrocardiography, high sensitive troponin T (hsTnT), N-terminal pro-BNP (pro-BNP) and echocardiography has been conducted in patients with septic myocarditis.

**Methods and results:** Out of 204 patients with sepsis enrolled, 111 patients satisfied the inclusion criteria and 103 completed the study. Myocardial injury was defined by elevation of hsTnT  $> 25$  pg/ml. Initial hsTnT, pro-BNP and 2D echocardiography were repeated if sepsis progresses. End points were in hospital mortality and left ventricular dysfunction (LVD). Simple sepsis was diagnosed in 45%; 19% had septic shock and 36% developed severe sepsis. Sinus tachycardia was present in 65% and T inversion in inferior leads in 32%. Systolic dysfunction (SD) was present in 42%, diastolic dysfunction (DD) in 21% and 21% had both SD and DD. HsTnT was elevated in 84% of the patients. Both HsTnT and pro-BNP significantly correlated with LVD ( $p < 0.001$ ). Though pro BNP and HsTnT vary in different levels of LVD (table 1). Both levels were lesser in DD than SD. Grade III DD was associated with severe SD. Pro-BNP had significant correlation with pro-calcitonin level ( $p < 0.001$ ) and APACHE II score ( $p < 0.001$ ); HsTnT had significant correlation with APACHE II score ( $p < 0.001$ ). In hospital mortality was 8%. In survivors hsTnT was 158pg/ml and pro-BNP was 6400 pg/ml. In non-survivors hsTnT was 256 pg/ml ( $p < 0.047$ ) and pro-BNP was 21805pg/ml ( $p < 0.001$ ). Pro BNP had better correlation with survival. ROC curve showed that pro-BNP level  $> 8530$  pg/ml signified with mortality (sensitivity-100% and specificity-80%) and HsTnT level  $> 178$ pg/ml correlated with mortality with 88% sensitivity and 71% specificity. Base line creatinine was normal in all our patients; **CONCLUSION** :- Pro-BNP value  $> 8530$  pg/ml signified decreased survival with 100% sensitivity. The significant elevation of pro-BNP with minimal elevation of hsTnT indicated that the pathophysiology is mainly myocardial stretch and not myocardial necrosis in sepsis; with full recovery in survivors.

Table 1: distribution of pro-BNP and HsT

ECHOCARDIOGRAPHY	%	Mean pro-BNP(pg/ml)	Mean HsTnT(pg/ml)
Normal	16	2433 (700-4100)	76 (<25-160)
Mild LV SD	11	5481 (3200-9200)	210 (80-360)
Moderate LV SD	13	9608 (5400-16100)	254 (150-480)
Severe LV SD	18	16844 (7200-25000)	268 (148-450)
Grade I DD	8	3132 (1024-5250)	117 (60-220)
Grade II DD	13	6596 (3500-9000)	125 (26-240)

Table 1: distribution of pro-BNP and HsTnT in LVD (\*21% had combined LVD)

## P917

**Left ventricular non-compaction - a magnetic resonance guided clinical and morphological correlation**

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**Introduction:** Left ventricular non-compaction (LVNC) is a rare, relatively recently described congenital cardiomyopathy, whose prevalence is continuously rising due to the improved accessibility of modern imaging techniques. It is considered to result from the defective development of the myocardial architecture in the late-stages of embryogenesis and is characterized by a hypertrabeculated myocardial structure. Its pathophysiological and clinical implications are the subject of continuous investigation.

**Purpose:** The purpose of the study was to establish a correlation between the clinical presentation and the morphological aspect of the left ventricle (LV), as described by the cardiac magnetic resonance imaging (MRI) examination.

**Methods:** We retrospectively evaluated 35 patients diagnosed with LVNC between Jan 2010 and Jan 2015 based on the echocardiographic Jenni criteria (end-systolic ratio of non-compacted to compacted myocardium above 2). Only patients with the diagnosis confirmed by cardiac MRI, according to the criteria established by Petersen (the diastolic ratio of non-compacted to compacted myocardium greater than 2.3) and Jacquier (trabeculated left ventricular mass above 20% of the total myocardium), were finally included in the study. The medium follow-up period was 3.5 years.

**Results:** 14 patients were included in the final analysis, with a medium age at diagnosis of 45.5 years. The most common form of presentation was heart failure, followed by ventricular arrhythmias. 64.2% of patients had some form of intraventricular conduction disorder, the most frequent being left bundle branch block. Regarding the distribution of the non-compacted myocardium, the lateral wall of the LV was most frequently involved (92.8%), followed by the anterior wall (78.5%), the apex (57.1%) and the inferior wall (42.8%). 78.5% of patients had depressed LV systolic function, defined as an LV ejection fraction below 50%. There was a positive correlation between the extension of the non-compacted myocardium and the severity of the systolic dysfunction. 71.5% of patients had some form of diastolic dysfunction, with an equal distribution between the impaired relaxation and restrictive pattern. During follow-up, there were two readmissions for decompensated heart failure. One patient received an implantable cardioverter-defibrillator for the secondary prevention of sudden cardiac death and one benefitted from cardiac resynchronization therapy. No thromboembolic complications were recorded. There was one fatality, due to massive acute pulmonary oedema.

**Conclusions:** LVNC is a rare cardiomyopathy, with considerable implications on cardiac function. Echocardiography is considered the standard diagnostic method, but it frequently over- or underestimates the disease prevalence. Therefore, cardiac MRI has become an important tool in confirming the diagnosis. There are still many questions to be answered and a need for more precise echocardiographic diagnosis criteria.

## P918

**Effects of adaptation to intermittent normobaric hypoxia in the patients with ischemic cardiomyopathy**

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The purpose of this research was to study the effects of intermittent normobaric hypoxia adaptation (NIHA) in the patients with ischemic cardiomyopathy (ICMP) and chronic heart failure (CHF).

**Materials and Methods:** Cohort of 90 ICMP patients with HF class II-IV NYHA (n = 45 in the main and control groups) were included into the research. The patients of the main group underwent a 10-days NIHA course before cardiac surgery (CABG).

**Results:** The initial CHF severity in the both groups was determined by depressed

left ventricle systolic function (LVEF less than 35%) against maladaptive LV remodeling, multiple myocardial perfusion defects with the prevalence of sympathetic activity nervous system (NS) and the changes in the endothelial dysfunction (ED) markers. After NIHA course we revealed the significant decrease in the area of myocardium with slight and moderate hypoperfusion as well as the prevalence of parasympathetic NS activity with reduction in the number of ventricular arrhythmias (VA). It was also marked the significant decrease in the level of the concentration of biochemical ED markers such as endothelin-1, TNF-alpha, interleukin-6, homocysteine and the increase in brachial artery diameter and Gosling's pulsatility index during reactive hyperemia test. The main group patients were characterized with a more favorable recovery during the intra- and early postoperative period after CABG with significantly less frequent of the low cardiac output syndrome with prolonged inotropic support. We also noted EF improvement, significantly less frequent of ventricular fibrillation during artificial circulation and the number of perioperative myocardial infarction with high grade VA.

**Conclusion:** The use of NIHA course before CABG for the patients with ICMP helps to protect from reperfusion injury and improve the endothelium functional state and microcirculatory processes in the myocardium with reduces the prognostically unfavorable VA after CABG..

### P919

#### Cirrhotic cardiomyopathy-a new entity?

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Liver cirrhosis is associated with a number of secondary cardiovascular changes. New clinical entity, cirrhotic cardiomyopathy (CCM) is already recognized, but still much underdiagnosed. Diagnosis is based on a combination of clinical, echocardiographic and electrocardiographic findings, associated with bioenergetic markers. The aim of the study was to analyze the incidence and prevalence of these data in order to obtain an early diagnosis.

**Methods:** The study group was represented by 53 cirrhotic patients hospitalized in the period January-May 2015 in Tirgu Mures (Romania) County Hospital, Department of Gastroenterology.

**Results:** The study group consisted mostly of men, 60%, with average age of 59.6 years. 43,75% of the 53 patients met the criteria of cirrhotic cardiomyopathy. These patients had a slightly higher average age, 61.3 years. Etiology was mainly ethanol (60%), but frequently postviral type C (40%). Most patients in the study group were placed in Child B stage of cirrhosis, but in the Child C stage 80% confirmed diagnosis of CCM. Among the most common electrocardiographic signs we can remember chronotropic incompetence with basal tachycardia, disturbed circadian variability and QT prolongation (56.6%). Among the most obvious signs of echocardiographic findings was left atrial dilation (83,21%), tricuspid reflux (76,47%) and diastolic dysfunction type altered relaxation in 56.66% of patients with CCM.

**Conclusions:** CCM is relatively common and easily diagnosed new clinical entity, but rarely diagnosed in gastroenterology wards. Cirrhotic cardiomyopathy incidence correlates with the stage of hepatic impairment (Child-Pugh score), particularly by increasing the QTc interval and altered relaxation type diastolic dysfunction.

### P920

#### Endomyocardial fibrosis in Argentina: therapeutic options

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**Introduction:** Endomyocardial fibrosis (EMF) is a non-frequent restrictive cardiomyopathy in our country. Its characteristics are fibrotic thickening of the endocardium with apex obliteration of one or both ventricles and involvement of the mitral/tricuspid valvular apparatus. Medical treatment is palliative. Objectives To assess the therapeutic options in patients (p) with EMF referred for treatment of this restrictive cardiomyopathy to our Centre.

**Material and methods:** We analyzed retrospectively 15 p with EMF between 1995 and 2015. Images techniques, clinical and histopathological criteria were used for diagnosis. Continuous variables were expressed as mean  $\pm$  SD or median and range and the categorical variables in numbers and percentages. Results Mean age was 44 (3-71) years, 13 p (87%) were female, all Caucasians, 7 p (47%) were from Argentinean Northwest and Mesopotamia provinces (subtropics areas). Three p (3%) had eosinophilia history. At admission, 11 p (73%) were in NYHA FC III-IV; 8 p (53%) presented atrial fibrillation; 4 p (26%) had severe left ventricular systolic dysfunction; 5 p (33%) moderate to severe right ventricular systolic dysfunction; 13 p (87%) moderate to severe mitral regurgitation; 11 p (73%) moderate to severe tricuspid insufficiency and 12 p (80%) developed pulmonary hypertension (mean pulmonary systolic pressure: 59  $\pm$  29 mmHg). Diagnosis of EMF was confirmed by images and/or pathological tests, confirming 80% (12/15 p) of biventricular compromise. Patients in NYHA FC I-II (4/15, 27%) continued with the medical treatment and clinical follow up. The remaining p on NYHA FC III-IV (73%; 11/15) were eligible either for

surgical treatment or heart transplantation listing. Four of 11 p (27%) on NYHA FC III-IV underwent endomyocardial resection and mitral and tricuspid valve replacement (one p died due to non cardiovascular cause at long term follow up). The rest of the p (7/11; 47%) were listed for heart transplantation due to decompensated heart failure (HF) and cardiogenic shock: 4/7 p (47%) underwent uneventful heart transplantation and 3 p died on waiting list. Conclusion Patients with the diagnosis of EMF in advanced NYHA FC should be consider for endomyocardial resection, valvular repair or replacement surgery when presented clinically compensated. Heart transplantation was the therapeutic of choice for p with refractory HF. Due to the high mortality rate while in waiting list, it should be considered the assistance circulatory support as bridge to transplant.

### P921

#### Isolation as a factor predisposing to takotsubo cardiomyopathy

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**Background:** Takotsubo cardiomyopathy (TTC) mimics acute coronary syndrome (ACS) and is accompanied by reversible left ventricular wall motion abnormalities. Typically TTC is preceded by acute emotional stress and is also known as "stress cardiomyopathy", "apical ballooning syndrome" or "broken-heart syndrome." The symptoms are similar to ACS. The pathophysiology remains unclear.

**Methods:** 120 consecutive female patients with TTC were analysed to prove association with stress factor (Table 1) and compared with 120 consecutive female patients with acute myocardial infarction with ST segment elevation (STEMI). All patients had echocardiography and coronary angiography performed.

**Results:** There were no differences between age, BMI, risk factors like hypertension, diabetes, smoking, hypercholesterolemia, family history in both groups. There weren't differences in comorbidities like: chronic obstructive pulmonary disease, hypothyroidism, stroke, status post hysterectomy, cancer. There weren't differences in drug or alcohol addiction too. The most interesting finding was that pts with TTC were more often lonely- single, divorced or widowed than pts with STEMI. They also more often lived alone. These differences were strongly statistically significant.

**Conclusion:** It is known that TTC is associated with stress factor. We suppose that not only occurrence of sudden stress is important to develop TTC. Being alone and lack of daily support from loved ones cause that some people may have TTC.

#### Kind of stress in pts with TTC

lack of stress factor	10%
psychological stress	67%
physical stress	4,5%
operation	4,5%
exacerbation of chronic disease	12%
head trauma	2%

### P922

#### Cardiac involvement in the two main genotypes of sickle cell disease: specificities of hemoglobin sickle cell compared to sickle cell anemia.

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**Background:** Hemoglobin SC (HbSC) and sickle-cell anemia (SCA) are the most frequent genotypes of sickle-cell disease. While SCA cardiac involvement was well characterized, the heart remodeling associated to HbSC was never specifically investigated.

**Purpose:** Considering the pathophysiological differences of both genotypes the aim of the study was to investigate the cardiac remodeling related to HbSC compared to SCA.

**Methods:** Using a case-control design, 60 adult HbSC patients (median age 31 years, 25 men) underwent an echocardiography and were compared to 60 SCA patients and 60 controls matched for age and gender. Left ventricular ejection fraction (LVEF), LV mass index (LVMI), cardiac index and peak tricuspid regurgitation velocity (TRV) were measured as recommended. LV filling pressures were assessed using the ratio of early peak diastolic velocities of mitral inflow and annular mitral plane (E/e').

**Results:** The LVMI was higher in both genotypes compared to controls. However, whereas LV hypertrophy was observed only in 3 (5%) patients with HbSC, this condition was diagnosed in 27 (45%) patients with SCA. While cardiac index and systolic pulmonary pressures were similar in HbSC patients compared to controls, SCA patients exhibited elevated cardiac output and pulmonary pressures. LVEF was similar in the three groups. However, both genotypes had a higher E/e' ratio compared

to controls. In HbSC patients, LVMI, E/e' and TRV were associated to the presence of hypertension and/or obesity comorbidities and not to anemia and hemolysis. In contrast, hematological variables were independently related to cardiac involvement in SCA.

**Conclusions:** Cardiac phenotype and its correlates are different in HbSC compared to SCA. In HbSC cardiovascular monitoring should focus on patients with non-hematological comorbidities.

### P923

#### Inflammatory and cardiac biomarkers in Takotsubo cardiomyopathy

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**Purpose:** Takotsubo cardiomyopathy's (TTC) presentation typically mimics the clinical and imaging findings of an anterior wall ST-segment elevation myocardial infarction (MI). Despite a growing knowledge base on this entity, its pathophysiology is still incompletely understood and its diagnosis requires exclusion of MI by coronary angiography. On the contrary, inflammation is known to have a fundamental role in the pathophysiology of MI. Following on this, we compared changes in inflammatory and cardiac biomarkers in both groups.

**Methods:** We retrospectively analysed the clinical files of patients (pts) with a diagnosis of TTC at our hospital between 2005 and 2015 and of a random sample of pts without known coronary heart disease admitted for anterior MI. Demographic, clinical and laboratory data was collected; the latter included collection of neutrophil count, admission C-reactive protein (CRP), albumin, brain natriuretic peptide (BNP) and maximum troponin I levels. These values were used to calculate BNP/troponin, BNP/left ventricular ejection fraction (LVEF) and troponin/LVEF ratios.

**Results:** We identified 58 pts with a TTC diagnosis (55 female), with a mean age of 66 years (33 to 88 years), and 21 age-matched MI controls. LVEF on admission was similar between the two groups (mean 38 ± 6 vs 37 ± 7%, respectively).

While values outside the reference range were frequent in all inflammatory parameters analysed, a statistical difference between the two samples was found only for albumin levels, which were lower in TTC pts (35.9 ± 4.8 vs 38.3 ± 2.2g/L, p = 0.004). This difference, however, lost significance after excluding 10 pts diagnosed with TTC during an ongoing hospitalization for other reason.

Regarding cardiac biomarkers, TTC pts had significantly higher brain natriuretic peptide (705 ± 132 vs 198 ± 102pg/mL, p = 0.004) and lower troponin I levels (2.8 ± 0.4 vs 120.4 ± 16.7ng/mL, p < 0.001) when compared to MI controls. BNP/troponin (584.3 ± 951.3 vs 2.2 ± 3.7, p < 0.001), troponin/LVEF ratios (8.8 ± 10.3 vs 367.1 ± 276.0, p < 0.001) and BNP/LVEF (1796 ± 1469 vs 684 ± 1582, p < 0.001) were significantly different as well. Furthermore, on ROC curve analysis, the former ratios showed highly significant power in differentiating TTC and MI: a BNP/troponin ratio > 13.2 identified TTC pts with 99% specificity and 94% sensitivity (AUC = 0.996, p < 0.001), while a troponin/LVEF ratio > 70 identified anterior MI pts with 99% specificity and 93% sensitivity (AUC = 0.996, p < 0.001).

**Conclusions:** Common biomarkers are altered in both TTC and MI. However, no statistically significant difference in inflammatory parameters was found between TTC and anterior MI. On the other hand, cardiac biomarkers available in the first 48h of hospitalization were significantly different between the two samples and BNP/troponin and troponin/LVEF ratios actually had significant power in distinguishing both entities.

### P924

#### Cardiac amyloidosis: imaging characterization and prognostic information

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**Purpose:** Cardiac amyloidosis (CA) is a challenging diagnosis, with an ominous prognosis. Biopsy remains the gold standard to diagnosis, but imaging techniques have emerged as attractive non-invasive alternatives. Different parameters have been used to predict outcome in these patients (pts). We studied the prognostic significance of clinical, echocardiographic and cardiac magnetic resonance (CMR) parameters in our population of pts with CA.

**Methods:** Clinical, standard echocardiographic and CMR parameters were collected and analysed in pts with histologically proven amyloidosis and a high suspicion of cardiac involvement. Mortality data was considered as the endpoint. Echocardiographic, CMR and clinical variables were evaluated using cox-proportional hazards model. Categorical variables are shown as percentages and continuous are presented as mean ± standard deviation. A p value less than 0.05 was considered statistically significant.

**Results:** We enrolled 32 pts with a mean age of 72.59 ± 10.78 years. Heart failure was the presentation form in 59.4%, with a BNP of 1701.26 ± 152.96 pg/mL. Concerning echocardiographic evaluation, the majority (53.1%) had normal left ventricle (LV) ejection fraction (EF) and half had normal right ventricular (RV) systolic function. LV mass index for body surface area (BSA) was increased (248.23 ± 81.77g/m<sup>2</sup>)

as well as interventricular septum and posterior wall thickness (14.9 ± 2.80 mm and 13.73 ± 2.82 mm). It was documented elevation in LV filling pressures (E/E' 22.84 ± 6.77) with E/A 1.91 ± 0.93. Left atrial (LA) volume indexed for BSA was also increased (41.54 ± 10.33 ml/m<sup>2</sup>) and the majority of pts had pulmonary hypertension (PSAP 42.35 ± 10.73 mmHg). CMR was performed in 14 pts. LV and RV indexed end diastolic volumes were increased (67.23 ± 12.10 and 69.31 ± 14.96 ml/m<sup>2</sup>). LV EF was slightly decreased (47.64 ± 12.11%) while RV EF was normal (49.50 ± 9.17%). Late gadolinium enhancement (LGE) was found in all pts, mainly the diffuse subendocardial pattern (85%). RV and atrial LGE was found in 85% and 50% of pts, respectively. On univariate analysis, the only 1-year mortality predictor was BNP (p = 0.005) with a BNP ≥ 768 pg/mL having a sensitivity of 94% and a specificity of 73% to predict 1-year mortality. This group of pts had a mean survival of 5.35 ± 5.34 months.

**Conclusion:** Echocardiography and CMR are of major importance in the suspicion of cardiac amyloidosis, as they provide important clues to diagnosis. We found biventricular and LA dilation and signs of LV systolic and diastolic dysfunction. Length of survival is strongly associated with BNP compared to echocardiographic or CMR parameters. Moreover, our study indicates that BNP may be used to detect patients at high risk of mortality and help early initiation of aggressive management and treatment.

### P925

#### Clinical significance of giant negative T-waves in patients with takotsubo cardiomyopathy

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**Background:** Takotsubo cardiomyopathy (TTC) mimics acute myocardial infarction. Electrocardiographic changes include ST-segment elevation during the acute phase and widespread T-wave inversion during follow-up. Some patients develop giant negative T waves ≥ 1 mV resembling those in apical hypertrophic cardiomyopathy (AHCM). This study assessed the frequency and clinical significance of giant negative T waves in patients with TTC.

**Methods:** Over a 9-year period, we observed 76 TTC patients (69 f, 7m; 70 ± 12 years). By angiography, 45 patients (59%) had apical ballooning (AB) and 31 (41%) mid-ventricular ballooning (MB) of the left ventricle (LV). ECG on admission, at the time of maximal T-wave inversion, before discharge and the daily QTc-interval were compared.

**Results:** Giant negative T waves ≥ 1 mV were seen in 16/76 patients (21%). All were documented in the precordial leads V2 (n = 3), V3 (n = 9), V4 (n = 10), V5 (n = 4) and V6 (n = 1). Patient with giant negative T waves were older (75 ± 11 vs 69 ± 12 years, p = 0.05) and they had significantly more frequent the apical ballooning variant (88% vs 12%, p < 0.01). Time interval from symptom onset to first ECG (7.8 ± 7.7 vs 8.6 ± 8.9 hours, p = ns), heart rate on admission (96 ± 25 vs 87 ± 21/min, p = ns) and the number of leads with ST-segment elevation on the admission ECG (4.3 ± 1.6 vs 3.8 ± 2.4, p = ns) were not different in patients with and without development of giant negative T waves. Cardiac markers, LV ejection fraction and LV end-diastolic pressure were comparable in both groups. In patients with giant T there was a trend towards more complications during the acute phase (69% vs 43%, p = 0.06).

The maximal QTc interval was significantly longer in patients with giant negative T waves during follow-up (606 ± 70 vs 559 ± 71 msec, p < 0.02), however, the occurrence of ventricular arrhythmias and atrial fibrillation was not different. Time to ECG normalization was similar (59 ± 21 vs 68 ± 82 days, p = ns). As assessed by echocardiography, 15/16 patients with giant negative T waves developed wall thickening in the apical area within 2 weeks of presentation with a ratio of apical to posterobasal wall thickness > 1.5:1 fulfilling the criteria for AHCM. Cardiac MRI performed in 6 of these 15 patients disclosed myocardial oedema in the apical area. Time to complete normalisation of LV function was significantly longer in patients with giant negative T waves (32 ± 24 vs 20 ± 15 days, p < 0.02).

**Conclusion:** Giant negative T waves ≥ 1 mV in the precordial leads resembling those in AHCM develop in 21% of patients with TTC. They are associated with apical wall thickening due to myocardial oedema, a higher complication rate and a longer time interval to complete normalisation of LV function.

### P926

#### Improved diagnostics and management of Danon disease in the Czech Republic.

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**Introduction:** Danon disease (DD) is an X-linked deficiency of LAMP2 protein clinically affecting both males and X-heterozygous females. DD most often presents



as a hypertrophic cardiomyopathy (HCM) with rapid progression to end-stage heart failure (HF).

**Purpose and methods:** We present an overview of diagnostic strategy, clinical manifestation and management of patients with DD in the Czech Republic.

**Results:** DD has been diagnosed in five Czech families since 2009. In three families, LAMP2 protein deficiency was identified by skeletal muscle biopsy and/or flow cytometry (FC) in peripheral white blood cells (WBC). Patients from the two remaining families were originally diagnosed with mitochondrial cardiomyopathy or Wilson disease and their DD status was first established by next-generation sequencing (NGS). Pathogenic LAMP2 mutations were confirmed by Sanger sequencing in all patients/families. To validate, LAMP2 protein deficiency was confirmed by FC in all currently living DD patients (4 male and 3 female patients). As a further evidence of practical diagnostic utility, the de-novo mutated female proband was the only affected individual in one of the families tested by FC. Clinical data were available for 6 male (54%) and 5 female (46%) DD patients (2 obligatory heterozygotes not tested for the LAMP2 mutation are included). 8 patients (73%) presented with HCM (including 2 females) and 3 females (27%) with dilated cardiomyopathy. In addition, six males (54%) had mild skeletal myopathy, elevation of aminotransferases and mild cognitive impairment, whereas females had isolated cardiac involvement. Median age at diagnosis of cardiomyopathy was 11 years (6-15). A total of 8 patients (72%) developed HF – median age of HF manifestation was 22 years (19-26) and median age of survival without necessity of heart transplantation (HTx) or ventricular assist device (VAD) was 26 years (20-28). In 5 patients having cardiac resynchronization therapy, we observed a poor response with median time to death, HTx or VAD of 9 months (5-27).

**Conclusions:** To allow appropriate non-pharmacological treatment of advanced HF early diagnosis of Danon disease can be facilitated by LAMP2 flow cytometry in peripheral WBCs. NGS testing can be suggested as a useful alternative particularly in DD patients/families with atypical clinical phenotypes.

## P927

### Association of anemia and transfusion with adverse outcomes in 22,991 patients hospitalized with takostsubo cardiomyopathy

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**Background:** Takostsubo cardiomyopathy (TTCM) is a rare form of acute nonischemic cardiomyopathy characterized by acute LV dysfunction in a multi-vessel distribution without obstructive coronary artery disease. Due to its rarity, comparatively little is known about predictors of poor outcomes. Anemia and transfusion have been associated with adverse outcomes in other kinds of acute and chronic heart failure. We hypothesize that these factors are associated with poor short-term outcomes in TTCM.

**Objective:** To describe the association between anemia, transfusion and other risk factors for poor outcomes in TTCM.

**Methods:** Hospital records from 11 US states were obtained from 2006-2013. All records reporting TTCM (ICD-9 CM code 429.83) were included in the analysis. Anemia, transfusion, and other patient procedures and characteristics were identified using ICD-9 codes and data documentation. A major adverse event (MAE) was defined as death, mechanical ventilation, cardiac arrest, shock, or placement of intraaortic balloon pump. Associations between anemia, transfusion, other patient characteristics and outcomes were determined by chi-square testing and multivariate logistic regression.

**Results:** In total, 22,991 TTCM cases were identified including 2479 (11%) men and 19327 (89%) women. Where race was reported, there were 15728 (78.6%) white patients, 1916 (9.6%) patients of African Ancestry (AA), 459 (2%) Asian patients, 1687 (8.4%) Hispanic patients and 230 (1.1%) of other or mixed race (2971 race). Anemia was present in 5598 (24%) of patients and 2339 (10%) of all patients received transfusions. Of anemic patients, 1805 (32%) had an MAE compared with 3270 (19%) non-anemic patients ( $p < 0.001$ ). Of patients receiving transfusion, 1133 (48%) had an MAE compared with 3942 (19%) who did not receive a transfusion. In multivariate analysis including age, gender, race, anemia, atrial fibrillation, heart failure, hyperlipidemia, hypertension, mood disorders, intracranial hemorrhage, stroke, and acute renal failure, anemia (OR 1.3, 95% CI 1.2-1.4,  $p < 0.001$ ) and transfusion (OR, 2.4 95% CI 2.1-2.7,  $p < 0.001$ ) remained significant predictors of MAE. Asian patients who have been shown to have worse outcomes in TTCM had significant higher rates of anemia (37%) and transfusion (18%) than non-Asian patients (25% and 10% respectively,  $p < 0.001$ ).

**Conclusion:** Anemia and transfusion during hospitalisation predict poor outcomes in TTCM.

## P928

### Clinical profile and outcomes of restrictive cardiomyopathies

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**Background:** Restrictive cardiomyopathy (RCM), a heterogeneous group of heart muscle conditions characterized by impairment of ventricular filling during diastole, remains the least common type of cardiomyopathies without uniformly accepted diagnostic criteria. Unlike the other cardiomyopathies that are classified according to morphological criteria, RCM is a functional classification. The clinical profile, therapeutic options and survival outcomes of a cohort of patients with RCM are shown.

**Method:** We analysed between 2010 and 2015, 15 patients (20 to 95 years old (mean, 64 ± 19 years), 7 females) meeting criteria for RCM the last consensus of the European Society of Cardiology.

**Results:** Fatigue, dyspnoea on exertion and oedema were the most frequent symptoms at the time of diagnostic. Twelve patients (80%) were in NYHA class ≥ III. Amyloidosis (n=9) was the predominant diagnosis. Other etiologies were: idiopathic (n=2), scleroderma (n=1), glycogenosis type III (n=1), hemochromatosis (n=1) and hypereosinophilic syndrome (n=1). No patient had a myocardial biopsy but biopsies from different tissues were performing to obtain a definitive diagnosis. A cardiac magnetic resonance scan was done in 8 patients supporting the etiologic diagnosis in all cases. Atrial fibrillation was noted in 8 patients (53%). One patient required pacemaker implantation for atrioventricular block. Left ventricle systolic dysfunction was present in 7 patients. In addition to the specific aetiology treatment, all patients received loop diuretics (53% combined with aldosterone antagonists). Among those who received ACE inhibitors (n=10) and beta blockers (n=8), we find his interruption due to poor tolerance of 20% and 50% respectively and one heart transplant was performed with good results. The overall mean follow-up was 3,3 years (median 3.1; range, 0.5 to 4,5 years). Total mortality was 33% due to terminal heart failure in 80% and infection in 20%. In the analytical appreciated that in addition ProBNP, Gamma glutamyl transpeptidase (GGTP) has relation with a poor prognosis and mortality, it is noteworthy that no other liver marker maintained this relationship (including Score Child-Pugh).

**Conclusions:** Our patients had findings similar to those described in the universal literature, echocardiography was important to evaluate the morphological and functional criteria and cardiac magnetic resonance provided an incremental value in etiologic diagnosis, the conventional treatment may be poor tolerated. The GGTP could be helpful in the prognosis of these patients, but further studies are needed for confirmation.

## P929

### Biomarkers in idiopathic dilated cardiomyopathy- different predictors of pharmacological reverse remodelling and clinical severity

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**Introduction:** Biomarkers in heart failure can play a play a hormonal role, can be related to inflammatory response, to oxidative stress, to myocyte injury, to myocyte stress or to matrix remodelling. Our aim was to see the role of some biomarkers in reverse remodelling (RR) and in clinical severity in pts with idiopathic dilated cardiomyopathy (IDCM). We also try to find association between those biomarkers and echocardiographic measures.

**Methods:** Prospective study of 50 IDCM pts (28 men, aged 59 ± 10 years, in sinus rhythm, followed for 39 ± 22 months), with ejection fraction <40%. Excluded secondary and reversible causes. At baseline we performed a clinical, bio humoral and echocardiographic evaluation. During follow-up, RR was defined as an increase of 10 units of ejection fraction (EF) and decrease of diastolic left ventricular diameter (LVD) in the absence of resynchronization therapy.

**Results:** Baseline EF was 25.4 ± 9.8% and LVD/BSA was 34.2 ± 4.5 mm/m<sup>2</sup>. RR occurred in 34% of pts within 17.6 ± 15.6 months. Pts with RR had a final EF of 49.6 ± 7.3% and LVD/BSA of 28.8 ± 2.9 mm/m<sup>2</sup>. RR was associated to lower BNP at the end of follow-up (143.5 ± 137.5 vs 36.9 ± 34.3,  $p < 0.01$ ).

Baseline predictive factors of RR ( $p < 0.05$ ) were: younger age (60.6 ± 8.8 vs 54.7 ± 10.8,  $p = 0.04$ ), smaller LVD/BSA (mm/m<sup>2</sup>) (35.2 ± 4.1 vs 32.3 ± 4.8,  $p = 0.03$ ), higher RV Tei index (0.46 ± 0.16 vs 0.52 ± 0.32,  $p = 0.02$ ), lower BNP (pg/ml) (163.1 ± 587.7 vs 81.3 ± 198.4,  $p = 0.05$ ), lower levels of adrenalin (pg/ml) (46.2 ± 38.6 vs 29.9 ± 16.8,  $p = 0.02$ ) and renin (U/ml) (228.4 ± 446.7 vs 84.1 ± 90.9,  $p = 0.02$ ). No correlation was found between 25-OH-vit D, CA 125, hs CRP, Lp (a) and reverse remodelling. Pts who presented with poor NYHA class (III-IV) had higher levels of: CA 125 (U/ml) (21.6 ± 58.1 vs 116.0 ± 255.3) cystatin C (mg/l) (0.76 ± 0.16 vs 0.92 ± 0.05), BNP (pg/ml) (257.5 ± 391.0 vs 968.5 ± 950.1) and hs CRP (mg/l) (2.6 ± 3.4 vs 10.9 ± 13.4) ( $p > 0.05$ ). Pts with pulmonary congestion or ankle edema had also higher levels of CA 125, BNP and hsCRP ( $p < 0.01$ ).

CA 125 was correlated to BNP levels ( $r = 0.61$ ), to hs CRP ( $r: 0.56$ ) and uric acid ( $r = 0.52$ ) (all  $p = 0.01$ ). CA 125 correlated with some echocardiographic variables: LA volume/BSA ( $r: 0.46$ ,  $p < 0.01$ ), E/A ratio ( $r: 0.60$ ,  $p < 0.01$ ), pulmonary systolic artery pressure ( $r: 0.49$ ,  $p < 0.01$ ). hs CRP was correlated with LV EF ( $r = -0.28$ ,  $p = 0.05$ , LV tei index ( $r: -0.41$ ,  $p < 0.01$ ) and with LV diastolic volume/BSA ( $r = 0.32$ ,  $p = 0.05$ ).

**Conclusions:** RR occurred in one third of IDCM pts, especially in younger pts, with less sympathetic and neuro humoral activation, smaller LVD and better RV function. CA125, BNP, hsCRP were predictors of clinical severity. CA 125 correlated with

measures of diastolic dysfunction and pulmonary pressure, while hs CRP correlated with LV systolic dysfunction. CA 125 correlated with hs-PCR and uric acid, indicating a potential pathogenic link between inflammatory activation and this marker of systemic congestion.

### P930

#### Differential regulation of Receptor for Advanced Glycation End products (RAGE) in ischemic and post-inflammatory dilated cardiomyopathy

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**Background:** Chronic heart failure is associated with a pro-inflammatory state. Activation of the Receptor for Advanced Glycation End products (RAGE) by its ligands (Advanced Glycation End products (AGEs) like Carboxymethyllysine (CML)) induces inflammatory responses and elicits oxidative stress and cardiac remodelling. The decoy receptor soluble RAGE (sRAGE) comprising only the RAGE-ectodomain and neutralizing RAGE-ligands exerts anti-inflammatory beneficial effects and has been shown to be a prognostic factor for heart failure. The aim of this study was to evaluate plasma and myocardial sRAGE/RAGE/CML expression in ischemic and post-inflammatory chronic heart failure.

**Methods:** Plasma samples from patients with chronic heart failure (n = 15 ischemic cardiomyopathy ICM, n = 15 post-inflammatory dilated cardiomyopathy DCM) and from age-matched healthy volunteers (controls n = 15) were analyzed for sRAGE and CML by quantitative Western blot. Additionally, myocardial tissue samples from explanted hearts from patients with chronic heart failure (n = 5 ICM; n = 5 DCM) and from non-failing hearts (n = 5) were investigated for RAGE/sRAGE and CML expression by Western blot.

**Results:** In patients with DCM sRAGE plasma levels were significantly decreased as compared to healthy controls (50% decrease). Additionally, patients with DCM showed increased CML plasma levels (4.2fold increase and 3.6fold increase versus controls and versus ICM), indicating a profound pro-inflammatory dysbalance in DCM. Myocardial RAGE expression was significantly increased in both DCM and ICM patients (3.9fold and 4.5fold increase versus controls). However, in ICM myocardium RAGE increase was counterbalanced by a concomitant 2.7fold sRAGE increase (compared to controls). Contrary to this, in DCM myocardial anti-inflammatory sRAGE was reduced (53% reduction versus controls) and the pro-inflammatory AGE CML was additionally increased (3fold increase).

**Conclusions:** Chronic heart failure is associated with increased myocardial RAGE expression. However, pro-inflammation is more profound in dilated cardiomyopathy as depicted by reduced myocardial and plasma sRAGE content and increased levels of the AGE Carboxymethyl-lysine. These novel observations might help develop new diagnostic and therapeutic strategies in chronic heart failure.

### P931

#### Insights into mildly dilated cardiomyopathy: temporal evolution and long-term prognosis

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**Background:** Mildly Dilated Cardiomyopathy (MDCM) is a 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.

**Purpose:** To characterize and assess the long-term natural history of MDCM.

**Methods:** From 1988 to 2010 we analyzed all DCM patients consecutively enrolled in the Trieste Heart Muscle Disease Registry. MDCM was defined as LV ejection fraction  $\leq 45\%$  and index LV end-diastolic volume (LVEDVI)  $\leq 70$  ml/m<sup>2</sup> in women and  $\leq 89$  ml/m<sup>2</sup> in men. Results. Among a whole population of 638 patients, 226 (35%) fulfilled the criteria for MDCM. They presented features of a less advanced disease at baseline and an overall lower rate of all-cause mortality/heart transplant (D/HTx) in the long-term follow-up (D/HTx at 10 years 15% vs 30%, in MDCM and DCM respectively;  $p < 0.001$ ). However, throughout the follow-up, 55 MDCM patients (24%) evolved in non-MDCM by increasing LVEDVI. Their prognosis consistently worsened approaching that of DCM patients in the long-term. On the other hand, among persistent MDCM patients, restrictive filling pattern (HR 5.30; 95%CI 2.34-12.01  $p < 0.001$ ) and non-sustained ventricular tachycardia (HR 2.21, IC 95% 1.003-5.11  $p = 0.047$ ) were independently associated with D/HTx at multivariate analysis.

**Conclusions:** MDCM identifies a consistent subgroup of DCMs diagnosed at an earlier stage and therefore presenting an apparent better evolution. However, some MDCMs progress towards DCM condition despite adequate medical therapy, whereas among persistent MDCMs those presenting with non-sustained ventricular arrhythmias and restrictive filling pattern were characterized by a very poor long-term outcome.

### P932

#### Improved prediction of major arrhythmic events in patients with unexplained cardiomyopathy who underwent endomyocardial biopsy

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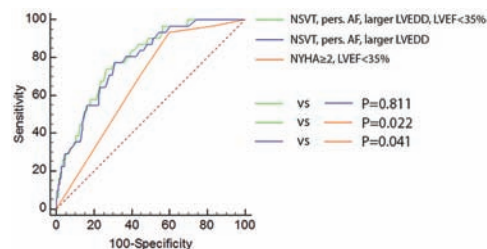
**Background:** The current ESC guidelines recommend an implantable cardioverter-defibrillator (ICD) in heart failure patients with a low LVEF  $< 35\%$  and NYHA-class  $\geq 2$ . Whether EF and NYHA-class are also ideal predictors of major arrhythmic events (MAE) in patients with unexplained cardiomyopathy (CMP) is not well established. The present study investigated which parameters best predicts MAE and compared it to the predictive value of LVEF and NYHA  $\geq 2$ .

**Objectives:** To identify prognostic factors predicting MAE in CMP patients who all underwent endomyocardial biopsy (EMB).

**Methods:** Within the Maastricht Cardiomyopathy registry, 459 patients with initially unexplained CMP – excluding ischemic, valvular, hypertensive, and congenital heart disease – were enrolled between 2004 and 2015. Patients with a history of ventricular tachycardia (VT) and/or ventricular fibrillation (VF) were excluded. All patients underwent complete work-up including electrocardiography, echocardiography, Holter registration and EMB. Primary endpoint was MAE defined as sustained VT, VF or sudden cardiac death (SCD). Secondary endpoint was event-free survival including all-cause mortality and/or heart transplantation (HTx).

**RESULTS.** A total of 459 consecutive DCM patients (290 males) were included, mean age of  $54 \pm 12$  yrs, NYHA  $\geq 3$  in 132 (29%), and LVEF  $< 35\%$  in 282 (61%) patients. Increased cardiac inflammation with or without significant viral load ( $> 500$  c/mcg DNA) and significantly increased myocardial fibrosis  $> 10\%$  was found in 182 (40%) and 143 (33%) patients, respectively. After median follow-up of 50 [20-75] months, a total of 32 (7%) patients had a MAE (14 SCD & 18 sustained VT/VF). Independent predictors included non-sustained VT (HR 2.18, 95% CI 1.12-4.83,  $P = 0.046$ ), persistent atrial fibrillation (HR 3.16, 95% CI 1.3-7.9,  $P = 0.014$ ), LVEDD (HR 1.08 per mm increase, 95% CI 1.04-1.13,  $P < 0.001$ ) and LVEF  $< 35\%$  (HR 3.40, 95% CI 0.7-15,  $P = 0.12$ ). This model was better as compared to LVEF  $< 35\%$  and NYHA  $\geq 2$  (area under the curve (AUC) of 0.80 vs 0.67 (Figure 1,  $P = 0.022$ ). Using all predictors except LVEF  $< 35\%$  still showed superiority as compared to ICD indications (Figure 1: AUC 0.79 vs 0.67;  $P = 0.041$ ). EMB-related markers did not further improve the model. Secondary endpoint was reached in 38 (8%) patients (36 deaths & 2 HTx.) Independent predictors included older age (HR 1.03, 95% CI 1.01-1.07,  $P = 0.038$ ), longer duration of symptoms (HR 1.01, 95% CI 1.00-1.01,  $P = 0.038$ ), NYHA  $\geq 2$  (HR 2.01, 95% CI 1.0-3.9,  $P = 0.042$ ) and LVEF  $< 35\%$  (HR 4.27, 95% CI 1.3-14,  $P = 0.019$ ).

**Conclusion:** A better prediction model for major arrhythmic events is found using the presence of NSVT, persistent AF, LVEF  $< 35\%$  and LVEDD – even without LVEF  $< 35\%$  in the model – as compared to guideline-based LVEF  $< 35\%$  and NYHA-class in patients with CMP. In contrast, both LVEF  $< 35\%$  and NYHA-class independently predict HTx-free survival, illustrating the importance to differentiate between arrhythmic and heart-failure related outcome.



AUCs for prediction models

### P933

#### Morpho-functional phenotypes of dilated cardiomyopathy due to lamina gene mutation/polymorphism

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Objective of the study was to assess morpho-functional phenotypes in patients with dilated cardiomyopathy (DCM) due to lamina gene mutation/polymorphism.

**Methods:** The study enrolled 160 patients (pts) with DCM (aged  $46 \pm 12$ ; 70 % male, NYHA  $2.7 \pm 0.4$ ; LVEF  $25.8 \pm 8.2\%$ ). Genetic testing was performed by SSCP and sequencing of exons and intron-exon lamina (LMNA) gene. Genetic finding, data by

SNPs and mutation LMNA gene in DCM				
polymorphic locus	nucleotide substitution specifying codon	localization in lamin gene	replacing an amino acid residue in the protein lamin	patients (n)
rs397517894	c.150 C > T	exon 1	Arg50Arg	1
art rs267607571	c.569G > C	exon 3	rg190Pro**	1
rs12117552	c.612G > A	Exon 3	Leu204Leu	2
rs11264442	c.639+56G > T	intron between 3 and 4exons	-	5
rs11264443	c.639+73C > T	intron between 3 and 4exons	-	5
rs538089	c.861 T > C	exon 5	Ala287Ala	16
rs553016	c.1489-41C > T	intron between 8 and 9 exons	-	16
rs267607557	c.1558T > C	exon 9	h520Arg	1
rs57629361	c.1583C > G	exon 9	hr528Arg	1
rs4641	c.1698C > T	exon 10	His566His*	25

Note: \* heterozygous carrier replacement s.1698 C > T was detected in 23 patients, homozygous carrier - 2 pts; \*\* de-novo mutation

EchoCG, ECG\24h-Holter with estimation of QTc dispersion, heart rate turbulence (HRT), microvolt T-wave alternans (mTWA), also age, gender and serum BNP, CPK levels were analyzed.

**Results:** We genotyped LMNA (SNPs and mutations are represented in Table below); 16\43 (37%) from 43\160 (26,%) pts showed carriage in two and more loci. A positive correlation between missens-mutations (exons 3, 9) and atrioventricular block ( $k=0,66$ ;  $p=0.001$ ), with CPK level ( $k=0,61$ ;  $p=0.002$ ) and muscle disorders ( $k=0,52$ ;  $p=0.02$ ) were revealed. Substitution of nucleotide C to T in codon 566 (exon 10) as result of SNP rs4641 which still codes for Histidine was detected in 25 pts. The LMNA rs4641 T-allele was associated with non-sustained ventricular tachycardia (Spearman  $k=0,65$ ;  $p=0.001$ ), with positive mTWA test ( $k=0,64$ ;  $p=0.0001$ ) and pathological HRT0 ( $k=0,53$ ;  $p=0.01$ ). SNP associated with rs4641 is very important as it is located in splice site at exon 10; alternative splicing at this site leads to the production of either lamin A or C transcripts or protein. The obtained results support the fact this SNP can affect signal transduction processes.

**Conclusions:** Thus, we consider that T allele rs4641 in LMNA is one of the major genetic risk factor for the pathogenesis of DCM other than mutation in LMNA.

### P934

#### Predictors of cardiac magnetic resonance-assessed reverse remodeling in non-ischaemic dilated cardiomyopathy

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**Purpose:** Reverse remodeling (R2) in non-ischaemic dilated cardiomyopathy (NIDCM) is associated with reduced morbidity, improved quality of life and survival. There is still scarce knowledge on predictors of R2, relevant for guide to treatment and device implantation. We aimed to identify predictors of R2, assessed by serial cardiac magnetic resonance (CMR) imaging, among several clinical, instrumental and biochemical variables in NIDCM.

**Methods:** We prospectively enrolled patients with clinical diagnosis of NIDCM, according to the World Health Organization criteria; significant coronary artery disease was excluded by coronary angiography. All patients received a baseline clinical, biochemical (including neurohormones, galectin-3 and ST2) and instrumental characterization, as well as contrast-enhanced CMR. CMR study was performed again 24 months after baseline evaluation. R2 was defined according to three different criteria, all present within literature: 1) > 15% decrease in left ventricular end-systolic volume index (LVESVi) (criterion 1); 2) increase in LV ejection fraction, LVEF, > 10U with a > 10% decrease in LV end-diastolic volume index (LVEDVi) (criterion 2); 3) an increase in LVEF > 10U or a > 10% decrease in LVEDVi (criterion 3).

**Results:** We recruited 86 patients (males 64%, age  $55 \pm 15$  years, LVEF  $38 \pm 10\%$ , LVEDVi  $118 \pm 32$  ml/m<sup>2</sup>, LVESVi  $75 \pm 32$  ml/m<sup>2</sup>). R2 was observed in 48, 26 and 50% of patients, according to criterion 1, 2, 3, respectively. Independent predictors were:

as for criterion 1, absence of diabetes ( $p=0.034$ ), introduction of mineralocorticoid receptor antagonist -MRA- after baseline evaluation ( $p=0.032$ ), greater baseline LVESVi,  $p=0.040$ ; as for criterion 2: MRA introduction ( $p=0.028$ ), higher C-reactive protein ( $p=0.017$ ), and higher baseline LVESVi ( $p=0.040$ ); as for criterion 3, higher baseline aldosterone only ( $p=0.044$ ).

**Conclusions:** Greater baseline LV volumes and aldosterone levels predict R2, with a possible interaction with MRA therapy. Neurohormonal activation may therefore identify the subset of patients with a more pronounced response to pharmacological neurohormonal antagonism.

### P935

#### Early phase 99Tc-HMMP scintigraphy: a rapid and reliable technique for the diagnosis and typing of cardiac amyloidosis

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**Background:** The usefulness of bisphosphonate-scintigraphy in diagnosing and typing cardiac amyloidosis (CA) has been reported in several studies. However, the procedure is time-consuming and may be regarded as inadequate especially in frail patients.

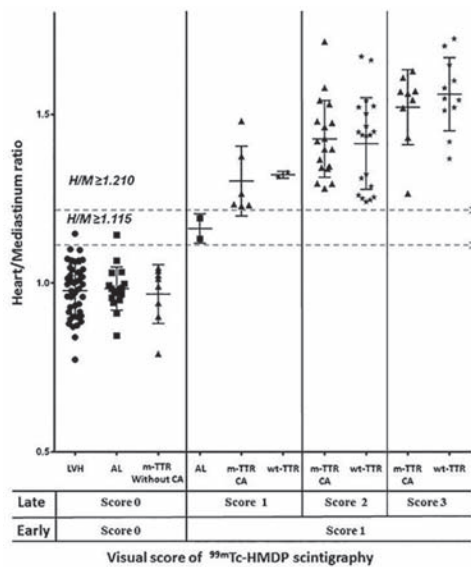
**Objective:** To compare accuracy of early (10min) and late (3h) cardiac fixation of 99mTc-HMMP scintigraphy in diagnosing and typing CA.

**Methods:** 135 patients referred for suspicion of CA were prospectively evaluated using 99mTc-HMMP-scintigraphy. Myocardial tracer accumulation was semi-quantitatively measured and visually scored at early and late phases.

**Results:** CA was diagnosed in 19 AL (light-chain) and in 33 wt-TTR (wild-type-transthyretin). Among m-TTR (mutated-transthyretin) 33 had CA, 5 had isolated neuropathy without CA and 3 were asymptomatic carriers. 31 patients with LVH (left-ventricle-hypertrophy) and without amyloidosis served as controls. Early 99mTc-HMMP cardiac uptake was found in 68 patients whose late visual score was  $\geq 1$ . Early uptake was undetectable in all the 57 patients with a null visual score at 3h. Early heart retention was strongly correlated to late heart retention ( $r=0.914$ ,  $p<0.0001$ ). An early 99mTc-HMMP heart/mediastinum ratio  $\geq 1.115$  predicts a late visual score  $\geq 1$  which differentiated CA from other causes of LVH (100% sensitivity, 97% specificity). Early heart/mediastinum ratio  $\geq 1.210$  discriminated TTR-CA from AL with perfect accuracy (100% sensitivity and specificity).

**Conclusions:** Early phase 99mTc-HMMP-scintigraphy perfectly predicts late phase finding. It is accurate to differentiate TTR-CA from AL and from other causes of LVH. This could be of particular benefit for frail patients and in centres with limited availability of scintigraphy.





Agreement between H/M and visual score

**P936**

**Apical hypertrophic cardiomyopathy: less heart failure symptoms but the same prognosis**

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**Introduction:** Apical hypertrophic cardiomyopathy (ApHCM) is the less frequent form of HCM. Despite described as benign, the natural history is less known.

**Aim:** Comparison between ApHCM vs asymmetrical or concentric HCM concerning clinical, ECG and genetic characteristics.

**Methods:** Retrospective, multicentre study including all HCM patients from ten hospitals. We compared clinical characteristics, genetics, ECG and 24 hours Holter between patients with ApMCH and patients with concentric or asymmetrical HCM.

**Results:** We included 476 HCM patients: 73 with ApHCM and 403 with concentric or asymmetrical HCM. Mean age 65 ± 15 years for ApHCM vs 62 ± 15 years (p=0,045). Mean follow up of six years. Patients with ApHCM had less dyspnea (45% vs 59%, p=0.034) and more angina (30% vs 17%, p=0.009). Genetic study was positive in 39% of patients in both groups. Mutations in TNNI3 gene were more frequent in ApMCH (14.3% vs 0.7%, p<0,001). In 12 lead ECG atrial fibrillation (18% vs 10%, p=0,045), left ventricular strain pattern (64% vs 42%, p<0,001), ST segment depression (29% vs 15%, p=0,002) and negative T waves (68% vs 34%, p<0,001) were more frequent in patients with ApHCM. 24h Holter revealed more frequently supraventricular tachycardia in patients with ApHCM.

No differences were found in the other variables tested including ventricular arrhythmias, stroke or death in the follow up.

**Conclusions:** This large multicentre study showed that ApHCM patients had more frequently symptoms of angina and less frequently dyspnea. TNNI3 mutations were more frequent. The ECG of patients with ApHCM has more frequently left ventricular strain pattern, negative T waves and ST segment depression. Despite more supraventricular arrhythmias on 24h Holter, there were no differences in ventricular arrhythmias, stroke or death in the follow up. Despite clinical and ECG differences, with found similar prognosis in patients with ApHCM and concentric or asymmetrical HCM upon a follow up of six years.

**P937**

**Nt-proBNP and high sensitive troponin in Friedreich ataxia's cardiopathy**

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**Background:** Friedreich Ataxia (FRDA) is the most common autosomal recessive neurodegenerative ataxia, resulting of mitochondrial disorder, caused by repetition of GAA expansion in frataxin gene. Hypertrophic cardiopathy is associated with FRDA and is known to be the first cause of death. Patients have abnormal ECG without acute coronary syndrome symptomatology. Cardiac biomarkers, high sensitive (hs) troponin and Nt-proBNP could be useful for the management of these patients.

**Purpose:** To establish the role of high sensitive troponin and Nt-proBNP plasma levels in the diagnosis and prognosis of cardiopathy in FRDA.

**Methods:** From december 2012 to january 2015, 76 genetically confirmed Friedreich ataxia's patients were included in our Hospital and had a cardiac evaluation: clinical examination, ECG 12 leads, echocardiography and plasma level of hs troponin and Nt-proBNP.

**Results:** Patients were aged of 38 ± 12 years, (mean ± standard deviation). 4 patients had palpitations, 2 dyspnea and no patients had chest pain. 89% had negative T waves on the ECG. 2 groups of patients were defined according to cardiac hypertrophy (Henrys'Nomogram). 37 patients had hypertrophy and 39 patients had no hypertrophy. Patients with hypertrophy were younger: 34 ± 10 years versus 42 ± 14 years, and age at onset of the disease was earlier 15 ± 6 years versus 21 ± 15 years. Myocardial wall thicknesses were respectively 12,6 ± 1,7mm versus 10,2 ± 1,2mm for septum wall thickness and 11,3 ± 1,5mm versus 9,4 ± 1mm for posterior wall thickness. Left ventricle ejection fraction were normal and not different between the two groups. High sensitive troponin t was higher in the group with hypertrophy: 22 ± 21ng/L versus 10 ± 7ng/L, p<0,01. Value of Nt-proBNP was similar in the 2 groups: 104 ± 170 ng/L versus 64 ± 122 ng/L. In multivariate analysis, hs troponin increases with interventricular wall thickness, p<0,01. A number of 12 patients had Nt-proBNP > 125ng/L: 42% experienced atrial fibrillation and 17% heart failure.

**Conclusion:** High sensitive troponin could be a diagnostic marker of hypertrophic cardiomyopathy in FRDA patients. Nt-proBNP is associated with cardiac events and could be rather a prognostic marker in these patients. Follow up studies are needed to study the evolution and the prognostic value of these biomarkers.

**P938**

**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 10 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 476 patients with HCM. Heart failure was present in 56.5% of patients. In patients with HCM, the factors associated with the development of heart failure were female gender (53.4% vs 27.7%, p<0.001), older age (66 ± 14 vs 58 ± 16 years, p<0.001), hypertension (17.8% vs 9.7%, p=0.011), presence of angina pectoris (22.3% vs 15%, p=0.044), history of surgical miectomy (5.2% vs 0%, p<0.001) and atrial fibrillation on clinical presentation (14.4% vs 7%, p=0.011). Patients with HCM and heart failure had higher frequency of death in the 6 years of follow up (3.7% vs 0.5%, p=0.020). In the multivariate analysis, older age (p=0.002) was identified as an independent predictor 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, hypertension, presence of angina pectoris, history of surgical miectomy and atrial fibrillation on presentation. Older age was identified as independent predictor of heart failure in patients with HCM.

**CO-MORBIDITIES**

**P939**

**Factors associated with medication adherence of elderly patients with chronic heart failure**

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Understanding the factors associated with medication adherence over time is important for the prevention of disease progression and good outcomes among patients with heart failure. However, little is known regarding the factors associated with medication adherence among elderly patients with heart failure and osteoporosis.

The objective of this study was to analyze the factors associated with medication adherence of elderly patients with chronic heart failure and osteoporosis in primary care.

**Methods:** Fifty-three outpatients suffering from NYHA class II-III CHF (40 F, 13 M, aged 60 - 88 years) due to ischemic heart disease and/or arterial hypertension entered the study. All patients had clinical, laboratorial evaluation, ECG, Echo CG measurements. Validated questionnaire Moriski-Green Test is being used to evaluate adherence to treatments. Bone mineral density (BMD) in the lumbar spine (L1-L4) and femoral neck (FN) were examined using dual-energy X-ray absorptiometry (DXA). BMD was expressed by T-score. All patients were under optimal HF therapy based upon the HFA guidelines. Statistical analysis was made using software packages SPSS 16.0. Results. Osteoporosis (T-score < -2.4 SD) was present in 33 (62.3%) patients (29 F, 4 M; group 1) and absent in 20 (37.7%) patients (11 F, 9 M; group 2). Patients of both groups were similar by age, NYHA class, hemodynamic parameters, atrial fibrillation and arterial hypertension cases. Diabetes mellitus was found in 45% patients with osteoporosis and in 18.2% patients without osteoporosis, = 0.036. MMLVI was  $111,1 \pm 5$  g/m<sup>2</sup> in patients with osteoporosis and  $122 \pm 6,0$  g/m<sup>2</sup> - without osteoporosis, = 0.038. Blood concentration of N-proBNP was  $1418,5 \pm 170,1$  pg/ml in patients with osteoporosis,  $228,6 \pm 179,5$  pg/ml - without osteoporosis, = 0.001. Patients with osteoporosis had higher rates of past bone fractures compared to those without osteoporosis, < 0.001. Adherent to treatments was 14 (42.4%) patients with osteoporosis and 9 (45%) - without osteoporosis. Moriski-Green Test mean score was  $3,3 \pm 0,7$  in patients with osteoporosis and  $3,25 \pm 0,8$  - without osteoporosis. There was correlations between high medication adherence and systolic BP (< 0.001,  $r = -0,44$ ), diastolic BP (= 0,04,  $r = -0,27$ ) and past osteoporotic bone fractures ( $p = 0,039$ ,  $r = 0,46$ ).

**Conclusion:** Medication adherence was similar in two groups of elderly HF patients and correlated with disease severity (due to N-proBNP) and past osteoporotic bone fractures. Our finding raises the fact that osteoporosis fractures could be a mere marker of disease severity and it should become a routine additional assessment of HF outpatients' adherence to medical treatment

## P940

### Renal denervation as a supportive treatment to chronic heart failure

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**Introduction:** Heart failure (HF) is a syndrome in which an abnormal cardiac function causes symptoms and signs of inadequate blood flow and oxygen delivery to the metabolizing tissues. The prevalence of HF in developed countries is increasing with the age and varies from 1-2% in the whole population to over 10% in the group of ≥85 years old. The costs of HF in Germany are between 3417€ to 5576€ per patient per year and are rising with the progression of the disease. The medication and device therapy should be addressed to slow and prevent worsening of HF. Cardiac resynchronization therapy (CRT) reduces annual mortality from 18,9% to 10,5% in patients who have severely depressed ejection fraction (EF ≤35 %). However, all the patients do not respond equally to CRT. 25-45% of the patients are non-responders and one of the greatest challenges is to improve the prognosis and the quality of life in this group. Renal sympathetic overactivation is present in chronic systolic heart failure and predicts adverse outcome. Sympathetic overdrive can effectively be reduced by renal denervation in patient with drug-resistant hypertension. Reach-Pilot trial demonstrated that renal denervation can safely be performed to patients with chronic systolic heart failure.<sup>2</sup>

**Purpose:** The aim of this study is to examine renal denervation (RDN) as a complementary treatment to optimal medical therapy and CRT to the non-responders for CRT.<sup>3</sup>

**Methods:** There are 13 patients who are non-responders for CRT with the criteria NYHA III-IV symptoms in spite of optimal medical therapy and CRT, the lack of reverse remodelling in left ventricle (LV), unchanged or worsened EF after CRT and walking distance in 6 minute walking test (6MWT) <400m with dyspnoea as a walking limiting symptom. All patients are > 18 years old. Patients were openly divided in two groups according to waiting list. Seven patients received RDN soon after signing of informed consent and six patients received RDN six months after signing informed consent. The follow-up will last two years. The primary end points are mortality, changes in 6MWT, th size of LV, EF and the quality of life measured by EQ-5D. The secondary end point is change in P-Pro-BNP. The group of early denervation and the group of late denervation will be compared to each other. The study will last until year 2017.

## P941

### Heart failure and the risk of perioperative cardiovascular complications in noncardiac surgery

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**Background:** History of heart failure /HF/ is an independent predictor for increased cardiovascular risk in noncardiac surgery. The incidence of HF among the European population varies from 0.4 to 2%, and it increases with age, the same way as the rate of noncardiac surgery increases with age.

**Methods and**

**Results:** A survey of the hospital stay of 561 surgically treated patients in the departments of general surgery in the University hospital of Pleven and multiprofile hospital for active treatment Rousse in the period 2012-2013 was performed. One hundred and sixty two patients /28.9%/ had history and clinical manifestation of HF in the past or at the moment of hospitalization. All the patients were evaluated for different cardiovascular complications - hypertensive crisis, long lasting hypotension requiring administration of catecholamines, angular pain, acute coronary syndrome, newly registered rhythm and conduction disorders, pulmonary thromboembolism, sudden cardiac death, acute or acutely decompensated chronic HF, acute manifestation of cerebrovascular disease, as well as death of any reason. The incidence of perioperative cardiovascular complications in patients with HF was 37.7% against 19.3% for the patients without HF. Thus the probability for complications in patients with history and / or clinical data for HF at admission was evaluated /OR=2.53; 95% CI=1.69-3.78 ( $p < 0.001$ )/. The concrete cardiovascular complications which increased the risk for HF patients turned out to be: newly registered ventricular rhythm disorders / $p = 0.007$ /, sudden cardiac death / $p = 0.024$ /, acute or acutely decompensated chronic HF / $p < 0.001$ / and overall death / $p = 0.004$ /. Additional analysis showed that the longer the history of HF and the higher the NYHA functional class of HF the higher the risk of perioperative cardiovascular complications. Thus a patient with one year history of HF has a 15% risk of perioperative cardiovascular complications, while a more than 5 year history of HF the risk increases to 57.6%, OR=4.66; 95% CI=2.27-9.58 ( $p < 0.001$ ). Similar are the results concerning the functional class of HF - complications were seen in 18.2% of the patients with NYHA class I, while in NYHA class III complications were registered in 66.7% of the patients, OR=7.21; 95% CI=3.5-14.86 ( $p < 0.001$ ).

**Conclusions:** With means of cross tabulation and unifactor analysis we proved that both the presence and duration of HF as well as the NYHA functional class of HF /acute and chronic/ have great importance for the occurrence of perioperative cardiovascular complications in non cardiac surgery.

## P942

### Contrast-induced nephropathy in a population with acute myocardial infarction and diabetes mellitus

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**Introduction:** Contrast-induced nephropathy (CIN) often complicates the invasive coronary procedures, appearing to associate with an adverse prognosis in acute myocardial infarction. In patients (P) with diabetes mellitus (DM), seems to be an intensification of oxidative stress and renal hypoxemia induced by contrast, making this population at increased risk of CIN.

**Aim:** To determine the prevalence of CIN after primary angioplasty in P with DM, the factors associated with its occurrence and its prognostic impact.

**Methods:** Retrospective study based on 250 P with DM admitted for ST-segment elevation myocardial infarction (STEMI) for 5 years. P requiring chronic peritoneal or hemodialysis treatment and cardiogenic shock at admission were excluded. CIN was defined by an elevation in creatinine values (cr) ≥ 0.5mg/dl 48 hours after angioplasty and there were determined 2 groups. We evaluated the occurrence of in-hospital death and at 6 months.

**Results:** The prevalence of CIN was 10.4% and these patients were older ( $p = 0.009$ ). There were no differences in demographic characteristics. The volume of contrast (VC) used was similar between the groups, but the ratio VC/eGFR was higher in P with CIN ( $p = 0.007$ ). P with CIN had more frequent anemia ( $p = 0.008$ ), left ventricular systolic dysfunction ( $p = 0.001$ ) and heart failure (HF) ( $p < 0.001$ ). The presence of anemia ( $p = 0.03$ ), eGFR <60ml/min and HF at admission ( $p = 0.009$ ) were predictors of CIN. The in-hospital mortality and at 6 months was higher in G1 (23.1% vs 4.5%,  $p < 0.001$  and 34.6% vs 8.0%,  $p < 0.001$ ), although the presence of CIN does not persist as an independent predictor of these events.

**Conclusion:** It is central to identify early P of higher risk in order to avoid side effects of therapy. In our population, the presence of anemia, eGFR <60 ml/min and HF are CIN predictors. Although the CIN is associated with an adverse prognosis, was not a predictor of mortality, remaining the doubt that this is only a marker of clinical severity.

**P943**

**Is there any benefit of early revascularization in patients with non-ST-elevation myocardial infarction and kidney disease?**

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**Introduction:** Kidney Disease (KD) is common amongst patients with non-ST-elevation myocardial infarction (NSTEMI) and it is associated with higher morbi-mortality. Due to renal impairment, the percutaneous coronary intervention (PCI) is sometimes differed. It is still not consensual when is the best time to perform PCI in these patients.

**Purpose:** Evaluate the outcomes of early versus late PCI in patients with KD, admitted for NSTEMI.

**Methods:** Single-center registry of 552 consecutive NSTEMI patients, with moderate or severe KD (evaluated by Glomerular Filtration Rate < 60ml/min/1.73m<sup>2</sup>) measured by the Cockcroft-Gault formula (previous validated for our population), between the years 2010-2014. Patients submitted to conservative therapy were excluded from this study. They were divided in 2 groups according to the moment PCI was performed, after NSTEMI was diagnosed. Group A: patients submitted to PCI ≤24h (n=241); Group B: patients submitted to PCI> 24h (n=311). Groups were compared regarding mortality rate and a primary composite endpoint (re-ML, stroke, and cardiovascular mortality) at one year follow-up.

**Results:** Group A was younger (A=72.10 ± 10.2 vs B=76.0 ± 8.9, years; p < 0.01). They had less history of arterial hypertension (A=70.5% vs B=79.4%; P < 0.05), Diabetes Mellitus (A=24.0% vs B=35.2%; p < 0.01), heart failure (A=5.8% vs B=14.8%; p < 0.01) and myocardial infarction (A=16.2% vs B=28.3%; p < 0.01).

At admission, Group A had higher glomerular filtration rate (A=43.3 ± 11.7 vs B=40.9 ± 13.5, ml/min/1.73m<sup>2</sup>; p < 0.05) and inferior prevalence of Killip Class>1 (A=13.5% vs B=25.3%; p < 0.01).

During hospitalization, they had lower Killip Class>1 at 72h (A=17.3% vs B=26.8%; p < 0.05), cardiogenic shock (A=8.7% vs B=15.8%; p < 0.01) and ischemic arrhythmias (A=12.2% vs B=21.6%; p < 0.01). They were less medicated with intravenous diuretics (A=25.8% vs B=34.0%; p < 0.05). At 1-year follow-up, Group A had an inferior mortality rate (A=20.3% vs B=29.6%; p < 0.01) and primary composite endpoint (A=23.2% vs B=34.4%; p < 0.01).

**Conclusion:** In this real-world cohort of patients with kidney disease, performing percutaneous coronary intervention in the first 24h after the setting of NSTEMI was beneficial, as patients showed long-term survival.

**P944**

**A simple depression screening tool and its association with outcomes in Asian patients with heart failure**

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**Background:** Few studies have examined the prevalence of depression and its association with outcomes in Asian patients with HF. The Patient Health Questionnaire-9 (PHQ-9) is a simple screening tool to evaluate depressive symptoms. PHQ-9 has never been evaluated in an Asian population with HF. PurposeOur aim was to compare the characteristics and outcomes of HF patients with and without depression as defined by the PHQ-9. MethodsThis was a prospective study enrolling consecutive patients hospitalised with HF to a tertiary centre in Singapore between 2010-2013. All patients were invited to take the PHQ-9 on admission. Depression was defined by PHQ-9 ≥5 or question 9 positive. Patient characteristics on admission and 1 year outcomes were collected. A t-test was used to compare means, a z-test for proportions and logistic regression to examine the independent association of PHQ-9 with outcomes. Results1450 consecutive patients were screened with the PHQ-9 questionnaire. 15.4% had depression. Depressed patients were younger (64 v 70 years, p < 0.05), had a lower LVEF (32v35%, p < 0.05) and were more likely to have symptoms of paroxysmal nocturnal dyspnea(42v31%, p < 0.05) and orthopnea(66v52%, p < 0.05) on admission. Patients with depression had higher rates of HF hospitalisation at 30days and 1 year, and death or CV hospitalization at 1 year. Depression (as defined by PHQ-9) was an independent predictor of death or CV hospitalisation at 1 year: OR 1.59 (1.13-2.2, p=0.008). Conclusion- Depression as defined by PHQ-9 is common in Asian patients with HF. The PHQ-9 questionnaire is a simple tool that can be used to screen for patients at high risk of adverse events. Further studies examining interventions for depression in this population are warranted.

Characteristics and outcomes

	Not depressed (PHQ-9 <5) (n = 1227)	Depressed (PHQ-9 ≥5 or question 9+ve) (n = 223)	p-value
Female (%)	39.5	39.0	n.s.
Ischemic heart disease (%)	69.3	65.5	n.s.
Previous stroke (%)	16.2	15.7	n.s.
Hypertension (%)	74.2	68.6	n.s.
Diabetes (%)	52.6	56.5	n.s.
NTproBNP (pg/ml)	4034	4419	n.s.
HF admission 30days (%)	6.5	10.8	p < 0.05
HF admission 1 year (%)	31.2	43.0	p < 0.05
Death or cardiovascular admission 30 days (%)	11.1	14.9	n.s.
Death or cardiovascular admission 1 year (%)	49.9	59.6	p < 0.05

n.s. - not significant

**P945**

**Impact of diabetes mellitus in the predictive value of heart failure biomarkers**

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**Background:** Diabetes mellitus (DM) entails a worse prognosis in heart failure (HF) patients. DM usually carries an increased atherosclerotic load and also a low-degree inflammation status. The use of biomarkers for HF risk stratification is growing. Biomarkers of different pathophysiological processes have been successfully used in predicting the risk of death in HF patients. Whether DM interferes their stratification ability is not completely elucidated. Objective: We sought to explore whether a panel of biomarkers have different prognostic value in patients with HF based on the presence or absence of DM.

**Patients and methods:** 1069 patients were included in the study (age 66.2 ± 12.8 years, 72% male, 51% of ischemic aetiology, mean LVEF 33.5% ± 13.3, 36% with DM). Serum concentrations of NT-proBNP (n=1030), high-sensitivity troponin T (hs-TnT) (n=803), ST2 (n=814), Galectin 3 (n=811), high-sensitivity C reactive protein (hs-CRP) (n=773) and Nephilysin (n=1069) were measured in consecutive ambulatory HF patients followed during 4.9 ± 2.8 years (6.6 ± 2.3 for alive patients). All-cause and cardiovascular deaths were the primary end-points.

**Results:** 534 patients died during follow-up, 283 of them from cardiovascular causes. As expected, mortality was higher in diabetic patients (57.7% vs. 45.6%, p < 0.001). NTproBNP (p = 0.07), hs-TnT (< 0.001) and Galectin-3 (p < 0.001) serum concentrations were higher in diabetic patients. We found no interaction between the majority of the biomarkers and DM in the prediction of risk of all-cause or cardiovascular death: NTproBNP, p = 0.98 and p = 0.66 respectively; hs-TnT, p = 0.39 and p = 0.78 respectively; Galectin-3, p = 0.78 and p = 0.96 respectively; hs-CRP, p = 0.19 and p = 0.90, respectively (after excluding those patients with very high levels due to other diseases); and Nephilysin, p = 0.98 and p = 0.19 respectively. However, ST2 significantly interacted with DM for all-cause death (p = 0.02) and cardiovascular death (p = 0.03). HR for ST2/10 were 1.27 [95%CI 1.16-1.40], p < 0.001 and 1.23 [95%CI 1.09-1.39], p = 0.001 for all-cause and cardiovascular death, respectively in diabetic patients; and 1.53 [95%CI 1.35-1.73], p < 0.001 for all-cause death and 1.64 [95%CI 1.31-2.05], p < 0.001 for cardiovascular death in non-diabetic patients.

**Conclusions:** We did not find an interaction between DM and NTproBNP, hs-TnT, Galectin-3, hs-CRP and Nephilysin in the prediction of risk of all-cause or cardiovascular death in a long-term follow-up of a cohort of ambulatory patients with HF. However ST2, a significantly predictor for both all-cause and cardiovascular death together in diabetic and also non-diabetic patients, conferred an appreciably higher risk in the non-diabetic patients.

**P946**

**Comparative long term effects of Nebivolol and Carvedilol in hypertensive heart failure patients**

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**Background:** Beta-blockers improve left ventricular (LV) systolic function and prognosis in chronic heart failure (CHF) patients, but their different pleiotropic properties may influence their cardiovascular effects.

**Aim** This study compared the effects of long term treatment with nebivolol versus carvedilol on left ventricular ejection fraction (LVEF), in hypertensive CHF patients. Secondary endpoints were to assess the effect of the two beta-blockers on exercise capacity and clinical outcome.

**Methods:** 160 hypertensive CHF patients, LVEF <40% and in NYHA class I, II or III were randomly assigned to receive nebivolol or carvedilol for 24 months. At baseline and at the end of treatment, all patients underwent clinical evaluation, echocardiogram and 6-minute walking test.

**Results:** Compared with baseline values LVEF increased by a similar extent in the carvedilol (C) and nebivolol (N) groups (C: from 36.1% (SD 1.5) to 40.9 (SD 1.9)  $p < 0.001$ ; N: from 34.1% (SD 1.8) to 38.5% (SD 2.2)  $p < 0.001$ ). Heart rate, NYHA class decreased significantly in both groups, while the 6-minutes walk distance (6MWT) increased (C: from 420 m (SD 104) to 490 m (SD 115)  $p < 0.001$ ; N: from 421 m (SD 118) to 487 m (SD 138)  $p < 0.001$ ). During 24 months 21 (26%) of carvedilol recipients and 18 (22%) nebivolol recipients had cardiac events, including 3 and 4 deaths, respectively.

**Conclusion:** In the long-term, nebivolol and carvedilol appear to be similarly effective in the treatment of hypertensive CHF patients.

#### P947

##### Hypertension, obesity, diabetes, and myocardial infarction are the major determinants of heart failure phenotype

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**Introduction:** It has been suggested that comorbidities drive myocardial dysfunction and remodeling in heart failure with preserved ejection fraction (HFpEF). We hypothesized that comorbidities determine whether a patient develops HFpEF or HF with reduced EF (HFrEF).

**Purpose:** To evaluate the contribution of comorbidities to the development of HF phenotype, HFpEF or HFrEF.

**Patients and methods:** 1019 consecutive HF patients (age  $71.7 \pm 12.3$  years, male 56.9%, mean LVEF  $42.8 \pm 14.4\%$ , HFpEF 46.6%) referred to the outpatient HF Clinic of a tertiary University Hospital were screened for major HF comorbidities, from January 2014 to December 2015.

**Results:** The prevalence of major HF comorbidities was: hypertension 72.3%; myocardial infarction 39.8%; atrial fibrillation 26.2%; diabetes 21.3%; chronic obstructive pulmonary disease 13.6%; obesity 39.4%; chronic kidney disease 18.9%; anemia 28.2%. Univariable and multivariable logistic regression analyses demonstrated that only hypertension, myocardial infarction, obesity and diabetes determined the HF phenotype (HFpEF or HFrEF) (Table), with an area under the curve of 0.90 (Figure).

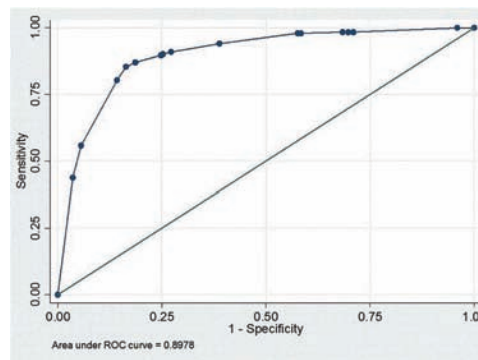
**Conclusion:** Hypertension, myocardial infarction, obesity, and diabetes were the only determinants of the HF phenotype. The contribution of other comorbidities was not significant.

Table

Variable	Odds ratios* (95% CI)	P value
Hypertension	9.43 (5.85, 15.17)	< 0.0001
Myocardial infarction	0.06 (0.04, 0.09)	< 0.0001
Obesity	3.24 (2.23, 4.69)	< 0.0001
Diabetes	0.57 (0.37, 0.90)	0.01

\*Higher odds for: i) HFpEF, if OR > 1.0; ii) HFrEF, if OR < 1.0

Multivariable logistic regression analysis



ROC curve for the prognostic model

#### P948

##### Long-term prognosis of patients with moderate to severe sleep apnea with preserved left ventricular systolic function and systolic dysfunction after myocardial infarction

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**Purpose:** Sleep apnea (SA) has a high prevalence in patients after myocardial infarction (MI). While SA might be a modifiable risk factor, recent data suggest that SA is severely underdiagnosed in patients after MI. There is a limited evidence about long-term prognosis of patients with moderate to severe sleep apnea with preserved (PEF) and reduced (REF) left ventricular ejection fraction after MI. We therefore prospectively investigated differences in the prognosis of these two groups of patients.

**Methods:** We prospectively studied 782 consecutive patients admitted to the hospital with the diagnosis of acute MI. The study was conducted in two tertiary care institutions, where primary percutaneous coronary intervention (PCI) is the standard of care in the treatment of acute MI. All subjects underwent sleep evaluations using a portable diagnostic device after at least 48 hours post-admission, provided they were in stable condition. Patients were followed for median follow-up of 44 months.

**Results:** Almost all patients (98%) underwent urgent coronary angiography and 91% of patients underwent primary PCI. 175 (22.4%) patients had technically inadequate limited sleep studies (less than 4 h recording time or inability to score study due to excessive artifact). We therefore analyzed the data from 607 patients who had good quality sleep study records. SA was present in 63% of patients after MI with PEF and in 72% of patients with REF (LVEF < 45%),  $p = 0.05$ . Moderate to severe SA was present in 33.1% of patients after MI. There was a higher total mortality in REF (21.7%) than in PEF (10.6%) patients after MI in the group of moderate to severe SA,  $p = 0.033$ . Independent predictors of mortality according to the multivariate analysis were type 2 diabetes mellitus (OR 5.003, 95% CI 1.968 to 12.717,  $p = 0.001$ ), history of previous MI (OR 4.633, 95% CI 1.832 to 11.718,  $p = 0.001$ ), age (OR 2.326, 95% CI 1.417 to 3.819,  $p = 0.001$ ) and apnea index (OR 1.216, 95% CI 1.023 to 1.445,  $p = 0.027$ ).

**Conclusion:** MI patients with moderate to severe SA and left ventricular systolic dysfunction had worse long-term prognosis than those with preserved systolic function. Whether treatment of SA after MI will significantly improve outcomes in these patients remains to be determined.

#### P949

##### Prevalence, severity and prognostic value of sleep apnea syndromes in cardiac amyloidosis

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**Background:** Sleep disordered breathing (SDB) occurs frequently in heart failure and is a marker of bad prognosis but its prevalence and consequence are unknown in cardiac amyloidosis (CA).

**Purpose:** Our aims were to assess prevalence, severity and prognosis value of SDB in the three main CA types i.e., light-chain (AL), transthyretin-related familial (m-TTR) or senile (WT-TTR).

**Methods:** Patients consecutively referred for CA diagnosis work-up underwent a night polygraphy. SDB was defined as apnea-hypopnea index (AHI)  $\geq 5/h$ . Multivariate analysis was used to identify predictors of major cardiovascular events (MACE) defined as death, heart transplantation and acute heart failure.

**Results:** Seventy CA patients were included (31 AL, 22 m-TTR, 17 WT-TTR). The mean (SD) age and LVEF were  $71 \pm 12$  years and  $49 \pm 13\%$  and median(IQR) NT-proBNP was 3932pg/ml (1607;7028). The prevalence of SDB was 90% without difference between amyloidosis types. SDB was central in 27% and obstructive in 73%. AL had less frequent severe SDB compared to m-TTR and WT-TTR ( $p = 0.015$ ) but higher time with  $SaO_2 < 90\%$  ( $p = 0.037$ ). After 7.5 (2.8; 14.9) months of follow-up, 49% patients experienced MACE. Time with nocturnal  $SaO_2 < 90\%$  were the only independent predictor of MACE with a threshold time superior to 30min indicating bad prognosis (Log-rank X2: 8.01,  $p$ -value = 0.005). Determinants of time with nocturnal  $SaO_2$  were NYHA and logNTproBNP but not AHI. Conclusion. Prevalence of SDB is high (90%) in CA population, most having an obstructive pattern. Nocturnal time spent with oxygen saturation less than 90% was an independent prognosticator of bad outcome and determined by heart failure severity.

**P950**

**Anaemia and the cardiorespiratory adaptation to exercise in chronic heart failure**

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**Introduction:** Anaemia (AN) in chronic heart failure (CHF) leads to worse symptoms and prognosis. Since haemoglobin (Hb) is implicated in O<sub>2</sub> and CO<sub>2</sub> transport, the presence of AN may be associated with more severe derangement in the control of ventilation (VE) during exercise.

**Purpose:** to evaluate the effect of AN on cardiopulmonary response to exercise in CHF.

**Methods:** We analysed 60 CHF patients (ejection fraction  $\leq 45\%$ ) on optimized therapy who consecutively performed a cardiopulmonary exercise test between 2014 and 2015. AN was defined according to WHO criteria (women: Hb  $< 12.0$ ; men  $< 13.0$  g/dL).

**Results:** 41 patients (68%) had AN. Demographics and echocardiography were similar in AN and non-AN. AN presented more advanced NYHA class, higher serum creatinine and higher prevalence of atrial fibrillation. At peak exercise, they had lower oxygen uptake (VO<sub>2</sub>) and lower heart rate (HR) than non-AN, while respiratory quotient did not differ. Exercise-induced hyperventilation, defined by the slope between VE and carbon dioxide production (VCO<sub>2</sub>), as well as the prevalence of exercise oscillatory breathing (EOV) did not differ between the two groups. NYHA class ( $r = -0.483$ ;  $p < 0.001$ ), creatinine ( $r = -0.382$ ;  $p = 0.003$ ), peak VO<sub>2</sub> ( $r = 0.371$ ;  $p = 0.04$ ) and peak HR ( $r = 0.303$ ;  $p = 0.019$ ) were all related to Hb values.

**Conclusions:** in our population, AN is associated with a more impaired functional capacity but not with worse ventilatory control during exercise. Somehow counter-intuitively, limitation in AN seems to be secondary to chronotropic incompetence more than to a reduction in the delivery/peripheral extraction of O<sub>2</sub>.

	Anemia	No anemia	P
Age [years]	72,6 ± 8,8	69,2 ± 10,1	0,091
BMI [Kg/m <sup>2</sup> ]	25,7 ± 5,3	26,9 ± 4,1	0,387
LVEF [%]	35,4 ± 5,8	33 ± 5,3	0,106
Hb [g/dL]	11,3 ± 0,9	14,1 ± 0,9	< 0,001
Creatinine [mg/dL]	1,6 ± 1,1	1,1 ± 0,2	0,032
NYHA class	2,2 ± 0,6	1,6 ± 0,5	0,002
HR@ peak [beats/min]	93.2 ± 17.3	105.8 ± 21.9	0,040
RQ @ peak	1,1 ± 0,1	1,1 ± 0,06	0,595
VO <sub>2</sub> @ peak [L/min]	1,0 ± 0,3	1,3 ± 0,4	0,026
O <sub>2</sub> pulse @ peak [mL/beat]	11,1 ± 3,2	12,1 ± 3,4	0,323
VE/VCO <sub>2</sub> slope	30,7 ± 5,2	30 ± 6	0,635
EOV%	12,2%	15,8%	0,704

Principal characteristics of our study population

**P951**

**Prognostic significance of anemia in patients with chronic heart failure**

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The aim of our study was to determine the prevalence of anemia in patients with chronic heart failure (CHF), the impact of anemia on quality of life, a correlation between the severity of CHF and anemia, the relationship between the severity of anemia and left ventricular function, the impact of anemia on the length of hospitalization.

**Methods:** The study included 205 patients with CHF. To assess the quality of life of patients we used Minnesota Living With Heart Failure Questionnaire - MLWHFQ. Standard echocardiography examination was performed. The functional capacity of patients was assessed by the six minute walk test (6MW). Results We examined 109 men and 96 women,  $62.67 \pm 8.38$  years old, the average duration of CHF was 37.7 months. The anemia was diagnosed in 25.4% patients. There was a significant difference in the values of MLWHFQ ( $p < 0.01$ ), significantly higher in patients with anemia. Analysis of variance showed statistically significant difference in average values MLWHFQ in according NYHA class in both groups. By comparing the two groups of patients examined on the basis of the distance traveled during the 6MW was found highly statistically significant ( $p < 0.01$ ). Patients with anemia had bigger dimensions of left ventricle and lower ejection fraction. Severity of mitral regurgitation was significantly higher in patients with anemia and CHF ( $p < 0.01$ ). Patients with anemia required significantly longer hospital treatment ( $p < 0.01$ ). Predictor factors for death during the period of 6 months follow-up after hospitalization in patients with CHF were hematocrit and serum creatinine. Our study showed that anemia is a common co-morbidity in patients with CHF and requires more aggressive treatment.

**P952**

**Anemia and low haemoglobin levels are associated with worse functional status in patients with chronic heart failure: results from TREAT HF**

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**Purpose:** Anemia has been demonstrated to be prevalent in patients with heart failure (HF) and associated with worse clinical outcomes. NYHA functional class has also been known to be a strong marker of poor prognosis. TREAT HF (Turkish Research Team-HF) data were analyzed for the assessment of any association of anemia or haemoglobin levels with NYHA functional class categories in patients with chronic HF and reduced ejection fraction (HFrEF).

**Methods:** TREAT HF is a network which undertakes multicenter, national, observational studies designed to evaluate HF patient's clinical characteristics and current treatment modalities. 924 patients with the diagnosis of chronic HFrEF and  $> 18$  years of age who had haemoglobin measurement were included in this analysis. Anemia was defined as a haemoglobin level  $< 13$  g/dL in men and  $< 12$  g/dL in women. Out of 924 patients, 113 patients (12.2%) were in NYHA class I, 409 patients (44.2%) in NYHA class II, 356 patients (38.5%) in NYHA class III and 46 patients (5%) in NYHA class IV. Patients with recent acute coronary syndromes, severe hepatic or renal dysfunction, severe chronic obstructive pulmonary disease, hematological disease, ongoing systemic inflammatory conditions, cancer, hyper-/hypothyroidism and pregnant women were excluded from the study.

**Results:** Anemia was found in 437 patients (47.3%) in our study population. Mean haemoglobin level was  $12.6 \pm 2.1$  g/dL in the study population,  $13.2 \pm 1.9$  g/dL in those with NYHA class I,  $12.9 \pm 2.0$  g/dL in those with NYHA class II,  $12.2 \pm 2.2$  g/dL in those with NYHA class III and  $11.4 \pm 2.2$  g/dL in those with NYHA class IV and overall, mean haemoglobin levels were found to gradually and significantly reduce across NYHA functional class categories ( $p = 0.001$ ). Anemia was found in 40 patients (35.4%) in those with NYHA class I, 163 patients (39.9%) in those with NYHA class II, 200 patients (56.2%) in those with NYHA class III and 34 patients (73.9%) in those with NYHA class IV and overall, the prevalence of anemia was also found to gradually and significantly increase across NYHA functional class categories ( $p < 0.001$ ). There was no significant difference between NYHA I and NYHA II in terms of the incident of anemia ( $p = 0.446$ ) while patients with NYHA IV showed significantly higher prevalence of anemia when compared patients with NYHA III, NYHA II or NYHA I ( $p = 0.015$ ,  $p = 0.001$  and  $p = 0.001$ , respectively). Also significantly more patients with NYHA III have had anemia as compared to those with NYHA II ( $p = 0.001$ ).

**Conclusions:** These results suggest that anemia and low haemoglobin levels are associated with worse functional status in patients with HFrEF.

**P953**

**Comparison of the effect of EPO treatment and intravenous iron treatment by patients in chronic heart failure with anaemia.**

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**Purpose.** The aim of investigation were to study the effect of intravenous (iv) iron sucrose (Venofer) and metoxipoliethylen glicol epoietin beta (MEB) in patients with CHF with anemic syndrome.

**Material and methods:** 63 patients with NYHA class II-IV CHF and LVEF 40 % or less with anemia and hypererythropoietinemia or hyporeythropoetinaemia were obtained. Mean age of patients  $67,9 \pm 8,5$  years. The level of Hb was  $Hb < 11$  g/dl and iron deficiency (ID) was diagnosed at serum ferritin 30-99  $\mu g/l$  or 100-299  $\mu g/l$ , if the transferrin saturation (TSAT)  $< 20$  %. It should be noted that patients with absolute ID. Echocardiographic indices of LV systolic and diastolic function and RV function, 6 minute walked distance and plasma NT pro BNP, erythropoietin (EPO), ferritin, TSAT were assessed at baseline and posttreatment. 63 patients

with anemic CHF were obtained and were randomly into two groups. I groups included 33 patients were treated with treatment of iv Venofer in dose either as 5 iv bolus injections of 100-200 mg iron per dose or as a fast high-dose infusion at baseline and of II groups included 30 patients were treated with percutaneous MEB in dose 50 IU in day in one month in follow-up 6 months. Control groups included 31 patients in CHF II-IV class without anemia. The level of Hb  $12.63 \pm 0.9$  g/dl, EPO-14,  $19 \pm 3.45$  IU, serum ferritin  $147.9 \pm 19.2 \pm \mu\text{g/l}$ , NT pro BNP  $1739 \pm 145.3$  pg/ml, TSAT  $> 20\%$ , LVEF  $< 40\%$  or less, 6-minute walking test  $340 \pm 65$  meters. Results. The treatment patients with anaemic CHF with ID and hypererythropoietinemia of Venofer there was a significant increase Hb (to  $10.32 \pm 0.18$  g/dl to  $10.8 \pm 0.22$  g/dl) ( $p < 0.001$ ), decrease EPO-36,  $7 \pm 14.8$  IU to  $13.1 \pm 2.8$  IU ( $p = 0.194$ ), increase ferritin  $88.4 \pm 14.9$   $\mu\text{g/l}$  to  $150.2 \pm 25.5$   $\mu\text{g/l}$  ( $p < 0.05$ ), TSAT  $> 20\%$ , NT pro BNP decrease  $2505.4 \pm 136.3$  pg/ml to  $1886.4 \pm 192.7$  pg/ml ( $p < 0.001$ ), LVEF increase  $35.8 \pm 1.6\%$  to  $37.4 \pm 1.6\%$  ( $p = 1.292$ ) a significant NYHA class from  $3.4 \pm 0.2$  to  $2.2 \pm 0.3$  ( $p < 0.05$ ), a longer endurance on exercise testing from  $243 \pm 34$  to  $384 \pm 75$  meters ( $p < 0.01$ ). But the treatment patients with anaemic CHF without ID and hypererythropoietinemia of MEB there was a significant increase Hb (to  $9.36 \pm 0.32$  g/dl to  $10.4 \pm 0.32$  g/dl) ( $p < 0.001$ ), increase EPO  $1.3 \pm 0.4$  IU to  $32.8 \pm 5.7$  IU ( $p < 0.01$ ), increase ferritin  $158.4 \pm 20.8$  to  $160.5 \pm 22.2$   $\mu\text{g/l}$  ( $p = 0.3$ ), increase TSAT  $< 20\%$  to TSAT  $> 20\%$ , NT pro BNP decrease  $1816.5 \pm 145$  pg/ml to  $991.6 \pm 142.9$  pg/ml ( $p < 0.001$ ), LVEF increase  $39.4 \pm 1.6\%$  to  $44.4 \pm 1.7\%$  ( $p < 0.05$ ) a significant NYHA class from  $3.4 \pm 0.2$  to  $2.2 \pm 0.3$  ( $p < 0.05$ ), a longer endurance on exercise testing from  $243 \pm 34$  to  $7.5$  meters ( $p < 0.01$ ). Conclusion. Therefore the treatment patients with anaemic CHF with hypererythropoietinemia of Venofer there was a significant increase Hb, ferritin, TSAT  $> 20\%$ , a longer endurance on exercise testing and decrease the level of NT pro BNP. The treatment patients with anaemic CHF and hypererythropoietinemia of MEB there was a significant increase Hb, EPO, LVEF and decrease NT pro BNP, NYHA class, 6-minute walking test.

#### P954

##### Oral iron therapy with polysaccharide iron complex may be useful in increasing ferritin level at short time in patients with dilated cardiomyopathy

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**Introduction:** It has been shown that iron therapy improves symptoms, exercise capacity and quality of life in HF patients with reduced ejection fraction. Polysaccharide-iron complex (PIC) is an oral iron supplement which allows the iron to be absorbed intact through the small intestine without coming into contact with the upper GI tract. In this study we aimed to investigate if oral PIC is effective in increasing ferritin level in dilated cardiomyopathy patients with absolute iron deficiency and what is the incidence GI side effects.

**Methods:** Thirty patients with a diagnosis of non-ischemic dilated cardiomyopathy were recruited according to the following inclusion criteria; LVEF equal or less than 35%, NYHA function class of I-III and serum ferritin level less than 100 microgram/lit. For all study participants one capsule of Feramax-150 (BioSyntPharmalnc) was prescribed on daily basis for 12 weeks. The study variables (table 1) were measured at baseline and after 12 weeks. All patients were asked to report any GI side effect they may have.

**Results:** A total of 30 patients (12 male) with a diagnosis of non-ischemic dilated cardiomyopathy were included. The mean (SD) of age was  $43.2(13.4)$  years. The mean of LVEF was 23 % (between 10-35%). The mean (SD) of ferritin level was  $48.8(27.7)$   $\mu\text{g/l}$  at baseline. After 12 weeks treatment with feramax-150 the mean (SD) of ferritin level increased to  $69.9(42)$  which was statistically significant ( $P < 0.001$ ). There was also statistically significant increase in 6 MWT and decrease in pro-BNP level after 12 weeks treatment with Feramax-150 (Table 1). No one of patients showed gastrointestinal side effects.

**Conclusion:** PICs would be a good and well-tolerated medicine in the treatment of iron deficiency in patients with heart failure.

Table 1

Variable	Baseline	After 12 weeks	P value
NYHA class of I, I-II, number(%)	7(24)	10(33)	0.04
NYHA class of II, II-III, III, number(%)	23(76)	20(67)	
Hemoglobin, g/l, mean(SD)	13.4(1.4)	13(1.4)	0.4
Iron, $\mu\text{g/dl}$ , mean(SD)	80(20)	87.2(35.7)	0.7
TIBC, $\mu\text{g/dl}$ , mean(SD)	344(62)	346(47)	0.8
Ferritin, $\mu\text{g/l}$ , mean(SD)	48.8(26.7)	69.9(42)	$< 0.001$
Pro BNP, ng/dl, median(IQR)	1375(132-3292)	1035(98-2400)	$< 0.001$
6MWT, meter, mean(SD)	354(83)	385(84)	0.02

The clinical and laboratory characteristics of study population at base line and after 12 weeks

#### P955

##### Iron deficiency predicts respiratory muscle weakness in men with heart failure with reduced ejection fraction

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**Introduction:** Dysfunction of respiratory muscles constitutes an important pathophysiological feature of heart failure (HF) and contributes to decreased exercise capacity in these patients. Preserved iron status is essential for effective functioning of muscle tissue, and therefore iron deficiency (ID) could potentially contribute to respiratory myopathy in patients with HF.

**Methods:** We evaluated respiratory muscle strength, exercise capacity and systemic iron status in 51 male outpatients with stable HF with reduced ejection fraction (HFrEF) (age:  $64 \pm 11$  years; NYHA class I/II/III: 35/49/16%; ischaemic aetiology: 82%; all with LVEF  $\leq 40\%$ ). None of them was diagnosed with asthma or COPD. Respiratory muscle function was assessed as maximal inspiratory pressure (MIP) at the mouth using a portable device (the average value of 5 measurements). We also assessed spirometry parameters (percentage of predicted value, the average value of 3 tests), i.e. forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1) and peak expiratory flow (PEF). Exercise capacity was evaluated using a 6-minute walking test distance (6MWD). ID was defined as serum ferritin  $< 100$   $\mu\text{g/L}$  or serum ferritin  $100-299$   $\mu\text{g/L}$  with transferrin saturation (TSAT)  $< 20\%$ .

**Results:** Mean MIP, FVC, FEV1 and PEF were  $74 \pm 23$  cm H<sub>2</sub>O,  $101 \pm 26\%$ ,  $89 \pm 28\%$ , and  $66 \pm 27\%$ , respectively. MIP was reduced in men with higher NT-proBNP ( $r = -0.31$ ,  $p = 0.03$ ), but was not related to NYHA class, aetiology of HF or BMI, and there was a trend towards lower MIP in older patients ( $p = 0.056$ ). Spirometry parameters correlated neither with the severity (NYHA class, NT-proBNP) nor aetiology of HFrEF (all  $p > 0.16$ ). Age was not associated with spirometry parameters, whereas subjects with lower BMI had greater FVC ( $r = -0.44$ ,  $p = 0.001$ ) and there was a trend towards higher FEV1 in these patients ( $p = 0.059$ ). Patients with ID had lower MIP than subjects without ID ( $67 \pm 20$  vs.  $83 \pm 23$  mm H<sub>2</sub>O,  $p = 0.02$ ), without any differences in spirometry parameters. In a two-variable linear regression model, both ID and anaemia independently predicted lower MIP ( $\beta = -0.29$ ,  $p = 0.03$ ; and  $\beta = -0.28$ ,  $p = 0.04$ ; respectively), and similar associations were also seen in a model comprising serum ferritin (but not TSAT) and haemoglobin. After the adjustment for haemoglobin and NT-proBNP, lower ferritin remained an independent predictor of lower MIP ( $\beta = 0.35$ ,  $p = 0.01$ ). Spirometry parameters were lower in subjects with anaemia (FVC:  $r = -0.28$ ; FEV1:  $r = -0.35$ ; PEF:  $r = -0.43$ ; all  $p < 0.05$ ), but correlated neither with ID nor serum ferritin. Importantly, in studied patients with HFrEF, lower MIP was an independent predictor of lower 6MWD after the adjustment for NT-proBNP and NYHA class ( $\beta = 0.40$ ,  $p = 0.004$ ).

**Conclusions:** In men with HFrEF respiratory muscle weakness correlates with ID and predicts decreased exercise capacity. Respiratory muscle dysfunction due to ID can partially explain decreased exercise capacity in iron-deficient men with HF.

#### P956

##### Kynurenine levels correlated with depression, functional capacity, and muscle performance in heart failure patients

the European Commission under the FP7

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**Background:** Lower functional capacity in heart failure (HF) patients is considered to be multifactorial, where depression and skeletal muscle wasting may play some roles. Recently, exercise-induced degradation of kynurenine (a metabolite from essential amino acid tryptophan) in skeletal muscle has been reported preferably affecting for maintaining resilience against psychological stress and depression.

**Methods and Results:** We assessed serum kynurenine levels in 249 HF patients (mean age:  $67 \pm 11$  years, 21% women) and 45 non-HF patients who participated in the Studies Investigating Co-morbidities Aggravating Heart Failure (SICA-HF). Kynurenine levels were higher in 173 HF patients with reduced ejection fraction (EF) and 76 patients with preserved EF than 45 non-HF patients ( $3.5 \pm 1.5$ ,  $3.4 \pm 1.3$ , and  $2.4 \pm 1.1$   $\mu\text{mol/L}$ , respectively,  $p < 0.001$ ). In HF with reduced EF, kynurenine levels had inverse correlation with handgrip (Pearson's  $r = -0.26$ ,  $p < 0.01$ ), peak O<sub>2</sub> consumption ( $r = -0.29$ ,  $p < 0.01$ ), and 6-min walk distance ( $r = -0.23$ ,  $p < 0.01$ ), and had positive correlation with parameters of kidney/liver function and depression assessed by questionnaire. No correlation was observed between kynurenine and muscle mass. In multivariable logistic regression analysis, kynurenine could identify those with lower peak O<sub>2</sub> consumption (below median;  $17.2$  ml/min/kg) even after



the adjustment by age, gender, and body mass index (odds ratio; 1.36, 95% confidence interval 1.02-1.81, for 1  $\mu\text{mol/L}$  increase in kynurenine,  $p=0.04$ ).

**Conclusions:** Kynurenine may have some roles linking depression, functional capacity, and muscle performance in HF. Further analysis assessing prognosis or implication in treatment would be warranted.

#### P957

##### Relationship between skeletal muscle mass and cardiac function during exercise in chronically ill older adults

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**Introduction:** The clinical interrelationship between skeletal muscle and cardiac function remains unknown. The aim of the study is to investigate the relationship between skeletal muscle mass and cardiac functional parameters in older adults during cardiopulmonary exercise testing (CPET).

**Methods:** Sixty-eight chronically ill older adults were enrolled. The participants consisted of 22 men and 46 women (mean age, 78 years; range, 52–97 years). Cardiac functional parameters during exercise were assessed using the CPET. Skeletal muscle mass index (SMI) was calculated from the appendicular lean mass, which was measured with dual-energy X-ray absorptiometry, divided by height in square centimeters. We divided the subjects into two groups based on their SMI as follows: men with SMI  $\geq 7.0$  kg/m<sup>2</sup> and women with SMI  $\geq 5.4$  kg/m<sup>2</sup> (Preserved-SMI group); or men with SMI  $< 7.0$  kg/m<sup>2</sup> and women with SMI  $< 5.4$  kg/m<sup>2</sup> (Reduced-SMI group). These criteria were derived from the Asian Working Group for Sarcopenia.

**Results:** There were significant positive correlations between SMI and peak VO<sub>2</sub> ( $r=0.609$ ,  $p<0.001$ ), and between SMI and peak VO<sub>2</sub>/HR ( $r=0.691$ ,  $p<0.001$ ). However, only peak VO<sub>2</sub>/HR was significantly different between the Preserved-SMI group and the Reduced-SMI groups in both sexes. Multiple linear regression analyses showed that SMI was the only independent determinant of peak VO<sub>2</sub>/HR after adjusting for potential confounders.

**Conclusions:** Peak VO<sub>2</sub>/HR, an index of stroke volume at peak exercise, was strongly associated with skeletal muscle mass. This result showed for the first time that reduced skeletal muscle mass might affect the impaired cardiac function during exercise, which might be the case with older patients with heart failure and preserved ejection fraction.

#### P958

##### N-terminal pro-B-type natriuretic peptide and high sensitive-Troponin I in the prognosis stratification of HF.

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The aim of our study was to evaluate the role of the NT-proBNP and hs-TnI in the prognosis stratification of HF. We studied 226 patients affected by chronic HF with EF  $< 35\%$ , whose 9 (3 heart transplant recipients and 6 lost to follow up). During the last follow up 69 clinical events were recorded, of which 53 hospitalizations for acute HF and 16 cardiovascular deaths (19% of the overall population). Baseline spheric levels of NT-proBNP, instead, which were three times higher in dead patients, was related to this clinical event ( $p=0.001$ ). Kaplan Meier analysis demonstrated that concentrations of NT-proBNP  $> 1250$  pg/ml are predictors of reduced survival ( $p=0.0003$ ). We assessed by univariate Cox analysis that, unlike hs-TnI, an increase of 500 Units of NT-proBNP were related to a relative risk of cardiovascular death of 22.4% ( $p<0.001$ ); similar results at the univariate logistic regression. As regard the second study end point (hospitalization for acute HF), in hospitalized patients serum levels of NT-proBNP and hs-TnI were higher than health patients (in particular: NT-proBNP  $> 1250$  pg/ml, hs-TnI  $> 0.009$  ng/ml); we demonstrated through regression analysis a significant correlation between an increase of the risk of hospitalization and serum concentrations of both biomarkers ( $p<0.001$ ). Applying the statistical illness-death model, we observed 122 transitions: 53 from health to illness (transition 1), 53 from illness to health (transition 3) and 16 from health to death (transition 4). None transition from illness to death (transition 2) verified, because all patients hospitalized were discharged home (Fig.1). We demonstrated, through Cox model, that a statistical correlation existed between an increase of 500 Units of NT-proBNP, compared to baseline, and the risk of transition both from health to illness (HR 1.278,  $p<0.001$ , IC 1.215-1.343) and from health to death (HR 1.234,  $p<0.001$ , IC 1.124-1.356); we were not able to evaluate the role of this biomarker to favour transition from illness to health (transition 3) because of the lack of its serum values at discharge. We studied also the composite of CV mortality and hospitalization; we demonstrated that high serum levels of

NT-proBNP were correlated to an increased risk of composite endpoint, unlike hs-TnI. Stratifying our population according to the serum levels of NT-proBNP and hs-TnI, we found that the risk of CV death combined to hospitalization was significantly associated with concentrations of NT-proBNP and hs-TnI respectively major than 1250 pg/ml and 0.009 ng/ml; we obtained similar results through univariate Cox analysis. The independent prognostic role of NT-proBNP was then confirmed by multivariate regression.

In our study NT-proBNP represents a strong predictor of cardiovascular outcomes: an increase of 500 Units of NT-proBNP is correlated to an increase of the relative risk of cardiovascular death and it influences the "transition" from the state of health to the state of illness/death.

#### P959

##### Acute cardio-renal syndrome: the role of inferior vena cava collapse

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The size and shape of the inferior vena cava (IVC) is correlated with central venous pressure (CVP) and intravascular volume status. Lung ultrasound with counting B-lines is a simple way to assess extravascular lung water. We assume that in patients with acute decompensated heart failure (ADHF), not only were with venous congestion strongly associated with renal perfusion, but also renal function impairment.

**Purpose:** To determine the interaction between the inferior vena cava collapse as a noninvasive ultrasound method of CVP assessment and counting B-lines and the risk of acute kidney injury (AKI) of patients with ADHF.

**Methods:** A prospective observational cohort study of patients admitted for ADHF. We enrolled 62 patients (69% male) with a mean age of 62 years. The main cause of ADHF was a combination of coronary artery disease and arterial hypertension - 36 (58%). AKI was diagnosed and classified according to the KDIGO Recommendations (2012). According to the Recommendations on pre-hospital and early hospital management of acute heart failure (2015) we carried out bedside thoracic ultrasound for signs of interstitial oedema and abdominal ultrasound for assessment of inferior vena cava diameter. Result: Acute cardiorenal syndrome (CRS type 1) was diagnosed in 33 (53%) patients with ADHF. On the basis of the AKIN staging system, 23 (70%) patients were classified as stage 1, 9 (27%) as stage 2, and 1 (3%) as stage 3. Patients needing replacement renal therapy were not found. Mean age was similar between both (63.3 (SD 11.9) in the development cohort, 61.5 (SD 11.7) in the validation cohort). In general, patients with ADHF and AKI during the first day of hospitalization had larger diameter of IVC ( $18.9 \pm 5.4$  mm vs.  $14.7 \pm 5.3$  mm resp.,  $p=0.05$ ) and variations of IVC diameter were significantly lower ( $12.4 \pm 4.7$  mm vs.  $7.2 \pm 4.7$  mm resp.,  $p=0.01$ ). Subsequently, during the 7th day of therapy of patients with ACS type 1 diameter IVC remained larger ( $21.2 \pm 5.2$  mm. vs.  $13.1 \pm 5.7$  mm resp.,  $p=0.01$ ), and the value of collapse IVC became lower compared with patients with ADHF without AKI ( $13.1+9.2$  mm vs.  $5.5+5.3$  mm resp.,  $p=0.04$ ). By the 10th day of intensive medical therapy diameter IVC correlated with the presence of AKI ( $r=0.73$ ;  $p=0.02$ ). Optimal cutoff points for predicting AKI were 8,7 mm for IVC collapse (sensitivity 73%, specificity 69%). Receiver operator curves demonstrated area under the curves of 0.77 for IVC collapse. The study showed no interaction between the count of B-lines and the risk of AKI.

**Conclusion:** Study showed that AKI affected 1% of patients with ADHF. Majority of patients (70%) had AKI stage 1. Development AKI when CRS type 1 may be associated increased venous congestion leading to renal dysfunction. Increasing CVP, IVC diameter and reducing IVC collapse leads to the AKI development of patients with ADHF. The study showed no interaction between the count of B-lines and the risk of AKI.

#### P960

##### Prognostic effect of dynamic renal function in chronic heart failure: is kidney more than a surrogate marker of cardiac function?

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**Background:** Chronic kidney disease (CKD) is a frequent comorbidity in heart failure (HF), associated with increased mortality. The prognostic value of dynamic kidney function is largely unknown.

**Purpose:** We evaluated the effect of longitudinal variation of renal function in all-cause mortality among ambulatory HF patients.

**Methods:** We retrospectively analyzed data from 560 HF patients with left ventricular systolic dysfunction followed for a median of 25.1 months at an outpatient HF

clinic. Demographics and comorbidities were abstracted from clinical records. Kidney function was assessed by estimated glomerular filtration rate (eGFR) and was categorized into three classes based on KDIGO guidelines. Extended Cox models were performed to study the association between dynamic changes in eGFR and death.

**Results:** Patients' median age was 70.0 years, 70% were men, 46% had ischemic etiology and the majority had moderate to severe LVEF. Half of the patients had CKD. Comorbidities were more prevalent in these patients. The eGFR declined about 12 mL/min/1.73m<sup>2</sup> over 5 years. After adjustment for baseline eGFR, time-varying eGFR had a marginally significant dose-dependent association with death [hazard ratio (HR)=1.26, 95% confidence interval (95%CI): 0.93-1.71; HR:1.37, 95%CI: 0.93-2.01, for eGFR between 30 to 60 and under 30 mL/min/1.73m<sup>2</sup>, respectively]. The prognostic value of dynamic eGFR was totally explained by baseline comorbidities, indicators of HF severity and drugs (adjusted HR=1.1, 95%CI: 0.79-1.54; HR=1.16, 95%CI: 0.75-1.79, for eGFR 30-60 and <30 mL/min/1.73m<sup>2</sup>, respectively).

**Conclusion:** Dynamic kidney function is not independently related to poor prognosis. Rather than directly affect survival, renal impairment is probably a surrogate marker of HF severity.

### P961

#### Correlation of laboratory biomarkers with echocardiographic parameters in patients with cardiorenal syndrome

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**Background:** Cardiorenal syndrome is associated with higher morbidity and mortality than in isolated chronic heart or kidney disease. NT-proBNP is a biomarker of heart failure that is currently used in all heart failure patients, though the number of studies concerning the use of biomarkers in diagnosing heart failure in chronic kidney disease patients is limited.

**Purpose:** We evaluated associations between biomarkers and echocardiographic parameters in patients with chronic heart failure and chronic kidney disease in hemodialysis program.

**Methods:** We included all patients with heart failure currently treated with chronic hemodialysis in our center. Echocardiography imaging was performed in all patients (LVEF, VTI, Sm, Em, E/A, E/Em) and blood samples were analysed for NT-proBNP, troponin T and iPTH. We evaluated the possible correlations between echocardiographic parameters and biomarkers with multiple regression analysis.

**Results:** We enrolled 22 patients with concurrent end-stage kidney disease and chronic heart failure (50% men, mean age 65.5 ± 11.7 years, mean NT-proBNP 1425 ± 1226 pg/ml, mean LVEF 57.1 ± 13.0%, 45% with HFrEF). Higher troponin T was the most important prognostic factor of lower LVEF (Pearson=-0.637, p=0.001; R<sup>2</sup>=0.406, F(1,20)=13.69, p=0.001), lower VTI (Pearson=-0.678, p=0.000; R<sup>2</sup>=0.459, F(1,20)=16.98, p=0.001), lower Sm (Pearson=-0.576, p=0.003; R<sup>2</sup>=0.331, F(1,20)=9.91, p=0.005) and higher E/A (Pearson=0.700, p=0.000; R<sup>2</sup>=0.490, F(1,20)=19.20, p=0.000). NTproBNP was a statistically significant prognostic factor of lower Em (Pearson=-0.489, p=0.010; R<sup>2</sup>=0.239, F(1,20)=6.30, p=0.021) and higher E/Em (Pearson=0.644, p=0.001; R<sup>2</sup>=0.415, F(1,20)=14.18, p=0.001). Indirect PTH was a statistically significant but not a prognostic factor of lower VTI and lower Sm. None of the tested laboratory or echocardiographic parameters were associated with heart failure hospitalizations in previous two years, but low VTI was a prognostic factor of longer hospital stay due to heart failure in same period (Pearson=-0.526, p=0.006; R<sup>2</sup>=0.277, F(1,20)=7.66, p=0.012).

**Conclusions:** Troponin T demonstrated better associations with echocardiographic parameters than NT-proBNP in patients with chronic heart failure and chronic kidney disease in hemodialysis program.

### P962

#### Acute cardiorenal syndrome in decompensated heart failure: impact on outcomes after hospital discharge in Brazil.

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**Background:** Acute cardiorenal syndrome (ACRS) is associated with poorer in hospital prognosis in patients with decompensated heart failure (DHF). There is no general agreement on its impact on outcomes after hospital discharge.

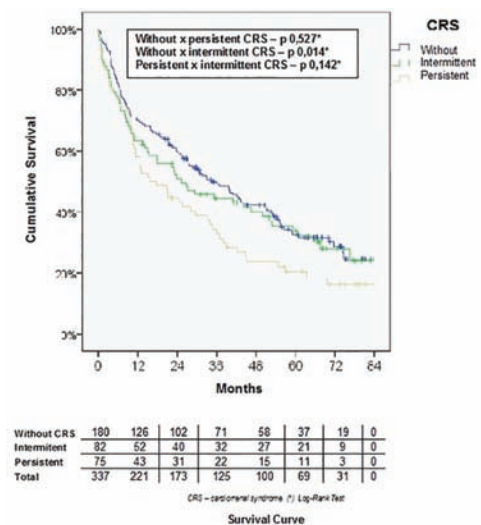
**Objectives:** To assess the association between ACRS and mortality after hospital discharge and readmission due to DHF and to compare the impact of ACRS in any moment during admission with the impact of persistent ACRS.

**Methods:** Patients admitted for DHF in a university hospital, between 01/01/06 and 12/31/11, were included in a cohort study. Deaths after discharge were identified through record linkage with the State of Rio de Janeiro mortality database. ACRS was defined as an absolute increase in serum creatinine ≥0.3mg/dL during hospitalization. ACRS was stratified in intermittent when creatinine levels

decreased until discharge and persistent when levels remained increased until discharge. The study excluded patients who had less than two creatinine measurements during hospitalization. Kaplan-Meier curves were built for overall survival and rehospitalization-free survival and were compared using the log-rank test. Cox multivariate analysis was used to assess the independent prognostic value of ACRS compared to outcomes after hospital discharge.

**Results:** Data from 395 patients showed that 53.3% were men, with mean age of 64 ± 14 years, 83.15% had systolic dysfunction and 37.6% ischemic etiology. ACRS incidence was 43.3%, being persistent in 22.3% of patients. The median follow-up time was 25,6 months (minimum of 12 and maximum of 83,9). Mortality after hospital discharge was 67.9% and hospital readmission rate for DHF was 41.4%. The accuracy of deaths search was 99.44%. Persistent ACRS was associated with mortality after discharge in uni- and multivariate analysis (OR1,52, 95% CI 1.12 to 2,08, p0,008). There was no association between ACRS and readmission regardless of the definition used.

**Conclusion:** Persistent ACRS is associated with higher mortality after hospital discharge. ACRS is no associated with readmissions due to DHF.



Survival after discharge and CRS

### P963

#### The heart failure and kidney injury in elderly patients with IE

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**Purpose:** To study the features of heart failure and kidney injury in elderly patients with infective endocarditis (IE).

**Material and methods:** 80 patients (50 men) with IE (Duke 2015) were included, of which the elderly (≥60 years) were 54 (43.2%) patients (group 1), young adults (group 2) — 26 (20.8%). The anamnesis, echocardiogram, renal function (GFR, proteinuria, microscopic hematuria, serum Cystatin C, urinary KIM-1), heart failure (NYHA) rates and NT-proBNP levels, acute kidney injury (AKI, KDIGO 2012) and mortality rates were evaluated. Early AKI was defined as AKI at the moment of admission to the hospital, AKI developed during hospitalization was considered as late AKI. Results. The median age in group 1 was 73 [66-79], in group 2 — 42 [32-52] years. Concomitant diseases were more common in group 1 than in group 2: hypertension [50 (92.6%) vs. 11 (42.3%), p<0.05], atrial fibrillation [25 (46.3%) vs. 3 (11.5%), p<0,05], coronary artery disease [22 (40.7%) vs. 3 (11.5%), p<0.05], cerebral infarction [20 (37.0%) vs. 3 (11.5%), p<0.05] and diabetes mellitus [13 (24.1%) vs. 4 (15.4%), p<0.05]. Groups did not differ in incidence of secondary forms, subacute IE. Median left ventricular EF in groups were comparable [53.8 ± 8.7 (28-72) vs. 58.3 ± 7.1 (39-72), p>0.05]. Heart failure occurred more frequent in group 1 than in group 2 [45 (83.3%) vs. 16 (61.5%), p<0.05], that was consistent with higher values of NT-proBNP — 3103 [1091-4890] pg/ml vs. 2030 [301-3499] pg/ml, p<0.05. The median GFR in group 1 was 47.9 [31-58] ml/min, in group 2 — 77.0 [45-91] ml/min (p<0.05). AKI in group 1 were more common than in the group 2 [29 (53.7%) vs. 12 (46.2%), p<0,05] and was presented by early AKI [6 (11.1%) vs. 3 (11.5%), p>0.05] and late AKI [23 (42.6%) vs. 9 (34.6%), p<0.05]. Laboratory changes in urine also prevailed in group 1 [45 (83.3%) vs. 17 (65.4%), p<0.05] and was presented by proteinuria [39 (72.2%) vs. 17 (65.4%), p<0.05] and hematuria

[28 (51.9%) vs. 9 (34.6%),  $p < 0.05$ ]. Elderly patients had significantly higher levels of serum Cystatin C – 3.1 [2.3-3.9] vs. 2.0 [1.8-2.4]  $\mu\text{g/ml}$  ( $p < 0.05$ ), KIM-1 in urine – 2.6 [2.5-2.8] vs. 1.6 [1.4-1.8]  $\text{ng/ml}$  ( $p < 0.05$ ). Mortality in the group of elderly was 2.5 times higher than in the young adults group [21 (38.9%) to 4 (15.4%),  $p < 0.05$ ]. Conclusion. IE in elderly patients is characterized by frequent association with comorbidities, heart failure (mainly III-IV FC) and AKI, by increased levels of NT-proBNP, Cystatin C, KIM-1, and by higher mortality rate.

#### P964

##### The relationship between renal resistance index values and worsening of renal function

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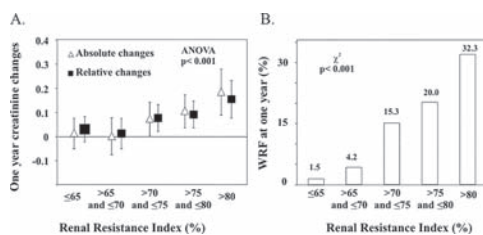
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**Background:** Arterial Renal Resistance Index (RRI) is a Doppler measure, which reflects abnormalities in renal blood flow, which can be determined by structural and functional abnormalities of kidneys. The aim of this study was to verify the association between RRI values and worsening renal function (WRF) in a group of chronic heart failure (CHF) outpatients.

**Methods:** We enrolled 266 patients (Age  $64 \pm 14$  years, 79% males, NYHA class  $2.2 \pm 0.7$ , left ventricular ejection fraction, LVEF,  $33 \pm 9\%$ ) in stable clinical conditions and in conventional therapy. All patients underwent a clinical evaluation, a routine chemistry and an echocardiogram. Peak systolic velocity and end diastolic velocity of a segmental renal artery were obtained by pulsed Doppler flow and RRI was calculated. WRF was defined as an increase in serum creatinine of  $\geq 0.3$   $\text{mg/dl}$  associated with a change  $> 25\%$  or a decrease in GFR  $> 20\%$  at 1 year follow-up.

Results. During follow-up, thirty-four (13%) patients showed WRF. RRI was associated with WRF at univariate analysis (OR: 1.13; 95%CI: 1.07-1.20). In a multivariate forward stepwise regression model including the other univariate predictors, i.e. age, high diuretic dose, GFR-EPI, log NT-proBNP, CVP  $> 5$  mmHg and acute decompensated heart failure within 1 year, only RRI (OR: 1.09; 95%CI: 1.03-1.16;  $p: 0.005$ ) and CVP  $> 5$  mm Hg (OR: 2.62; 95%CI: 1.04-6.63;  $p: 0.041$ ) remained significantly associated with WRF. As shown in Figure 1A, a progressive increase of relative and absolute creatinine changes was observed in subgroups of patients with greater RRI values as well as an increase in the risk of WRF occurrence (Figure 1B). At ROC curve analysis, the RRI showed an AUC of 0.74 (95% CI 0.67–0.82) for WRF occurrence. The best cut-off of RRI was 70 (sensitivity 91%; specificity 50%).

**Conclusions:** Quantification of arterial renal perfusion provides a new parameter whose greater values are independently associated with a progressive increase of the risk of WRF in CHF outpatients, thus helping to better define the risk of cardiorenal syndrome progression.



Figure

#### P965

##### Serum cystatin C is associated with left ventricular hypertrophy and impaired left ventricular relaxation in patients with stage 2 or 3 chronic kidney disease

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**Background:** In this cross-sectional study, we aimed to determine the associations between serum cystatin C levels and structural and functional cardiac changes in patients with stage 2 or 3 chronic kidney disease (CKD).

**Methods and Results:** We enrolled 429 consecutive patients (aged 24–97 years) with CKD stage 2 or 3 and left ventricular (LV) ejection fraction (LVEF)  $> 40\%$ . Echocardiographic parameters, including LV mass index (LVMI), early diastolic mitral annulus velocity ( $e'$  velocity), left atrial volume index (LAVI), and N-terminal of the prohormone brain natriuretic peptide (NT-proBNP) were measured. Patients were categorized into quartiles according to serum cystatin C levels. Cystatin C was associated with LAVI ( $p = 0.0055$ ), LVEF ( $p = 0.0432$ ), LVMI ( $p = 0.0409$ ),  $e'$  ( $p = 0.0051$ ),  $E/e'$  ( $p = 0.0027$ ), and log-transformed NT-proBNP ( $p < 0.0001$ ) according to multivariate linear Regression analysis, after adjustment for confounding factors including creatinine-based estimated glomerular filtration rate (eGFR<sub>creat</sub>) and urinary albumin to creatinine ratio. Incidence of eccentric and concentric hypertrophy increased

with increasing cystatin C (Q1, 38%; Q2 49%; Q3, 51%; Q4, 66%,  $p = 0.0008$ ), mainly because of increasing concentric hypertrophy (Q1, 30%; Q2, 39%; Q3, 39%; Q4, 51%,  $p = 0.0187$ ).

**Conclusion:** A high serum cystatin C is strongly associated with structural cardiac abnormalities such as LVH and left atrial enlargement, impaired LV relaxation, and an increased NT-proBNP, independently of eGFR<sub>creat</sub> in patients with stage 2 or 3 CKD.

#### P966

##### Primary prevention of anthracycline-induced subclinical cardiotoxicity in breast cancer

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**Introduction:** There is no effective method for prevention of anthracycline-induced cardiotoxicity.

**Purpose:** To investigate the preventive effect of concomitant administration of candesartan or carvedilol in the anthracycline-induced subclinical cardiotoxicity.

**Methods:** 110 patients from prospective registry (Pros) for prediction and prevention of chemotherapy induced cardiotoxicity in breast cancer of our institution were selected. All patients were administered candesartan or carvedilol concomitantly with doxorubicin contained chemotherapy. 85 patients from retrospective registry (Retros) of breast cancer of our institution were selected for control. Both group evaluated cardiac function by transthoracic echocardiography (TTE) before chemotherapy for baseline and followed up at least twice during chemotherapeutic period. The incidence of subclinical cardiotoxicity (SC) was evaluated.

**Results:** Intervals between TTE evaluation was  $12 \pm 1$  weeks in Pros, but intervals between TTE in Retros was rather irregular. Left ventricular ejection fraction (LVEF) of Pros showed no change during follow up, however, LVEF of Retros showed gradual decrement (Table 1). Incidence of SC was higher in Retros (Table 2). Number of SC with mild LV dysfunction (LVEF  $< 55\%$ ) was higher in Retros.

**Conclusion:** Concomitant administration of candesartan or carvedilol with chemotherapy can reduce incidence of SC and prevent aggravation of LV dysfunction of SC developed patients.

#### P967

##### Assessment of atrial and ventricular electromechanical delay, as a cardiotoxicity parameter in patients with trastuzumab chemotherapy for breast cancer patient.

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**Backgrounds:** The atrial electromechanical delays (AEMD) and ventricular electromechanical delays (VEMD) on echocardiography was noninvasive indicator of atrial and ventricular conduction delay. We hypothesized that cardiotoxicity of Trastuzumab may affect to cardiac conduction disorder and it maybe occur before significant decrease in LVEF and evaluated AEMDs and VEMDs before and after trastuzumab chemotherapy in breast cancer patients.

**Methods:** The breast cancer patients who underwent chemotherapy with Trastuzumab from 2011 to 2015 in a national university hospital were selected. Among this patients, Total 57 patients have 6  $\pm$  2 month follow up echocardiography after chemotherapy, and we analyzed this echocardiographic parameters compared with baseline echocardiography. Left and Right VEMDs was defined as the time intervals from initiation of QRS wave of electrocardiography (ECG) to the initiation (LVEMDi, RVEMDi) and peaks (LVEMDp, RVEMDp) of left and right ventricular outflow tract time-velocity integrals on pulse wave (PW) doppler echocardiography. AEMD was defined as the time interval between the onset of ECG P wave and the initial (AEMDi) or peak a' wave (AEMDp) on the medial mitral annular tissue Doppler velocity curve (TDI) or PW Doppler at the mitral valve inflow level. We also measured GLS (global longitudinal strain), known as parameter of early predictor of cardiotoxicity in patients receiving cancer therapy. We compared these echocardiographic parameter between before and after 6 months trastuzumab chemotherapy with other echocardiographic parameters. Paired t-tests were used to compare all parameter at 6 month with baseline.

**Results:** There were significant elongation of time in RVEMDi, RVEMDp, LVEMDi, LVEMDp, AEMDi at TDI, and AEMDp at TDI between baseline and after 6 month follow up echocardiographic data (RVEMDi,  $90.31 \pm 20.11$  vs.  $97.09 \pm 19.34$ ,  $p$  value = 0.04, RVEMDp,  $220.81 \pm 35.57$  vs.  $237.40 \pm 34.91$ ,  $p$  value  $< 0.001$ ,  $84.77 \pm 14.83$  vs.  $95.91 \pm 18.31$ ,  $p$  value = 0.009, LVEMDp,  $179.18 \pm 26.60$  vs.  $199.82 \pm 26.01$ ,  $p$  value = 0.004, AEMDi at TDI,  $57.88 \pm 15.71$  vs.  $63.50 \pm 13.73$ ,  $p$  value = 0.001, AEMDp at TDI,  $114.02 \pm 19.84$  vs.  $119.84 \pm 18.94$ ,  $p = 0.001$ ). Particularly, LVEMDi and LVEMDp showed an increase of 10% or more. GLS average was also changed after trastuzumab chemotherapy, but mean difference was very small (GLS average,  $-16.15 \pm 3.69$  vs.  $-15.10 \pm 3.64$ ,  $p$  value = 0.044) LVEF was significant statistical difference between baseline and 6 month follow up echocardiographic data, but both data was in normal value, this results was no clinical significance. ( $62.55 \pm 2.98$  vs.  $60.16 \pm 3.64$ ,  $p < 0.001$ )



**Conclusion:** AEMDs and VEMDs was a good parameter to early detect of Trastuzumab cardiac toxicity in breast cancer patients before LV systolic dysfunction occurred. Especially, LVEMDI and LVEMDp showed great difference at 6 months follow up after initiation of trastuzumab chemotherapy.

**Purpose:** Even though chemotherapy-induced cardiotoxicity is one of the commonest side-effects of anthracyclines, it is unclear whether hospital-based clinicians routinely ensure thorough diagnostic, management and cardiac specialist referral of oncology patients.

61194 Table 1. Changes of LVEF during follow up.

	Baseline TTE	1 <sup>st</sup> F/U TTE	2 <sup>nd</sup> F/U TTE	
LVEF Pros (n = 110)	65.3 ± 8.3	64.9 ± 5.6	64.3 ± 5.4	No significant
LVEF Retros (n = 85)	63.9 ± 4.6	62.3 ± 4.7	60.1 ± 5.7	Significant
	P = 0.180187	P = 0.000546	P < 0.00001	
Table 2. Development of subclinical cardiotoxicity in both groups				
	Pros (n = 110)	Retros (n = 85)		
Subclinical cardiomyopathy	13 (11.8% 13/110)	20 (23.5% 20/85)		
LVEF < 55% in any F/U	4 (3.6%, 4/110)	11 (12.9%, 11/85)		
Reduction of LVEF more than 10% in 1 <sup>st</sup> F/U	6 (5.4%, 6/110)	5 (5.8%, 5/85)		
	Recovered at 2 <sup>nd</sup> F/U from SC at 1 <sup>st</sup> F/U	3 (50%, 3/6)	2 (40%, 2/5)	
	Aggravation at 2 <sup>nd</sup> F/U from SC at 1 <sup>st</sup> F/U	3 (50%, 3/6)	3 (60%, 3/5)	
Reduction of LVEF more than 10% in 2 <sup>nd</sup> F/U	9 (8.2%, 9/110)	16 (18.8%, 16/85)		

## P968

### Relationship between left ventricular diastolic stiffness, trastuzumab, and cardiac function and toxicity

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**Purpose:** Trastuzumab (T) 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 (DS) in patients treated with T.

**Methods:** We studied 157 consecutive breast cancer patients (all females; mean age, 57.1 ± 10.8 years) who received T for more than 6 months. These patients were categorized into the following two groups: DWS ≤ 0.63 (group A; mean age, 56.8 ± 10.8 years; n = 79) and DWS > 0.63 (group B; mean age 57.4 ± 11.3 years; n = 78). Echocardiography was performed before and after administration of T, 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). Data were then compared between the two groups.

**Results:** Symptomatic heart failure was observed in five cases. Overall, no significant changes were observed in the indices of cardiac function, including IVSTd, PWTd, E/A, e', RWT, and IVC. After treatment with T, significant increases were observed in LAD, LVDd/s, LVED(S)V, E/e', TI, LVM, LVMI, PASP, LVEDP, and BPs (p < 0.001) and significant decreases were observed in IVSTs (p < 0.05), PWTs, LVEF, and DWS (p < 0.001). In both groups, no significant changes were observed in IVSTd, IVSTs, E/A, e', and IVC, and significant increases were observed in LVDd, LVDs, LVEDV, LVEDVI, LVESV, LVM, LVMI, and BPs. Further, significant decreases were observed in LVEF and DWS. With regard to indices of cardiac function, including LAD, E/e', T-I, PASP, and LVEDP, significant increases were observed only in group A. Furthermore, a significant decrease was observed in RWT only in group A.

**Conclusion:** Administration of T resulted in an increase in DS with LV diastolic dysfunction, a tendency towards eccentric hypertrophy with an increase in LVM, and heart failure with reduced ejection fraction. The tendency for LV diastolic dysfunction and eccentric hypertrophy was more common in patients with lower DWS than in those with higher DWS before treatment with T.

## P969

### Forgotten but not forgiven: current practices in surveillance and prevention of anthracycline-induced cardiomyopathy

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**Methods:** retrospective review of cardiac function investigations, management and follow-up practices of patients with diffuse large B-cell lymphoma (DLBCL) undergoing anthracycline-based chemotherapy between 2010 and 2015.

**Results:** Sixty-seven patients with DLBCL received anthracycline-based chemotherapy (34 males, 33 females; average age 59.7 ± 15.3 years). Forty-seven patients (70.1%) underwent echocardiography prior to chemotherapy, only 19 patients (28.8%) underwent subsequent evaluation of cardiac function after receiving anthracyclines. Eleven patients (16.4%) did not receive any form of imaging surveillance either prior or after treatment. Twelve patients (18%) were referred to a cardiology specialist either during or after treatment. Pre-existing cardiovascular comorbidities were significantly more prevalent in patients receiving cardiac review such as hypertension (66.7 vs 25.5%, p < 0.05), diabetes (33.3 vs 9.1%, p < 0.05), dyslipidaemia (41.7 vs 12.7%, p < 0.05) and coronary artery disease (33.3 vs 5.5%, p < 0.05). Current or prior smoking history did not differ (41.6 vs 41.8%, p > 0.05). Importantly, cardiology specialist review led to a significantly higher proportion of patients undergoing follow-up assessments by echocardiography (91.7 vs 27.8%, p < 0.0001), receiving heart failure therapies angiotensin-converting enzyme inhibitors/angiotensin receptor antagonists (75.0 vs 9.4%, p < 0.0001) and beta-blockers (58.3 vs 9.4%, p < 0.005).

**Conclusion:** There is still a significant under-referral in the assessment, management and follow-up of cardiac function in patients undergoing well recognized cardiotoxic chemotherapies. These results suggest that there is substantial opportunity for early detection and management of chemotherapy-induced cardiomyopathy by promoting a stronger collaboration between oncologists and cardiologists. This approach has had a positive and significant impact on the implementation of post-chemotherapy cardiac surveillance practices and instigation of evidence-based heart failure treatments, known to prevent or reverse anthracycline-induced cardiomyopathy.

## P970

### The outcome of hypertensive patients with diastolic dysfunction under doxorubicin therapy assessed by echocardiography

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**Premises and objectives:** Potential life-threatening cardiac toxicity limits the dose of doxorubicin. Echocardiography is the standard noninvasive method for monitoring the patients on chemotherapy. The purpose of this study was to assess the outcome in hypertensive oncological patients with diastolic dysfunction and to identify potential risk factors associated with early induced doxorubicin cardiotoxicity.

**Material and method:** The study group consisted of 50 consecutive hypertensive patients (P) with oncological pathology on doxorubicin chemotherapy and 25 control hypertensive P. A Siemens Acuson X300 unit was used for echocardiographic measurements. The data recorded included: demographics, clinical and echocardiographic measurements, (Table 1). In all 50 P data collection and follow-up were

done in outpatient and cardiology department prior to treatment, 6 w after initiation of treatment and at 6 m. Statistical analysis was made using paired t test for patient data and unpaired t test for comparison between the control and study group.  
**Results:** There were no significant differences between control and study P regarding demographic parameters. The study P had a poorer hypertension control, LV hypertrophy and diastolic dysfunction and at 6 weeks and 6 months showed

echocardiographic evidence of SAVS. One-year mortality was 6% for OP- and 19% for NON-OP. Any cause hospitalization (at least an overnight stay) this year was in days and incidence rate per million patient years (IR): 2364 (46) and 362 (142) for OP and NON-OP, respectively. Number (IR) of any cause hospitalization (3 times or more) was for OP 39 (0,8) and 15 (5,8) for NON-OP (p=0,08). Table displays paired analyses for additional outcomes.

Table 1

Parameters	Control (n = 25)	Baseline (n = 50)	6 weeks (n = 50)	6 months (n = 50)	P value
Age (years)	55.0 ± 7.9	56.9 ± 11.9	56.9 ± 11.9	56.9 ± 11.9	0.396
Males (n)	13 (52%)	23 (46%)	23 (46%)	23 (46%)	0.478
SBP (mmHg)	138.9 ± 12.9	147.0 ± 24.7	149.0 ± 12.6 (0.5)	151.0 ± 11.2(0.2)	0.003*
DBP (mmHg)	78.6 ± 10.3	89.4 ± 12.3	91.2 ± 9.7 (0.3)	92.8 ± 11.2 (0.1)	0.0004*
EF (%)	66.8 ± 12.9	58.6 ± 14.5	57.3 ± 12.5 (0.7)	54.7 ± 13.2 (0.1)	0.001*
E/A	1.3 ± 0.4	0.98 ± 1.21	0.97 ± 1.11 (0.9)	0.95 ± 2.3 (0.9)	0.001*
IVRT (ms)	79.9 ± 17.4	100.8 ± 27.9	101.2 ± 22.4 (0.8)	102.0 ± 25.9 (0.7)	0.001*
LVMI (g/m <sup>2</sup> )	64.4 ± 19.0	86.4 ± 36.1	87.2 ± 28.2 (0.9)	88.3 ± 37.8 (0.8)	0.006*

\* Statistically Significant; SBP - Systolic blood pressure; DBP - diastolic blood pressure; EF - ejection fraction; IVRT - izovolumic relaxation time; LVMI - left ventricular mass index. Data are expressed as mean followed by " ± " mean standard deviation (SD).

an decrease in EF and deterioration of diastolic function, without reaching statistical significance (table 1).

**Conclusions:** The hypertensive P treated with doxorubicine have a good cardiovascular prognosis at 6 months. There is, however, a tendency of deterioration in diastolic and probably in systolic LV function. Therefore a more intensive additional echocardiographic follow-up at, 3 months would be more appropriate.

**Conclusion:** The present study demonstrates that aortic valve replacement for severe aortic stenosis is associated with improved functional outcome, while being declined AVR is associated with high mortality, more hospitalizations, unaltered functional status and a tendency to loss of independence.

VALVULAR HEART DISEASE (DIAGNOSIS, MANAGEMENT AND INTERVENTIONAL THERAPIES)

P971

Comparing one-year outcomes beyond mortality in operated versus non-operated patients with severe aortic valve stenosis.

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**Introduction:** Aortic valve replacement (AVR) improves survival and quality of life in patients with severe aortic valve stenosis (SAVS). Few clinical studies compare outcomes beyond mortality-rates in operated versus non-operated patients.

**Purpose:** To compare functional- cognitive- and morbidity-outcomes in the year following AVR or not in patients with SAVS. Method Of 480 patients with SAVS evaluated for AVR, 351 had surgical- and 38 transcatheter-AVR (OP), while 91 were declined operation (NON-OP). At inclusion and one year follow-up, we obtained data on Six-Minute Walk test (6MWT), New York Heart Association-scale (NYHA) and Canadian Cardiovascular Society-scale (CCS). Cognitive function was assessed by the mini-mental state examination (MMSE). Questionnaires and medical records provided information on home situation, level of independence and hospitalizations.

**Results:** Mean (SD) age was 74 (10) and 81 (9) years, and gender (% women) was 41 and 52 for OP and NON-OP, respectively. At inclusion, all patients had

P972

Comparing one-year patient reported outcomes (PROs) in operated versus non-operated patients with severe aortic valve stenosis (SAVS)

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**Introduction:** Advancements in surgical techniques make high risk and progressively older patients with SAVS eligible for aortic valve replacement (AVR). Current guidelines emphasize the importance of improving PROs as an outcome after AVR.

**Purpose:** To compare PROs at inclusion and one year for operated versus non-operated patients with SAVS.

**Method:** Of 480 patients with SAVS evaluated for AVR, 351 had surgical- and 38 transcatheter-AVR (OP), while 91 were declined operation (NON-OP). We collected data on SF-36v2; Physical-(PCS) and Mental-(MCS) Component Summary, EuroQol-5 Dimensions (EQ-5D), visual analogue scale (EQ-VAS), and Hospital Anxiety and Depression Scale (HADS).

**Results:** Mean (SD) age was 74 (10) and 81 (9) years, and 41 and 52 % were women for OP and NON-OP patients, respectively. Physical- and general health increased for OP patients, while anxiety decreased. In the NON-OP group there was a tendency towards decreased physical health. Table displays paired analyses of selected PROs.

**Conclusion:** Aortic valve replacement improves PROs assessed as perception of overall health and physical health, and reduces anxiety in patients with SAVS. Patients with SAVS declined for operation tend to experience a decrease in physical health over a one-year period. Our results advocate AVR in patients with SAVS.

Additional	outcomes					
	Operated (OP), n = 389			Non-operated (NON-OP), n = 91		
	Inclusion	Follow-up	p-value	Inclusion	Follow-up	p-value
Six-Minute Walk test, meter	465	442	< 0.01	412	369	0.05
NYHA functional class						
I/II/III or IV (%)	5/49/46	67/24/9	< 0.01	30/42/28	33/33/33	0.08
CCS functional class						
0, I, II, III or I (%)	54/13/27/6	95/3/1/1	0.01	80/6/8/6	86/8/6/0	0.08
No help or home nurse, n(%)	298(98)	276(96)	0.15	44(100)	41(93)	0.08
MMSE, mean total score	28.5	28.1	0.03	27.4	26.9	0.11

**P973**  
**new insights into cardiac functional status after MitraClip: the role of cardiopulmonary exercise test**

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**Background:** Whereas haemodynamic and echocardiographic studies suggest clinical benefits after MitraClip system in advanced heart failure (HF) patients, there are limited data on changes in functional capacity evaluated by cardiopulmonary exercise test (CPET).

**Purpose:** to assess the functional status in HF patients undergoing MitraClip using CPET and to evaluate whether preoperative echocardiographic data could predict the effects of this therapy.

**Methods:** Out of 46 patients undergoing MitraClip at our institute, 23 performed a maximal symptom-limited bicycle CPET with ramp protocol, transthoracic echocardiography (TTE) and clinical assessment before and after 6 months from the procedure. All patients (mean age 61,9 ± 8 years, 72.7% males) were affected with severe left ventricle (LV) systolic dysfunction (mean LV ejection fraction, LVEF 24 ± 7.9%) in optimal HF medical therapy, 7 were in waiting list for heart transplantation, the others were judged not eligible from HF team because of multi-organ failure or relative contraindications. 75% of patients were implanted with implantable cardioverter defibrillators (ICDs), 57% of whom received CRT-D. The main mechanism of MR was functional (FMR) 87%; ischaemic 45.2%; no-ischaemic 41.9%. Baseline functional status was poor: 85% in NYHA Class III/IV, mean VO<sub>2</sub>max 10.58 ± 3ml/Kg per min (43.6 ± 9.4% of predicted value, p.v.), mean slope VE/VCO<sub>2</sub>: 37.24 ± 8.7, mean work rate 63 ± 25 Watt (47.8 ± 14.1 % of p.v.). Results MitraClip significantly reduced MR from 3+/4+ to 1+/2+ in 94% of cases (p < 0,0001), increased LVEF from 24 ± 7.9% to 28.5 ± 7,0% (p < 0,001), decreased pulmonary systolic pressure (Δ PAPs ~10mmHg; p value < 0.005), with a substantial clinical benefit (97% of patients in NYHA Class III/IV, improved to I/II Class; p < 0,0001) at 6 month follow up. On the contrary, among CPET parameters only the exercise capacity improved after MitraClip (Δ Watt % ~7.4; p = 0.02). Among pre-procedural TTE parameters, evaluated at multiple linear regression analysis, only tricuspid annular plane excursion (TAPSE), resulted significantly related to the improvement of the maximum workload achieved at CPET (p = 0.022).

**Conclusions:** MitraClip resulted in a little increase of exercise capacity without any functional or ventilatory efficiency improvement in our patients at 6 months follow-up. TAPSE resulted the only TTE parameter able to predict exercise response at CPET after MitraClip. Further analysis of this cohort are needed to reveal the correlations among CPET parameters and haemodynamic/echocardiographic findings able to explain the clinical benefits of this therapy beyond NYHA Class.

**Introduction:** Tricuspid regurgitation (TR) is an acquired valvular abnormality that is most frequently encountered during the evaluation of left heart valve disease. Uncorrected significant TR during mitral valve surgery can result in inferior early and late outcomes due to progression of TR and underlying right heart failure. The purpose of this study was to report the clinical characteristics of patients undergoing tricuspid annuloplasty.

**Methods:** It was a retrospective study that included 91 patients who underwent Tricuspid annuloplasty in a Tunisian tertiary cardiovascular center. Clinical and echocardiographic data of patients who underwent Tricuspid annuloplasty were recorded.

**Results:** Ninety-one patients underwent tricuspid annuloplasty for TR as part of their cardiac surgical procedure. De-Vega annuloplasty was performed in 46 patients and ring annuloplasty in 45 patients. Tricuspid annuloplasty was associated to mitral replacement in 59 patients (64.8%), to aortic replacement in 3 patients (3.3%) et to a mitro-aortic replacement in 26 patients (28.6%). The mean age of the study population was 43.58 ± 12.56 years. The female gender was predominant (72.8%). Six patients (6.5 %) had a history of percutaneous mitral balloon valvuloplasty and 17 patients (18.6 %) had previous left-sided valvular surgery. The comparison of preoperative clinical characteristics showed no significant difference between the 2 groups of patients (Ring annuloplasty versus De-Vega annuloplasty).

**Conclusion:** TR is an important condition which is associated with adverse clinical outcomes. Based on numerous trials and registries, concomitant surgical repair of TR at the time of mitral valve surgery should be considered the current. It is important to select patients for tricuspid annuloplasty during operative management of left-sided valvular heart disease to improve outcomes.

**P975**

**Long-term follow-up of mitral stenosis after percutaneous mitral balloon valvuloplasty treatment. Inoue versus balt single balloon technique**

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Percutaneous mitral balloon valvuloplasty (PMBV) has emerged as an alternative to surgical treatment for mitral stenosis. Objective: This study aimed to demonstrate that mitral balloon valvuloplasty (MBV) with the Balt single balloon (BSB) has similar outcome and long-term follow-up (FU) than MBV performed with the Inoue worldwide accepted technique.

**Methods:** From 1987 to 2013 a total of 526 procedures were performed, being 312 with a FU, 56 (17,9%) with Inoue balloon (IB) and 256 (82,1%) with BSB.

	Inclusion	Follow-up	p-value	Inclusion	Follow-up	p-value
SF-36v2, mean						
PCS	40.1	45.8	< 0.01	37.0	34.5	0.06
MCS	50.9	51.1	0.8	49.4	46.2	0.2
EQ-5D, proportion without limitation, %						
Mobility	113(39)	97(34)	0.2	26(57)	27(59)	0.8
Self-care	18(6)	26(9)	0.2	9(20)	11(24)	0.6
Usual activities	139(47)	115(39)	0.05	23(50)	30(65)	0.1
Pain / discomfort	188(65)	152(53)	< 0.01	28(61)	29(63)	0.2
Anxiety / depression	111(39)	82(29)	0.01	18(39)	18(39)	0.1
EQ-VAS, mean	60.3	71.9	< 0.01	62.2	56.8	0.2
HADs, mean						
Anxiety	5.3	4.6	< 0.01	5.6	5.8	0.7
Depression	5.4	5.2	0.2	6.2	6.2	0.8

**P974**

**Clinical characteristics of patients undergoing tricuspid annuloplasty in a tunisian tertiary cardiovascular center**

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The mean FU in IB group was 33 ± 27 (2 to 118) and 55 ± 33 (1 to 198) months, p < 0.0001. Univariate analysis (UA) and multivariate Cox analysis (MVA) were utilized to determine independent predict variables of survival and event free survival (EFS) in both techniques groups. The major events (ME) were death, cardiac surgery and new MBV.

**Results:** In IB and BSB groups there were, respectively: female 42 (75.0%) and 222 (86.7%); mean age 37.3 ± 10.0 (19 to 63) and 38.0 ± 12.6 (13 to 83) years, p = 0.7138; sinus rhythm 51 (91.1%) and 215 (84.0%), p = 0.1754; echo score (ES) 7.6 ± 1.3 (5 to 10) and 7.2 ± 1.5 (4 to 14) points, p = 0.0528; echo mitral valve area (MVA)



pre-MBV  $0.96 \pm 0.18$  and  $0.93 \pm 0.21$  cm<sup>2</sup>,  $p = 0.2265$ ; post-MBV mean MVA (Gorlin) were  $2.00 \pm 0.52$  and  $2.02 \pm 0.37$  cm<sup>2</sup>,  $p = 0.9554$ ; MBV dilatation area  $6.09 \pm 0.27$  and  $7.02 \pm 0.30$ ,  $p < 0.0001$ . At the end of the FU, there were in IB and BSB groups, respectively: echo MVA  $1.71 \pm 0.41$  and  $1.54 \pm 0.51$  cm<sup>2</sup>,  $p = 0.0552$ ; new severe mitral regurgitation in 5 (8.9%) and 17 (6.6%) patients,  $p = 0.5633$ ; new MBV in 1 (1.8%) and 13 (5.1%),  $p = 0.4779$ ; mitral valve surgery in 3 (5.4%) and 27 (10.4%),  $p = 0.3456$ ; deaths 2 (3.6%) and 11 (4.3%),  $p = 1.000$ ; cardiac deaths 1 (1.8%) and 9 (3.5%),  $p = 1.000$ ; ME 5 (8.9%) and 46 (18.0%),  $p = 0.1449$ . In UA and MCA the BSB or IB technique do not predict survival or EFS. The independent risk factors to survival (MCA with 2 models with 5 and 6 variables) were: age  $< 50$  years ( $p = 0.016$ , HR = 0.233, 95% IC 0.071 - 0.764), ES  $\leq 8$  ( $p < 0.001$ , HR = 0.105, 95% IC 0.34 - 0.327), MBV dilatation area ( $p < 0.001$ , HR 16.838, 95% IC 3.353 - 84.580) and no mitral valve surgery in the FU ( $p = 0.001$ , HR 0.152, 95% IC 0.050 - 0.459). Independent risk factors to EFS: no prior commissurotomy ( $p = 0.012$ , HR = 0.390, 95% IC 0.187 - 0.813) and post-MBV MVA  $\geq 1.50$  cm<sup>2</sup> ( $p = 0.001$ , HR = 7.969, 95% IC 3.413-18.608).

**Conclusion:** MBV with BSB and IB were equally efficient, there were similar survival and EFS in the FU. Independent predictors of survival were: age  $< 50$  years, ES  $\leq 8$  points, MBV dilatation area  $> 7$  mm<sup>2</sup> and no mitral valve surgery in the FU. Independent risk factors of EFS were no prior commissurotomy and post-MBV MVA  $\geq 1.50$  cm<sup>2</sup>

### P976

#### Magnesium orotate may be a new promising therapy of heart failure in operated valvular heart disease

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**Background:** Successful surgery for valvular heart disease prolongs life and generally improves symptoms and cardiac function. Nevertheless, myocardial dysfunction and health-related quality of life (HRQoL) impairment may persist and worsen post-operatively.

**Purpose:** We hypothesized that long-term nonsteroidal anabolic magnesium orotate might help improve symptoms and HRQoL after valve replacement.

**Methods:** 100 patients [aged  $56.2 \pm 3.5$  years; 62% males; 68% NYHA class III, 32% NYHA class II; 35% concomitant SCAD, 18% CABG; median (IQR) 6-min walk distance (6-MWD) 348 (152-442) m; mean (SE) left ventricular ejection fraction (LVEF) 55.6 (2.4)%] 2-4 weeks after conventional aortic ( $n = 58$ ) or mitral ( $n = 42$ ) valve replacement by mechanical prostheses (38% due to degenerative, 32% rheumatic, 13% myxomatous, 11% congenital valve diseases and 6% infective endocarditis) were randomized 1:1 to receive either optimal standard therapy or magnesium orotate 500 mg t.i.d. added to conventional treatment. Efficacy endpoints included changes from preoperative baseline in 6-MWD, NYHA functional class, echo-parameters, heart failure hospitalizations and all-cause mortality. HRQoL was assessed by the Short Form (SF-36 v.1) Health Survey.

**Results:** There were no significant differences between magnesium orotate and control groups at baseline. Patients reported poor postoperative HRQoL. At month 12, patients receiving magnesium orotate ( $n = 50$ ) had a mean increase in 6-MWD of 191 m ( $p < 0.0001$ ); control patients ( $n = 50$ ) had a mean 6-MWD increase of 135 m ( $p < 0.001$ ), with a control-adjusted difference of +56 m ( $p = 0.022$ ). NYHA status improved by two classes in 48% of magnesium orotate versus 32% of controls ( $p = 0.028$ ), by one class in 52% versus 68% ( $p = 0.028$ ). Magnesium orotate delayed the time to clinical worsening ( $p = 0.0063$ ) and reduced the heart failure admissions ( $p = 0.0042$ ). Improvements were noted in control-adjusted changes in supraventricular ( $p = 0.0027$ ) and ventricular arrhythmias ( $p = 0.035$ ) and in postoperative heart remodeling, e.g. in mean LVEF (+4.8%;  $p = 0.0018$ ), left ventricular end-diastolic diameter (-6.3 mm;  $p = 0.0012$ ), and end-systolic diameter (-3.9 mm;  $p = 0.0038$ ). Combination therapy with magnesium orotate was well tolerated. In both groups, SF-36 scores substantially rose after follow-up. Magnesium orotate patients had significant higher improvements in HRQoL over time compared to controls. One patient died in the control group ( $p = 0.63$ ).

**Conclusion:** Long-term magnesium orotate treatment for patients with mechanical aortic/mitral valve prostheses improves symptom status, cardiac function and HRQoL. This study provides the evidence that the metabolically acting agent magnesium orotate may be a new additional therapy for patients after proceeding with surgical valve replacement.

### P977

#### Percutaneous mitral valvuloplasty with balt single balloon. long-term follow-up of 25 years.

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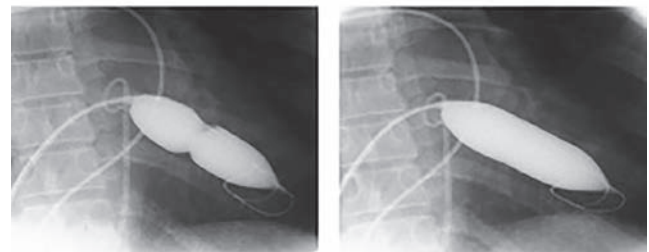
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**Introduction:** Percutaneous mitral valvuloplasty has been proven to be an effective and safe method for treatment of patients with severe mitral valve stenosis and single balloon is a less expensive technique to perform the procedure of mitral balloon valvuloplasty. **Objective:** To evaluate the long-term follow-up (FU) of mitral balloon valvuloplasty (MBV) with Balt single balloon (BSB) technique and to determine independent predictors of survival and event-free survival (EFS). **Method:** From 1987 to 12-31-2013, 526 procedures of MBV were performed, 404 (77.1%) with BSB. There were 256 procedures with long-term FU. Balloon diameter: 25 mm in 5 procedures, 30 mm in 251; mean dilatation area:  $7.02 \pm 0.30$  cm<sup>2</sup>. FU was  $156 \pm 144$  months. Multivariate Cox analysis to determine IPS and EFS.

**Results:** Mean age:  $38.0 \pm 12.6$  (13 to 83) years, 222 (86.7%) female gender, 215 (84.0%) sinus rhythm, echo score (ES)  $7.2 \pm 1.5$  (4 to 14) points and echo mitral valve area (MVA) pre-MBV  $0.93 \pm 0.21$  cm<sup>2</sup>. Mean pre and post-MVA (Gorlin):  $0.90 \pm 0.20$  and  $2.02 \pm 0.37$  cm<sup>2</sup>, respectively ( $p < 0.001$ ). Success (MVA  $\geq 1.5$  cm<sup>2</sup>): 241 (94.1%) procedures. Mean pulmonary artery pressure pre and post-MBV:  $27 \pm 10$  and  $20 \pm 7$  mmHg, respectively. Three (1.2%) patients began the FU with severe mitral regurgitation (SMR). At the end of FU 119 (46.5%) patients were in NYHA functional class (FC) I; 70 (27.3%) in FC II; 53 (20.7%) in FC III; 3 (1.2%) in FC IV; 11 (4.3%) deaths; 17 (8.2%) patients with SMR; 20 (4.7%) were submitted to a new MBV; 27 (10.5%) to mitral valve surgery and 70 (26.3%) without any medicine. Independent predictors of survival were: ES  $\leq 8$  points ( $p < 0.001$ , HR 0.116, 95% IC 0.035-0.384), age  $\leq 50$  years old ( $p = 0.011$ , HR 0.203, 95% IC 0.059-0.693) and absence of mitral valve surgery in the FU ( $p = 0.004$ , HR 0.170, 95% IC 0.050-0.571). Independent predictors of EFS were: absence of prior commissurotomy ( $p < 0.002$ , HR 0.318, 95% IC 0.151-0.667), female gender ( $p = 0.036$ , HR 0.466, 95% IC 0.229-0.951) and MVA post-MBV  $\geq 1.50$  cm<sup>2</sup> ( $p < 0.001$ , HR 0.466, 95% IC 4.884-28.457).

**Conclusions:** Success in 94% of procedures. At the end of follow-up (25 years) only 4.3% of mortality. The independent predictors of survival were: ES  $\leq 8$  points, age  $\leq 50$  years old and absence of mitral valve surgery in the FU. Independent predictors of EFS were: absence of prior commissurotomy, female gender and MVA post-MBV  $\geq 1.50$  cm<sup>2</sup>.

Balt Balloon 30mm



### P978

#### Early hemodynamic improvement after percutaneous mitral valve repair evaluated by noninvasive pressure-volume analysis

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**Purpose:** Mitral regurgitation represents a volume load on the left ventricle (LV) leading to congestion and symptoms of heart failure. This study aimed to investigate the early hemodynamic changes after successful percutaneous mitral valve repair (MVR) with catheter-based clip implantation.

**Methods and Results:** 46 consecutive patients with symptomatic high-grade mitral valve insufficiency (mean age, 72 years; 54 % men) were prospectively included. 70% of patients had secondary mitral regurgitation. Noninvasive pressure-volume loops were reconstructed from echocardiography with simultaneous blood pressure measurements. MVR reduced left ventricular (LV) end-diastolic volume index from  $87 \pm 41$  ml/m<sup>2</sup> to  $80 \pm 40$  ml/m<sup>2</sup> ( $p < 0.0001$ ). End-systolic volume index was  $55 \pm 37$  ml/m<sup>2</sup> before versus  $54 \pm 37$  ml/m<sup>2</sup> after repair ( $p = 0.52$ ). Hence total stroke volume decreased from  $60 \pm 23$  ml to  $49 \pm 16$  ml ( $p < 0.0001$ ), as did ejection fraction ( $41 \pm 14\%$  to  $37 \pm 13\%$ ,  $p = 0.002$ ) and global longitudinal strain ( $-11 \pm 4.9\%$  vs.  $-9.1 \pm 4.4\%$ ,  $p = 0.0001$ ). Forward stroke volume and forward cardiac output remained constant ( $43 \pm 12$  ml vs.  $42 \pm 11$  ml and  $3.2 \pm 0.9$  l/min vs.  $3.4 \pm 0.8$  l/min, respectively). Parameters of LV contractility (end-systolic elastance, peak power index) and measurements of afterload (arterial elastance, end-systolic wall stress, total peripheral resistance) were similar before and after MVR. Total mechanical energy assessed as pressure-volume area decreased

(10,903 ± 4,410 mmHg×ml vs. 9,124 ± 2,968 mmHg×ml,  $p = 0.0007$ ) due to a reduced stroke work (5,546 ± 2,241 mmHg×ml vs. 4,414 ± 1,412 mmHg×ml,  $p < 0.0001$ ).

**Conclusions:** Noninvasive pressure-volume analysis shows that percutaneous mitral valve repair preserves left ventricular contractility and forward cardiac output while unloading the left ventricle through reducing the end-diastolic volume. Mitral valve repair is associated with a reduced total myocardial work and an economized cardiac function.

#### P979

##### Long-term outcomes after transcatheter aortic valve implantation with the corevalve prosthesis in the first patients

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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 December 2010, 144 patients underwent TAVI for the treatment of severe symptomatic aortic stenosis with the CoreValve prosthesis

**Results:** the mean age and euroSCORE were 79.6 ± 6.4 years and 20.8 ± 14% respectively. Mean aortic valve gradient decreased from 50.8 ± 16 mmHg to 8.8 ± 4 mmHg after TAVI, to 11.3 ± 9 mmHg at 4 years and 19.7 ± 12 mmHg at 5 years ( $p$  for post-TAVI trend 0.03). Mean aortic valve area increased from 0.62 ± 0.19 cm<sup>2</sup> to 1.61 ± 0.4 cm<sup>2</sup> after TAVI to 1.47 ± 0.27 at 4 years and 0.98 ± 0.4 cm<sup>2</sup> ( $p$  for post-TAVI trend 0.01). Mean left ventricular ejection fraction increased from 62.8 ± 14 mmHg to 67.1 ± 10 mmHg after TAVI, to 60.7 ± 8 mmHg at 4 years and 53 ± 16 at 5 years ( $p$  for post-TAVI trend 0.001). Late mortality after a mean of 52.1 ± 26 months was 44.4% and in only 15 p was cardiovascular mortality. Survival rates at 1 to 6 years were at 88.8%, 75.6%, 72.2%, 61.8%, 50.57% and 45.5% respectively. At 5 years, 2 patients had severe prosthetic valve dysfunction (severe stenosis and moderate transvalvular regurgitation). Median survival time after TAVI was 3.55 years (95% confidence interval [CI]: 3.26 to 3.84), and the risk of death was significantly increased in patients with stroke (adjusted hazard ratio [HR]: 29.9; (95% CI: 3.4 to 262),  $p = 0.002$  and new-onset atrial fibrillation HR 3.53; (95% CI 1.54 to 8.11)  $p = 0.003$

**Conclusions:** Our study demonstrated favourable long-term outcomes after TAVI. Signs of prosthetic valve failure were observed in 1.4% of patients.

## DEVICES / CRT / ICD

#### P980

##### Clinical screening for pacing induced cardiomyopathy is not enough

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**Background:** Prolonged pacing from the right ventricular apex (RV) is associated with left ventricular (LV) dyssynchrony leading to progressive left ventricular dysfunction and increased morbidity and mortality. Currently the diagnosis is based on development of heart failure symptoms.

**Purpose:** The aim of this study is to analyze the efficiency of clinical screening for pacemaker induced cardiomyopathy.

**Methods:** We analysed retrospectively the patients upgraded in our center from conventional pacemaker to biventricular device for pacing induced cardiomyopathy between the years 2010-2013. The diagnosis was based upon questioning for heart failure symptoms during pacemaker follow up visits. Symptomatic patients performed cardiac echo and were upgraded to a CRT device if LVEF was lower than 35%. We excluded from our group those patients with abnormal LVEF at the initial implant, patients with ischaemic cardiomyopathy or significant valvular disease. The 32 patients were divided in two groups – a group of 16 patients with LVEF at diagnosis ≤25% and a group of 16 patients with LVEF >25% at diagnosis. Echocardiographic and clinical follow up was performed at one year after the implant in all patients.

**Results:** Average duration between the initial implant and diagnosis was 51,7 months. NYHA class, age comorbidities and symptom duration did not differ significantly between groups. Patients with LVEF ≤25% (average 16,37%) had an increase to 29,5% while those with LVEF >25% (average 31,05%) reached an LVEF of 47,64% at one year. LVEF >25% was associated with normalisation of LV systolic function (LVEF >45%) at one year after CRT upgrade ( $p < 0,05$ ).

**Conclusions:** LVEF >25% at diagnosis was a predictor of normalized systolic function at one year after CRT. Using heart failure signs and symptoms for screening half

of the patients had LVEF ≤25% at diagnosis, showing the need for better screening strategies.

#### P981

##### Reducing heart failure mortality through remote nursing telemonitoring

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**Introduction:** Heart failure is often the result of the clinical evolution of several common diseases such as ischaemic heart disease, arterial hypertension, and cardiomyopathy, with an incidence of 2 million cases per year in the world, 470,000 in Europe, and 66,000 in Italy. Heart failure is the most frequent cause for hospitalization in older people. The use of Health Technology Assessment, pacemakers and defibrillators has rapidly increased in the last decade following clinical advances. Implanted heart devices play an important role in monitoring heart failure. Telemonitoring systems enable to check at any time current and previous data produced by the implanted devices, for an early detection of arrhythmia or incipient anomaly of the stimulation or heart defibrillation system. Purpose To identify to what extent telemonitoring affects survival rates and patient adherence to follow up. Methods From June 2014 to October 2015, out of a total of 65 patients with an implanted cardiac defibrillator and an initial diagnosis of heart failure, 40 accepted to participate in this study. One of our nurses educated and trained the patients, entered the data into the website, reviewed and screened transmitted data, and identified any critical cases, and if necessary contacted a physician specialized in arrhythmia, keeping in contact with the patient and checking adherence to treatment through the reports received. Six months after patient enrolment, a semi-structured interview was conducted to study how patients perceived the quality of this service. Results Telemonitoring enabled to identify 84% of the adverse clinical events and intervene immediately for urgent cases and on average within three days for other cases. Patients expressed high levels of acceptance and satisfaction, positively perceived monitoring, and their quality of life improved. The control group after one year presented a higher incidence of adverse events (27.5%) than the intervention group (18.9%). We received 211 transmissions, and avoided 51 outpatient consultations. Telemonitored patients presented lower mortality rates (3.4% vs. 8.7%). Conclusion The data that emerged from this study, despite the small size of our sample, confirmed the data reported by guidelines and the most important studies in this area. Remote follow up performed using implanted devices ensure an early detection of any clinical events or device malfunctions, a 50% reduction of inappropriate shocks, a better quality of life, better compliance and patient satisfaction.

#### P982

##### Two ways for measuring B-type natriuretic peptide, either from capillary blood or venous sample. a comparison of diagnostic accuracy in patients with chronic heart failure in NYHA classes I-III

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**Background:** In recent years, several systems have been implemented to achieve quick and non-invasive measurements of B-type natriuretic peptide (BNP). Among them, a detection system with very innovative properties has been patented, consisting in a one-step immunoassay that uses biotinylated anti-BNP monoclonal antibody and streptavidin-coated magnetic solid-phase particles to attract the immune binding of latex particles coupled with horseradish peroxidase and a monoclonal antibody fragment. It represents the most recent advancement in its field and is termed here as Heart Check (HC) BNP test, so as not to include in the report any trademark symbol, according to the rules and regulations governing the present submission. This system is a rapid point of care immunoassay (POC), projected for measuring BNP directly from a capillary whole blood sample.

**Purpose:** This study aimed at comparing the analytical and clinical performances of this new POC with our reference method, namely the lab-based test Architect system which obtains the BNP measurement from plasma derived from venous blood sample, subsequently treated with ethylenediaminetetraacetic acid (EDTA).

**Methods:** 111 patients with stable chronic heart failure (CHF) referring to two cardiac rehabilitation centers were enrolled from December 2013 to January 2015. These patients were subjected to a simultaneous capillary (HC) and plasma (Architect system) BNP measurements. Clinical and analytical performance of HC were assessed and compared to the reference method. Results Capillary BNP showed a good correlation with the reference method ( $r = 0.94$ ,  $p < 0.0001$ ), although the values diverged when BNP was higher than 1500 pg/mL. Indeed, the HC had a relatively poor precision and the coefficient of variability was 10.1% and 18% for low and high controls, respectively. However, both methods showed similar diagnostic performances in discriminating the patients with heart failure in NYHA class I from those belonging to NYHA classes II-III, with values of area under the curve (AUC) of 0.983 and 0.984, respectively, and equivalent sensitivity, specificity, and positive and negative likelihood ratios.

**Conclusions:** The HC BNP test is a good POC able to provide reliable information

about the hemodynamic status of CHF patients, especially of those belonging to NYHA classes I-III.

**P983**

**Trend of echocardiographic parameters in pediatric patients with Berlin Heart EXCOR LVAD: a prospective observational study**

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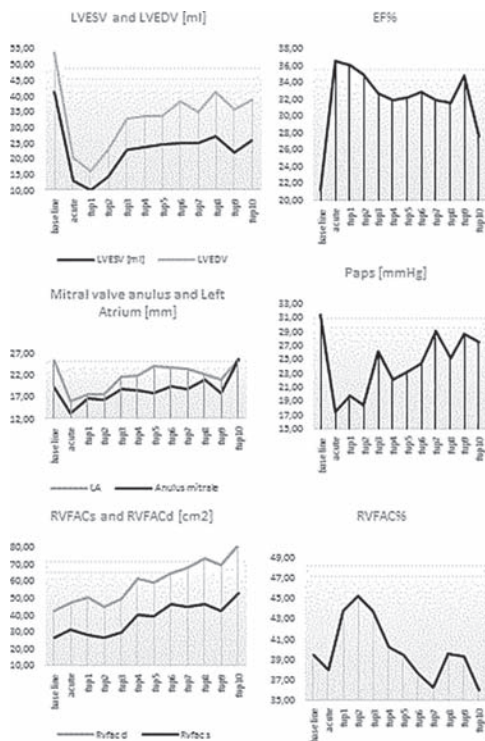
**Background:** LVAD is an important treatment for bridging pediatric patients to heart transplant or to heart recovery assuring an adequate cardiac output and the left ventricular unloading.

**Purpose:** This work aim at evaluating the trend of echocardiographic parameters in pediatric patients undergoing Berlin Heart EXCOR LVAD.

**Methods:** Data of Children implanted from 2013 to 2015 were prospectively collected before the LVAD implantation and at the monthly follow-up till the LVAD explantation.

**Results:** 12 patients were enrolled. 9 patients (75%) were affected by an idiopathic dilated cardiomyopathy, 2 patients (17%) by a non compacted left myocardium and 1 patient (8%) by a restrictive cardiomyopathy. At the implantation, average patients age and weight were 13.1 ± 11.1 months and 7.2 ± 3.7Kg, respectively. Average LVAD staying was 226 ± 104 days. Six patients (50%) were successfully transplanted, one (8%) was weaned from the LVAD, three (25%) died for a major neurological complication and two (17%) are still on LVAD. Left ventricle was significantly unloaded by the LVAD with a statistically significant reduction in left ventricular end diastolic volume (LVEDV) (p<sub>acute</sub>=0.0001, P<sub>fup1</sub>=0.0004, p<sub>fup2</sub>=0.0006, p<sub>fup3</sub>=0.02, p<sub>fup4</sub>=0.03, p<sub>fup5</sub>=0.05), Left ventricular end systolic volume (LVESV) (p<sub>acute</sub>=0.0003, P<sub>fup1</sub>=0.0003, p<sub>fup2</sub>=0.0003, p<sub>fup3</sub>=0.03, p<sub>fup4</sub>=0.04) and a statistically significant improvement of left ventricular ejection fraction (EF) (p<sub>acute</sub>=0.01, P<sub>fup1</sub>=0.02, p<sub>fup2</sub>=0.02). However, after the initial unloading, the LVESV and LVEDV increase and the EF decreases. A similar trend is shown by the left atrial size, mitral valve annulus, mitral regurgitation and right ventricular pressure (Paps). Right Ventricular Fractional Area Change (RVFAC) is initially improved by the LVAD. However, right ventricular end systolic (RVFACs) and end diastolic (RVFACd) area and tricuspid valve annulus showed a progressively increment and then the RVFAC decreases.

**Conclusion:** Berlin Heart EXCOR LVAD could successfully bridge patients till the heart transplantation. However, results show that the left ventricular unloading provided by the LVAD in the short term follow up decreases in time resulting in both left and right ventricular dilatation.



Trend of Eocardiographic Data

**P984**

**Ventricular assist devices do not treat ventricular arrhythmias. Significant morbidity persists after implantation**

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**Purpose:** Left Ventricular assist devices (LVADs) have emerged as a life saving treatment option for patients with advanced heart failure. Despite robust left ventricular unloading, the right ventricle remains unsupported and susceptible to hemodynamic perturbations, including those from ventricular arrhythmias (VAs). Little is known about the epidemiology and influence of sustained VAs on outcomes in patents with VADs.

**Methods:** We retrospectively reviewed and analyzed data from all consecutive patients receiving a continuous flow VAD at our hospital from October 2003- December 2015. Patient demographics, medical therapies, and outcomes were recorded. Descriptive statistics were generated and multivariable logistic regression was used to assess the independent association of clinical variables on post-implant VAs.

**Results:** Thirty – five patients underwent the implantation of left ventricular assist devices. Fifteen out of 35 patients (43%) had sustained VAs after VAD. The majority with post-implant VAs were male (95%), had history of HTN (55%) and hyperlipidemia (30%), and had non-ischemic cardiomyopathy (75%). Compared with patients who did not experience VAs after VAD, patients with post-VAD VAs more often had pre-VAD VAs (67% v. 20%), an ICD (86% vs. 43%), and appropriate ICD discharge prior to mechanical circulatory support (44.4% v. 12.5%). The length-of-stay during implant hospitalization was similar regardless of post-VAD VAs, but those with VAs had twice the rate of rehospitalization (2.8 v. 1.6 admissions/patient) and required more anti-arrhythmic medications (2.3 v. 0.6 antiarrhythmics/patient). Post-VAD VAs were often refractory to medical therapy, requiring electrical cardioversion in the majority of cases (75%). Using multivariable logistic regression, only history of prior VAs was found to be associated with the development of post-VAD VAs.

**Conclusions:** Vas following VAD implantation are often refractory to conservative therapy and are associated with frequent hospital readmissions. Since only pre-implant ventricular tachycardia was associated with post-VAD VAs, arrhythmia burden may have a significant impact on future outcomes. Additional study should focus on utilizing arrhythmia burden to optimize patient selection for VAD.

**P986**

**Right ventricular failure and left ventricular assist device: a 14-year, single-centre experience.**

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**Background:** Right Ventricular Failure (RVF) is life-threatening complication after 20-50% of the implantation of a LVAD and contributes to increase postoperative morbidity and mortality. This complication has a poor prognosis and is generally unpredictable. RVF may often need temporary mechanical assistance and is most commonly associated with TVR.

**Purpose:** To study institutional experience over 14 years in LVAD implantation, to investigate effectiveness of TV annuloplasty in reducing the weaning time from temporary RV mechanical support in patients with mild-to-moderate TVR.

**Methods:** We evaluated our institution's LVAD database and analyzed all patients who received a LVAD as a bridge to transplant (BTT) or destination therapy (DT) from 2002 to 2015. We identified 64 patients, of which 54 were implanted as BTT (84.4%) and 10 received the device as DT (15.6%)

**Results:** The mean age was 54 ± 7.3 years, 79% were males, the INTERMACS medium level was 3.25 ± 0.45. The 17.2% of the patients (n = 11, Group A) required a temporary magnetically levitated rotary pump to support the RV without tricuspid annuloplasty (RVSWI 5.2 ± 3.1, PCWP 25.2 ± 5.2 mmHg, SVR 1611 ± 2950 dyne/sec /cm-5/m2, PVR 244 ± 90 dyne/sec /cm-5/m2). In 9 patients (14.1%, Group B), temporary RV support was combined by TV annuloplasty (RVSWI 6.1 ± 3.5, PCWP 24.4 ± 4.5 mmHg, SVR 1591 ± 270 dyne/sec /cm-5/m2, PVR 254 ± 110 dyne/sec /cm-5/m2). We compared the outcome of 2 groups of patients. They were similar regarding preoperative risk variables. Incidence of RHF after LVAD is successful weaning from mechanical RV support occurred in 9 patients in group A (81 %) and 8 patients in group B (88%). Weaning time, need of inotropic support, time of recovery were significantly shorter for group B as compared to that of group A (9 ± 2.1 days group B versus 21.1 ± 8.1 days group A: p < 0.001; 7.8 ± 0.9 patients of group B versus 25 ± 2.6 patients of group A: p = 0.002; 29.4 ± 4.5 days group B versus 61.8 ± 1.8 days group A: p = 0.004). Also, data of Group B evidenced a reducing of the early postoperative complications (such as dialysis, perioperative mortality, revision for bleeding) and less time of recovery in ICU (Table 1).

**Conclusion:** Our single-centre experience suggests that the associated procedure LVAD implantation and TV annuloplasty, in patients with TVR at least mild-moderate grade, may reduce the mechanical and pharmacological support as well as recovery time, risk of infections and costs of hospitalization.



	All Samples	Hb <10	Hb 10-12	Hb 12-14	Hb > 14
Sample number; n(%)	212	104 (49)	79 (37)	22 (10)	8 (4)
Haemoglobin; median (IQR)	10 (8.5-11.3)	8.4 (7.8-9.2)	10.8 (10.2-11.3)	12.6 (12.3-13.1)	14.9 (14.4-15.7)
Mean Corpuscular Volume; median (IQR)	85 (80-90)	86 (80-91)	83 (80-87)	83 (76-89)	93 (86-97)
Red Cell Distribution width; median (IQR)	17 (15-19)	18 (16-20)	17 (15-19)	16 (15-19)	17 (15-18)
Transferrin Saturation; median (IQR)	12 (9-17)	11(6-15)	11 (9-17)	18 (11-22)	16 (14-19)
Ferritin; median (IQR)	76 (30-200)	118 (33-272)	62 (29-118)	39 (18-89)	42 (37-125)
Estimated Glomerular Filtration Rate; median (IQR)	69 (54-90)	64 (46-75)	57 (49-66)	75 (50-90)	69 (59-73)
Lactate Dehydrogenase; median (IQR)	526 (443-604)	510 (428-620)	536 (447-595)	499 (444-595)	497 (452-542)
C Reactive Protein; median (IQR)	18 (8-46)	35 (12-63)	12 (5-32)	9 (3-13)	17 (12-36)

### P987

#### Impact of different types of implanted long-term left ventricle assist devices on outcomes after heart transplantation

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**Background:** Continuous-flow left ventricle assist device (CF-LVAD) implantation has become the therapeutic standard for management of advanced heart failure patients awaiting heart transplantation (HTx) as a bridge-to-HTx. The aim of our study was to determine association between LVAD device type and short-term outcomes following the HTx.

**Patients and methods:** We retrospectively analyzed a total of 23 patients, who underwent LVAD implantation at our institution between 1/2009 and 6/2015. 11 patients received the type HM II, 12 type HW. There was no statistical difference between the two groups in age, gender, BMI, diagnosis and pulmonary vascular resistance. They were all transplanted from the urgent order. The only significant difference between the two groups was the time on the waiting list, in the group of the HMII it was in average 342 days compared to 166 days in the HW group ( $p=0,039$ ). There were no significant differences in following donor characteristics: age, gender, cause of death, BMI, EF of left ventricle and cold ischemia time.

**Results:** The average duration of extracorporeal circulation was in the HMII group 163 minutes, in HW 170 minutes ( $p=0,902$ ), blood losses were 1836 ml versus 1946 ml ( $p=0,224$ ), the need for implantation of ECMO 2 versus 1, renal failure with hemodialysis 4 versus 5 ( $p=1,0$ ). The incidence of failure of wound healing 2 versus 3 ( $p=1,0$ ), the incidence of acute rejection grade 1B and higher 5 versus 3 ( $p=0,40$ ), length of stay in the ICU was 21 days versus 18 days ( $p=1,0$ ) and total duration of hospitalization after HTx 37 versus 39 days ( $p=0,926$ ). Survival according to Kaplan Meier was significantly different in favour of HW group: the one and three year survival was 100%, compare to HMII group 64% and 55% respectively.

**Conclusions:** According to our pilot results, in patients undergoing HTx from different types of implanted LVADs there was no significant difference in the incidence of postoperative complications and in length of hospitalization. However, based on our limited sample data, patients transplanted from HW device support had a statistically significantly better survival.

### P988

#### Iron deficiency in patients with ventricular assist devices - how common is it?

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**Introduction:** Patients with ventricular assist devices (VAD) often suffer from bleeding events, multiple or persistent infections and develop acquired Von Willebrand Disease, which may all contribute to iron deficiency (ID). Traditionally, ID is associated with decreased haemoglobin, microcytosis and a low serum ferritin (FER). However, FER increases in response to inflammation, which may render it unreliable in patients with cardiac disease. An alternative method of assessing ID is transferrin saturation (TSAT).

**Purpose:** We sought to assess the prevalence of ID and anaemia in a population of VAD patients.

**Methods:** Blood iron profiles, with associated full blood count, renal function and C reactive protein (CRP) were retrospectively collated.

**Results:** From 77 patients (median age 48, IQR 41-56; 67 men) who had a VAD implanted between 2007 and 2015, 212 relevant blood samples taken after VAD implantation were available. Median length of VAD support was 439 days (IQR 266-808). For all samples, median (IQR) TSAT was 12 (8-17) and FER was 74 (29-195); 27 (34%) patients had at least one TSAT <20%, 59 (75%) had at least one FER <100ug/L and only 20 (25%) had at least one FER > 300ug/L. At one year, Hb was <10g/dL in 25 patients, 10-12g/dL in 35 patients, 12-14g/dL in 12 patients and > 14g/dL in 5 patients. Indices suggesting ID were common in all Hb categories. TSAT but not FER declined as Hb fell. RDW, eGFR and LDH were similar in each Hb group. Conclusion VAD patients are often anaemic and most fulfill criteria for ID regardless of Hb category. In this population, FER may be acting as an inflammatory marker rather than a measure of ID. TSAT may be a more reliable marker of both absolute and functional ID in this clinical setting. Further studies are needed to assess the clinical relevance and importance of correcting ID in this population.

### P989

#### Ventricular energetics in pediatric LVAD patients: a retrospective clinical study

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**Background:** The continued decline in donor hearts' availability prolonged the LVAD support duration and leads to an increased interest in the use of LVAD as a bridge to heart recovery in pediatrics. Left and right ventricular energetic parameters were proposed in literature to evaluate ventricular unloading and recovery.

**Purpose:** The aim of this study is to estimate the trend of right and left ventricular energetic parameters in pediatric patients implanted with LVAD.

**Methods:** Echocardiographic data of 12 pediatric LVAD patients implanted from December 2013 to December 2015 were retrospectively analyzed at the baseline, in the acute phase after the LVAD implantation and at the monthly follow ups till the LVAD explantation. Data were used to estimate left and right ventricular energetic parameters.

**Results:** A significant relationship between the left and right ventricular energetic parameter trends along all the study period has been found. Left ventricular end systolic pressure-volume relationship (LVE<sub>max</sub>) showed a statistically significant improvement till the follow-up of two months ( $p=0.002$ ) and then it progressively decreases. Left attero-ventricular coupling (LAVC) significantly decreases after the LVAD ( $p=0.04$ ) and right attero-ventricular coupling (RAVC) decreases in the short term follow up. Left ventricular external work (LVEW), potential energy (LVPE) and pressure-volume area (LVPVA) decrease at the short term follow up and then increase progressively. The right ventricular external work (RVEW), potential energy (RVPE) and pressure-volume area (RVPVA) increase after the LVAD implantation. Finally the left (right) cardiac mechanical efficiency (LVCME and RVCME) is improved (decreased,  $p=0.02$ ) by the LVAD.

**Conclusion:** The trend of energetic variables shows that the benefits provided by the LVAD could decrease over time. A continuous and patient tailored LVAD parameter programming could contribute to prolongue LVAD benefits. The introduction of energetic parameters could lead to a more complete evaluation of LVAD patients outcome which is, typically, a multiparametric process.



Ventricular Energetic Trends

**P990**

**Value of BNP monitoring in patients with left ventricle mechanical circulatory support in outpatient care.**

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**Background:** Implantation of left ventricle assist devices (LVAD) can be lifesaving procedure for eligible patients with terminal heart failure. Early identification of complications during post LVAD outpatient care using BNP levels monitoring has not been well documented.

**Purpose:** The aim of our study was evaluation of BNP as a marker of severe clinical events in patients with LVAD Heart Mate II (HM II) in outpatient care.

**Methods:** We analysed BNP levels in patients with HM II implanted as a bridge to transplant from 02/08 to 6/15 in our institution who were discharged from hospital to outpatient care, n = 109. In all patients we evaluated the most increased BNP level during follow-up ("BNP max") and we calculated the percentage change in relation to BNP level prior to implantation ("% BNP before") and to the lowest one ("% BNP min"). To each BNP max level we assigned any clinical event (0 = no clinical event, 1 = hypervolemia without need of parenteral therapy, 2 = arterial hypertension with mean BP ≥ 100mmHg, 3 = less severe infection, 4 = severe infection, 5 = heart failure without pump dysfunction, 6 = pump dysfunction according to echo and angiography findings). We divided patients into 3 groups by the severity of clinical events, Group A (clinical event 4, 5, 6) = serious, Group B (clinical event 1, 2, 3) = not serious and Group C (0 = no clinical event). We compared mean BNP max levels of Groups A, B, C one another. Consequently we used ROC analysis to identify the strongest predictors of any event and the serious one.

**Results:** In Group A we included 16 pts (with event 4 = 7pts, 5 = 4 pts, 6 = 5 pts), in Group B 34 pts (with event 1 = 14pts, 2 = 11pts, 3 = 9 pts) and in Group C 59 pts. There was statistically significant difference in log of mean "BNP max" between A and B Groups p=0,001, A and C p < 0,001 and B and C p < 0,001 (Tukey-Kramer

test). Using ROC analysis we found "% BNP before" as the strongest predictor of the serious event. The cut off point was increased BNP level amounting ≥ 40% of BNP level before HM II implantation with 100% sensitivity and 81% specificity. Using ROC analysis we identified "%BNP min" as the strongest predictor of any event (Groups A+B) with cut off point 167% with sensitivity 92% and specificity 85%.

**Conclusion:** Our findings showed that BNP monitoring is an important part of post LVAD outpatient care. High sensitivity and specificity of BNP changes allow identification of clinical events with need for further diagnostic and therapeutic interventions. Of special importance is BNP monitoring ability to reveal life threatening situations. Furthermore we believe that this approach could decrease frequency of visits in outpatient VAD departments in stable pts.

**P991**

**RESPIRATE-2 project: a co-management telemedicine-based programme between hospital (HF clinic) and field (general practitioner) for ICD-CRTD heart failure patients. final results**

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**Background:** The effectiveness of telemedicine and Remote Monitoring (RM) in heart failure is not established. RM systems can transmit device data and clinical data (for e.g. Transthoracic impedance, Heart Rate Variability, Physical Activity). Today these data are managed only by HF specialist or Electrophysiologist (EP). RespiRATE-1 was a pilot-project about Remote Patient Management (RPM) that involved HF specialist, EP (Hospital HF Clinic) and general practitioners (GP) (Outpatient Clinic). The aim of this Project was to create a network between the hospital and the field. RespiRATE-2 followed the same program but involved a greater number of GP and was supported by the local healthcare business of Bergamo.

**Purpose:** the primary aim of this project is to develop, implement, and test the feasibility and efficacy of RPM program (telephone support, network care and device-assisted monitoring) co-managed by HF specialist and GP.

**Methods:** HF specialist and GP used a common remote access technology and followed agreed simple flow-charts, in order to view and to share clinical and device data and to plan diagnostic or therapeutic actions if necessary (increase diuretic's dosage, prescribe blood tests or X-rays, etc.). A teleconsultation between patient and HF Clinic (physician or nurse) or Outpatient Clinic (GP) was allowed, if necessary.

**Results:** 10 GP were trained about HF management and RPM. 6 transmissions (tx) per pt was scheduled on a monthly basis from June 2014 to November 2014 and Alert tx was activated. GP was the first clinical data reviewer. Clinical actions, if needed, were shared by HF specialist and GP, following agreed flow-chart. During the study we reported: -60 scheduled transmissions, all co-managed by GP and HF specialist, with no need for pt's hospital access.-7 Alert Tx: 3 of these due to ICD shock on VF, that required patient's hospitalization; 4 of these due to fluid accumulation, all managed by GP in Outpatient Clinic. The use of RPM technology was perceived positively by patients and physicians.

**Conclusions:** A remote HF patient co-management with GP seems to be feasible but requests clear and simple flow-chart. The acceptance by patients and primary physicians is necessary for the implementation of RPM via implantable electronic devices as part of the out-patient HF-care program.

**P992**

**Heart failure risk status and medical management: Insights from the TRIAGE-HF trial.**

Medtronic

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**Background:** TRIAGE-HF was a Canadian prospective observational post-market study to evaluate the performance and clinical usability of the heart failure risk status (HFRS) feature on CareLink. HFRS is a Health Canada approved integrated diagnostic tool. HFRS is based on existing commercially available device diagnostic parameters and is a dynamically updated tool to assess individual patient risk (low, medium or high) of having a heart failure (HF) hospitalization in the next 30 days.

**Purpose:** One of the TRIAGE-HF study objectives was to correlate HFRS burden with participant's medical management. Since prescription of mineralocorticoid receptor antagonists (MRA) in HF is a marker of advanced disease, we hypothesized that MRA prescription will be associated with less modifiable HFRS scores despite optimal HF care in TRIAGE-HF.

**Methods:** TRIAGE-HF enrolled 100 patients with systolic HF implanted with a Medtronic high performance device and followed at 3 Canadian HF centers. Study follow-up was up to 8 months. The sum of HFRS scores from 30 days

prior to both the baseline and study exit visits was computed. The data were summarized for each visit (baseline and study exit) by the presence or absence of MRA treatment. All patients included in the analysis received background therapy with beta-blockers and ACE-inhibitors/angiotensin receptor blockers or nitrates/hydralazine. Non-parametric testing was used to compute p-values within and between groups.

**Results:** 69% of patients remained in the same medication group at study entry and exit. HFRS scores improved over the study period in both groups and this achieved statistical significance in those patients who were not treated with an MRA ( $p=0.03$ ). HFRS scores were higher at study entry and exit in MRA treated patients (see Table 1).

**Conclusions:** In the TRIAGE-HF study, HFRS was high in both MRA and non-MRA groups at baseline and improved over the study duration. This decrease was large and statistically significant only in the non-MRA group. This may be due to more advanced HF in MRA treated patients, which is more difficult to impact even with optimal HF care.

Table 1: HFRS and MRA Use

		no MRA		MRA		p-value
Baseline	Mean (SD) Median (IQR)	1.59 (1.29)	1.25 (0.80-1.76)	1.99 (2.39)	0.99 (0.79-1.87)	0.68
Exit	Mean (SD) Median(IQR)	1.19 (0.87)	1.07 (0.73-1.41)	1.49 (1.31)	1.08 (0.79-1.49)	0.51
Difference	Mean (SD) Median (IQR) p-value	-0.39 (1.51)	-0.13 (-0.60, 0.10)	0.03	-0.49 (2.21) -0.06 (-0.93, 0.43)	0.60 0.33

### P993

#### Correlation between pulmonary pressure and thoracic impedance measured by remote monitoring devices

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**Background:** The increase in ventricular filling pressures is considered the first event causing acute decompensation in Chronic Heart Failure (CHF). Neurohormonal activation would then take place and, finally, peripheral and pulmonary edema would cause symptoms of overt acute heart failure. Left ventricular filling pressure can be estimated from diastolic Pulmonary Artery Pressure (dPAP) and monitored by means of telemetric sensors; pulmonary congestion is associated to reduction of Thoracic Impedance (TI), which can be monitored remotely by ICDs. The purpose of our study was to investigate the temporal relationship between sustained variations of left ventricular filling pressures and pulmonary congestion.

**Methods:** 11 CHF patients (Age  $71 \pm 9$ ; EF  $27 \pm 4$ ; NYHAIII) with ICDs measuring TI were implanted with a PAP sensor. TI was measured daily and transmitted automatically every 15 days. PAP was transmitted daily; for three months CHF specialists were blinded to PAP and no medical intervention was guided by PAP. We defined: TI as decreasing and dPAP as increasing, when their value was lower or higher than the average of the previous week; a decrease or increase period when TI or PAP had been decreasing or increasing for three or more days

**Results:** we received 691 PAP transmissions (compliance 77%). 7 patients suffered from  $1,82 \pm 2.64$  episodes of mild AHF requiring therapy adjustment. There were no hospitalizations. We recorded 35 TI decrease periods and 47 dPAP increase periods. Most (74%) TI decrease periods were "subthreshold", i.e. not associated to impedance alert conditions, according to the algorithms of the ICDs. dPAP increases preceded TI decreases by  $6.83 \pm 3.1$  days. A weak, though significant, correlation between the increase of dPAP and the decrease of TI recorded 7 days later was observed ( $R=0.22$ ;  $p<0.001$ ). The association of 1) increasing PAPd and 2) PAPd absolute value  $> 22$  mmHg was evaluated as a predictor of decrease of TI taking place 7 days later: specificity was 59%, sensitivity 42%, PPV 36%; NPV 65%.

**Conclusions:** Our observations confirm the strict correlation between filling pressure and pulmonary impedance. dPAP increase is associated TI decrease, occurring about 1 week later, mainly subthreshold, possibly indicating subclinical pulmonary congestion. It can be hypothesized that PAP and TI remote monitoring may be combined for more reliable and timely early detection of impending AHF.

### P994

#### HF-RADD; Early experience of risk monitoring in ambulatory heart failure patients using device-reported parameters

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**Introduction:** The majority of heart failure (HF) risk assessment tools apply models of care based on population studies rather than predicting acute, possibly preventable, events in individuals. A number of variables have been associated with worsening HF. An integrated diagnostic algorithm, considering the combined impact on risk of

a number of such HF variables monitored by implantable cardiac device provides us with opportunity to monitor dynamic risk in individual patients even remotely. It has been shown that a patient at 'high' risk by this algorithm faces nine times the risk of hospitalisation at that time.

**Purpose:** To consider the feasibility of providing a clinical response for all patients with cardiac device reporting 'high' risk status. To consider the opportunity for intervention and the feasibility of a prospective study of the impact of such intervention.

**Methods:** The Cardiac rhythm management (CRM) team applied an integrated diagnostics algorithm to HF patient data sent by remote download as part of routine device surveillance. They monitored reported risk. Patients at 'high' risk were referred to the HF team at that point. The HF team reviewed the clinical status of all those patients by telephone. Intervention was offered to those with symptom change. No additional visits were arranged unless indicated in response to condition change. Treatment change was delivered via pacing clinic, specialist HF teams or primary care physicians.

**Results:** Over 1 year, 762 remote downloads were considered (381 patients, assessed remotely twice/year). 37 patients were monitored by another study and therefore excluded. 22/762 downloads reported 'high risk'. 19/22 patients reported worsening HF symptoms prompting intervention, 13/19 were referred to local HF team, 5/19 to their primary care practitioner, 1 to cardiologist for management of new arrhythmia. 9/19 had resulting medication change. 3/22 patients reviewed by telephone were asymptomatic and therefore had no action.

**Conclusion:** The Integrated diagnostics algorithm is a means of focusing clinical teams on a patients' current risk of event. It highlights change in condition for which intervention might prevent clinical deterioration, perhaps optimising resource utilisation. We are able to report that only a small proportion of HF patients with device, face such a change at any one time. Specialist response is feasible. In our organisation closer collaboration between CRM and HF teams has been welcomed by both. We have now activated real time device alerts in all patients and are offering clinical review as a 'high alert' is reported. We are collecting data prospectively in order to better describe the reasons for an alert, the opportunity for intervention and with control group are considering the impact of such intervention on outcome. We are expanding the population to include neighbouring HF centres managed by different specialist teams.

### P995

#### Influence of biventricular pacing on clinical status and left ventricular diastolic parameters in patients with preserved ejection fraction after radiofrequency AV node ablation. Case series.

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**Introduction:** After radiofrequency AV node ablation and implantation of conventional pacemaker some patients present with clinical picture of diastolic heart failure with preserved left ventricular systolic function. We observed several patients with described problem who were undergone upgrade to CRT procedure.

**Materials and methods:** Three patients with preserved systolic function were included into study (table 1). As the criteria of assessment the following parameters were used: early diastolic myocardial velocity - e' and E/e' ratio. In all patients left ventricular endocardial lead was optimally implanted into lateral left ventricular wall. Follow-up was conducted after 1, 3 and 6 months after the procedure. Results. All the patients initially had 100% right ventricular pacing with QRS duration 180-200 msec, signs of left ventricular diastolic dysfunction, which was reflected in delayed early diastolic myocardial velocity and increased E/e' ratio. After CRT upgrade QRS duration decreased by 60-70 msec and was 130-140 msec. In all patients we observed increase of distance of six minute walk test, increased quality of life score. Early diastolic myocardial velocity increased by 1-2 cm/sec, E/e' ratio decreased by 1-3. Ejection fraction increased by 6-8%, left ventricular end diastolic volume decreased by 10-20 ml and remained the same in third patient. Mitral regurgitation degree decreased in 2 patients and did not change in one patient.

**Conclusion:** CRT upgrade is one of the possible methods of management of left ventricular diastolic dysfunction in patients with implanted conventional pacemaker, clinical picture of heart failure and preserved ejection fraction.



Table 1. Patient data.

Sex	Age, yrs	BMI	EF, %	QRS, msec	Quality of life score	Six minute walk test, meters	Mitral regurgitation
female	66	44	62	180	78	147	moderate
male	69	38	57	200	61	145	moderate
male	66	33	55	200	58	294	moderate

BMI - body mass index, EF - ejection fraction

### P996

#### Optimization of interventricular delay with contrast echocardiography in end-stage heart failure patients with biventricular pacing

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**Background:** More than 25% of patients with cardiac resynchronization therapy (CRT) are not-responders. By now few is known about features predicting CRT success. In this scenario, the optimization of interventricular delay has not been widely assessed so far, as predicting variable for CRT responding.

**Methods:** 13 patients with end-stage heart failure on ICD-CRT underwent to contrast echocardiography after a mean time of 4.7 years. During contrast injection interventricular (IV) delay was modified according to following protocol: left ventricular (LV) stimulation was anticipated 20, 40 and 60 msec with respect to right ventricular (RV) stimulation and vice versa. At every modification, 3 cardiac cycles echocardiographic clips were recorded. Then offline analysis of LV vortex was performed using a dedicated software (HyperFlow version 6.2, AMID s.r.l.) to evaluate the best configuration to achieve a physiological flow direction (from basis to apex and then to left ventricular outflow tract). To corroborate our hypothesis we evaluated the patient's quality of life using Kansas City Cardiomyopathy Questionnaire. Pro-BNP was also estimated both before modifying pacing configuration and one month afterwards.

**Results:** In 5 patients no change of ventricular pacing features were needed. Conversely, in 8 patients IV delay was changed according to offline vortex analysis. We found a decrease in end diastolic ventricular diameters as well as a contractile function an improvement of ejection fraction (EF) (respectively end diastolic left ventricle diameter  $65 \pm 9$  vs  $64 \pm 7$  and EF  $30 \pm 11$  vs  $32 \pm 8$ ). One month after CRT modification pro-BNP values was significantly reduced ( $1438$  vs  $1123$ ,  $p=0.04$ ).

**Conclusion:** This is a pilot study aimed to verify the possible clinical use of intraventricular vortex examination in order to find the best interventricular delay to optimize CRT and increase the rate of responders. A further analysis with a larger cohort of study is mandatory to confirm this initial findings.

### P997

#### Usefulness of cardiac resynchronization therapy in elderly patients: predictors of response at long term follow up

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**Background:** proportion of elderly patients included in studies of cardiac resynchronization therapy (CRT) is low. Therefore response to CRT has not been well studied in this population. We aimed to determine useful predictors of response to CRT in elderly patients ( $\geq 75$  years old).

**Methods:** A total of 49 patients (mean age  $79.2 \pm 2.9$  years; 79.6% men) undergoing CRT implantation between June 2006 and October 2014 were included. Response was defined if patients met a composite endpoint (alive status, improvement in NYHA class  $\geq 1$  and no need for HF admission).

**Results:** At implantation, mean functional class (FC) was  $2.4 \pm 0.8$ , left ventricular ejection fraction (LVEF) was severely impaired (mean  $23.4 \pm 6.7$  %) and left ventricle was severely dilated (mean end diastolic diameter  $60.4 \pm 6.6$  mm). Heart failure was due to non-ischemic cardiomyopathy in 25 patients. Population was under optimal medical treatment (Beta blockers: 87.5%; ACEI (angiotensin-converting enzyme inhibitors)/ARB (angiotensin II receptor blockers): 64.6/27.1% respectively and aldosterone antagonists: 68.8%). Left bundle branch block (LBBB) was present in 67.3% of the overall population, and mean QRS duration was of  $155.4 \pm 25$ ms. After 37.1 months of follow-up, 68% of patients remained alive and both average FC ( $2.1 \pm 0.9$ ) and LVEF ( $30.8 \pm 13.7$ ) were improved. A total of 17 patients (35.4%) met the clinical endpoint. Response to CRT was more frequently observed in more symptomatic patients (mean FC in responders  $2.7 \pm 0.4$  Vs  $2.3 \pm 0.7$  in non-responders;  $p=0.049$ ) and in those with LBBB ( $p < 0.005$ ). After multivariable analysis, both functional class (HR 3.4; 95% CI 1.02-11.45) and LBBB (HR 8.5; 95% CI 1.03-70.10) emerged as predictors of clinical response in elderly patients.

**Conclusion:** response to CRT was seen in 35.4% of elderly patients ( $\geq 75$  years), which is slightly less than in general population. Two reliable predictors of positive

response emerged: poorer functional class and LBBB were found to be useful markers after long-term follow up. These factors can be used to select those elderly candidates to CRT more suitable to obtain a positive response.

### P998

#### real world on CRT in a colombian heart failure clinic

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Cardiac resynchronization therapy has been shown to improve outcomes in heart failure. Patients enrolled in clinical trials are highly selected and do not represent the real-life scenario.

**Objective:** To evaluate the response to resynchronization therapy in NYHA class, echocardiographic criteria, hospitalizations and survival after 6 months follow-up.

**Methods:** Retrospective observational analytical cohort.

**Results:** 96 patients were included, 59.4% were male, 31.3% of patients had non-ischemic and 68.8% ischemic heart disease. The mean ejection fraction was  $18.9\% \pm 7.1\%$ . The functional class before the implant was: NYHA I 4.2%, NYHA II 31.3%, NYHA III 52.1% and NYHA IV 12.5%. 90.6% had left bundle branch block on with a QRS of  $152\text{ms} \pm 21.4\text{ms}$ . There were no cases of death or cardiac transplantation at six months, 53.1% of the patients were free of hospitalizations after implant, 62.5% improved the NYHA class, the mean ejection fraction improvement was  $29.2\% \pm 13.6\%$  and 22.9% decreased ventricular diameters.

**Conclusions:** response to cardiac resynchronization therapy in our real life scenario is closer to reported in literature, mainly in the improvement of NYHA and the number of hospitalizations. All patients with CRT must be followed in a heart failure clinic to get the best results of this therapy.

### P999

#### The correlation between six minute walking test distance and noninvasive cardiac output measurements before and after cardiac resynchronization therapy optimization

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**Background:** Optimization is performed in patients unresponsive to cardiac resynchronization treatment (CRT) to increase the effectiveness of treatment. Six minutes walking test (SMWT) is a practical test and commonly used test to evaluate the clinical response to optimization. CRT devices are programmed to achieve the highest cardiac output during optimization by echocardiography and other methods as well. In this study; we aimed to compare the relationship between SMWT distance and cardiac output values measured by different methods before and after CRT optimization.

**Methods:** Fifty non-responder patients were enrolled in the study. Patients were divided into two groups. In group 1, cardiac output values were measured by non-invasive cardiac output measurement (NICOM) device and optimizations were performed. In group 2, cardiac output measurement and optimization were performed by conventional echocardiographic methods. Both groups performed SMWT before and after optimization and the correlation between cardiac output values and SMWT distance were investigated.

**Results:** After the optimization, SMWT distances revealed significant increase in both groups ( $244 \pm 62$  m vs.  $254 \pm 61$  m and  $235 \pm 39$  m vs.  $261 \pm 5$  m,  $p < 0.05$ ). In group 1, pre-optimization SMWT distance and cardiac output values showed moderately positive significant correlation ( $r=0.460$ ,  $p=0.021$ ). In this group, postoptimization values again showed a good positive significant correlation ( $r=0.557$ ,  $p=0.004$ ). In Group 2, no significant correlation was observed in SMWT distances and cardiac output values before and after optimization ( $r=0.094$  vs.  $r=0.347$ ,  $p > 0.05$ ).

**Conclusion:** Results of this study showed that NICOM based cardiac output measurement and optimization is practical, reliable and not operator dependent

method compared to echocardiography. Additionally, cardiac output values measured by NICOM device showed stronger correlations with SMWT distances. Therefore NICOM method can be used as an alternative for CRT optimization in selected patients.

### P1000

#### Galectin 3 predicts improvement in LV volumes after Cardiac Resynchronisation Therapy

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**Background/Introduction:** Cardiac Resynchronisation Therapy (CRT) is commonly used in the management of patients with chronic systolic heart failure (CHF). However, up to 30-50% patients with severe CHF who receive CRT derive no benefit. The exact mechanisms underlying this phenomenon are poorly understood and there are no well-established biomarkers to predict the response to CRT. It has been suggested that fibrosis, as occurs in most forms of CHF, may play a role in determining the response to CRT. Galectin 3 is a soluble  $\beta$ -galactoside-binding lectin that has regulatory roles in fibrosis, inflammation and tissue repair. Several recent clinical studies have reported an association between circulating galectin 3 levels and cardiac remodeling as well as adverse clinical outcomes in patients with CHF. However, the association between baseline galectin 3 levels and response to CRT in severe CHF has not been established.

**Purpose:** To investigate the relationship between baseline plasma galectin 3 levels and physical performance and reverse remodeling in patients undergoing CRT implantation.

**Methods:** 28 patients (aged 71.2  $\pm$  9.4) with predominantly severe CHF (70% NYHA class III or IV) and planned CRT irrespective of the aetiology of heart failure were studied. Transthoracic echocardiogram (TTE), 6-minute walk test (6MWT), maximum oxygen uptake (VO<sub>2</sub> max) and blood collection for routine biochemistry, NT pro-BNP and galectin 3 levels were performed prior to and 6 months post-CRT implantation. Galectin 3 levels were assayed with commercially available ELISA kits. Univariate analyses were performed to investigate the relationship between the measures of physical performance (6MWT and VO<sub>2</sub> max), echocardiographic measures of response to CRT (LVESV and LVEDV) and baseline galectin 3 levels. Multivariate analyses were then performed to establish the independent baseline predictors of these parameters.

**Results:** On univariate analyses, baseline galectin 3 levels were inversely correlated with baseline and end-of-study 6MWT ( $p=0.002$ ), VO<sub>2</sub> max ( $p=0.003$ ) and improvement in LVESV ( $p=0.01$ ) and LVEDV ( $p=0.02$ ). On multivariate analyses, galectin 3 remained the only independent predictor of the improvements in LVESV ( $p=0.015$ ) and LVEDV ( $p=0.02$ ), while galectin 3 ( $p=0.03$ ) and NYHA class ( $p=0.01$ ) were independent predictors of baseline VO<sub>2</sub> max after adjustment for age, gender, NT pro-BNP and NYHA class.

**Conclusion:** Plasma galectin 3 levels predict poor baseline status and are the inverse predictor of response to CRT implantation in patients with severe symptomatic CHF. Thus, galectin 3 is a promising biomarker of physical performance and response to CRT, potentially being a surrogate for myocardial fibrosis.

### P1001

#### CRT survey II

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**Background/Introduction:** CRT reduces mortality and morbidity in patients with heart failure with electrical dyssynchrony and therefore receives strong recommendations in current guidelines. However, despite these recommendations and the expanding indications for CRT, the increase in the rate of CRT has been modest across Europe. Therefore, actions to increase the awareness of the indications for CRT as well as to increase both the quality and level of care for follow-up over EHRA countries are needed.

**Purpose:** The two ESC associations, EHRA and HFA have designed the CRT Survey II, which is an 8 month snapshot Survey created to describe clinical practice regarding implantation of CRT devices in a broad sample of hospitals in ESC member countries. It should reflect changes in clinical practice due to the substantial modifications in ESC device guideline recommendations by both the HFA and EHRA Methods Patients enrolled are both those with new implantations of a CRT-P/CRT-D and upgrades. There is a one-time, site description questionnaire completed by each site. This information gathered by this questionnaire describes the organisation of

the device programme for each site and provides information useful for assessing health resource utilisation. The second and patient related electronic case report form (eCRF) is completed at each enrolment. This eCRF includes patient demographics, aetiology of heart failure, pharmacological therapy, ECG morphology and QRS duration, indication for CRT implantation, procedural details, complications, discharge status, and follow-up plans. CRT Survey II began collecting data on 1st October 2015, is currently operating in > 40 countries and should complete data collection by June 2016. Conclusion This pan-European Survey hosted by two ESC Associations will collect essential data permitting national and international benchmarking of clinical practice with regard to CRT. The data collected should provide information relevant for assessing healthcare resource utilisation, help to identify the major obstacles to implementation of CRT therapy and thus create a basis for enhancement of therapy access. Ultimately, we hope that the results will serve to increase CRT implementation for appropriate heart failure patients in Europe.

## DISEASE MANAGEMENT PROGRAMMES

### P1002

#### Acute heart failure in three disease management programs, retrospective study in colombia

Novartis Colombia S.A.

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**Introduction:** Acute heart failure is a major public health problem. However, there is little information on the clinical characteristics, management patterns and outcomes of patients with acute heart failure (AHF) in Latin America.

**Purpose:** To describe the demographics, clinical profile, comorbidity, treatment, use of resources in hospitalization, and mortality in a population of AHF patients treated in three Colombian institutions with comprehensive disease management programs from 2012 to 2014.

**Methods:** A retrospective descriptive study in which medical records were reviewed. The information was consolidated using a standard software tool, and analyzed by basic central tendency statistical measures

**Results:** The results are presented based on the sample size (n) for each of the variables. Demographics: 408 patients, 181 women, 227 men, age (67  $\pm$  16 years). Clinical Profile: reduced function 79% (n=330), preserved function 21% (n=330), etiology of heart failure: n=288 [ischemic 45%, valvular 19%, non-ischemic dilated 7%, hypertrophic 2%, chagasic 1%, others 72%], blood pressure n=407 [systolic 122  $\pm$  22 mmHg, diastolic 72  $\pm$  14 mmHg], heart rate 79  $\pm$  21 (n=407), main NYHA at the time of admission 57% NYHA III (n=260), main NYHA upon discharge 53% NYHA II (n=171), LVEF 36.4  $\pm$  17.7 (n=393), creatinine 1.4  $\pm$  1.4mg/dl (n=384), BUN 32.1  $\pm$  17.2 (n=193), BNP 2366.4  $\pm$  5546.5 (n=181), positive troponin 25% (n=150). Comorbidity: hypertension 65% (n=392), diabetes 64% (n=408), coronary artery disease 37% (n=406), atrial fibrillation, 26% (n=337), anemia 23% (n=314), chronic kidney failure 19% (n=200), COPD 18% (n=403), stroke 9% (n=269), previous hospitalization for AHF 48% (n=266). Treatment: ACE inhibitors 23% (n=383), ARB 36% (n=381), beta blockers 52% (n=383), diuretics 53% (n=314), digitalis 5% (n=314). In-hospital treatment: Inotropes [levosimendan 7% (n=408), dobutamine 6% (n=325), milirone 3% (n=326)] Vasopressors n=326 [dopamine 3%, norepinephrine 18%] Diuretics [IV 48% (n=318), PO 47% (n=198)]. Use of resources: hospital bed days 11  $\pm$  16 (n=268), ICU days  $\pm$  8 (n=268). Mortality: General death 11% (n=189), cardiovascular death 13% (n=182).

**Conclusions:** The study population is a high-risk population with a high profile of comorbidities, with an elevation of biomarkers and advanced functional class. However, hospital stay, ICU stay and mortality are similar to those reported in the literature. These data suggest that the comprehensive treatment right from the acute phase of decompensation promotes a proper use of resources and an optimum management in accordance with the guidelines.

### P1003

#### In patients with systolic dysfunction, what does being young imply?

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**Background and objectives:** Patients (P) with systolic dysfunction benefit from close monitoring, such as that provided in cardiac rehabilitation programs (CRP). We aimed to determine whether age influences their results or their efficacy.

**Methods:** We studied a cohort of 509 P. with low ejection fraction (EF) (EF < 51%) referred to a CRP between 2006 and 2014. The reason for inclusion was a recent

acute coronary syndrome (93.6%) or heart failure (4.8%). EF was calculated using the Simpson method at the beginning of the program and before the end of it. Functional status was evaluated with a treadmill exercise test. The CRP lasted for six weeks and included supervised exercise training twice a week. According to the age, P. were classified in two groups: P. under the age of 50 (n=378, 74.3%) and P. over 50 (n=131, 25.7%). We compared their baseline characteristics, functional status improvement and achievement of program's targets.

**Results:** Mean age was 42.76 years (range: 29-49) and 62.98 (range: 50-86) respectively; 88.6% (451 P) were male. Hypertension (53.7% vs 32.1%,  $p < 0.01$ ) and diabetes (27.3% vs 16.9%,  $p = 0.018$ ) were more prevalent in the over-50 group, whereas smoking was more frequent among young P. (45.6% vs 79.4%,  $p < 0.01$ ). There were no significant differences in the prevalence of dyslipemia or obesity. The rates of prescription of ACE inhibitors (80.9% vs 81.9%,  $p = 0.81$ ), betablockers (94.1% vs 96.1%,  $p = 0.40$ ), aldosterone antagonists (51.1% vs 55.1%,  $p = 0.43$ ) or ivabradine (8.9% vs 10.2%,  $p = 0.65$ ) did not differ between both groups, although there is a trend toward a more common use of diuretics in older P. (17.7% vs 11%,  $p = 0.075$ ). Considering only P. with moderate or severe systolic dysfunction (EF  $< 40\%$ ), young P. showed better functional status (9.1 vs 11.4 METs,  $p < 0.01$ ) and greater exercise capacity increase during the CRP (3.22 vs 3.88 METs increment,  $p = 0.05$ ), despite no significant differences were found in EF improvement (11.70% vs 12.41% increase,  $p = 0.632$ ). Targets were achieved in the same proportion in both groups: HbA1c  $< 7\%$  (72.7% vs 72.2%,  $p = 0.96$ ), LDL  $< 70$  mg/dL (50.8% vs 45.2%,  $p = 0.44$ ), smoking cessation (82.1% vs 77.4%,  $p = 0.37$ ) and abdominal perimeter (96.99 cm vs 98.89 cm,  $p = 0.16$ ).

**Conclusion:** Although age does not influence medical treatment or goals of a CRP, young P. with systolic dysfunction represent a group of growing importance who get the maximal benefit from these programs thanks to a greater improvement in functional status. Moreover, a long-standing correction of young patients' lifestyle is mandatory in order to improve their outcomes.

#### P1004

##### The impact of the multidisciplinary team approach on early mortality and acute cellular rejection after heart transplantation

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**Background:** In 2008, the University Hospital of Lausanne established the multi-disciplinary Heart Transplantation (HTx) team to improve quality of respective pre- and postoperative care. This study investigates its impact on mortality and morbidity early post-transplant. Methods and

**Results:** A total of 140 patients underwent HTx between 2000-8/2014 with 66 patients operated between 2000-2007 and 74 thereafter. Mean age was 53.5 years (IQR 47.3-59.8 years), 80% were males, donor/recipient gender mismatch was 38.3%, length of in-hospital stay was 34 days (IQR 26-61 days), donor age was 41 years (IQR 26-51 years); characteristics were not different between groups. In HTx recipients of 2008-2014, dilated cardiomyopathy of non-ischemic origin was less prevalent (43.2 vs 63.6%;  $p = 0.024$ ), assist device treatment was more frequent (24.3 vs. 9.1%;  $p = 0.030$ ). Cardiovascular risk factors, burden of comorbidity, and baseline hemodynamic, clinical, and echocardiographic parameters were not different between groups. In-hospital and 1-year all-cause mortality (ACM) was lower in HTx recipients of 2008-2014 (22.2 vs. 16.2%; 25.8% to 18.9%, respectively;  $p = 0.4711/0.4708$ ). Diabetes mellitus was a predictor of in-hospital and 1-year ACM in patients operated 2000-2007, acute cellular rejection (ACR) of  $\geq$  moderate grade was associated with in-hospital mortality in 2000-2007 but not in 2008-2014; mean individual grade of ACR was lower in 2008-2014 (0.2 vs. 0.65;  $p < 0.0001$ ).

**Conclusion:** The multidisciplinary HTx team approach increased the number of HTx recipients and increased quality of care in HTx with a lower mean ACR grade within the first year post-transplant, improved treatment of risk factors, and non-significant decrease of in-hospital and 1-year ACM.

#### P1005

##### Coding of acute decompensated heart failure admissions and patient enrolment in a disease management programme

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**Background:** Acute decompensated heart failure (ADHF) contributes to about 5% of all emergency hospital admissions and 27% of the total cost of all hospitalisations.

Disease management programmes are well established as the optimal management strategy for patients discharged following an acute decompensation of heart failure. Coded hospital discharge data is an important information source for research and health planning services.

**Purpose:** We sought to evaluate all admissions coded as ADHF - to assess how many of these patients were enrolled in a heart failure disease management programme (DMP) and to look at reasons for not enrolling patients. We also sought to identify any coding errors.

**Methods:** We obtained a list of all admissions to an acute tertiary hospital coded as a primary diagnosis of ADHF for a four month period. We then compared this to a list of ADHF patients identified and followed by our heart failure unit from the same hospital and same time period. We reviewed the medical records of the patients that were "missed" - i.e. not followed by our heart failure unit and investigated into the reasons for same.

**Results:** A total of 95 patients were coded as having a primary diagnosis of ADHF. Of these 62% were enrolled in a DMP. The reasons for not enrolling were: 1. Incorrect coding - a total of 7.37% were inappropriately coded as primary ADHF admissions although the admission was unrelated to ADHF 2. RIP on admission 3. Patients were dialysis dependent 4. Geographical- living too far from the heart failure unit 5. Heart failure was a secondary rather than primary diagnosis 6. Not referred to the heart failure team 7. Significant comorbidity or poor compliance impacting on ability to engage with the programme A further 6 patients were identified as having had an admission with primary ADHF during that period and not coded as same.

**Conclusions:** This highlights the level of inappropriate coding of hospital admissions which can lead to an inaccurate estimation of the burden of ADHF admissions and unreliable calculation of length of stay for ADHF admissions. It also gives insight into the activity of the heart failure unit and the patients most appropriate for a disease management programme.

#### P1006

##### Heart failure patient post discharge follow up by phone calls by nurse call center 24/7/365

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**Purpose:** Since June 2013 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. We try 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 8 questions which depending on the answer given will determine different actions, as per protocol. • Correct answers: Advice regarding, diet, exercise, weight and indications to take the medications prescribed correctly. • Adherence or knowledge problems: New appointment with the Nurses in the community to see the patient in their homes in the next 24-48h. • Symptoms or drug side effects: Nurses arrange an appointment with their GPs to see the patient in their homes in the next 24-48h. • Severe symptoms of Congestive Heart Failure: Nurses will contact emergency services. Nurses also remind the patient of their next scheduled appointment to see their GPs.

**Results:** Average age 80 years of age and 48% were women. 60% of patients with preserved ejection fraction. We have performed 600 phone calls: 35% generated an appointment with their nurses in community as aspects of adherence to treatment and self caring habits needed reinforcing. 22% required an early appointment with their GP due to medication side effects or weight gain. 9% required emergency services due to dyspnea at rest or temperature and no specific actions were performed after 32% call phones.

**Conclusions:** Problems related to adherence to treatment were the ones that generated most alarms. The 72h follow up phone call helps us to improve patient adherence after discharge. 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.

#### P1007

##### Verification of guidelines-adherent medical therapy in patients with sinus rhythm hospitalised due to worsening of heart failure

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**Background:** Hospitalization of patients with heart failure (HF) is a good opportunity to re-evaluate patient care including optimizing present and planning future management. The aim of our study was to analyze medical management in patients with sinus rhythm hospitalized due to worsening of HF, who were included in an ongoing Optimize Heart Failure Care program.

**Methods:** The Optimize Heart Failure Care program is an international, multi-center patient support program based on pre-discharge patient education, pre- and post-discharge check-lists over a period of 12 months. This analysis included data collected over 3 months from 317 patients (mean age  $62.9 \pm 0.6$  years, 70% male) with sinus rhythm hospitalized due to worsening of HF, NYHA II-IV (mean  $2.81 \pm 0.03$ ), left ventricular ejection fraction (LVEF)  $<40\%$  (mean  $31.1 \pm 0.5\%$ ), mean systolic/diastolic blood pressure  $128.6 \pm 1.3/80.8 \pm 0.7$  mm Hg and mean heart rate (HR)  $85.1 \pm 1.0$  bpm.

**Results:** The prescription rate of angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs), beta-blockers (BBs) and mineralocorticoid receptor antagonists (MRAs) before discharge from hospital were 92.4%, 82.6% and 90.5%, respectively. Diuretics and digoxin were recommended in 98.8% and 17.7% of patients with HF, respectively. However, despite high baseline HR, ivabradine was prescribed in 25.5% of patients with HF only. Interestingly, baseline HR in this group of patients was significantly higher than in patients who did not receive ivabradine ( $91.2 \pm 1.7$  bpm vs.  $83.4 \pm 0.9$  bpm,  $p < 0.05$ ). There were no differences in terms of age, sex, NYHA functional class, LVEF between the groups of patients receiving and not receiving ivabradine. Thus, ivabradine was prescribed in patients with excessively high HR only. On the other hand, ivabradine therapy was characterized not only with good safety, but also with a significant reduction of the rate of repeated hospitalizations after 3 months of follow-up (3.7% versus 17.7% in patients without ivabradine therapy,  $p < 0.05$ ).

**Conclusion:** Despite the high adherence among cardiologists to prescribing neurohumoral antagonists and diuretics in patients hospitalized due to worsening of HF, additional efforts are needed in order to improve the adherence to HR lowering therapy with ivabradine.

#### P1008

##### NT-proBNP guided care versus standard care for heart failure in outpatient setting

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It remains unclear whether treating chronic heart failure (HF) in outpatient setting based on the follow-up with serial NT-proBNP evaluation would be associated with better outcomes compared to standard follow-up alone. The goal of the study was to evaluate whether patients (pts) with HF would benefit from NT-proBNP guided care (GC), compared to standard care (SC) with LVEF but not NT-proBNP serial controls in outpatient setting. In a prospective single-centre trial, 186 subjects (age:  $63 \pm 12$  years, man/female: 90/96, LVEF:  $<40\%$ , mean  $29 \pm 10\%$ ) with NYHA class II-IV due to left ventricular systolic dysfunction were randomized 1:1 to receive SC for HF or GC (NT-proBNP evaluation on regular basis at each visit) with a goal of keeping pts compensated longer reducing numbers of hospitalizations and lowering the biomarker plasma levels. The primary endpoint was total hospitalization events in both groups compared using generalized estimating equations. Secondary endpoints included effects of the each type of care on LVEF and NT-proBNP levels at the end of follow-up. Echocardiographer making the assessment of LVEF was blinded of NT-proBNP levels.

Through a mean follow-up period of  $18 \pm 2$  months, GC significantly improved hospitalization-free survival compared with SC (68 events vs. 110 events, HR = 0.71; 95% CI 0.55–0.98;  $P = 0.04$ ). Kaplan-Meier curves demonstrated significant differences in time to first hospitalization event, favouring GC ( $p = 0.02$ ). No age and sex interactions were found, with elderly pts (age  $\geq 65$ ) benefitting similarly from GC as younger subjects (age  $< 65$ ). Although there was no significant difference in LVEF improvement at the end of follow-up in both groups neither in interaction ( $32 \pm 8\%$  in SC group,  $p = 0.2$  vs.  $36 \pm 9\%$  in GC group,  $p = 0.3$ , interaction  $p = 0.5$ ), the mean NT-proBNP levels, achieved at the end of follow-up period in GC group were significantly lower against those in SC group ( $1,254 \pm 480$  ng/l vs  $3,824 \pm 560$  ng/l,  $p = 0.01$ ).

NT-proBNP-guided therapy can improve long-term hospitalization-free survival of HF pts versus standard therapy in outpatient setting. Possibly, this attributes to on time and appropriately intensified complex HF medication based on the dynamic changes in serial NT-proBNP measurements. It argues, that individually tailored and

targeted, but not "blind" due to symptoms or LVEF results carpet bombing with drugs, approach is appropriate for HF pts in outpatient setting.

## DRUG THERAPY, OTHER

#### P1009

##### Efficacy of trimetazidine on functional capacity in symptomatic patients with moderately reduced or left ventricular dysfunction and CAD: a subgroup analysis of the VASCO trial

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Trimetazidine (TMZ) is a metabolic agent of proven efficacy in improving functional capacity in patients with angina, in monotherapy or combined with beta-blockers. VASCO was a 12-week multicentre randomised double-blind controlled trial aimed to assess the anti-anginal efficacy and safety of modified-release TMZ (TMZ 70 mg/d, TMZ 140 mg/d) on top of background therapy with beta-blockers in patients with coronary heart disease. The trial demonstrated that TMZ is effective in improving total exercise duration (TED) measured by the treadmill exercise stress test (ETT) in symptomatic angina patients. Therefore, we conducted a retrospective subgroup analysis of the VASCO trial, aimed at further investigating the efficacy of the two doses of TMZ on TED and time to 1-mm ST segment depression (T1), in the subgroup of symptomatic patients with moderately reduced or impaired left ventricular function. TED significantly increased both in the group allocated to TMZ 140 mg/d than placebo ( $p = 0.004$ ), and in the group allocated to TMZ 70 mg/d than placebo ( $p = 0.01$ ). These improvements were dose-dependent with a greater TED variation observed in TMZ 140 mg/d than in TMZ 70 mg/d. In conclusion this post-hoc analysis of the VASCO study confirms the effectiveness of TMZ in improving exercise capacity in patients with moderately impaired and in patients with left ventricular dysfunction and coronary artery disease.

#### P1010

##### Pharmacological treatment of chronic heart failure during cardiac resynchronization therapy

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**Background:** Cardiac resynchronization therapy (CRT) is associated with improved morbidity and mortality in patients with chronic heart failure (HF). Optimal medical therapy also plays an important role for CHF patients prognosis and quality of life.

**Purpose:** To evaluate pharmacological treatment changes of HF patients during 1-year follow-up of CRT.

**Methods:** We evaluated 85 consecutive HF patients pharmacological treatment during 1-year follow-up of CRT. Medication consumption data were assessed before CRT, at the time of hospital discharge following CRT implantation and 1-year follow-up visit. Statistical analysis was performed using SPSS version 21.0.

**Results:** Beta-blockers were used in 81.2% of patients before CRT, consumption increased after CRT implantation (96.5% at 1-year follow-up visit) ( $p < 0.002$ ). Angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB) consumption and dose didn't changed statistically significant during study. The average dose of spironolactone changed statistically significant comparing spironolactone dose before CRT with the discharge from the hospital period ( $p = 0.02$ ). The use of diuretics was significantly higher after CRT device implantation, compared with period before CRT from 62.4% to 84.7% - at discharge and at 1-year follow-up visit ( $p < 0.001$ ), but doses of torsemide hasn't changed statistically significant, comparing the period before CRT with both, hospital discharge ( $p = 0.5$ ) and 1-year follow-up periods ( $p = 0.8$ ). Cardiovascular medications consumption was significantly lower before CRT  $4.6 \pm 2.1$ , compared with discharge  $5.6 \pm 1.8$  ( $p < 0.001$ ) and follow-up  $5.5 \pm 1.8$  ( $p < 0.001$ ) periods.

##### Conclusions:

1. Beta-blockers, ACEI and diuretics were the most frequently used medications.
2. Beta-blockers consumption increased after CRT implantation.
3. The use of diuretics was significantly higher after CRT device implantation, but average dose of the loop diuretic after CRT remained almost the same.
4. Cardiovascular medications consumption was significantly lower before CRT.

#### P1011

##### Effect of levosimendan on left and right ventricular function in patients with acute and chronic heart failure: a review of echocardiographic studies

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**Background:** Levosimendan infusion induces a rapid improvement in haemodynamic parameters in patients with congestive heart failure (HF) with maximal effects occurring 1-3 days after starting the infusion, but the effects are sustained for up to at least a week, thanks to its long-lived metabolite, OR-1896. According to the recent ESC guidelines, i.v. infusion of levosimendan may be considered to reverse the effect of beta-blockade if beta-blockade is thought to be contributing to hypoperfusion (Class IIb, Level of Evidence C). In the recent literature, there has been interest in the use of i.v. levosimendan in chronic advanced HF, also for planned repetitive use to potentially avoid acute decompensation and frequent rehospitalisation.

**Purpose:** To summarize current knowledge on the effects of levosimendan therapy on the echocardiographic indexes of systolic and diastolic left ventricular (LV) and right ventricular (RV) function and to present future prospects for the effects of this drug on myocardial deformation studied by a newer echocardiographic technique of speckle tracking echocardiography (STE).

**Methods:** We reviewed all the previous studies published so far about the effects of levosimendan in patients with acute and chronic heart failure on echocardiographic parameters of systolic and diastolic biventricular functions.

**Results:** Echocardiographic studies have shown improved LV and RV systolic and diastolic function in HF; levosimendan therapy produced beneficial effects via the improvements in left ventricle ejection fraction (LVEF), mitral annular plane systolic excursion (MAPSE), the E/A ratio, early diastolic transmitral flow peak wave/early diastolic tissue Doppler velocity (E/e') ratio, LV wall stress and left atrial performance.

**Conclusion:** Levosimendan has shown positive effects in a range of conditions requiring inotropic support, not only on LV impairment but also on RV dysfunction which often complicates advanced LV HF.

### P1012

#### Two drugs comparison of bisoprolol in efficiency influence on the heart rate from a position of pharmacoeconomics

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**Objective:** To compare the efficiency of two drugs bisoprolol (original and generic) on the effects on heart rate (HR). To perform clinical and economic analysis with using the method of "cost-effectiveness" (CER).

**Materials and methods:** 60 patients with coronary artery disease (CAD) were studied. Patients of group A received the original bisoprolol, patients in group B - generic. All patients were matched for baseline dates ( $p > 0.05$ ). Treatment correction was performed on the 3rd and 14th day. Target HR was considered as 60 b.p.m or less. Ivabradine (Coraxan, Servier, France) was administrated to main therapy in the cases of target HR absence and there was not opportunity to increase the dose of beta-blockers (BAB). BAB dose was picked individually with focusing on HR, blood pressure level, tolerance and efficacy. HR was evaluated on electrocardiogram at baseline and after 6 weeks therapy. Cost/efficiency was calculated as  $CER = DC/Ef$ , where CER is cost-effectiveness result; DC - direct costs; Ef- therapy efficiency.

**Results:** Significant HR reduction ( $p < 0.05$ ) was in both groups by 6 therapy weeks. However, it was found that the original bisoprolol decreases HR more significantly in comparison with the generic in assessing the degree of HR ( $\Delta\%$  HR). In group A  $\Delta\%$  HR was  $16.55 \pm 7.55\%$ , in group B  $12.5 \pm 7.5\%$  ( $p < 0.05$ ). Ivabradine was administrated to 4 patients (13.3%) in the group A, in group B to 7 patients (23.3%). The treatment cost for HR reduction on 1 heart beat was 48.46 rubles in group A, in group B - 69.40 rubles during 6 weeks therapy.

**Conclusion:** It is more efficiently to use the original bisoprolol in patients with CAD from the pharmacoeconomic analysis.

### P1013

#### How many patients with chronic heart failure will be eligible for LCZ696 in the community?

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**Background:** LCZ696 is a new class of agent for the treatment of heart failure (HF) but it is unknown how many patients might be eligible for treatment with it in clinical practice. The product is licensed for use in patients with symptomatic chronic heart failure with reduced ejection fraction (HFrEF); there are few contra-indications other than pregnancy. However, the PARADIGM clinical trial required that patients tolerated enalapril 10mg bd and had an elevated NT-proBNP ( $\geq 600$ ng/L or  $\geq 400$ ng/L if hospitalized in prior 12 months).

**Methods:** Between 2001 and 2014, all patients referred to a community HF clinic with suspected HF were enrolled in a prospective observational study.

**Results:** Of 6131 referrals, 1,980 patients had HFrEF, of whom 1,396 had NTproBNP measured concurrently and would have been eligible for LCZ696 according to its license. However, only 379 patients were on target doses of ACE-I or ARB at baseline and, of these, only 45% ( $n = 172$ ) fulfilled the PARADIGM criteria; lack of limiting symptoms (32% in NYHA I) and NT-proBNP  $< 600$ ng/L (49%) were the commonest

reasons for exclusion. At 4 and 12 month follow-up visits, only a few new patients became eligible for LCZ 696 (22 and 13 patients, respectively). When the analysis was expanded to patients with HFREF on any dose of ACE-I or ARB at the baseline visit ( $n = 1,144$ ), 570 patients were potentially suitable for LCZ696 treatment, but the number fell to 360 when restricted only those already receiving beta-blockers.

**Conclusions:** The number of patients who require switching from LCZ696 will depend greatly on whether clinicians follow the licensed indication or the PARADIGM inclusion criteria. We await with interest the ESC guidelines on this issue.

### P1014

#### The ACEi switchback study

Servier

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**Background/Introduction:** ACE inhibitors (ACEi) have been studied extensively in the treatment of heart failure (HF) and have been shown to be beneficial in all its stages. Studies with the use of ARBs in chronic HF have not shown the equivalent results of ACEi trials. However, many patients are on ARB pharmacotherapy and some patients appear to have never been treated with an ACEi. Registry data have shown very few patients had absolute contraindications to ACEi. Guidelines recommend ACEi first line to treat HF as they reduce morbidity and mortality, hence all HF patients should be on ACEi therapy unless clear contra-indications exist.

**Purpose:** To assess among patients on ARBs the percentage of these patients who are truly ACEi-intolerant by determining the percentage who will tolerate a switch to an ACEi.

**Methods:** HF patients with indication for ACEi but on an ARB (no absolute contraindication to ACEi) were enrolled from 6 HF clinics in Canada. These patients had LVEF  $\leq 35\%$ , NYHA class I-IV, treated with beta-blockers as well as followed in HF clinic and stable for  $> 3$  months (except diuretic dose). Patients with documented intolerance with prior ACEi use, were excluded candidates from this study. Enrolled patients were switched from ARB to ACEi (perindopril); dosage was determined by ARB dosage. Patients were instructed to watch for ACEi side effects and given a contact to call in the event of side effects. Perindopril was stopped if abnormalities in renal function ( $> 25\%$  change in creatinine value), kalemia ( $> 5.2$ mmol/L) or important adverse events occurred. The primary end-point was medication tolerance recorded at 3-6 months post-switch. Patients who continued on ACEi beyond 3 months were considered a positive SwitchBack patient. Results 65 HF patients were enrolled from the 6 HF clinics. 48 patients were included in the preliminary analysis. 71% of the patients analyzed were tolerating Perindopril at 3-6 months post-switch. The main reason for intolerance to perindopril at 3-6 months was cough.

**Conclusion:** These preliminary results are showing that most HF patients who were on ARB were not true ACEi-intolerant as once switched back on the ACEi perindopril, they were tolerating the drug after 3 months.

### P1015

#### Assessment of the understanding of a standardized medication plan by patients with chronic heart failure

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**Background/Introduction:** A medication plan (MP) template has been implemented by national law as part of the German Action Plan for Medication Safety issued by the Federal Ministry of Health. The MP depicts all medicines taken including active ingredient, brand name, strength, form, dosage, unit, instructions for use, and indication. However, patients' understanding of a MP has never been explored in detail.

**Purpose:** To evaluate the understanding of the national MP in  $n = 50$  patients with the diagnosis of chronic heart failure (CHF) compared to  $n = 40$  general internal medicine (GIM) patients, each taking  $\geq 5$  drugs regularly.

**Methods:** We developed an "Evaluation Tool to test the handling of the Medication Plan" (ET-MP) that rates patients' medication management skills from 0-100%. The ET-MP is based on an individual test providing the patient with a standardized MP listing 6 drugs with different morning/noon/afternoon/at bedtime doses. Patients were asked to fill a pillbox according to the MP for 2 days. The pillboxes were photographed and both days rated by the ET-MP. The cut-off, distinguishing if patients understand the medication regimen, was set at 90%. For the CHF patients, we also tested for signs of depression (PHQ-9), level of selfcare (EHFScB-9), and impaired cognitive function (Mini-Cog). The study was approved by the local ethics committees.

**Results:** Both cohorts were comparable with a mean ( $\pm$  SD) age of  $69 \pm 13$  years and they took  $8 \pm 3$  drugs chronically. 53% were male, 33% lived alone. The CHF patients (78% NYHA I/II, LVEF  $51 \pm 14\%$ ) had a lower level of education ( $p = 0.004$ ). The mean ( $\pm$  SD) ET-MP Score for the CHF cohort was  $78 \pm 23\%$  and  $86 \pm 19\%$  for the GIM patients ( $p = 0.16$ ). 38% of the CHF patients achieved a score  $>90\%$  compared to 50% of the GIM cohort ( $p = 0.29$ ). Overall, we found a moderate correlation between the score and the level of education ( $r = 0.45$ ) and age ( $r = -0.46$ ), both  $p < 0.001$ , but not living alone ( $p = 0.19$ ). Cognitive impaired CHF patients (46%) achieved a lower score ( $p = 0.03$ ). Signs of depression (PHQ-9  $\geq 10$ : 26%) or a lower level of self-care behaviour (EHFScB-9 scale  $<$  median) were not associated with a lower score.

**Conclusions:** The ET-MP is suitable to explore CHF patients' understanding of a medication plan (MP) but less than 50% reached a score  $>90\%$ . Higher age ( $>75$ y) and lower level of education ( $< 10$ y) but not the diagnosis of CHF per se correlate with lower medication management skills. Apart from providing a written MP, a significant number of CHF patients might benefit from further counselling and continuous care e.g., via weekly prepared dosing-aids.

#### P1016

##### Pre-hospital treatment of acute heart failure - vasodilators in combination with diuretics or diuretics alone?

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**Background:** The most common drugs used in patients with acute heart failure (AHF) are intravenous loop diuretics. The combination of drugs with vasodilatory action (nitrates) with diuretics (furosemide) is very challenging and especially data from early administration in pre-hospital setting are poor.

**Purpose:** We have investigated whether adding of intravenous nitrate to furosemide in pre-hospital area has additional effect on short and mid-term outcome in patients with suspicion for AHF.

**Methods:** We used data from CARE PRE-H registry (aCute heARt failurE in PRE-Hospital care), multi-centric observational study performed by 21 ambulance teams of the emergency medical system in a region with the total population of 1.17 million inhabitants. During the study period between January 2010 and December 2011 overall 1118 patients with suspected AHF were enrolled. Propensity score method was used to compare balanced population of 211 patients treated with intravenous nitrate (isosorbide dinitrate, glyceryl trinitrate) in addition to furosemide, to 211 patients receiving furosemide alone. Assessed were 30-day up to 3-year overall mortality.

**Results:** Compared populations (nitrates and furosemide vs. furosemide alone) were balanced (with no statistically significant difference) in terms of age (78.0 vs. 79.0

**Conclusion:** Pre-hospital administration of intravenous nitrate when added to loop diuretic furosemide did not significantly changed outcome of patients with suspected AHF, nevertheless trend for lower mortality rates and need of tracheal intubation in these patients was observed. These findings require further research in larger studies.

#### P1017

##### Dose reduction and contraindication of the novel oral anticoagulant in patients with heart failure and reduced ejection fraction during a follow-up of 27 month. Data from CORONA Trial

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**Aim:** The non-vitamin K antagonist oral anticoagulants (NOACs) exhibit varying degrees of renal elimination. Their dose should be altered by renal function. Patients with heart failure (HF) often have fluctuating renal function. We estimated the need for dose adjustment in patients with HF using data from the Controlled Rosuvastatin Multinational Trial in Heart Failure (CORONA)

**Methods:** We calculated creatinine clearance using Cockcroft-Gault formula in 779 patients with AF at baseline, 15 and 27 months. The proportion of patients requiring NOAC dose reduction or discontinuation was estimated according to EU prescribing guidance.

**Results:** The estimated proportion of patients requiring dose reduction at baseline and during follow-up according to EU guidance was respectively: apixaban 9.7% and 9.3%, dabigatran 26.3% and 5.5%, rivaroxaban 34% and 17% and edoxaban both 35% and 16%. US guidance yielded similar proportions in reductions for all NOACs except dabigatran, for which 3.7% and 7.5% of patients would need dose reduction. With the exception of EU guidance for dabigatran and US for edoxaban, the NOACs are only contraindicated with creatinine clearance less than 15 ml/min, which was rare in this trial population.

**Conclusion:** Renal function is often impaired and fluctuates in patients with HF, necessitating NOAC dose reduction. The proportions of patients requiring dose reduction varying substantially between the different NOACs. Physicians should carefully consider renal function when prescribing NOACs and ensure adequate monitoring of renal function

n = 779 (% relative to baseline)	Dose reduction at baseline	Dose reduction following baseline	Dose reduction overall including baseline	Contraindication at baseline	Contraindication overall including baseline
Europe					
Apixaban	76 (9.7)	73 (9.3)	149 (19.1)	0 (0)	4 (0.5)
Dabigatran	205 (26.3)§	43 (5.5)*	248 (31.8)§	29 (3.7)§	88 (11.3)§
Rivaroxaban	267 (34.3)§	129 (16.5)§	396 (50.8)§	0 (0)	4 (0.5)
Edoxaban	275 (35.3)§	127 (16.3)§	402 (51.6)§	0 (0)	4 (0.5)
US					
Apixaban	66 (8.4)	57 (7.3)	123 (15.8)	0 (0)	4 (0.5)
Dabigatran	29 (3.7)§	59 (7.5)	88 (11.3)*	0 (0)	4 (0.5)
Rivaroxaban	267 (34.3)§	129 (16.5)§	396 (50.8)§	0 (0)	4 (0.5)
Edoxaban	267 (34.3)§	129 (16.5)§	396 (50.8)§	34 (4.3)§	64 (8.2)§

Dose reduction and contraindication at baseline and follow-up according to EMA and FDA recommendations \* $< 0.05$  vs apixaban § $< 0.001$  vs apixaban

years), gender (male 48.8% vs. 54.0%), medical history (coronary artery disease 51.7% vs. 45.0%, diabetes 39.8% vs. 40.8%, hypertension 82.9% vs. 84.8%), initial blood pressure (systolic/diastolic - 160/90 vs. 160/90 mmHg) and oxygen saturation values (85.0% vs. 84.0%), incidence of pulmonary oedema (64.5% vs. 67.8%) and the need of tracheal intubation (2.8% vs. 4.3%). Only higher heart rate was observed in subgroup receiving nitrates (107.0 vs. 100.0 beats/min,  $p = 0.025$ ). Short-term (30-day) mortality did not significantly differ in compared groups (21.3% vs. 21.8%,  $p = NS$ ). A trend to lower 1-year mortality (42.2% vs. 46.4%) and 3-year mortality (63.6% vs. 69.1%) was observed in population receiving nitrates, nevertheless without statistical significance ( $p = NS$ ).

#### P1018

##### A novel oral partial adenosine A1 receptor agonist for the treatment of heart failure: safety and tolerability in healthy volunteers pretreated with beta-blocker

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**Introduction:** Activation of adenosine A1 receptors (A1R) is a key mechanism for protecting the heart from injury and energetic imbalance in various pathophysiological conditions like heart failure (HF). The development of A1R agonists for HF is supported by encouraging preclinical evidence in animal models. However, therapy with a full A1R agonist is limited by side effects, notably higher degree AV blocks, in particular with the concomitant use of beta-blocker. A partial A1R agonist might overcome these undesired effects, while preserving the beneficial potential. This is the first study to investigate the safety and tolerability of BAY 1067197, a novel oral partial A1R agonist, in healthy subjects pretreated with beta-blocker.

**Methods:** 11 male healthy volunteers (mean age  $33 \pm 8$  years) were pretreated with 95mg metoprolol-succinate (MS) alone for 6 consecutive days followed by a co-administration of placebo on day 7 and a single dose of 50mg BAY 1067197 at day 8. Blood samples were collected for safety monitoring and pharmacokinetics. Standard ECG, 48h Holter ECG and vital signs were monitored. Results After co-administration of BAY 1067197, all subjects' Holter ECG recordings were interpreted as normal by a central ECG reader. The heart rate (HR) measured over 1 minute was slightly lower following MS+BAY 1067197 vs. MS + placebo (HR -1.1 beats/min,  $p = 0.06$ , ANCOVA), whereas the PR interval corrected for HR was not significantly different ( $p \geq 0.13$ , ANCOVA). No changes in blood pressure (BP) were observed in the BAY 1067197 treatment arm. BAY 1067197 co-administration had no effects on MS exposure. Conclusion The novel partial A1R agonist BAY 1067197 was safe and well tolerated following a single oral dose co-administered with a beta-blocker. Notably, no higher degree AV block, relevant decreases in HR or BP were observed. We conclude that co-administration of BAY 1067197 with a beta-blocker does not increase the risk of AV blocks in healthy volunteers. The development of a partial A1R agonist may overcome the undesired effects of a full A1R agonist on AV conduction. The safety of co-administration with a beta-blocker needs to be confirmed in patients with HF and for longer treatment duration.

## HORMONES / NEUROHUMORAL REGULATION

### P1019

#### The potential role of 123I-MIBG imaging in left ventricular non-compaction

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**Introduction:** Left ventricular noncompaction (LVNC) is characterized by excessive and prominent myocardial trabeculations associated with deep recesses. The clinical spectrum is very wide, including ventricular arrhythmias and sudden cardiac death (SCD). Algorithms for SCD stratification are lacking, especially in those with preserved ejection fraction. 123I-MIBG imaging evaluates sympathetic nervous system function and has been shown to lead to better risk stratification in heart failure and coronary artery disease, with lower heart/mediastinal ratio (HMR) and higher myocardial washout rate (WR) being associated with worse outcome. The use of 123I-MIBG imaging in LVNC has not been systematically studied.

**Purpose:** We aimed to evaluate cardiac adrenergic activity in LVNC patients and compare it to dilated cardiomyopathy (DCM) patients and respective family members.

**Methods:** We evaluated 6 patients with LVNC and no left ventricular dysfunction (LVD), 10 with LVNC+LVD, 27 with DCM and 14 family members of DCM patients, with no LVD (unknown genetic background). For 123I-MIBG imaging anterior projection planar images of the thorax were obtained, 20min and 4h after intravenous administration of 370 MBq of 123I-MIBG (early and late images). HMR and WR were calculated twice by 2 independent blinded observers; the final result was the mean of the average of each operator.

**Results:** Patients with isolated LVNC presented the highest late HMR ( $2.11 \pm 0.24$  vs  $1.65 \pm 0.15$  vs  $1.74 \pm 0.27$  vs  $1.93 \pm 0.15$ ,  $p = 0.000$ ) and the lowest WR ( $22.5 \pm 11.6$  vs  $39.9 \pm 10.4$  vs  $42.6 \pm 11.5$  vs  $31.8 \pm 9.3$ ,  $p = 0.000$ ) compared to patients with LVNC+LVD, DCM and no LVD, respectively. Early HMR results did not present significant differences, although there was a trend in the same direction of late HMR results. Only 17% of patients with isolated LVNC presented abnormal results of WR (> 30%) comparing with 80%, 85% and 64% of patients with LVNC+LVD, DCM and no LVD, respectively. However, when analyzing 123I-MIBG parameters according to the presence of LVNC in patients with and without LVD (isolated LVNC vs no LVD / LVNC+LVD vs DCM), we found no significant differences.

**Conclusion:** In our group of patients, 123I-MIBG imaging indexes were not significantly affected by the presence of LVNC, beyond left ventricular ejection fraction. Additionally, in LVNC patients with no LVD, we found markers of better cardiac adrenergic activity than in family members of DCM patients, a result that warrants further investigation.

### P1020

#### Sympathetic cardiac activity evaluated by 123I-MIBG scintigraphy in left ventricular non-compaction patients

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**Introduction:** Left ventricular non-compaction (LVNC) is an increasingly recognized cardiomyopathy, characterized by a distinctive spongy appearance of the myocardium. The clinical presentation is very heterogeneous and includes heart failure, thromboembolic events, conduction disturbances, supraventricular or ventricular arrhythmias and sudden cardiac death (SCD). Cardiac 123I-MIBG scintigraphy evaluates adrenergic activity and has been shown to be related with outcomes in heart failure and ischemic coronary artery disease, with lower heart/mediastinal ratio (HMR) and higher myocardial washout rate (WR) being associated with worse prognosis. However, the usefulness of 123I-MIBG cardiac uptake imaging in the setting of LVNC has not been systematically studied.

**Purpose:** We aimed to evaluate cardiac adrenergic activity, using 123I-MIBG imaging, in LVNC patient.

**Methods:** We evaluated 16 patients (50% men, mean age  $47 \pm 17$  years) with LVNC, assessed by cardiac magnetic resonance (CMR), which underwent 123I-MIBG cardiac uptake imaging. For 123I-MIBG scintigraphy, anterior projection planar images of the thorax were obtained 20 minutes and 4 hours after intravenous administration of 370 MBq of 123I-MIBG (early and late images). HMR and WR were calculated twice by 2 independent blinded observers, with the final results being the mean of the average of each operator.

**Results:** Mean early and late HMR and WR were  $1.81 \pm 0.21$ ,  $1.82 \pm 0.29$  and  $33.4 \pm 13.6\%$ , respectively. Ten patients presented left ventricular (LV) dysfunction (mean ejection fraction and LV end-diastolic volume of  $36 \pm 8\%$  vs  $66 \pm 4\%$ ,  $p = 0.000$ , and  $123 \pm 35\text{mL}$  vs  $90 \pm 15\text{mL}$ ,  $p = 0.067$ , respectively). There was no significant differences in the age of patients of both groups  $53 \pm 17$  vs  $38 \pm 14$  years,  $p = 0.093$ , in patients with and without LV dysfunction, respectively. Early and late HMR were significantly lower in patients with LV dysfunction ( $1.71 \pm 0.18$  vs  $1.97 \pm 0.16$ ,  $p = 0.011$  and  $1.65 \pm 0.15$  vs  $2.11 \pm 0.24$ ,  $p = 0.000$ , respectively) and WR was higher ( $39.9 \pm 10.4$  vs  $22.5 \pm 11.6$ ,  $p = 0.008$ ). Late HMR was correlated with age ( $r = -0.502$ ,  $p = 0.047$ ) and both late HMR and WR were correlated with LVEF ( $r = 0.686$ ,  $p = 0.005$ ;  $r = -0.688$ ,  $p = 0.005$ , respectively) and BNP levels ( $r = -0.635$ ,  $p = 0.036$ ;  $r = 0.661$ ,  $p = 0.027$ , respectively).

**Conclusion:** In our group of LVNC patients, the presence of LV dysfunction was associated with sympathetic denervation, usually present in severe forms of heart failure. Late HRM and WR were associated with other prognostic factors such as left ventricular ejection fraction and BNP. These findings are in accordance with those found in other forms of cardiomyopathies/heart failure conditions.

### P1021

#### Potential prognostic role of chromogranin a in patients with systolic heart failure: correlation with plasma levels of natriuretic peptide and left ventricular function

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In patients with chronic heart failure plasma chromogranin A (CgA) concentrations are increased and represent an independent prognostic indication of mortality. Recently the measurement of some CgA fragments has been set up in our Institute: compared to intact CgA, single fragments seem to yield a different pathophysiological role in different diseases. In this study the potential correlation between plasma concentration of CgA and its dosable fragments with ejection fraction (EF) and proBNP plasma levels in patients with systolic heart failure was evaluated. 77 patients (54 males, age  $72.5 \pm 10$  years) with systolic heart failure (EF < 45%) (24 post-ischemic) were studied. Patients were NYHA class I (10 patients), class IIA (30 patients), class IIB (21 patients), class III (16 patients), on optimal therapy with  $\beta$ -blockers, ACE-inhibitors/ARBs, diuretics and, if necessary, anti-aldosterone drugs and digoxin. In all patients one blood sample was collected in basal conditions and proBNP, CgA and its fragments (non processed CgA or Cg439, Cg436, Cg373, Cg76, fragments lacking C-terminal or FRs, Cg439+Cg436, total CgA, N-terminal fragmentation index, C-terminal fragmentation index, and Cg373/Cg439 and Cg373/Cg76 ratios) were measured. On the basis of the recognised effect of PPI therapy and aging on CgA plasma levels (and the effect of aging on proBNP plasma concentration), age (in years) and PPI therapy (as a dichotomic variable) have been inserted as control variables in each model. proBNP showed significant associations with basal levels of Cg76 (0.156,  $p$ -value < 0.001), FRs (0.118,  $p$ -value = 0.031), total CgA (0.107,  $p$ -value = 0.038), C-terminal fragmentation index (-0.017,  $p$ -value = 0.040) and Cg373/Cg76 ratio (-0.076,  $p$ -value = 0.005). Unlike proBNP, no CgA fragment but Cg373/Cg439 ratio (-0.022,  $p$ -value = 0.020) was significantly associated with EF. In conclusion, total CgA plasma levels are significantly associated with proBNP, but not with EF. Considering the significant association

between proBNP and EF, the non-significant correlation between the absolute levels of CgA fragments and EF suggests that the evaluation of CgA and its fragments could be an independent and complementary marker to proBNP, as it is probably released through pathophysiological mechanisms which are different from other well-known mechanical and neuro-humoral phenomena involved in heart failure onset and progression.

#### P1022

##### Subclinical hypothyroidism(SCH) as a risk factor in elderly patients with chronic heart failure(CHF) -still a challenge for clinical practice

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**Background:** Subclinical hypothyroidism (SCH), defined as an isolated elevation of thyroid-stimulating hormone (TSH) levels (>5.0mIU/L) with a normal free thyroxine (fT4) level, became a common disorder, with a strong impact on the cardiovascular diseases outcome. The prevalence of SCH is relatively high, ranging from 4% to 20% in the adult population, more often in women and elderly people.

**Purpose:** This study was undertaken to assess the prevalence of SCH in elderly with chronic heart failure (CHF) and the relationship between SCH and clinical, biomolecular, echocardiographic and echovascular parameters.

**Methods:** Data were collected on 874 patients, aged >65 years (mean age 73 years), women 63%, admitted to our hospital with the clinical syndrome of CHF. The New York Heart Association (NYHA) heart failure classification on admission was: 62% of patients had class IV, 25% had class III criteria and 13% met class II. Exclusion criteria were: known previous thyroid diseases, amiodarone therapy, atrial flutter and fibrillation. Among the analyzed cases, 52% had heart failure (HF) resulting from coronary artery disease, 11% had HF attributable to valve disease, 9% had a dilated cardiomyopathy and 28% had HF as a result of arterial hypertension. In each patient measurement of ejection fraction (EF) was performed by the quantitative 2D(biplane Simpson) method and all cases underwent pulsed-wave Doppler examination of mitral inflow for diastolic evaluation, as well as carotid artery intima-media thickness measurements. Based on TSH level, patients were divided into two groups: group I, with SCH and CHF (10.8%), comprised 94 cases and group II, without SCH (89.2%), comprised 780 cases. The correlations were performed using Student's t-test. Results. Patients in group I were, compared with those in group II, older, more often women, had higher body mass index, higher prevalence of diabetes, higher systolic blood pressure, higher levels of serum lipids and higher serum creatinine values ( $p < 0.05$ ). The CHF and SCH were associated more frequently with class III and IV NYHA and with a lower EF, compared with group with normal TSH ( $p < 0.001$ ). Also, patients in group I had a higher index of intima-media thickness of carotid artery and more atheroma plaques "at risk".

**Conclusions:** The presence of SCH (10.8% in our study) was associated for sure with a worse status of patients in CHF, but SCH could represent a potentially modifiable risk factor. The current determination of TSH threshold levels for the treatment of SCH remained a clinical controversy and the decision to treat or not to treat a SCH patient with CHF is still a challenge for clinician, in the light of known risk of hormonal replacement therapy.

#### P1023

##### Mid-regional pro atrial natriuretic peptide predicts increase in cardiac output during submaximal exercise in patients with heart failure.

The Research Fund, Rigshospitalet, Denmark. The Heart Center Research Foundation, Rigshospitalet, Denmark

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**Background:** Mid-regional pro-atrial natriuretic peptide (MR-proANP) is produced and secreted from the atria as a result of atrial distention in heart failure (HF). The association between MR-proANP and invasive hemodynamic parameters during exercise in patients with HF is unknown.

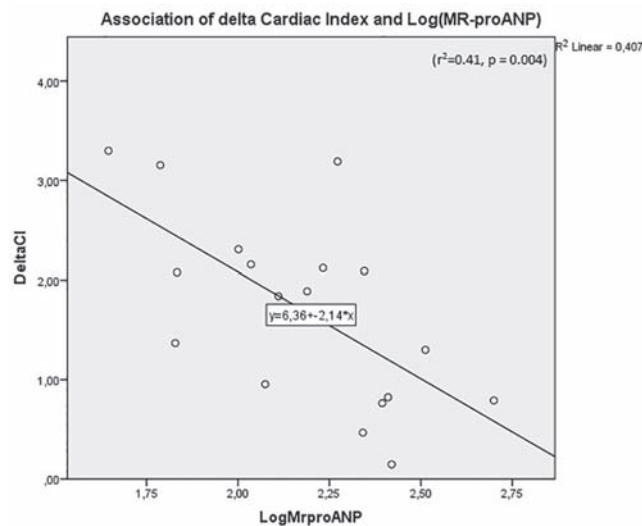
**Purpose:** The purpose was to investigate the association of MR-proANP and invasive hemodynamic measures during submaximal exercise.

**Methods:** Patients with chronic HF with a left ventricular ejection fraction (LVEF) <45 % performed a submaximal exercise test on a supine exercise bike. The individual submaximal exercise level was determined as 50 % of the maximal workload during maximal exercise testing one week prior. All patients underwent right heart catheterization with measurement of invasive hemodynamic parameters at rest and during submaximal exercise. Blood levels of MR-proANP were measured at rest and during exercise. MR-proANP was logtransformed for analyses.

**Results:** A total of 18 patients (89 % male) were included (mean age  $53 \pm 12$ , mean LVEF  $23 \pm 8$  %, mean  $VO_2\max$   $18 \pm 5$  l/kg/min, mean submaximal workload was  $52 \pm 18$  Watts). Pulmonary capillary wedge pressure (PCWP) increased from rest

( $15 \pm 8$  mmHg) to submaximal exercise: ( $34 \pm 11$  mmHg) ( $p < 0.05$ ). The increase in cardiac index (CI) from rest to submaximal exercise was  $2.3 \pm 0.5$  L/min to  $4.0 \pm 1.3$  L/min ( $p < 0.05$ ). Levels of MR-proANP also increased from rest to submaximal exercise:  $180 \pm 114$  pmol/L vs.  $238 \pm 142$  pmol/L ( $p < 0.05$ ). There was an inverse correlation between resting  $\log(\text{MR-proANP})$  and increase in cardiac index (CI) from rest to submaximal exercise ( $r^2 = 0.41$ ,  $p = 0.004$ ).  $\log(\text{MR-proANP})$  was also correlated with resting pulmonary capillary pressure (PCWP) ( $r^2 = 0.37$ ,  $p = 0.007$ ), but there was no association between  $\log(\text{MR-proANP})$  and PCWP during peak exercise ( $p = 0.09$ ). Increase in CO during exercise was also associated with resting PCWP ( $P = 0.005$ ). NT-proBNP was not associated with CI or PCWP at rest or during exercise in this study ( $p > 0.05$ ).

**Conclusion:** A low blood level of MR-proANP predicts a greater increase in cardiac output during submaximal exercise in patients with chronic HF. In systolic HF, MR-proANP is a predictor of resting PCWP, and hereby further predicts cardiac reserve during submaximal exercise.



Association: Cardiac Index and MR-proANP

#### P1024

##### Renin-angiotensin-aldosterone system stimulation in different stages of heart failure with reduced ejection fraction

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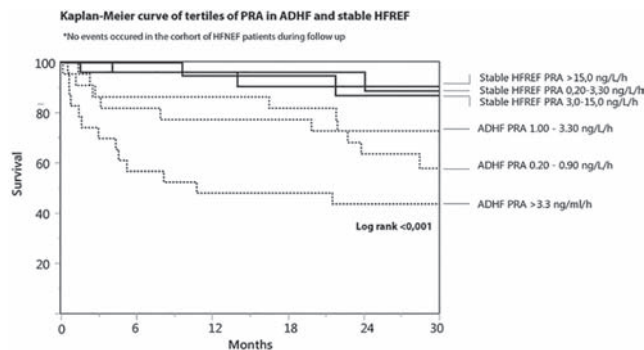
**Background:** Renin-angiotensin-aldosterone system (RAAS) stimulation in heart failure (HF) with reduced ejection fraction (HFREF) is detrimental through cardiac remodeling and water/salt retention. Cardiac function, hemodynamic alterations and HF therapies influence RAAS hormones.

**Aims:** This study aims to describe RAAS activation during different stages of HFREF and assesses their prognostic role.

**Methods and Results:** In 72 acute decompensated HFREF patients (ADHF), 78 stable chronic HFREF patients and 53 patients with HF with normalized ejection fraction (HFNEF), venous blood samples and hemodynamic parameters were obtained. Subjects were prospectively followed up to 30 months. RAAS hormones (plasma renin activity (PRA) and serum aldosterone) are significantly lower in ADHF compared to stable HFREF and HFNEF patients (all  $p < 0.05$ ) (Table 1). Volume status, blood pressure and HF medication seem to play an important role (all  $p < 0.05$ ). High PRA levels are associated with worse outcome in acute ADHF, which does not hold true in stable HFREF or HFNEF (Figure 1). There is a trend to lower PRA levels in HFNEF patients compared to stable HFREF ( $p = 0.06$ , not presented in table) which could not be accounted for by medication use or hemodynamic factors between these two groups.

**Conclusion:** High RAAS activity in stable HFREF and HFNEF patients is not associated with worse outcome in contrast to patients with ADHF. During acute decompensation the RAAS system remains appropriate responsive and is downregulated. In HFNEF patients RAAS activity declines possibly due to the reversal of cardiac abnormalities.

Characteristics of HFREF cohorts				
Acute decompensated HFREF n = 72	Stable chronic HFREF n = 78	HFNEF n = 53	p	
- Age - Male (%) - LVEF (%) - Systolic Blood pressure - diastolic blood pressure - > 1 clinical sign of congestion (%)	67 ± 11 76 25 ± 10 128 ± 23 71 ± 15 100 (inclusion criterium)	66 ± 12 77 32,8 ± 7,0 124 ± 17 63 ± 12 0 (exclusion criterium)	70 ± 8 50 X 121 ± 25 70 ± 16 0 (exclusion criterium)	0,21 <0,05 <0,05 <0,05 <0,05 <0,05
- ACE/ARB (%) - BB - MRA - Loop diuretic	50 72 49 64	87 97 81 49	90 94 70 8	<0,05 <0,05 <0,05 <0,05
- Creatinine (mg/dl) - NT-proBNP (ng/l) - PRA (ng/ml/h) - Aldosterone (ng/ml)	1,4 ± 0,7 4011[2018;10608] 1,5[0,8;5,7] 179 [134;292]	1,3 ± 0,5 608[271 ± 1407] 7,6[2,2;18,1] 213[144;374]	1,1 ± 0,4 363[145;490] 3,9[1,0;13] 257[210;371]	<0,05 <0,05 <0,05 <0,05



Kaplan-Meier curve of PRA tertiles

HEART FAILURE IMAGING

P1025

Longitudinal left ventricular strain in type 1 diabetes children

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**Introduction:** Diabetic cardiomyopathy is a new entity, defined as a form of heart failure with preserved LVEF, observed in diabetic patients, in the absence of coronary artery disease, hypertension and significant valvular heart disease. Application of a new echocardiographic tool, the 2D Strain is being evaluated. The aims of our study were to investigate the global longitudinal Strain (GLS) of the left ventricle (LV) and of the right ventricle (RV) and to determine the correlations between GLS and metabolic control evaluated by HbA1c. **Methods:** It was a retrospective study of 24 children with type 1 diabetes. The conventional echocardiographic parameters and GLS were studied. These data were compared to the measured parameters in 20 healthy children matched for age and sex.

**Results:** The mean age was 11,13 ± 0,54 years. The mean duration of diabetes was 7 years ± 0,54. Mean HbA1c was 8,79% ± 0,25. LVEDD was 41,8 ± 0,84 mm and LVESD was 26,33 ± 0,73 mm. LVEF was preserved with an average of 67,88 ± 1,18%. E/A ratio was 4,4 ± 2,08. The TDE was significantly shorter in the diabetic group (146,54 ms ± 3,69 Vs 161,42 ms ± 2,38 for the control group, p = 0,005). E/E' ratio was significantly higher in the diabetic group compared with the control group (6,72 ± 0,33 Vs 5,21 ± 0,15, p = 0,0011). RV function was preserved in the diabetic group: TAPSE was 20,33 ± 0,26 mm and S' Wave was 14 cm / s ± 0,002. The study of myocardial deformation showed a significant decrease in the GLS of diabetic patients compared to healthy subjects (-18,53% ± 0,5 Vs -25,52% ± 0,37, respectively; p < 0,001). RV longitudinal strain was preserved (-26,31% ± 0,51). No correlation was found between the GLS of the LV and the HbA1c (r = 152, p = 0,477).

**Conclusion:** Myocardial deformation analysis by Strain 2D can detect subclinical impairment of LV systolic function. It is an early marker of diabetic cardiomyopathy. It has a contributive value for screening early cases and for optimizing therapeutic management and consequently codifying the subsequent monitoring strategy.

P1026

Biventricular remodelling after pregnancies complicated by HELLP syndrome

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**Background:** Haemolysis, Elevated Liver enzymes and Low Platelets (HELLP) syndrome is a rare condition which can superimpose to pre-eclampsia (PE). PE is characterized by left ventricular subclinical alterations persisting after pregnancy. Nothing is known about similar consequences after HELLP syndrome.

**Purpose:** To evaluate biventricular function in patients with previous pregnancies complicated by HELLP syndrome, and to compare it to PE and healthy controls.

**Methods:** 50 women with a history of HELLP syndrome, 50 with a previous PE and 50 controls were examined from 6 months to 4 years after delivery. Left ventricular (LV) dimensions, volumes, ejection fraction (LVEF) and mass were measured. Right ventricular (RV) tricuspid annular plane systolic movement (TAPSE) and fractional area changing (FAC) were sampled. Diastolic filling (E/A and E/E' ratios) and tissue Doppler imaging were evaluated for both ventricles and myocardial performance index was calculated.

**Results:** HELLP group showed an earlier gestational age at delivery if compared to PE alone. LV concentric hypertrophy was present only in the HELLP group. LV concentric remodeling was identified also in the PE group together with consequent diastolic dysfunction (altered E/E' ratio) and reduced LVEF. Regarding RV parameters, only FAC and E/E' were slightly impaired in the HELLP group while the others were similar to controls.

**Conclusion:** The significant overlap among data related to women with a history of HELLP syndrome and those with previous PE alone seems to suggest that these disorders represent variations of the same pathophysiological process. However early onset of HELLP syndrome may lead to a more severe cardiovascular remodelling after delivery.

P1027

Speckle tracking echocardiography analysis of the left ventricular function in young athletes

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**Introduction:** In addition to the 2D standard echocardiographic parameters, the assessment of left ventricular (LV) function in young athletes is currently possible by deformation parameters (strain or speckle tracking echocardiography (STE)). The aim of this study was to assess the role of 2 D-STE for better characterize the heart performance in young athletes.

**Patients and methods:** Thirty-three footballers and 20 healthy untrained subjects were included in the study. The systolic LV function was evaluated by 2D conventional echo parameters, Doppler method and 2D-STE.

**Results:** The STE demonstrated a different pattern of LV deformation in the 2 study groups. A significant lower LV global longitudinal strain (GLS -20.68 ± 2.05 versus -22.99 ± 2.32 %, p < 0.001) and higher radial and circumferential strains have been found in the young athletes as compared with controls. A significant relationship between the GLS values and LVED (r = 0.299, p = 0.03) and LVMi was also reported in athletes.

**Conclusion:** STE could detect early changes in the LV systolic function. Deformation parameters showed a different pattern of LV mechanics in young footballers versus controls.



## 60651 Abstract

Variable	HELLP	PE	Controls	p
LVEF	7 (14.0%)*	13 (26.0%)*	0 (0.0%)	0.005
LV concentric remodeling LV concentric hypertrophy	23 (46.0%)* <sup>§</sup> 10 (20.0%)	28 (56.0%)* 0 (0.0%)	0 (0.0%) 0 (0.0%)	< 0.001
LV diastolic dysfunction	3 (6.0%)	0 (0.0%)	0 (0.0%)	0.1
LV E/e' > 15 E/e' > 8 e < 15	0 (0.0%)* 10 (20.0%)	0 (0.0%)* 6 (12.0%)	0 (0.0%) 0 (0.0%)	0.03
FAC	8 (16.0%)* <sup>§</sup>	6 (12.0%)*	0 (0.0%)	0.04
TAPSE	0 (0.0%)	0 (0.0%)	0 (0.0%)	1
sPAP	0 (0.0%)	0 (0.0%)	0 (0.0%)	1
RV diastolic dysfunction	0 (0.0%)	0 (0.0%)	0 (0.0%)	1
S' TDI	2 (4.0%)	0 (0.0%)	0 (0.0%)	0.2
RV MPI	0 (0.0%)	0 (0.0%)	0 (0.0%)	1

\* p < 0.05 vs controls; # p < 0.05 vs PE

## P1028

### Role of echocardiography and cardiac sonographer in outpatient evaluation for heart failure

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1. Heart failure (HF) is a complex syndrome due to structural or functional heart diseases that make heart unable to fill and/or pump at normal filling pressures. The definition of accurate diagnostic settings for its recognition is crucial for patients' management.

2. The aim of this study is to show the feasibility and usefulness of a focused echocardiographic examination performed by cardiac sonographer during the clinical evaluation of patients referred to an outpatient program dedicated to HF.

3. Between September and October 2015 68 patients (68% males, average age 74 years) were referred to the outpatient program dedicated to HF. For each patient we obtained clinical and instrumental data (age, sex, risk factors, symptoms, blood pressure, heart rate -HR, oxygen saturation, electrocardiogram) and an echocardiographic examination performed by a cardiac sonographer (level 1 of competence in echocardiography according to American Society of Echocardiography - ASE recommendations). The echocardiographic acquisition was limited to a minimal data set of 12 images (frames and loops). It was focus to obtain the following parameters: left ventricle (LV) dimensions, ejection fraction (EF; Simpsons' rule) and filling pressure estimation (E/A ratio, DTE, E/E' ratio), right ventricle (RV) systolic function (TAPSE), pulmonary artery systolic pressure (PASP) estimation (using tricuspid regurgitation peak pressure gradient and inferior cava vein dimensions and breath excursion). The images and the preliminary report performed by the sonographer were sent to a DICOM server and immediately evaluated by the cardiologist (level 2 of competence in echocardiography according to ASE recommendations) on his workstation.

4. According to clinical and echocardiographic data, 24 patients were not enrolled into the outpatient program dedicated to HF.

Forty-four patients (66% males, average age 75 y) were enrolled into the program. Only 60% of them was in sinus rhythm and echocardiographic examination shown a LVEF ≤50% in 68% (46,6% 40-50%, 46,6% 30-40% and 6,8% <30%), increased LV filling pressure in 93,2% (slightly 19,5%, moderately 61% and severely 19,5%), reduced RV systolic function (TAPSE ≤17 mm) in 18,2% and increased PASP in 38,6%. Only 7 patients shown bidimensional and Doppler signs of valve (mitral or aortic) disease and were referred to the Echo-Lab to perform a standard examination. The mean duration of echocardiographic examination performed by the sonographer was of 12 minutes and the mean global duration of the clinical outpatient evaluation was not significantly prolonged (35 minutes).

5. The echocardiographic evaluation performed by cardiac sonographer during the clinical evaluation of patients, referred to an outpatient program dedicated to HF is feasible, allows immediate information about structural and functional cardiac parameters useful for patients' management and avoids to refer all the patient to the Echo-Lab with evident economic advantages.

## P1029

### The study about 4D LV strain according to the changes of preload

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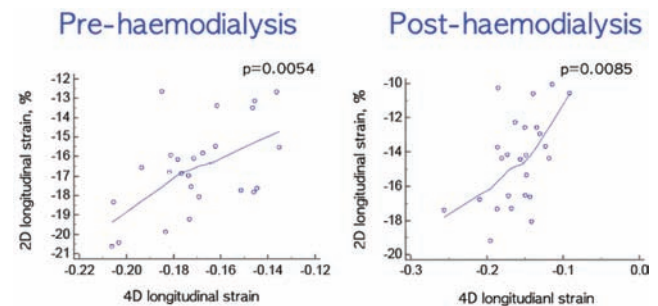
**Purpose:** Various peak strain values from 4D full volume image are novel indicator of left ventricular function. In this study, we investigated various 4D strain values to examine the effect of preload reduction in end-stage renal disease patients who were undergoing regular hemodialysis.

**Methods:** 56 subjects who underwent transthoracic echocardiography including 4D full volume image acquisition of left ventricle before and after haemodialysis were enrolled. Peak systolic longitudinal, circumferential, radial and area strain values were obtained from left ventricular 4D full volume image. (Table) All the values were significant decreased after preload reduction. 2D longitudinal strain values were also calculated from 25 subjects. And they were well correlated with the longitudinal strain values obtained from 4D image. (Figure)

**Conclusion:** 4D strain values are reliable parameter for left ventricular function. They can be more easily obtained from just one image. However, they are not preload-independent just like other conventional left ventricular systolic parameters.

### Strain values from 4D speckle tracking

	pre-haemodialysis	post-haemodialysis	p values
Longitudinal strain, %	-17.10 ± 2.35	-15.59 ± 3.23	p = 0.0004
Circumferential strain, %	-20.03 ± 3.21	-17.47 ± 3.71	p < 0.0001
Area Strain, %	-32.29 ± 3.83	-28.98 ± 5.00	p < 0.0001
Radial Strain, %	53.67 ± 9.66	45.87 ± 11.30	p < 0.0001



Correlation between 2D and 4D LS

## P1030

### Ventricular-vascular coupling after pre-eclampsia

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**Background:** Ventricular-arterial coupling (VAC) is a major determinant of left ventricular function and energy transfer to the aorta. Pre-eclampsia (PE) is associated to subsequent higher cardiovascular risk and development of arterial stiffness and heart failure.

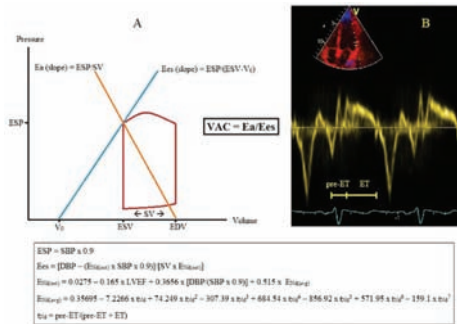
**Purpose:** To evaluate VAC few years after pregnancies complicated by PE.

**Methods:** 30 non-pregnant women with a previous singleton pregnancy complicated by early-onset (EO) PE, 30 by late-onset (LO) PE and 30 controls with a previous uncomplicated pregnancy underwent an echocardiographic evaluation 6 months to 4 years after delivery. Women with cardiovascular risk factors,

ongoing medical therapy, hypertensive or nephrologic or immunologic disorders were excluded. VAC was defined as the ratio between aortic elastance (Ea) and left ventricular end-systolic elastance (Ees), assessed by the echocardiographic single-beat method. Multivariate regressions were run to test the association between gestational age (GA) at PE onset and VAC parameters, after correcting for blood pressure and uterine artery pulsatility index at diagnosis of PE and for birth weight.

**Results:** VAC was normal in the whole study cohort. Ea and Ees were altered significantly more in the EOPE group than both LOPE and controls. Ea, Ees and VAC were independently associated with GA, after correcting for blood pressure and uterine artery pulsatility index at diagnosis of PE and for birth weight.

**Conclusions:** VAC as a marker of cardiovascular performance is maintained normal few years after pregnancies complicated by PE. Nevertheless, its single components (Ea and Ees) showed subclinical alterations principally in the EOPE group. This findings support the greater risk of cardiovascular diseases which affects these women later in life.



**P1031**

**Clinical and prognostic relationships of pulmonary artery to aorta diameter ratio in patients with heart failure. A cardiac magnetic resonance imaging study.**

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**Background:** The main pulmonary artery (PA) distends as a consequence of raised pulmonary artery pressure. Its diameter, and the ratio to the aorta diameter, might provide prognostic information in patients with chronic heart failure (CHF).

**Methods:** Patients with CHF and control subjects undergoing cardiac magnetic resonance imaging (CMRI) were evaluated. The main PA diameter and the transverse axial ascending aorta (Ao) diameter at the level of bifurcation of the main pulmonary artery were measured. The maximum diameter of both vessels was measured through the cardiac cycle and the PA/Ao ratio was calculated.

**Results:** 384 patients (mean age 69 years, mean left ventricular ejection fraction 40%, median amino terminal pro-brain natriuretic peptide (NT-proBNP) 1010 (IQR: 448-2262) ng/l) and 38 controls were included. Controls and patients with CHF had similar maximum Ao and PA diameters, and PA/Ao ratio. During a median follow up of 1759 days (998-2269), 181 patients with HF were hospitalised for HF or died. Neither PA diameter nor PA/Ao ratio predicted outcome in univariable analysis. In a multivariable model, only age and NT-pro BNP were independent predictors of adverse events.

**Conclusions:** the PA/Ao ratio is not a useful method to stratify prognosis in patients with heart failure.

**P1032**

**Hybrid SPECT/CT imaging in patients with heart failure and coronary artery diseases**

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**Background:** SPECT-CT is a hybrid technique whereby simultaneous non-invasive functional information about myocardial perfusion obtained by SPECT and anatomical information about the coronary arteries using CT is obtained. A hybrid SPECT-CT scanner can be used in heart failure patient with coronary heart diseases. In this kind

of imaging CT could correct the limitations of SPECT, and SPECT corrects limitations of CT.

**Material and Methods:** 48 patients (mean age 52.5 ± 10.1 years, 48.4% male) with stable symptoms of angina and mean ejection fraction < 35% assessed by echocardiography, were prospectively included in this study. Hybrid SPECT/CT was performed prior to conventional coronary angiography. Hybrid analysis was performed by combined interpretation of SPECT and CT images. The sensitivity, specificity, positive (PPV), and negative (NPV) predictive values were calculated for SPECT, CT, and hybrid SPECT/CT comparing with coronary angiography. Ejection fraction, regional wall motion, and regional wall thickening measured by echocardiography was compared with GSPECT parameters. Results Significant CAD was demonstrated in 32 patients (67%). SPECT had a sensitivity of 83%, specificity 72%, CT had a sensitivity of 100%, specificity 62%. Hybrid analysis of SPECT and CT improved the overall performance: sensitivity, specificity for the presence of significant CAD in heart failure pts to 96, 95% respectively. Conclusions Hybrid SPECT/CT is fast, complete and easy to obtain. It could diagnose or exclude coronary artery disease and identify coronary risk in patients with heart failure.

**P1033**

**Characterization of patients with diffuse aneurysmatic coronary artery disease by non-dimensional shape analysis and wall shear stress**

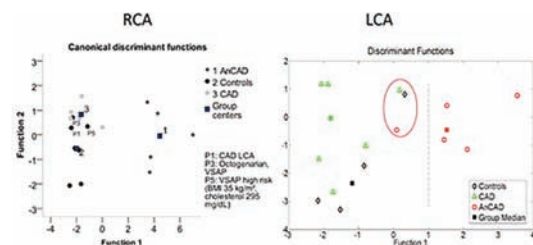
E Ernst Wellnhofer<sup>1</sup>; U Kertzscher<sup>2</sup>; K Affeldt<sup>2</sup>; B Pieske<sup>2</sup>; L Goubergrits<sup>2</sup>  
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**Purpose:** Aneurysmatic coronary artery disease (ANCAD) is a descriptive diagnosis based on local or diffuse ectasia of several coronary vessels. Patients with ANCAD may have poor prognosis due to early myocardial infarction resulting in heart failure. We evaluated whether a previously published classification model discriminating ANCAD by quantitative measures based on 3-D reconstruction and flow simulation in right coronary arteries may be validated in left coronary arteries of the same patients.

**Methods:** Patients with ANCAD (n=6; age: 50 ± 10 y, 1 f), with CAD ruled out by angiography (controls) (n=8; age: 53 ± 14y, 5 f) and with CAD without ectasia (n=9; age: 59 ± 10y, 3 f) with long-term follow-up (20 years) were selected by review of coronary angiograms performed between 1990 and 1994. Left and right coronary arteries were 3-dimensionally reconstructed from biplane angiograms by a validated method. Numerical flow simulations based on Navier Stokes equations in an appropriately refined mesh were performed. A previously published classification approach based on non-dimensional shape analysis and wall shear stress statistics was applied.

**Results:** There was fair agreement between the classifications irrespective whether it was applied to right or left coronary arteries. The three patients with different classification related to selected coronary vessel are identified by a red circle in the left part of the figure. Discriminant function 1 characterizes the "aneurysma factor" and function 2 reflects negative remodeling.

**Conclusion:** The novel classification approach based on non-dimensional shape analysis and wall shear stress statistics is a promising diagnostic tool to identify aneurysmatic coronary artery disease that should be further investigated. This could probably be easily done with CT data. Of particular interest is, whether the severity of disease or prognostic impact might be reflected by the discriminant functions.



Discriminant function

**BIOMARKERS**

**P1034**

**Diagnostic and prognostic accuracy of galectin-3 for acute heart failure**

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**Background:** The biomarker galectin-3 has been included in the 2013 ACCF/AHA guideline for additive risk stratification of patients with acute and chronic heart failure (HF). However, it remains unclear whether galectin-3 may be useful as an aid for the diagnosis of heart failure.

**Purpose:** To compare head to head the diagnostic and prognostic capabilities of galectin-3 and B-type natriuretic peptide (BNP) for HF in an emergency setting.

**Methods:** We studied 251 consecutive patients with dyspnoea as a chief complaint presenting to an emergency department. The diagnosis of HF was based on the Framingham score for HF plus echocardiographic evidence of systolic or diastolic dysfunction. All-cause mortality was assessed at one year. We measured plasma concentrations of galectin-3 and BNP by two commercially available assays from Abbott Diagnostics. The diagnostic and prognostic accuracies of galectin-3 and BNP were assessed by receiver operating characteristic (ROC) curve analysis.

**Results:** Of the 251 patients, 137 had dyspnoea attributable to acute HF and 114 had dyspnoea attributable to other reasons. BNP had a higher area under the curve (AUC) for the diagnosis of HF (0.91; 95% CI, 0.87-0.95) than galectin-3 (0.57; 95% CI, 0.51-0.64). Galectin-3 did not add to the diagnostic capability of BNP. Cut-off values with the highest diagnostic accuracies were 295 ng/L for BNP (sensitivity, 80%; specificity, 86%), and 26 ng/mL for galectin-3 (sensitivity, 41%; specificity, 75%). Of the 137 patients with acute HF, 41 died and 96 survived during follow up. The AUC of BNP for the prediction of one-year all-cause mortality in HF patients (0.72; 95% CI, 0.63-0.79) was not different from the AUC of galectin-3 (0.70; 95% CI, 0.62-0.78). A statistical model combining the predictive values of both biomarkers did not improve the prognostic capabilities of each analyte. Cut-off values with the highest prognostic accuracies were 925 ng/L for BNP (sensitivity, 68%; specificity, 69%), and 33 ng/mL for galectin-3 (sensitivity, 54%; specificity, 88%).

**Conclusions:** In this study, galectin-3 and BNP were equally useful for the prediction of one-year all-cause mortality in patients with acute HF. However, in contrast to BNP, galectin-3 was not useful as an aid in the diagnosis of acute HF in short of breath patients presenting to an emergency department.

### P1035

#### Serum concentrations of tumor markers carbohydrate antigen 125 (CA 125) in acute heart failure - clinical implications

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**Introduction:** Serum CA 125 is elevated in patients with congestive heart failure.

**Objective:** To examine the relationship between Ca 125 with different clinical presentations of acute heart failure (AHF).

**Methods:** In 86 patients who were hospitalized with AHF, the serum concentration of Ca 125 and BNP was measured 48-72 hours after hospitalization.

**Results:** Ca 125 is positively correlated with serum concentration of BNP, and negatively with EF. In patients with pleural effusions (47) Ca 125 is higher than in those without ( $121.7 \pm 108.4$  U / ml, vs.  $24.1 \pm 12.1$  U / ml,  $p < 0.001$ ), patients with dilated right ventricle (RV) (53) had higher of Ca 125 than those without ( $139.0 \pm 102.2$  / ml vs.  $20.8 \pm 14.9$  U / ml,  $p < 0.001$ ). Patients with Acute pulmonary edema (20) have lower values than those with no AHF (66) ( $25.3 \pm 10.5$  U / ml vs.  $131.4 \pm 98.0$  U / ml), patients with atrial fibrillation (29) had higher Ca 125 than those without ( $107.3 \pm 101.7$  U / ml vs.  $22.2 \pm 14.9$  / ml,  $p < 0.001$ ).

**Conclusion:** CA 125 is a good indicator of heart failure, particularly volume overload at the right ventricle decompensation

### P1036

#### Predictors of length of stay of heart failure hospitalizations in heart failure patients with normal and reduced left ventricular ejection fraction

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**Background and aims:** Factors associated with the length of hospital stay (LoHS) for patients with decompensation of chronic heart failure (HF) with normal and reduced left ventricular ejection fraction (HFpEF and HFrEF) have not been well described.

**Methods:** Demographic measurements, symptoms and signs, and standard blood tests were collected routinely from patients referred with suspected heart failure to a community heart failure service between 2000 and 2013. For this analysis, hospitalizations resulting in death were excluded. HF was defined as a clinical diagnosis confirmed by an NT-proBNP > 400 ng/L; patients were classified as HFpEF and HFrEF if their LVEF was above or below 40%. A multivariable model was developed to identify variables associated with a total of LoHS for HF > 7 days in the 5 years following enrolment. Pre-specified variables were: age, sex, body mass index (BMI), NYHA class, systolic BP, NT-proBNP, creatinine, haemoglobin, sodium, QRS, heart rate, sinus rhythm, COPD and diabetes.

**Results:** Of 4,055 patients with suspected HF evaluated with a follow-up of at least

5 years after first NT-proBNP measurements, 1,091 patients had HFpEF and 1,274 had HFrEF. Of patients with HFpEF, the median age was 77 (IQR: 72-83) years, 591 (54%) were men and 305 (28%) were in NYHA class III/IV. Of patients with HFrEF, the median age was 79 (IQR: 73-84) years, 944 (74%) were men and 469 (37%) were in NYHA class III/IV. The patients with HFrEF had a total of 5,141 hospitalizations over the following 5 years, of which 2,947 lasted > 24 hours, 1,274 of these were for HF and 444 (35%) lasted > 7 days. The patients with HFpEF had a total of 4,720 hospitalizations over the following 5 years, of which 2,527 lasted > 24 hours, 776 of these were for HF and 303 (28%) lasted > 7 days. 628 patients with HFrEF and 518 patients with HFpEF died within 5 years; 388 patients with HFrEF and 403 patients with HFpEF survived 5 years without a HF hospitalization (>=24 hours). For HFpEF, a total LoHS for HF > 7 days over 5 years was associated with increasing NT-proBNP, BMI, age, NYHA class, and decreasing haemoglobin and sodium and presence of COPD. For HFrEF, only increasing age (odds ratio (OR): 1.02 (95% CI: 1.01-1.03)), NYHA class (OR: 1.52 (1.17-1.97)), and diabetes (OR: 1.47 (1.10-1.97)) were associated with a total of LoHS for HF > 7 days.

**Conclusions:** Patients with HFrEF are more likely to have a total of LoHS for HF > 7 days than those with HFpEF. Older age and more severe heart failure predict longer LoHS.

### P1037

#### CT-pro-endothelin-1 in heart failure patients with reduced and preserved ejection fraction - useful or waste of resources? MOLITOR substudy.

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**Introduction:** N-terminal-pro-brain natriuretic peptide (NT-proBNP) has a diagnostic and prognostic role in heart failure (HF). The role of CT-pro-endothelin-1 (CT-pro-ET-1) in HF is unclear. Endothelin-1 increases with the rise of right ventricle systolic pressure (RVSP).

**Purpose:** The goal was to investigate the change of NT-proBNP and CT-proET-1 in patients with reduced and preserved left ventricle ejection fraction (HFrEF/HFpEF) one year after hospital admission due to acute HF.

**Methods:** We included 168 patients with acute HF, age  $68.18 \pm 9.9$  years, 70.8% being males, 83.7% with HFrEF.

**Results:** CT-proET-1 in HFpEF patients was  $122.1(86.4-143.8)$  at admission and  $92.34(72.3-106.46)$  pmol/L after 1 year ( $p=ns$ ). NT-proBNP at admission and 1 year after was  $1501(1018-1948)$  /  $854.4(388.6-1460)$  pg/mL,  $p=0.046$ . In HFrEF patients, CT-proET-1 at admission and after 1 year was  $112.7(80.9-191.6)$  /  $95.13(78.29-127.61)$  pmol/L,  $p=ns$ , while NT-proBNP was  $3414.5(1578.5-10989.5)$  at admission and  $1017.6(437.05-2581)$  pg/mL after 1 year ( $p=0.002$ ). The difference was found among patients with HFrEF and HFpEF in NT-proBNP values measured at admission ( $p < 0.01$ ). Left ventricle ejection fraction significantly changed in HFrEF patients during 1 year ( $33.47 \pm 10.77$  vs.  $29.91 \pm 9.08\%$ ,  $p < 0.001$ ), while in patients with HFpEF it was not the case ( $51.38 \pm 8.8$  vs.  $54.04 \pm 6.7\%$ ). SPDK did not change significantly in HFpEF and HFrEF patients during 1 year ( $28.56 \pm 15.03$  vs.  $30.56 \pm 22.83$ ) / ( $35.72 \pm 17.7$  vs.  $33.39 \pm 15.34$  mmHg).

**Conclusions:** NT-proBNP was higher in patients with HFrEF and was significantly reduced after 1 year in all patients. CT-proET-1 did not change as well as RVSP during 1 year in all our patients. CT-proET-1 could be the indicator of pulmonary hypertension in HF. However, its role in this setting is yet to be determined.

### P1038

#### The evaluation of early risk of lymphoproliferative diseases after heart transplantation: important but underutilized

The work was supported by the Ministry of Health of the Czech Republic (Grant number: AZV MZ 15-27579A).

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**Introduction:** Post-transplant lymphoproliferative diseases (PTLD) are one of the most frequent and severe complications after transplantation (Tx) with 40-70% mortality. There were 13 definitive diagnosis of PTLD in 603 patients after heart Tx (HTx). Monoclonal gammopathy (MG) is an independent risk factor of PTLD. Conventional tests for the detection of MG and/or polyclonal activation of the immune system include electrophoresis (PE) and immunofixation (IFE) of serum and urine proteins; the measurement of free light chains (FLC) is another option. However, these tests are usually not included in the guidelines for the management



of patients after HTx. Purpose To describe the common practice in the use of screening methods for PTLT risk. Methods Retrospective study: We searched the laboratory database for serum and urine PE and IFE in patients after Tx. We compared number of patients screened for MG with data from our institution transplant register. Pilot prospective study: 80 patients (67 men, 13 women, aged 21-68, median 52 years) after HTx (2010 – 2012, 4 sequential serum samples were obtained from each patient: before HTx and at 9th, 18th and 24th month after HTx). Serum and urine PE, IFE, and FLC were determined in an accredited laboratory using Sebia and Binding Site systems. Results The retrospective study is described in Table 1 (study 2005 - 2015). Pilot prospective study: No positive result (PE and/or IFE) was found in any of the 80 pts before HTx. Within 2 years, 2 pts developed MG, 6 pts biconal gammopathy and 3 pts developed oligoclonal gammopathy. The FLC determination revealed 12 pathologies before HTx and 18 pathologies within 2 years after HTx. Conclusions Screening for MG is protocol-based in patients after liver Tx, but only rarely ordered in other Tx patients (based on clinicians' judgment). The significant number of pathologies and more intensive immunosuppressant therapy after HTx encourage the screening use of PE and IFE together with FLC measurement. The utility of this regimen will be assessed in our prospective study.

Table 1. PE and/or IFE results

Organ	No. of Tx	No. of Pts.	No. of MG screenings (%)	No. of pathologies before (%)	No. of pathologies after (%)
Heart	884	745	36 (4.8 %)	0 (0 %)	5 (13.9 %)
Liver	1237	1103	818 (74.2 %)	15 (1.8 %)	46 (5.6 %)
Kidney	3766	2965	685 (23.1 %)	4 (0.6 %)	43 (6.3 %)
Total	6378	5264	1608 (30.5 %)	19 (1.2 %)	98 (6.1 %)

Pts. = patients

**P1039**

**Bio-humoral determinants of early LV dysfunction in patients with stable angina.**

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**Background:** In patients with stable coronary artery disease (CAD) LV function can be impaired as a result of repetitive myocardial ischemia. It is not known whether circulating biomarkers of atherosclerosis/ischemia are associated with early LV functional impairment in these patients.

**Purpose:** To evaluate whether particular biohumoral profiles are related with LV systolic function in patients with stable angina.

**Methods.** Clinical, functional and imaging data were collected in 362 patients (212 males, 150 females, mean age 60 ± 9 years) with stable angina and suspected CAD enrolled in the Evaluation of INtegrated Cardiac Imaging (EVINCI) study. All patients underwent baseline echocardiography measurements to assess LV function, stress imaging to detect myocardial ischemia (SDS>2) and coronary computed tomography angiography (CTA) to assess the presence of obstructive CAD (>50% stenosis of a major coronary vessel). Only patients with LVEF ≥50% were included in this substudy. Biohumoral profile involved 39 markers associated with atherosclerosis/ischemia including lipid/glucose, inflammatory and cardiac specific markers.

**Results:** LVEF was 60 [55-66] %, median [25-75 percentiles]. Myocardial ischemia was present in 90 patients (25%), obstructive CAD in 112 (31%), and myocardial ischemia + obstructive CAD in 46 (13%). At multivariate analysis including age, sex, cardiovascular risk factors, medical treatment, CTA and stress imaging results, high levels of adiponectin (Coefficient: -0.044 ± 0.01 (SE), p < 0.0001) and low levels of HDL cholesterol (0.055 ± 0.02, p = 0.0167) were predictors of lower LVEF independently of the presence of myocardial ischemia and/or obstructive CAD.

**Conclusions:** Adiponectin and HDL cholesterol are associated with low-normal systolic LV function in patients with stable angina independently of the presence of myocardial ischemia and obstructive CAD.

**P1040**

**Elevated parathyroid hormone is associated with left ventricular remodeling in elderly patients with mild to moderate chronic kidney disease**

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**Background:** Parathyroid hormone (PTH) plays an important role in bone metabolism. Aging and chronic kidney disease is recognized as an important factor associated with elevation in PTH. Although elevated PTH was associated with cardiovascular mortality, the association of PTH and left ventricular

remodeling in elderly patients with mild to moderate kidney disease has not been elucidated.

**Methods and results:** 238 patients over 65 years with CKD stage 2 or 3 were examined (101 male, 75 years). Subjects with LV dysfunction (LVEF <50%), atrial fibrillation and advanced chronic kidney disease (eGFR<15 ml/min/1.73m2) were excluded. Patients were divided into two groups according to intact PTH level: below 65pg/ml (normal PTH, n=201) and above 65pg/ml (high PTH, n=37). High PTH groups had lower creatinine-based estimated GFR (57+/-15 vs 63+/-13 ml/min/1.73m2, p<0.05) and higher cystatin C level (1.21+/-0.44 vs 1.01+/-0.30mg/L, p < 0.01). In echocardiography, high PTH group had lower e (5.3+/-1.6 vs 5.9+/-1.7 cm/sec, p < 0.05), higher E/e (16.1+/-21.9 vs 11.5+/-3.6, p < 0.01) and higher LVMI (119+/-28 vs 107+/-30g/m2, p < 0.05). The intact PTH was significantly associated with LVMI, even after adjustment for confounding factors. Also, high PTH group had high prevalence of LVH in multivariable logistic regression analysis. Conclusion In elderly patients with mild to moderate CKD, higher level of parathyroid hormone is associated with left ventricular remodeling, which may cause cardiovascular event in these patients.

**P1041**

**Differences in biochemical and genetic biomarkers in patients with heart failure of various etiologies**

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**Purpose:** To evaluate whether biomarkers reflecting pathophysiological pathways and selected single nucleotide polymorphisms differ between patients (pts) with heart failure (HF) with different etiologies.

**Methods:** 110 pts with HF (mean age 63 years, 69% males) were involved, including HF pts with preserved ejection fraction (HFpEF, n=51) with hypertensive origin, HF pts with reduced ejection fraction (HFrEF) with ischemic aetiology (ICM) (n=32) and HFrEF with dilated cardiomyopathy (DCM) (n=27). Functional polymorphisms were selected from six candidate genes: CYP27B1, NOS3, IL-6, TGF beta, TNF alpha, PPAR gamma. We also assessed the levels of selected HF biomarkers and performed echocardiographic examinations.

**Results:** Higher concentrations of TNF alpha were observed in pts. with hypertensive HFpEF compared to pts. with DCM (p=0.008). Pts. with HFpEF had higher concentrations of TGF beta 1 compared to pts. with DCM and ICM (p=0.0001 and p=0.0003, respectively). Compared to HFpEF and ICM pts., subjects with DCM had significantly higher values of syndecan 4 (p=0.03 and p=0.0001, respectively), cardiotrophin (p=0.02 and p=0.0003, respectively), and PIIINP (p=0.0008 and p=0.04, respectively). For the NOS3 -786 C/T rs2070744 polymorphism in DCM there were significantly more CT heterozygotes than in ICM and HFpEF. The only biomarkers distinguishing HFpEF vs HFrEF were TGF beta 1 and syndecan 4. The higher levels of syndecan 4 were connected with HFrEF and higher levels of TGF beta 1 were found in HFpEF.

**Conclusions:** Inflammation mediated through TNF alpha and TGF beta 1 may represent an important component of an inflammatory response that partially drives the pathophysiology of HFpEF. NOS3 -786 C/T rs2070744 polymorphism in DCM may serve as a marker for more rapid progression of heart failure. Finally, the only biomarkers independently distinguishing HFpEF and HFrEF are syndecan 4 and TGF beta 1.

Multivariate logistic regression					
Groups	Variable	OR	95%CI for OR	p-value	
Lower limit	Upper limit				
DCM	constant	x	x	x	0.001
TGF beta 1	0.381	0.233	0.621		0.001
Syndecan 4	3.241	1.570	6.692		0.001
ICM	constant	x	x	x	0.002
TGF beta 1	0.453	0.3	0.684		0.001
Syndecan 4	2.202	1.118	4.339		0.023

Model description statistically significant:  $\chi^2 = 132.06$ ;  $df=8$ ;  $p < 0.001$ , HFpEF group is reference group.

**P1042**

**The factors associated with heart failure hospitalization rates in heart failure patients with normal and reduced left ventricular ejection fraction**

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**Background and aims:** limited information from epidemiological studies on the causes and frequency of heart failure (HF) hospitalizations for patients with normal (HFneEF) and reduced (HFReEF) left ventricular ejection fraction exist. We explored these issues in a large, epidemiologically-representative cohort enrolled in a single regional centre which was also the sole provider of expert HF care.

**Methods:** Demographic measurements, symptoms and signs, and standard blood tests were collected routinely from patients referred with suspected heart failure to a community heart failure service between 2000 and 2013. Hospitalizations with admission and discharge on separate days were included (lasting >= 24 hours); for this analysis, hospitalizations resulting in death were excluded. Only patients with HF confirmed by an NT-proBNP >400ng/l were included and divided into those with an LVEF below (HFReEF) or above (HFneEF) 40%. A multivariate model was developed to identify the variables associated with HF hospitalization rates within 5 years follow-up for each group. Pre-specified variables included were: age, sex, body mass index (BMI), NYHA class, systolic BP, NT-proBNP, creatinine, haemoglobin, sodium, QRS, heart rate, sinus rhythm, COPD and diabetes.

**Results:** Of 4,055 patients with a follow-up of at least 5 years after first NT-proBNP measurements, 1,091 had HFpEF and 1,274 had HFReEF. Of patients with HFpEF, the median age was 77 years (IQR: 72-83), 591 (54%) were men, and 305 (28%) were in NYHA class III/IV. Of patients with HFReEF, the median age was 79 years (IQR: 73-84), 944 (74%) were men, and 469 (37%) were in NYHA class III/IV. HF hospitalization rates in HFpEF and HFReEF were 10.0 and 13.2 per 100 patient-years, respectively. For both HFpEF and HFReEF, the risk of >=1 HF hospitalizations in the following 5 years was associated with increasing NT-proBNP, NYHA class and age and with decreasing systolic BP, sodium and with the a diagnosis of diabetes. For patients with HFpEF, only increasing BMI and decreasing haemoglobin added to this model. For patients with HFReEF, no other variable added information unless NT-proBNP was excluded, in which case both creatinine and haemoglobin did.

**Conclusions:** Patients with HFReEF have a higher rate of HF hospitalizations compared to those with HFpEF. Variables that predict HF hospitalization rates are similar regardless of cardiac phenotype.

**P1043**

**Soluble ST2 and vitamin D, a potent deleterious interaction for the heart**

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**Background:** The increase of circulating soluble ST2 (sST2) levels is related to cardiac remodeling, fibrosis and to Heart Failure (HF). Recently, the regulation of the production of ST2 by vitamin D was demonstrated. A growing body of evidence is supporting the role of vitamin D and parathyroid hormone (PTH) in cardiac remodeling and worsening HF. These elements raise therefore the question of potent interrelations between vitamin D and mediators of fibrosis and inflammation such as sST2.

**Purpose:** Our objectives were therefore to determine the potential interrelation between sST2, 25(OH)D, 1,25(OH)2D and PTH levels in HF patients with reduced ejection fraction and to compare their prognosis value for cardiovascular death over a long-term follow-up.

**Methods:** One hundred HF patients with reduced left ventricular ejection fraction (mean age: 66 ± 14 years; males n=78; females n=22; NYHA II-IV; etiology: ischemic n=67, dilated cardiomyopathy n=33; mean left ventricular ejection fraction (EF): 23 ± 6%) were included. The primary outcome was cardiovascular death. Circulating levels of sST2, NT-proBNP, 25(OH)D, 1,25(OH)2D and PTH(1-84) were determined with immunoassays.

**Results:** Increased sST2, PTH(1-84) and NT-proBNP concentrations were significantly related to NYHA classes ( $p < 0.001$ ). The decreased levels of 1,25(OH)2D was related to NYHA classes but not to 25(OH)D. Levels of sST2 were significantly correlated with EF, 25(OH)D, 1,25(OH)2D, PTH(1-84) and NT-proBNP. In multiple regression analysis including age, EF, eGFR, 25(OH)D, 1,25(OH)2D, PTH(1-84), NT-proBNP, and the 1,25(OH)2D/PTH(1-84) ratio, the independent determinants of sST2 levels were NT-proBNP, 25(OH)D and 1,25(OH)2D. In univariate COX analysis, sST2, NT-proBNP, 1,25(OH)2D, PTH(1-84) and the 1,25(OH)2D/PTH(1-84) ratio were predictive of CV death in HF patients. The areas under the ROC curves were 0.70 for sST2, 0.71 for the 1,25(OH)2D/PTH(1-84) ratio, 0.68 for 1,25(OH)2D, 0.65 for PTH(1-84) and only 0.54 for 25(OH)D. In a backward stepwise multivariate Cox analysis only sST2, NT-proBNP and the 1,25(OH)2D/PTH(1-84) ratio remained significantly associated with CV death.

**Conclusions:** Our results suggest the potential interrelation between sST2 and the vitamin D / PTH(1-84) axis in patient with HF. Like sST2, the ratio between 1,25(OH)2D and PTH(1-84) is also a strong predictor of CV death. Our study might also open additional therapeutic perspectives through vitamin D or calcitriol supplementation.

**P1044**

**The association between BDNF levels and survival and prognosis in patients with decompensated heart failure**

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**Introduction:** The aim of this study is investigate the prognostic value and role of the BDNF levels in hospital and short term follow-up in patients with decompensated systolic heart failure

**Methods and Materials:** We examined 125 patients with decompensated heart failure that have NYHA III-IV functional capacity and left ventricle systolic dysfunction (EF<35) between the period of February 2013- March 2015. The control group consisted of 40 healthy volunteers who had no known history of cardiac disease. We measured serum NT pro-BNP and BDNF levels of patients and control subjects with ELISA method. In present study was aimed to examine the association of BDNF levels with primary endpoints including death and rehospitalization after at least six-month follow-up. We also pointed to examine the value of BDNF in secondary endpoints (in-hospital arrest, major arrhythmia, cardiorenal syndrom, mechanical ventilator, coronary care need, inotropic support).

**Results:** One variable analysis suggested that there is an significant association between BDNF levels and clinical status generate primary and secondary endpoints in patients with decompensated HF. However multiple variable analysis with Cox-regression analysis determined that increasing NT-proBNP (OR:1.071, 95% CI 1.01-1.13) were independent variable but the association between BDNF levels and survival was lost its significance. On the other hand, multiple variable analysis determine factors that affect the "time to rehospitalization" showed that increasing NT-proBNP (OR:1.004, 95% CI 1.002-1.006), decreasing BDNF level (OR:9.077, 95% CI 1.99-41.4) were independent factors.

**Discussion:** Serum BDNF levels were lower in hospitalized patients with decompensated HF than healthy individuals. Our results suggest that serum BDNF level is a independent prognostic factor to determine the "time to rehospitalization" in hospitalized patients with decompensated systolic HF. Unlike NT-proBNP, it is not found serum BDNF level is an independent prognostic factor to determine survival.

Cox regression rehospitalization					
	$\beta$	p	OR	95.0% CI for Exp(B)	
Lower	Upper				
age	.003	0.850	1.003	.975	1.031
Assit	-.016	0.934	0.984	.671	1.442
Troponin	.267	0.090	1.306	.960	1.778
eGFR	.001	0.856	1.001	.992	1.010
BDNF	2.206	0.004	9.077	1.990	41.410
NT-ProBNP	.004	<0.001	1.004	1.002	1.006

**P1045**

**Role of NT-proBNP evaluations in risk stratification of patients with heart failure within one year follow-up**

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**Background:** Ability of N-terminal-pro-B-type natriuretic peptide (NT-proBNP) to stratify risk in patients with heart failure (HF) is well established. Repeated measurements however, seem improve the risk stratification.

**Purpose:** We prospectively investigated the prognostic value of NT-proBNP levels and their changes during hospitalization in patients with HF. Method: We enrolled 135 patients with echocardiographic and clinical criteria of HF. 67 have HFrEF (EF  $\leq$  40%) while 68 have HFpEF (EF > 40% and abnormalities in E/e' ratio and/or increased left atrial volume). NT-proBNP was titrated within 24 hours from admission and at discharge. Median follow-up was 12 months. At census we administered the Minnesota Living with Heart Failure questionnaire to define their quality of life (QoL). Primary outcomes were mortality and the combined end-point of HF readmission and mortality. The evaluations were done in different ways: adding individual titrations, through percentage changes and classifying patients into categories of risk based on changes across threshold levels.

**Results:** NT-proBNP at discharge have the higher prognostic power for mortality (HFrEF 26,8% deceased: C-Index 0,85  $P < 0,0001$ ; HFpEF 14,7% deceased: C-Index 0,76  $P = 0,0004$ ) and combined end-point (HFrEF: C-Index 0,84  $P < 0,0001$ ; HFpEF: C-Index 0,67  $P = 0,01$ ). In multivariate Cox analysis it appears the most powerful and independent prognostic factor (HFrEF all  $P \leq 0,02$ ; HFpEF all  $P \leq 0,03$ ) and increases hazard ratio of models with only titrations at admission. The percentage changes stratify the risk only for mortality ( $\chi^2$  12,44  $P = 0,001$ ) conversely, categorical risk stratification shows a prognostic role for all outcomes (all log-rank  $P < 0,0001$ ) and provides independent prognostic informations when threshold values are specific for HFrEF or HFpEF compared to titrations. The categorical analysis seems define different profiles of QoL at 12 months census in patients still alive ( $P < 0,0001$ ). NT-proBNP at admission correlates with days of hospitalization ( $P = 0,0002$ ).

**Conclusions:** Levels of NT-proBNP at discharge have the highest prognostic value in inpatients subject with HF but a categorical classification based on repeated measurements and changes across threshold values of NT-proBNP specific for type of HF may be an independent strategy of risk stratification and may define differences in QoL in these patients.

#### P1046

##### ST2 in heart failure- a prognostic marker

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**Introduction:** ST2 (growth STimulation expression gene 2), a member of the interleukin family, has emerged as a novel biomarker in patients with heart failure (HF). It acts as a trigger for fibrosis and the cascade of events leading to cardiac remodelling. The heart is subjected to greater stress in the presence of high levels of soluble ST2, leading to cellular death and tissue fibrosis, reduced cardiac function, and increasing the rate of disease progression. While Brain Natriuretic Peptide (NTpro-BNP) is more useful for diagnosis of HF, ST2 is of particular value in prognostication. Patients with ST2 > 35 ng/ml are documented to have a 2.8x higher risk of adverse outcomes within 30 days. Good response of ST2 to therapy is associated with a better future course of the disease.

**Purpose:** To study and correlate ST2 biomarker release with NTpro-BNP, left ventricular ejection fraction (LVEF) and other parameters at the time of admission in patients presenting with heart failure in a single tertiary centre.

**Methods:** 150 patients, 93 males and 57 females who presented with clinical evidence of cardiac failure were evaluated with echocardiography and estimation of NTpro-BNP, ST2 and other blood investigations at time of admission. Patients were divided into four groups: GROUP A: 49 patients with ST2 < 35ng/dl (normals), GROUP B: 60 PATIENTS with ST2 between 35 to 100ng/dl and GROUP C: 41 patients with ST2 between 100 to 200ng/dl or more.

**Results:** Overall there was a correlation of ST2 with age, renal dysfunction and diabetes. There was also a significant correlation of ST2 with NTpro-BNP. Overall ST2 did not correlate with LVEF and 30% of HF patients on admission had normal ST2. However 43% of patients with ST2 over 100ng/dl had LVEF less than 30% compared with 26% when ST2 was normal. On follow up after discharge, no patient with normal ST2 (Group A) died, whereas 5 deaths and one cardiac transplant occurred in the abnormal groups put together (B, C and D). No difference was seen within groups B, C and D, suggesting any high value was associated with poorer prognosis.

**Conclusion:** Though there is a correlation between ST2 and NTpro-BNP values, ST2 is a better biomarker for risk stratification but not for diagnosis of HF. In this study, 30% of patients had normal ST2 levels on admission confirming this. ST2 was able to identify amongst HF patients those who had a poorer prognosis, as seen from the greater number of deaths in the high ST2 groups in this study. Correlation of high ST2 values with increasing age, renal dysfunction and diabetes in this study, could be a factor in poorer prognosis. We are closely following our patients for further clinical events and biomarker changes.

#### P1047

##### Biomarkers of cardiac damage in elderly people

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**Introduction and aims:** Chronic cardiac damage and heart failure represent the major cause of illness and death among elderly people. Since clinical signs and symptoms may be mild or even absent circulating biomarkers are of increased importance and utility for prognosis. Recently, high sensitive assays for cardiac troponin and specific markers for fibrosis have become available and we aimed to evaluate those in an apparently healthy population of elderly Italian people.

**Patients and methods:** A single plasma sample was taken after informed consent from 130 elderly persons (age > 65 years) living in hospices and with no overt signs of heart disease. Samples were tested by Vitros for cardiac troponin I (TnI) by a contemporary assay and by ARCHITECT for high sensitive (hs) TnI and also for BNP and Galectin-3, a fibrosis biomarker. Common tests for kidney function were also performed. Results. The mean age was 85.6±7.6 years with no significant differences between females (n=96) and males (n=34). Troponin I was detectable in 19 cases (14.6%) by the contemporary assays and in 124 (95.4%) cases by the hs assay; by the latter, measurable levels ranged from 2 to 110 ng/L and values exceeding the expected 99th percentile were found in 13.5% of females vs. 5.9 % of males ( $p < 0.01$ ). BNP and Galectin-3 levels exceeded the respective thresholds in 33.8% and 13.8% cases, respectively, with no gender differences. Mean creatinine levels were significantly higher in subjects with raised Galectin (1,70±0.77 umol/L) than in those with normal Galectin (1,06±0.39 umol/L) irrespective of BNP levels. An impaired renal function was detected in 6/9 subjects (66.7%) with both BNP and Galectin elevation (66.7%) compared to 30/121 (24.8%) of the other ( $p < 0.05$ ).

**Conclusions:** Our observation confirms that cardiac troponin is detectable by hs assays in almost all individuals, especially in elderly individuals that undergo a more active cardiac remodeling. The functional and structural biomarkers of heart failure are often altered in this population and reflect the general worsening of cardiac function in the late stages; whether the increase of the fibrosis biomarker is cause of consequence of the worsening of renal function is still to be investigated.

#### P1048

##### Clinical significance of growth differentiation factor-15 in patients with acute decompensated heart failure

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**Purpose:** Growth differentiation factor-15 (GDF-15) is emerging prognostic biomarker in various cardiovascular diseases. There is scarce information about it in patients with acute heart failure. The aim of our study was to determine the long-term prognostic value of GDF-15 in patients with acute decompensated heart failure (ADHF).

**Methods:** One hundred and seven consecutive patients (median age 70 [interquartile range, IQR: 60-73.5]; 36% women), hospitalized for ADHF, were examined. The primary and secondary end-points were to determine the differences in mortality and rehospitalization due to heart failure after two years, depending on the GDF-15 plasma level. Twenty-five healthy people of a similar age were in control group.

**Results:** The patients with ADHF had a significantly higher level of GDF-15 on admission (median 3481 [IQR: 2113-5090]), than the subjects in the control group (887.5 [IQR: 763.75-960.25] ng/L). A high GDF-15 level on admission remained a significant predictor for adverse outcome, shown by a multivariable regression analysis (hazard ratio [HR], 3.69; 95% confidence interval [CI], 1.58-13.53,  $p < 0.05$ ), together with B-type natriuretic peptide ( $p < 0.05$ ). A Kaplan-Meier curve analysis showed a significantly higher probability of death and heart failure rehospitalization in patients with higher levels of GDF-15. The highest mortality rate had patients with both GDF-15 and BNP levels above the median on admission.

**Conclusion:** The elevated GDF-15 value on admission was strong predictor of an adverse clinical outcome regarding mortality and HF rehospitalization 2-years after the initial hospitalization in patients with ADHF.



## P1049

**Calculated colloid osmotic pressure as an independent risk factor of mortality in chronic heart failure**J T Niedziela<sup>1</sup>; B Hudzik<sup>1</sup>; P Rozentryt<sup>1</sup>; N Niedziela<sup>2</sup>; A Ociessa<sup>1</sup>; J Nowak<sup>1</sup>; M Gasior<sup>1</sup><sup>1</sup>Medical University of Silesia, 3rd Department of Cardiology, SMDZ in Zabrze, Katowice, Poland; <sup>2</sup>Medical University of Silesia, Department of Neurology, SMDZ in Zabrze, Katowice, Poland

**Introduction:** Colloid osmotic pressure (COP) is determined by blood proteins and plays a pivotal role in the fluid balance between extra- and intravascular compartments. COP is associated with fluid shifts between compartments, which may result in the edema appearance. In critically ill patients COP was found to be a predictor of survival. Calculated COP (cCOP) based not only on plasma albumin (A), but also globulin (G) concentration, was found to be better correlated with measured COP than plasma albumin level itself.

**Purpose:** The purpose of this study was to assess the predictive role of cCOP in stable patients with heart failure with reduced ejection fraction (HFrEF) in 1-year follow-up.

**Methods:** Patients with stable HFrEF (without any clinical signs of congestion) treated in the heart failure outpatient clinic were included into the study. The cCOP was calculated using the Hoeffs equation:  $cCOP = A \times (1.058 \times G + 1.063 \times A + 3.11)$ . The cCOP was divided into quartiles. The probability of 1-year survival were compared between the groups using log-rank test. The multivariate survival analysis using COX's regression model adjusted for age, sex, LVEF, peak VO<sub>2</sub>, NT-proBNP levels, HF etiology and duration was performed. The forward regression was applied for 1-year follow-up.

**Results:** There were 999 patients included into the study; age  $52.8 \pm 10.4$  years, 13% of them were women, EF  $24.3 \pm 6.9\%$ , mean NYHA class  $2.6 \pm 0.7$ ; NT-proBNP  $2502 \pm 2992$  pg/mL and mean cCOP  $28.85 \pm 3.6$  mmHg. In the unadjusted survival analyses, the trend toward differences in 1-year mortality between the groups was found (log-rank  $p=0.07$ ). In the multivariate Cox model the Q4 of cCOP was associated with higher 1-year mortality than Q1 of cCOP.

**Conclusion:** In stable HFrEF patients the higher cCOP is an independent predictor of 1-year mortality. The effect of cCOP changes during albumin supplementation may be an interesting aim of further prospective studies.

Table. Multivariate analysis

	HR (95% CI)	p
Age [years]	1.03 (1.01 - 1.05)	0.001
NT-proBNP [pg/ml] (per 1000 pg/ml increase)	1.10 (1.06-1.15)	< 0.0001
Q1 cCOP	Reference	
Q2 cCOP	1.44 (0.86 - 2.42)	0.17
Q3 cCOP	0.97 (0.53 - 1.75)	0.91
Q4 cCOP	1.80 (1.08 - 2.99)	0.02
LVEF < 25%	1.86 (1.21 - 2.87)	0.005
peakVO <sub>2</sub> < 14 ml/kg/min	2.75 (1.83 - 4.14)	< 0.0001

Multivariate survival analysis using Cox's regression model - 1-year follow-up

## P1050

**Thyroid-stimulating hormone -predictor of long term mortality in heart failure with reduced ejection fraction**A Anca Breha<sup>1</sup>; C Delcea<sup>1</sup>; CA Buzea<sup>1</sup>; A Dima<sup>1</sup>; RA Popescu<sup>1</sup>; M Dobranici<sup>1</sup>; I Daha<sup>1</sup>; AR Dan<sup>1</sup>; C Baicus<sup>1</sup>; GA Dan<sup>1</sup><sup>1</sup>Colentina University Hospital, Bucharest, Romania

**Introduction:** Thyroid hormones exert important effects on cardiac structure and function. Both hypo- and hyperthyroidism could induce heart failure. However, data

regarding the clinical significance of thyroid-stimulating hormone (TSH) levels alone as a predictor of mortality in patients with HF with reduced ejection fraction (HFrEF) are sparse.

**Purpose:** We aimed to assess the value of TSH levels as a predictor for mortality in HFrEF patients.

**Methods:** We have retrospectively included patients with HFrEF aged over 18 years admitted to our clinic from January 1st to July 31st 2012. Acute coronary syndromes, pulmonary embolism, clinical manifest hypo- or hyperthyroidism, and in-hospital mortality were considered exclusion criteria. TSH levels were measured in all patients, while free T4 values were determined on individual basis. Survival was assessed at 3 years after hospital discharge for each subject.

**Results:** Our study group consisted of 150 patients with a mean age of  $72.71 \pm 10.31$  years, of which 82 (54.7%) patients were female. Median (minimum; maximum) TSH levels were 1.855 (0.005; 95.76) uIU/ mL. 18 (12%) patients had increased TSH levels (> 4.2 uIU/ mL) and 5 (3.33%) had decreased TSH levels (< 0.27 uIU/ mL). 3-year all-cause mortality was 28.7% for all group. Surviving patients had lower median TSH values of 1.65 (0.016; 52.53) compared to 2.27 (0.005; 95.76) in non-survivors,  $p=0.0138$ . Mortality increased with TSH value tertile from 10 (19.23%) patients in the first tertile to 20 patients (40.00%) in the highest tertile ( $p$  for trend = 0.0239). Patients in the highest TSH tertile had a fatality OR of 2.2 (95% CI 1.05 - 4.58),  $p=0.033$  compared to the rest of the sample. In ROC curve analysis, TSH predicted 3-year all-cause mortality with an AUC of 0.629 (95% CI 0.529 - 0.729),  $p=0.014$ . No correlation with mortality was found for decreased TSH levels.

**Conclusion:** TSH levels are correlated to survival in HFrEF patients, higher values indicating worse prognosis. We therefore emphasize the importance of thyroid function assessment in all heart failure patients.

## P1051

**Serial troponin assessment in the early phase of hospitalization for acute heart failure to identify high risk patients**R Zymliński<sup>1</sup>; M Sokolski<sup>2</sup>; J Biegus<sup>2</sup>; P Siwolowski<sup>1</sup>; J Todd<sup>3</sup>; J Estis<sup>3</sup>; S Florey<sup>3</sup>; EA Jankowska<sup>4</sup>; W Banasiak<sup>1</sup>; P Ponikowski<sup>2</sup><sup>1</sup>Centre for Heart Disease - Clinical Military Hospital, Wroclaw, Poland; <sup>2</sup>Wroclaw Medical University, Department of Heart Diseases, Centre for Heart Disease - Clinical Military Hospital, Wroclaw, Poland; <sup>3</sup>Singulex, California Inc. 1701 Harbor Bay Parkway Alameda, CA 94502, United States of America; <sup>4</sup>Wroclaw Medical University, Laboratory for Applied Research on Cardiovascular System, Department of Heart Diseases, Wroclaw, Poland

**Background:** New sensitive assays for cardiac troponins (Tn) are able to detect very low Tn concentrations. However, clinical interpretation of these findings, outside of acute coronary syndrome, remains unclear.

**Purpose:** The aim of the study was to interlink different patterns of Tn leak (measured with ultrasensitive assay) with clinical characteristics and outcomes in patients hospitalized with acute heart failure (AHF).

**Methods:** Ultra-sensitive cardiac TnI (us-TnI) was measured on admission, after 24, and after 48 hours using new diagnostic platform - immunoassay for plasma cardiac TnI by Single Molecule Counting technology (Singulex, USA). The following pattern of usTnI was defined as confirming 'myocardial damage' occurring early during AHF: A. usTnI above the 99th upper reference limit either at baseline or after 24 hours without significant (>20%) decrease in subsequent samples or B. a significant (>20%) increase from baseline in 24 and 48 hours. Remaining patients were classified as having 'no myocardial damage' usTnI pattern.

**Results:** We analyzed 91 patients with AHF (age:  $64 \pm 12$  years, 79% men, 24% AHF de novo) among whom 30 (33%) met the criteria for 'early myocardial damage'. These patients had on admission: lower systolic blood pressure ( $124 \pm 29$  vs  $140 \pm 36$ , mmHg), more often peripheral oedema (60% vs 34%), higher levels of NTproBNP (7116 [4893-14955] vs 4670 [2209-7980], pg/mL), creatinine (1.39 [1.20-1.75] vs 1.07 [0.90-1.30], mg/dL), urea (72 [49-100] vs 46 [37-58], mg/dL) and more common history of chronic heart failure (90% vs 69%) (all  $P < 0.05$ ). During hospital stay 13% from 'early myocardial damage group' required inotropic therapy and 3.3% pts died (vs 5% and 1.6% in the remaining patients). During 1-year follow-up cardiovascular mortality was significantly higher in patients with 'early myocardial damage' (40% vs 18%,  $p=0.023$ ; test log-rank:  $p=0.032$ ).

61734. Table

All-cause mortality	Model 1 (OPTIMAL)*	Model 2 (MAGGIC)#	CV mortality	Model 1 (OPTIMAL)*	Model 2 (MAGGIC)#			
	p	HR (95% CI)†		p	HR (95% CI)†	p	HR (95% CI)†	
log PICP µg/L	0.008	2.1 (1.2-3.6)	0.05	1.8 (1.0 -3.2)	0.006	2.7 (1.3-5.4)	0.08	2.0 (0.9-4.1)
log CITP µg/L	0.003	1.9 (1.2-2.8)	<0.0001	2.3 (1.4-3.7)	0.012	1.9 (1.2-3.2)	0.004	2.7 (1.4-5.2)
log PICP/CITP	0.200	0.8 (0.6-1.1)	0.057	0.7 (0.4-1.0)	0.55	0.9 (0.6-1.4)	0.17	0.7 (0.4-1.2)

\*model 1 including: age, gender, endsystolic volume, serum creatinine, hemoglobin. # model 2 including: age, gender, diabetes, previous HF, smoking, NYHA class, EF, ACE/ARB, betablockade, BMI, systolic blood pressure, serum creatinine. †Hazard ratios (HR) and confidence intervals (CI) for all-cause and cardiovascular mortality per 1 log unit change.

**Conclusion:** The pattern of us-TnI characterizing 'early myocardial damage' in patients hospitalized with AHF is associated with worse clinical status and poor outcome. Serial evaluation of us-TnI during early phase of hospitalization for AHF may be useful to identify high risk patients.

#### P1052

##### BNP and PCT utility in the management of acute heart failure patients with or without infections

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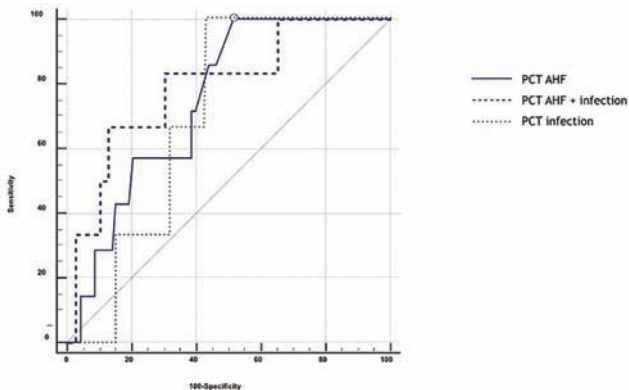
**Background:** Procalcitonin (PCT) is a protein up-regulated during bacterial infections and it has been demonstrated that in patients with heart failure, plasma PCT concentration are significantly higher than normal controls, and that there is a relation between PCT levels and 90-day mortality.

**Purpose:** Aim of this work was to evaluate the independent association between PCT and in-hospital mortality in patients admitted from ED with diagnosis of acute heart failure (AHF) with or without evidence of active infection.

**Methods:** This was a retrospective analysis of patients admitted for dyspnea with a final diagnosis of respiratory infection or AHF with or without infection. We evaluated the serum levels of PCT and BNP at ED arrival in these different groups and in order to determine the prognostic accuracy in terms of in-hospital mortality, we analyzed ROC curves and calculated the area under curves (AUCs).

**Results:** 351 patients classified in three groups: pulmonary infection (n 154), AHF without infection (n 146) and respiratory infection complicated by AHF (n 51). 18/351 (5.1%) patients died during hospitalization. Compared to the other two groups, in patients with AHF, the mean PCT values were significantly lower ( $0.24 \pm 0.56$  ng/ml). We divided patients with AHF without infection in three different classes based on BNP values and we found that the PCT was higher in patients with higher BNP values. PCT showed to be the best predictor of in-hospital mortality in all considered groups: AHF and infection (cut-off > 0.90 ng/ml, AUC 0.79,  $p < 0.004$ ); AHF alone (cut-off > 0.10 ng/ml, AUC 0.74,  $p < 0.0009$ ) and infection (cut-off > 0.17 ng/ml, AUC 0.70,  $p < 0.01$ ) (Fig. 1).

**Conclusions:** Beside its ability to detect the presence of bacterial infection, in patients presenting to ED with dyspnea due to AHF with or without infection PCT is a good predictor of in-hospital mortality. Our results could suggest that the activation of inflammatory response during AHF could interfere with PCT expression and may contribute to increase serum PCT levels.



PCT and in-hospital mortality

#### P1053

##### Disturbances of collagen type 1 metabolism are independent predictors of long-term mortality in systolic heart failure.

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**Purpose:** Disturbances of collagen metabolism may alter the myocardial collagen network and contribute to cardiac remodelling and 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 mortality in HF patients.

**Methods:** The Optimizing congestive heart failure outpatient clinic project (OPTIMAL) studied patients aged  $\geq 60$  years with NYHA class II–IV and HF with reduced left ventricular ejection fraction (HFrEF) hospitalised with acute HF during 1996–99. On entry, mean age was 75 years, blood pressure 134/80 mm Hg, ejection fraction 34 %, BNP 312 pg/ml; 55 % were in atrial fibrillation. Dates and causes of mortality were collected up until 2008.

**Results:** Follow-up was 9–13 years in all 132 patients, mean survival was  $5.5 \pm 4.0$  years. Multivariable Cox regression analyses were performed for all-cause ( $n = 101$ ) and cardiovascular mortality ( $n = 61$ ) by two models (Table). First, variables previously shown to predict mortality in OPTIMAL were included. Second, we used the variables in the heart failure risk calculator from Meta-analysis global group in chronic heart failure (MAGGIC).

**Conclusions:** Disturbances of collagen type I metabolism have independent prognostic implications for long-term all-cause and cardiovascular mortality in patients with HFrEF. We interpret that the results indicate degradation to be the predominant type associated with untoward prognosis.

#### P1054

##### Prognostic value of CA-125 in combination with N-terminal pro-brain natriuretic peptide in patients with acute decompensated heart failure

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**Background:** Carbohydrate antigen-125 (CA-125) is an emerging prognostic biomarker in heart failure. We aimed to test the long term prognostic value of CA-125 in combination with N-terminal pro-brain natriuretic peptide (NT-proBNP) in patients with acute decompensated heart failure.

**Methods:** A total of 457 patients ( $64.4 \pm 16.1$  years-old, 236 men) suffered acute decompensated heart failure between 2005. Jan and 2013. July were retrospectively enrolled. All-cause mortality was investigated for the prognosis of the patients.

**Results:** During follow-up ( $35.9 \pm 28.7$  months), 152 (33.2%) deaths were recorded. In multivariable analysis model, CA-125 was an independent prognostic marker (log CA-125 hazard ratio 1.241 [1.051–1.465],  $p = 0.010$ ) together with age, sex, NYHA class, systolic blood pressure,  $\beta$ -blocker use, inotropics use and NT-proBNP level. Kaplan-Meier analysis showed that patients with both elevated CA-125 and NT-proBNP level exhibited worse prognosis compared to those with any single marker solely-elevated (Figure 1). Likelihood ratio test showed that addition of NT-proBNP level to established risk factors increase the predictive power for mortality (global chi-square from 156.2 to 167.2,  $p < 0.001$ ). Addition of CA-125 on the top of the combination of NT-proBNP and established risk factors still more increased the predictive power for mortality (global chi-square from 167.2 to 173.7,  $p = 0.011$ ) in patients with acute decompensated heart failure.

**Conclusion:** CA-125 was an independent prognostic marker in patients with acute decompensated heart failure. Combined use of CA-125 and NT-proBNP provided a significant improvement in prognostic power for mortality in patients with acute decompensated heart failure.

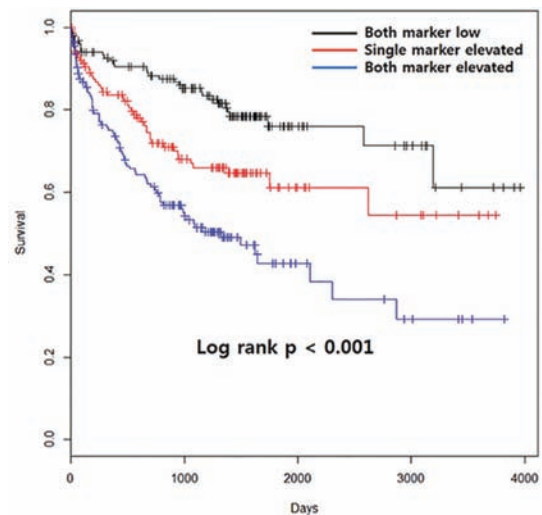


Figure 1

**P1055**

**Multi-biomarker profiling and recurrent hospitalizations in heart failure**

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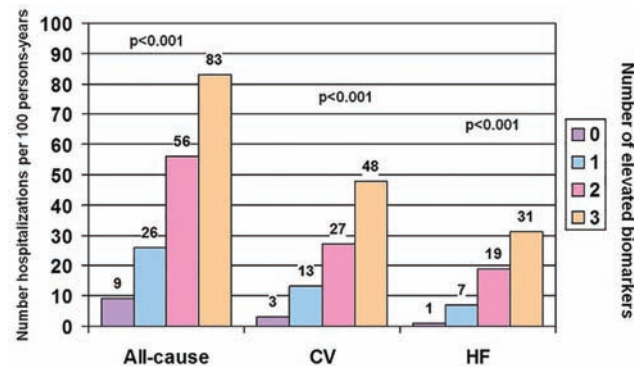
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**Background:** Despite current treatment with evidence-based drugs and devices, patients with heart failure (HF) are frequently admitted to the hospital because of symptom exacerbation, and once admitted, they are often readmitted. Risk prediction of recurrent hospitalizations has often been downplayed, with study endpoints focused on time-to-first event analysis and disregarding the impact of recurrent readmissions that frequently occur in HF. Objective: We sought to explore whether a multi-biomarker panel (including NT-proBNP, hs-TnT, and ST2) is superior to clinical assessment for long-term prediction of recurrent hospitalizations in HF.

**Methods:** NT-proBNP, high-sensitivity troponin T (hs-TnT), and ST2 levels were measured in 891 consecutive ambulatory HF patients. The state-of-the-art statistics were used. The independent association between the multi-biomarker panel and recurrent hospitalizations was assessed through a multivariable negative binomial regression and expressed as incidence rates ratio. McFadden pseudoR2 and goodness-of-fit measures were also used. The total number of unplanned hospitalizations (all-cause, cardiovascular [CV]-, and HF-related) were selected as the primary endpoints.

**Results:** At a mean follow-up of 4.2±2.1 years, 1623 all-cause hospitalizations in 498 patients (55.9%), 710 CV-related hospitalizations in 331 patients (37.2%), and 444 HF-related hospitalizations in 214 patients (24.1%) were registered. The crude incidence of all-cause, CV-, and HF-related recurrent hospitalizations was significantly higher for patients with the multi-biomarker panel above the cut-point (hs-TnT > 14 ng/L, NT-proBNP > 1000 ng/L, and ST2 > 35 ng/mL) (all P < 0.001) (figure). For all-cause, CV-, and HF-related recurrent hospitalizations, the McFadden R2, Akaike information criterion, and Bayesian information criterion supported the superiority of incorporating the multi-biomarker panel into a clinical predictive model.

**Conclusions:** A multi-biomarker approach that incorporates NT-proBNP, hs-TnT, and ST2 better identifies HF patients at risk for recurrent hospitalizations. Elucidation of new biophysiological targets for recurrent hospitalizations may identify patient profiles for focused intervention.



**P1056**

**Testing for soluble ST2 in heart failure patients: reliability of a point of care method**

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**Background:** Soluble ST2 (sST2) is a soluble decoy receptor able to quench the biological activity of IL-33, a cytokine preventing the apoptosis of cardiomyocytes and improving cardiac function. The increase of circulating sST2 levels is related to cardiac remodeling, fibrosis and to the severity of Heart Failure (HF).

**Purpose:** Our objectives were to determine the clinical validity of a recently developed point of care (POCT) assay for measurement of sST2.

**Methods:** Samples of forty-nine HF patients (NYHA II-IV; mean age: 67 years; median LVEF: 23%) were measured with the sST2 POCT assay and with a reference ELISA method. Circulating levels of BNP, NT-proBNP, Galectin-3 and PTH(1-84) were determined with automated immunoassays.

**Results:** The median sST2 levels measured with the POCT and ELISA assays were 37.7 ng/mL (range: 12.5–250) and 39.1 ng/mL (18.4–200), respectively. Both methods were significantly correlated (r = 0.93, p < 0.0001). Passing-Bablok regression analysis showed a slope of 1.5 and an intercept of 22.5. Bland-Altman plot

evidenced a bias between the methods with a mean bias of 5.2 ng/ml. However, the POCT method was faster by allowing a turnaround time of analysis lower than 30 minutes. Levels of sST2 determined with the POCT were significantly related to the left ventricular ejection fraction. Concentrations of sST2 measured by the POCT assay were also significantly and positively correlated to BNP (r = 0.75, p < 0.001), NT-proBNP (r = 0.57, p < 0.001), Galectin-3 (r = 0.40, p < 0.01) and PTH(1-84) (r = 0.39, p < 0.01).

**Conclusions:** Our results confirm the reliability of the sST2 POCT assay and its compatibility with clinical practices. Moreover, the POCT method allows a faster delivery of results to physicians.

**P1057**

**A new marker for poor NYHA functional class in heart failure with reduced ejection fraction: C-reactive protein / lymphocyte ratio**

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**Background and objectives:** Exercise intolerance and higher New York Heart Association (NYHA) classes predict poor prognosis in patients with heart failure with reduced ejection fraction (HFrEF). Heart failure (HF) is characterized by ongoing inflammation mediated by proinflammatory cytokines and inflammatory mediators. The studies demonstrated that increased C-reactive protein (CRP) level or decreased lymphocytes level is associated with poor functional capacity in patients HFrEF. However no data exists about the association between CRP/lymphocyte ratio and functional capacity in patients with stable HF. In this study, we aimed to investigate the relationship between functional status and CRP/lymphocyte ratio in outpatients with HFrEF.

**Methods:** A total of 246 consecutive patients with HFrEF diagnosis for at least 6 months duration who were admitted to outpatient cardiology clinic, were included in this prospective study. Patients were divided into 2 groups according to NYHA class: NYHA class I-II (group 1) and NYHA class III-IV (group 2).

**Results:** The mean age of patients was 43 ± 11 years. CRP value was statistically higher, and lymphocyte level was statistically lower in NYHA III-IV group. Furthermore, the median CRP/lymphocyte ratio (0.8 vs 0.2, p < 0.001) was significantly higher in NYHA III-IV group as compared to NYHA I-II group. In multivariate logistic regression model, CRP/lymphocyte ratio (OR: 1.393, 95% CI: 1.080-1.798, p = 0.011), hemoglobin level (OR: 0.809, 95% CI: 0.659-0.992, p = 0.042), LVEF (OR: 0.872, 95% CI: 0.805-0.945, p = 0.001), and digoxin usage (OR: 2.488, 95% CI: 1.132-5.647, p = 0.023) were remained associated with poor NYHA functional class in HFrEF outpatients (Table 1).

**Conclusion:** We demonstrated that CRP/lymphocyte ratio was strongly associated with poor NYHA functional capacity, independently from coronary heart disease risk factors in stable HFrEF outpatients.

Table 1. Univariate and multivariate predictors of poor NYHA functional class.

	Univariate			Multivariate		
	P	OR	95% CI	P	OR	95% CI
<i>Statistically significant variables</i>						
CRP, mg/L	0.001	1.207	1.074-1.356			
Lymphocyte, 10 <sup>9</sup> cells/mm <sup>3</sup>	0.047	0.694	0.484-0.985			
CRP/lymphocyte ratio	0.002	1.416	1.141-1.756	0.011	1.393	1.080-1.798
BUN, mg/dL	0.014	1.032	1.006-1.058			
Creatinine, mg/dL	0.047	2.721	1.014-7.304			
Male gender	0.032	2.914	1.094-7.761			
Hemoglobin, g/dL	0.002	0.759	0.638-0.903	0.042	0.809	0.659-0.992
Neutrophil, 10 <sup>9</sup> cells/mm <sup>3</sup>	0.025	1.205	1.204-1.419			
Neutrophil/lymphocyte ratio	0.005	1.315	1.088-1.590			
LV ejection fraction, %	<0.001	0.872	0.816-0.932	0.001	0.872	0.805-0.945
BNP > 35pg/mL, n (%)	0.023	10.366	1.378-77.983			
Furosemide use, n (%)	0.040	2.593	1.044-6.444			
Digoxin use, n (%)	0.034	2.002	1.056-3.798	0.023	2.488	1.132-5.647
Heart rate	0.032	1.022	1.002-1.043			
<i>Variables which correlated with CRP/lymphocyte ratio</i>						
Age (years)	0.613	1.007	0.979-1.037			
Fasting glucose, mg/dl	0.271	1.004	0.997-1.011			
Sodium, mEq/L	0.110	0.931	0.853-1.016			
Potassium, mEq/L	0.356	0.723	0.363-1.439			
ACEI use, n (%)	0.397	0.748	0.382-1.465			
Beta blocker use, n (%)	0.115	0.270	0.053-1.377			

Predictors of poor NYHA functional class



## P1058

### Magnitude of brain natriuretic peptide elevation in the emergency department is associated with all-cause cardiac diagnosis, but not necessarily acute decompensated heart failure

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**Background:** Brain natriuretic peptide (BNP) testing is effective in excluding acute decompensated heart failure (ADHF) in the Emergency Department (ED) due to high negative predictive value. However, BNP is elevated in other cardiac and non-cardiac conditions. The clinical utility of an elevated BNP in ED patients is less well defined.

**Purpose:** In patients presenting to an ED with no predefined protocol for BNP testing, we aimed to determine (i) the diagnoses associated with elevated BNP according to magnitude of BNP elevation, and (ii) the proportion of these patients with ADHF and left ventricular systolic dysfunction (LVSD).

**Method:** BNP results were identified from laboratory records over a 3-month period. For patients with elevated BNP, case records were reviewed for clinical features and echocardiographic findings. Primary and subsidiary diagnoses and mortality rates were determined from hospital coding statistics.

**Results:** 192 patients were included, of whom 62 had normal BNP levels (< 100 pg/ml) and 130 elevated: 60 with mildly elevated BNP (100-399 pg/ml; Group A) and 70 with significantly elevated BNP ( $\geq$ 400 pg/ml; Group B). As shown in the table, Group B patients were more likely to receive a primary ADHF diagnosis, and to have LVSD. A cardiac primary diagnosis (ADHF, acute coronary syndrome, arrhythmia and valve disease) was twice as likely in this group. A non-cardiac or respiratory diagnosis was more likely in Group A. 6-month mortality was similar between groups.

**Conclusion:** ADHF accounted for a minority of primary diagnoses in ED patients with elevated BNP, however ADHF and other primary cardiac diagnoses are more likely in patients with BNP  $\geq$ 400 pg/ml compared to those with BNP 100-399 pg/ml. ED physicians should have high index of suspicion for cardiac disease in patients with BNP  $\geq$ 400 pg/ml, however ADHF should not be diagnosed from elevated BNP alone.

#### Patient characteristics

	Group A (BNP 100-399, n=60)	Group B (BNP $\geq$ 400, n=70)
Mean age, years	75	77
Deaths at 6-months, n (%)	15 (25.0)	17 (24.3)
LVSD, n (% of patients receiving echo)	14 (36.8)	31 (57.4)
ADHF primary diagnosis, n (%)	7 (11.7)	24 (34.3)
ADHF primary or subsidiary diagnosis, n (%)	12 (20.0)	36 (51.4)
All-cause cardiac primary diagnosis, n (%)	18 (30.0)	42 (60.0)
Respiratory primary diagnosis, n (%)	15 (25.0)	15 (21.4)
Other organ primary diagnosis, n (%)	18 (30.0)	6 (8.6)
Diagnosis not determined, n (%)	9 (15.0)	7 (10.0)

## P1059

### Relation between left ventricular global longitudinal strain and B-type natriuretic peptide in patients with chronic heart failure

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**Introduction:** In the setting of chronic heart failure (CHF) patients, the finding of elevated levels of B-type natriuretic peptide or of the N-terminal fragment of the pro B-type natriuretic peptide (NT-proBNP) is a reliable marker of pathological increase in myocardial ventricular wall stress and detrimental rise in ventricular filling pressures. However, the ensemble of data concerning the relationship between longitudinal deformation indices and NT-proBNP is still rather vague and approximate.

**Methods:** We carried out a retrospective study that involved 118 CHF patients admitted to our clinic for CHF outpatients. For inclusion in the study, the CHF patients were required to have undergone at least a determination of global longitudinal strain (GLS) by means of two-dimensional speckle tracking echocardiography and to have practiced at least a determination of NT-proBNP. Furthermore, the two determinations should have been carried out in a condition of substantial simultaneity, that is, the former should have been done not more than 24 hours before or after the latter.

**Results:** Correlation between log (NT-proBNP) and GLS was highly significant ( $r=0.8247$ ;  $p<0.0001$ ). The observed correlation between log (NT-proBNP) and left ventricular ejection fraction (LVEF) was also significant, but explained a smaller magnitude of the variance ( $r=-0.335$ ;  $p=0.0019$ ). In CHF patients with reduced

ejection fraction (HFREF) and in those with preserved ejection fraction (HFpEF) analyzed separately, log (NT-proBNP) exhibited a stronger overall correlation with GLS (HFREF,  $r=0.8426$ ,  $p<0.0001$ ; HFpEF,  $r=0.8472$ ,  $p<0.0001$ ) compared with LVEF (HFREF,  $r=-0.3592$ ,  $p=0.1568$ ; HFpEF,  $r=-0.3437$ ,  $p=0.0502$ ). The median value of NT-proBNP (namely, 495 pg/mL) was used as a discriminating value for identifying relatively low (i.e., below the median) and relatively high (i.e., above the median) levels of natriuretic peptide. In this manner, higher (namely less negative) values of GLS were associated with significantly increased probability of higher levels of NT-proBNP (i.e.,  $>495$  pg/mL). On the contrary, higher values of LVEF were associated with significantly increased probability of reduced levels of NT-proBNP (i.e.,  $\leq 495$  pg/mL). However, the C-statistics for GLS were significantly higher than for LVEF [area under the curve (AUC): 0.949 (GLS) vs. 0.730 (LVEF)];  $p=0.0038$ ].

**Conclusions:** In CHF patients with apparently preserved systolic function as well in those with reduced ejection fraction, GLS is more accurate compared with LVEF in predicting increased levels of NT-proBNP.

## P1060

### Role of NT proBNP in preventing left ventricular dysfunction in hypertensive patients

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**Purpose:** To study the importance of NTproBNP in guiding treatment to prevent left ventricular dysfunction in hypertensive patients.

**Methods:** We included 168 patients with hypertension who were present at hospital for cardiology consultation for one and a half year. We excluded patients who are already diagnosed with heart failure, left ventricular systolic dysfunction. We randomized patients into 2 equal groups: a control group (84 patients) and an intervention group (84 patients). NTproBNP value was determined in all patients. In the intervention group patients were treated according to the NTproBNP value. Patients who had NTproBNP value  $<125$  pg / dl (36 patients) received standard treatment for their symptoms. Patients who had NTproBNP value  $>125$  pg / dl (52 patients) were the ones on which we intervened to prevent left ventricular dysfunction. They were investigated by cardiac ultrasound and other specific tests of 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 of their symptoms regardless of the NTproBNP value.

**Results:** The end points were: systolic or diastolic left ventricular dysfunction, and the rate of hospitalizations for cardiovascular pathology. After two year, in the control group 29 (34.5%) patients were diagnosed with left ventricular systolic dysfunction, compared to 21 (25%) in the intervention group. In control group were 56 (66.6%) patients diagnosed with left ventricular diastolic dysfunction, compared to 43 (51.1%) in the intervention group. Also, and rate of admissions for heart disease was higher in the control group 33 (39.2%) versus 16 (19%) patients 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 diastolic and systolic left ventricular dysfunction or cardiovascular events than patients in the control group. In conclusion medical intervention guided by NT proBNP can prevent or delay left ventricular dysfunction in hypertension patients.

## NURSING

## P1061

### Clinical, psychosocial and quality of life profile of hospitalized patients with de novo heart failure and reduced left ventricular ejection fraction, etific project

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**Background:** The profile of hospitalized patients with "de Novo" Heart Failure (HF) and Left Ventricular Ejection Fraction (LVEF) $\leq$ 40% is not well known. **Purpose:** To evaluate the clinical, psychosocial and quality of life characteristics of hospitalized patients with "de Novo" HF and LVEF $\leq$ 40%.

**Methods:** Multicenter cross-sectional study at discharge of admitted patients with "de Novo" HF and LVEF $\leq$ 40%, recruited in cardiology wards (March-September

60147. Table. Patient characteristics

Sociodemographic	n(%)	Clinical	n(%)
Female	14(23.7)	NYHA II/III	45(77.6)/13(22.4)
Age*	61.1(11.4)	LVEF $\leq$ 25%/26-40%	51(87.9)/7(12.1)
Educational Level $\leq$ 10 years	25(46.3)	6 min test **	370(120-460)
Quality of life questionnaires		Ischemic cardiomyopathy	11(18.8)
MLWHFQ	51.9(24)	Respiratory disease	8(13.6)
Physical/Emotional Dimension*	25.1(11.0)/9.3(7.2)	Cancer	3(5.1)
Euro-QoL-5D *	0.77(0.24)	Age-adjusted Charlson index*	3.6(1.9)
Visual analogic scale*	53.2(22.6)	Laboratory tests	
Cardiovascular risk factors		Nt-ProBNP at discharge*	2333(2126)
Hypertension	31(52.5)	Nt-ProBNP > 1000	36(76.6)
Dyslipidemia	21(35.6)	Systolic Blood Pressure(SBP)*	112(20)
Diabetes	16(27.1)	SBP $\leq$ 110	29(49.2)
Smoker	20(36.4)	Heart Rate*	75(14.9)
Alcohol consumption > 2 units	15(25.4)	Glomerular filtration 30-60	12(28.6)
Body Mass Index <20/20-30/> 30	7(12.5)/33(58.9)/16(28.6)	Haemoglobin<12	9(15.2)

\*result as mean(standard deviation); \*\* result as median (interquartile range)

2015). Sociodemographic, clinical and quality of life variables were recorded. Descriptive statistics were performed: mean (or median) and standard deviations (or interquartile range) were calculated. Otherwise, frequencies and percentages were computed. These statistical analyses were developed using SAS System v9.4.

**Results:** A sample of 59 patients were recruited, 14(23,7) being female. The mean age was 61,1 years, the Minnesota Living with HF Questionnaire (MLWHFQ) 51,9(24) and 51(87,9%) patients had LVEF $\leq$ 25% (Table)

**Conclusions:** Relatively young patients(older patients tend to be assigned to internal medicine), male(greater presence of women in preserved LVEF;possible selection bias), low educational level, quality of life greatly affected, most of them having severely depressed LVEF, CVRF and comorbidities despite probable under-registration). Specialized multidisciplinary holistic approach is crucial.

#### P1062

##### Is individual patient education a reliable tool to prevent heart failure in diabetes?

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**Background:** Diabetes is a strong predictor of Heart Failure (HF). Glycemic control, obesity and blood pressure (BP) can have a major role in the development of HF among diabetic patients. Therapeutic Patient Education (TPE) has a major role in diabetes management and in the improvement of all outcomes. PURPOSE. to evaluate whether individual TPE can reduce some risk factors for HF in diabetes.

**Methods:** All people followed for at least 24 months in the randomized controlled INTEND (Individual Therapeutic Education in Newly Diagnosed type 2 diabetes) study were recruited. Twenty-seven newly diagnosed type 2 diabetic patients who received an individual TPE (GROUP A) were compared to 27 age- and sex-matched newly diagnosed type 2 diabetic patients in usual care (GROUP B). The two study groups were comparable in age (62.9 $\pm$ 9.2 vs 61.0 $\pm$ 8.6 years), sex (males 40.7 vs 48.1%), HbA1c, BMI, systolic BP and diastolic BP at baseline. No patient had HF at baseline on the basis of clinical, ECG and echo criteria.

**Results:** After a 24-month follow-up period both GROUP A and GROUP B showed significantly (p<0.01) lower HbA1c (GROUP A: 9.0 $\pm$ 2.4 vs 6.5 $\pm$ 0.9%; GROUP B: 8.7 $\pm$ 1.5 vs 7.6 $\pm$ 0.9%), systolic BP (GROUP A: 168.0 $\pm$ 12.1 vs 144.1 $\pm$ 15.1 mmHg; GROUP B: 168.7 $\pm$ 14.8 vs 149.4 $\pm$ 15.9 mmHg) and diastolic BP (GROUP A: 83.4 $\pm$ 10.6 vs 70.7 $\pm$ 9.9; GROUP B: 84.3 $\pm$ 9.4 vs 75.1 $\pm$ 6.9 mmHg) than at baseline. BMI was significantly decreased at the end of the follow-up in the GROUP A (30.9 $\pm$ 4.9 vs 26.8 $\pm$ 10.1; p<0.01) but not in the GROUP B (29.9 $\pm$ 4.0 vs 30.9 $\pm$ 4.5). At the end of the follow-up HbA1c, BMI, systolic BP and diastolic BP were significantly lower in the GROUP A than in the GROUP B. In addition in 6 patients of the GROUP A and 14 patients of the GROUP B an intensification of therapy for diabetes and/or hypertension was needed. No patient developed HF during the follow-up.

**Conclusions:** Individual TPE may be a reliable tool to control risk factors for HF in type 2 diabetes

#### P1063

##### Role telenursing on quality of life and readmission patient with heart failure

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**Background:** The Nature of heart failure causes reducing the quality of life and higher readmission in patients.

**Purpose:** To measure the impact of tele nursing on patients discharged with heart failure.DESIGN: Experimental study (RCT).SAMPLE: 42 patients with heart failure were divided into two groups by using the purposive sampling method based on random allocation. Medical centers with traditional care (21patient) and traditional care plus telenursing (21patient).

**Methods:** This trial compared 2 post-hospitalization nursing care models for reducing congestive heart failure (CHF) readmission charges during 90 days of follow-up. Subjects received in-person visits at baseline and 60 days plus 1 of 2 care modalities in the interim: telenursing( telephone calls and message) and usual care. Minnesota's questionnaire of quality of life was completedFINDINGS: Telenursing patients indicated higher satisfaction. Overall costs for both types of visits were about equal. The control group have increased cost of 1.30 \$ per patient (P $\leq$ 0.002). The results showed telenursing was difference statistically significant) P <0/000).

**Conclusions:** Combining traditional care and and telenursing is feasible for supporting discharged patients with new heart failur and enhances traditional care, resulting in increased satisfaction overall.

#### P1064

##### Perception about heart failure telemonitoring of physicians and nurses from Japan and Sweden

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**Background:** Non-invasive telemonitoring of heart failure (HF) patients is increasingly addressed in research. However, little is known about perception of telemonitoring among healthcare professionals who are working with HF patients in daily clinical practice.

**Aim:** The aim of this study was (1) to describe perception of non-invasive HF telemonitoring among Japanese and Swedish physicians and nurses and (2) to compare the perception between physicians and nurses.

**Methods:** A cross-sectional questionnaire survey of non-invasive HF telemonitoring was performed in Japan and Sweden between November 2013 and May 2014. A total of 378 Japanese (120 cardiologists, 258 nurses) and 120 Swedish (39 cardiologists, 81 nurses) healthcare professionals from 165 Japanese and 61 Swedish hospitals/clinics nationwide (210 in Japan, 98 in Sweden approached) participated in the study. Participants were asked if they were familiar with HF telemonitoring (yes/no). They were also asked about good ways to follow up stable HF patients (multiple choice). In addition, participants were asked about main purpose for telemonitoring, reasons for introducing telemonitoring in HF patients as well as criteria

to select HF patients for telemonitoring with a questionnaire that was adapted from a previous Dutch study.

**Results:** There was a significant difference in familiarity of non-invasive HF telemonitoring between physicians (40%, n = 63) and nurses (16%, n = 55) ( $p < 0.01$ ). In total 24% of physicians (n = 38) and 27% of nurses (n = 92) thought that "Telemonitoring" was a good way to follow up stable HF patients. Regardless of profession, the most frequent purpose for choosing HF telemonitoring was "monitoring physical condition and noticing a decline" (physicians 93%, n = 144; nurses 93%, n = 309). Among nurses (64%, n = 215) "patient education" was more frequently seen as a purpose ( $p = 0.02$ ) compared with physicians (53%, n = 82). There were no differences in reasons for introducing telemonitoring rated on a scale from 0-10 (low-high): to reduce hospitalizations (8.4 in physicians and 8.0 in nurses), and to increase patients' self-care (7.6 and 7.8). Regarding criteria to select HF patients for telemonitoring, most of physicians (91%, n = 141) and nurses (79%, n = 263) chose "admission/readmission," meanwhile "patient education" and "support and advice" were more frequent criteria among nurses (57%, n = 191, 47%, n = 157, respectively; both  $p < 0.01$ ).

**Conclusions:** Nurses are less familiar with non-invasive HF telemonitoring than physicians. Regardless of profession, healthcare providers have expectations of telemonitoring to reduce patients' hospitalizations and increase patient self-care. More nurses have perception that telemonitoring could be a tool for helping patient education and support.

### P1065

#### The greek version of teamSTEPPS teamwork perceptions questionnaire and minnesota satisfaction questionnaire "short form"

Heart Failure Association - nurse training fellowship  
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**Background:** Teamwork and job satisfaction is important among the multidisciplinary team who care HF patients. TeamSTEPPS and Minnesota Satisfaction Questionnaire "short form" are both self-report questionnaires which examine multiple dimensions of perceptions of teamwork and job satisfaction, respectively within healthcare settings. Our aim is to examine the psychometric properties of the Greek versions of the TeamSTEPPS Teamwork perceptions questionnaire (GrT-TPQ) and Minnesota Satisfaction Questionnaire "short form" (GrMSQ-short). Method: A methodological study was conducted in order to assess the construct validity and reliability of the GrT-TPQ and GrMSQ-short. For that reason, 292 questionnaires were administered by Greek-Cypriot health care professionals (HCPs). Confirmatory factor analysis (CFA) and Exploratory factor analysis were conducted to examine the relationship between the five T-TPQ dimensions. Cronbach's  $\alpha$  was calculated as well.

**Results:** CFA of GrT-TPQ confirmed the initial scale structure with excellent fit indices ( $\chi^2$  (df) 1124.75 (550),  $p < 0.0001$ , AGFI = 0.986, TLI = 0.994, CFI = 0.994, RMSEA = 0.06, 90%, C.I.[0.055-0.065]). Furthermore, all dimensions were found to be correlated ( $r = 0.65$  to  $r = 0.88$ ) and internal consistency was found adequate (Cronbach's  $\alpha = 0.96$ ). Subscales also, demonstrated high internal consistency ( $\alpha = 0.87-0.95$ ). CFA for GrMSQ-short, did not confirm the initial scale's dimensions. In EFA items 1, 5, 6, 12 and 18 were eliminated from the analysis due to low communalities and multiple components loading. Two components were found representing the intrinsic and extrinsic aspects of job satisfaction.

**Conclusions:** GrT-TPQ and GrMSQ-short are construct-valid instruments for measuring perceptions of teamwork and job satisfaction. This has increased implications on future use and research on HCPs who care for patients with HF.

### P1066

#### Self-care behavior and its associated factors among heart failure patients in Pakistan.

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Abstract Heart Failure is a progressively worsening clinical syndrome associated with poor quality of life and higher hospital readmissions. Self-care in heart failure is considered equally important to its pharmacological management. Literature indicates that the level of self-care varies among different culture. However, little is known about the self-care behaviors and its predictors among HF patients in the developing countries. Therefore, this study aimed to determine the level of SCB and its associated factors among HF patients in Pakistan. The study was conducted using a sequential mixed method approach. The SCB of 230 heart failure patients were assessed using European Heart Failure Self-Care Behavior Scale\_9 (EHFScBS\_9) via a cross sectional survey. Moreover, eight patients were interviewed to explore the factors affecting their SCB. The mean score of the EHFScBS was 29.30 +/- 7.06. In multivariate Analysis, education, income and chronicity of the HF diagnosis were associated with better SCB ( $P < 0.005$ ). Moreover, analyses of the

qualitative data showed patients' financial status, family support, health education and support of the health care system as important factors affecting the SCB of HF patients. The overall level of the self-care was found to be sub-optimal. The convergence of the quantitative and qualitative findings revealed that patients' financial status, education and experience of the illness are the key determinants of SCB among HF patients in Pakistan. Hence, this study has implications for the health care providers, policy makers and donors to establish HF management programs for the patients in our culture.

### P1067

#### Nursing care in patients undergoing left ventricular assist devices (LVAD) implantation as bridge to transplantation therapy

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**Introduction:** the advent of implantable ventricular assist device (VAD) to treat advanced heart failure has changed dramatically this high mortality syndrome. The action of nursing in this context takes on a prominent role, especially in reducing driveline infection and major bleeding related to long term mechanical circulatory support. Propose: to describe the nursing care practices related to implantable VAD patients and correlate them to the incidence of driveline infection and major bleeding observed in a given period.

**Method:** qualitative and descriptive (observational) study correlating the standardization of nursing practices to patients treated with implantable VADs from October 10, 2013 to January 18, 2016 and the incidence of major bleeding and driveline infection as INTERMACS registry settings. The standardization followed the practices regarding: (i) patient and caregiver's education (self-care: bathing, exercise and oral hydration); (ii) dressing driveline changes (technical, frequency, materials, exit site wound classification and photographic record); (iii) the stability of driveline; (iv) alarm interpretation (batteries and self-test); (v) home visit (adaptation of day-by-day routines); (vi) oral anticoagulation control (outpatient protocol).

**Results:** since the beginning of the VAD implant program, a rate of 178 patients-day free of bleeding and/or infection of the driveline exit site according to INTERMACS setting was observed.

**Discussion(s):** the role of the specialized nursing team in mechanical circulatory support is crucial to major bleeding and driveline infection free survival for patients receiving durable VAD. The systematization and organization of nursing actions in specific protocols is the key. Educational guidance of nurses to patients after VAD implantation covers the surgical recovery process, the care of driveline's exit site and the device handling; contribute to self-post hospital care and possible improvement of symptoms while waiting for a heart transplant.

### P1068

#### Usefulness of a simple educational tool with 4-colour leaflets to increase adherence to medication and assessment of patients satisfaction with it

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**Background:** Patients with heart failure (HF) require complex pharmacological treatment to increase survival and quality of life. Health education is mandatory to promote patient's self-care and has demonstrated to improve outcomes. The use of simple educational tools may be key to achieve this goal.

**Purpose:** Primary objective: To assess the usefulness of a simple informational tool (4-colour leaflets, based on the 2012 HF Guidelines ESC) for increase the adherence to medication in HF with reduced ejection fraction (HFrEF) patients. Secondary objective: To assess the patient's acceptance and satisfaction on these informational tools.

**Methods:** Consecutive patients with HFrEF (defined as LEVf <40%) seen at our HF Unit and receiving any of the disease-modifying therapies for HFrEF drugs (RAAS inhibitors, beta-blockers, mineral receptor antagonists, and ivabradine) were invited to participate. The only exclusion criterion was refusal to participate and/or unavailability to understand the information. Changes in adherence to pharmacological treatment was assessed using the Morisky Medication Adherence Scale (MMAS-4) basal and after 6 months. MMAS (from 0% to 100% according correct response to 1 to 4 questions); 3-4 was considered "full adherence" and 0-2 "poor adherence". Patient's satisfaction was assessed with a survey of 5-point multiple Likert response questions (from 1 minimum to 5 maximum).

**Results:** Among 234 patients enrolled between March and June 2015, this preliminary analysis on adherence has been done on 174 patients (mean age 67.7 years SD 10.3; 80.5% male) who had completed baseline and 6-month MMAS by the time of data analysis. NYHA class status were as follows: I (37 patients, 21.3%), II (105 patients, 60.3%), III (31 patients, 17.8%) and IV (1 patient, 0.6%). The distribution of etiology was as follows: 77 (44.3%) ischemic, 68 (39.1%) dilated and 29 (16.7%)



other. Most patients (156/174, 89.7%) reported full-adherence by means of MMAS-4 already at entry, proportion that did not significantly changed at six months (152/174, 87.4%;  $p = n.s.$ ). Nevertheless, among patients with poor adherence at entry, 55.6% of them (10 out of 18) became full adherent after tool implementation ( $p < 0.001$ ). In addition, 64.2% of participants who completed the satisfaction survey showed high levels of satisfaction (4 or 5 in the Likert scale).

**Conclusions:** Even among patients with high adherence to recommended treatments as ours, identification of "low adherents" by means of MMAS and implementation of this well accepted educational tool may be of clinical utility.

#### P1069

##### Hospitalised heart failure patients: what is behind their satisfaction with nursing care?

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**Introduction:** There is an increasing interest on patient satisfaction in healthcare. Moreover, the satisfaction with nursing care is a relevant indicator for hospitals quality of care. Its measurement is also strategic to define and meet patients' needs in terms of care, particularly in patients with a chronic and multifaceted conditions, such as the chronic heart failure (HF). However, the relations between specific domains of clinical practice (i.e. carelessness, emotional support, relationship and caring times) and patient satisfaction with nursing care are not clear. Purpose The aim of this study is to assess which areas of clinical practice influence the patient satisfaction and to describe its relationship with socio-demographic characteristics in patients with HF.

**Methods:** An observational, cross-sectional and correlational study design was used, with a convenience sample of 201 hospitalized HF patients (NYHA class II-III) (mean age 66.8 years, SD 8.6; 63% men). After a written informed consent and the socio-demographic variables collection, patient satisfaction was assessed using the Newcastle Satisfaction with Nursing Scales (Italian version), measuring 6 domains (overall satisfaction, satisfaction with nursing care, carelessness, emotional support, relationship and caring times).

**Results:** Overall satisfaction and satisfaction with nursing care had high rating scores and there were no statistically differences considering gender, age and literacy ( $P > 0.05$ ). Considering different multiple regression models results, the domains of relationship ( $\beta 1$ ) and emotional support ( $\beta 2$ ) were the unique predictors of overall satisfaction ( $\beta 1 = 0.43$ ;  $P < 0.001$ ) ( $\beta 2 = 0.24$ ;  $P < 0.05$ ) and for the satisfaction related to nursing care ( $\beta 1 = 0.52$ ;  $P < 0.001$ ) ( $\beta 2 = 0.22$ ;  $P < 0.05$ ).

**Conclusion:** This study provides a preliminary description of the satisfaction of Italian patients hospitalized for HF: some peculiarities are conflicting with the majority of literature about satisfaction (e.g. no differences in scoring comparison between gender, age and literacy). The results highlight the important role played by relationships and emotional support in nursing clinical practice, being the unique predictors of satisfaction. Indeed, the results showed that the carelessness domain was not a negative predictor of satisfaction. Further multicenter investigations with wider samplings are needed for better understanding of satisfaction in hospitalized HF patients.

#### P1070

##### Thirst in patients with heart failure in daily life

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**Introduction:** Thirst is one of the distressing consequences of heart failure (HF) and can cause a decrease in quality of life, especially in patients with worsening HF. There is some knowledge on thirst in HF patients seeking health care for medical treatment in a controlled study setting with in- and exclusion criteria. However, it is unknown how often and to what extent thirst occurs in a regular HF population visiting a HF clinic.

**Purpose:** To assess thirst and thirst intensity in a regular patient population visiting a HF clinic in the Netherlands and to assess which variables are related to thirst intensity.

**Methods:** Data were collected in 2 HF clinics. In total 197 HF patients (mean age  $66 \pm 14$ ; 40% female) were asked whether they were thirsty at the moment of the visit and if they were thirsty in the week preceding the visit. An additional sample of 66 HF patients (mean age  $72 \pm 10$ ; 54% female; 75% NYHA-II) also assessed their thirst intensity using the visual analogue scale. This is a validated scale ranging from no thirst (0) to worst possible thirst (100). Patients were also asked what they perceived as a cause for their thirst and which interventions they undertook to relieve thirst (open question). HF nurses collected data on age, gender, NYHA-class, prescribed diuretics and fluid restriction.

**Results:** Of the total 197 patients, 17% reported thirst at the visit to the HF clinic and 28% of all patients experienced thirst the week before they visited the HF clinic.

No differences in age and gender between patients with and without thirst were found. Of the sample with additional data collection the mean thirst intensity was  $23 \pm 23$  (range 0-90). Most of the patients (65%) were prescribed a fluid restriction of 1750 ml; 30% had a restriction of 2000 ml. No significant differences were found in thirst intensity between patients with different amounts of fluid restriction (1750 of 2000 ml), men and women and patients in NYHA-II compared to patients in NYHA-III. Patients with a higher dose of loop diuretics ( $> 40$  mg Furosemide) reported significantly more thirst than patients without or with a lower dose of Furosemide (28 vs. 21;  $p = .01$ ). Most reported reasons for thirst were salty or spicy foods (15%), dry air, heat or exertion (12%) or a low fluid intake (11%). Interventions patients undertook themselves were drinking water, tea or other fluids (62%). Almost 30% of these patients reported to drink just a little bit, probably due to their fluid restriction.

**Conclusion:** Almost every 5th patient visiting the HF clinic reported to have thirst. Higher dose of loop diuretics was associated with higher thirst. Although most patients were in NYHA class-II, a considerable amount restricted their daily intake of fluids. Clinicians at HF clinics should ask their patients about thirst and help them to find individual management strategies in order to relieve increased thirst in patients with HF.

#### P1071

##### Understanding patient experience during emergency admissions for acute heart failure

Funded by Royal College of Nursing as a Mary Seacole Development Award Scholar

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**Background:** Acute Heart failure (AHF) is associated with frequent hospital admissions and unplanned admissions can be distressing to patients. Patient experiences have the potential to impact on treatment adherence and readmission rates. Initiatives to evaluate patient experience in the UK, such as the National Patient Survey Programme (NPS), have some limitations since it is not disease tailored and the generic questions posed may not be relevant to patients presenting in an acute setting.

**Purpose:** Since patient experience can be related to outcomes, we aimed to (1) understand the aspects of care patients with AHF thought were important to them during their emergency admission and acute inpatient care experience and (2) to ascertain patients' perceived importance of a 24-item structured 'AHF patient specific questionnaire' to assess their acute care experience.

**Methods:** A mixed methods approach was used. Individual semi-structured interviews elicited spontaneous and prompted descriptions of patient experience during emergency admissions with AHF. Interviews were transcribed, manually coded with thematic extraction using inductive and deductive approaches. Patients also completed a 24-item structured AHF patient specific questionnaire (adapted from a previous study), and completed a Likert-type ranking scale for each question pertaining to their perceived importance

**Results:** 31 patients were interviewed with a mean (SD) age of 72.7 (12.3) yrs. Six main themes came from interviews which included; patient perceived physical and emotional burden of heart failure, the need for good communication from clinical staff, co-operative working between health care professionals and co-management of their disease by patients, timely management, and a desire to be given a specific attention for their HF status. The 24-item structured questionnaires revealed that patients felt that they did not receive enough information about medications (56.6%) or their current condition (56.6%). From the structured questionnaire, 22/24 questions were ranked as 'very' or 'extremely' important with the exception of 'friends and family recommendation questions', which were seen to be less important.

**Conclusion:** Qualitative approaches reveal important insight about the patient experiences of their emergency admission with AHF. We also confirm that most questions posed in our AHF specific structured questionnaire were deemed at least 'very' important. Use of a disease-focused assessment questionnaire may be a more appropriate approach to assess experience and is the subject of ongoing work.

## POPULATION STUDIES / EPIDEMIOLOGY

#### P1072

##### Heart rate variability and systolic blood pressure: implication for heart failure, attainment by stages

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**Purpose:** Heart failure is one of the most prevalent and horrific conditions in prognostic utility for cardiovascular disease (CVD). Autonomic dysfunction may antedate development of symptomatic HF, is incorporated into pathogenesis of HF, and is a pawn in concept of adverse events (MESA).

**Methods:** We executed EPOCH, used power spectral analysis of resting heart rate (RHR), its variability (HRV, 15-min) and clock-time-dependent method narrow approach of diurnal systolic blood pressure (SBP) profile.

**Results:** If we should actually see in the evidence, theory pretty well off affirmed that elevated RHR and reduced HRV - both express the abruptly turned aside sympathetic/parasympathetic activities. From quite exalted achievement, increased RHR in patients with acute myocardial infarction (MI) is considered as independent of HF predictor of subsequent death, hypotension, shock, and etc. In an embarrassing admission, there is one point (PROSPER) which suggested that baseline RHR/HRV are integrated with worse functional ailments in older adults, unprejudiced toward CVD, - although it is and that is the foretelling items - and exists other point (ASCOT, VALUE) which mentioned that RHR mean levels are better provident factors for CVD events than baseline RHR. Hence, in Pearson pattern we defined ties of TP with day ( $r=-0.187$ ), night ( $r=-0.197$ ), crest ( $r=-0.229$ ), trough ( $r=-0.200$ ), high ( $r=-0.205$ ) and low ( $r=-0.220$ ) waves; VLFn with night ( $r=0.168$ ), trough ( $r=0.174$ ), low ( $r=0.189$ ) wave, high-low waves difference ( $r=-0.183$ ), night:day ratio ( $r=0.164$ ), night fall ( $r=-0.150$ ); LFn with day ( $r=0.225$ ), night ( $r=0.216$ ), crest ( $r=0.242$ ), trough ( $r=0.242$ ), high ( $r=0.232$ ) and low ( $r=0.245$ ) waves; HFn with day ( $r=-0.216$ ), night ( $r=-0.258$ ), crest ( $r=-0.238$ ), trough ( $r=-0.276$ ), high ( $r=-0.229$ ) and low ( $r=-0.277$ ) waves; LFn:HFn with day ( $r=0.222$ ), night ( $r=0.237$ ), crest ( $r=0.239$ ), trough ( $r=0.259$ ), high ( $r=0.231$ ) and low ( $r=0.261$ ) waves of SBP,  $P < 0.05$  for all. It is looked shrewdly and out of its depth, cardiac control services regulation of circulation and respiration. Moreover, HF - and, what are widely appointed, following MI - provide dysfunction of nervous system constituents. The scientific attention is not slipping concerning systolic hypertension as apprehensive factor for all-cause, CVD/non-CVD mortality (Syst-Eur). To be sure, in younger subjects link between SBP and HF risk is matched up with prehypertension.

**Conclusion:** Hopefully, yet archaic, we chased up delightful order of priorities for enlargement of patchy knowledge profitability to preserve human being welfare beleaguered by sickness.

### P1073

#### Adverse prognosis with acute myocardial infarction involving proximal left anterior descending artery occlusion

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**Background:** Mortality following myocardial infarction (MI) has markedly reduced with the introduction of primary percutaneous coronary intervention (PPCI) from well above 10% in the thrombolysis era to as low as 1-3% for those who reach the hospital. This is however dependent on the size of the infarct. Post PPCI survival is dependent on the extent of myocardium at risk. The left anterior descending (LAD) artery subtends at least 60% of the left ventricle. As such proximal LAD occlusion is a common cause of moderate left ventricular systolic dysfunction associated with adverse outcome. This report looked at the prognosis of proximal LAD MI in a large tertiary cardiac unit.

**Methods:** This review extracted data submitted by a Hospital to the British Cardiovascular Intervention Society (BCIS) PCI registry which is linked to the Office of National Statistics (ONS) that tracks country wide mortality in the United Kingdom Findings Between September 2005 and December 2014, 13200 PCI were performed, out of these, 3548 were PPCI and the proximal LAD was involved in 360 patients. The mean age was 61 (SD 14) years with 303 (84%) male patients. The median call to balloon time was 108 mins. Cardiogenic shock was present in 21.8%. Co-morbidities were; prior MI or CABG 14%, PCI 9.4%, smoking 52%, diabetes 14%, renal dialysis 1.4% and hypertension 62%. TIMI III was achieved in 92.5%. In-hospital mortality was 11.61%, 30 days 14.58%, 90 days 15.18% and 1 year 19.67%.

**Conclusions:** Despite PPCI, proximal LAD MI carries adverse prognosis with the rules of ten; 10% of MI, 10% in-hospital mortality and 10% post-discharge mortality at 1 year. The challenge is to develop strategies that limit infarct size and reduce sudden cardiac death in the community in this at risk patient group with post MI ischaemic cardiomyopathy.

### P1074

#### Readmission and death without readmission after acute heart failure hospitalization: an approach using competing risk analysis

Novartis Farma provided a grant for statistical analysis

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**Introduction:** The year after hospital discharge for acute heart failure (AHF) is an adverse event golden period. Death and readmission compete for patient path and one-year outcome, but they are often considered together as a composite endpoint in heart failure studies.

**Purpose:** This study aims to identify characteristics of patients discharged from an AHF hospitalization that independently influence the risk of readmission for acute heart failure (RAHF), considering death without RAHF as a competing risk.

**Methods:** Retrospective observational study that enrolled all patients hospitalized for AHF and discharged alive from an internal medicine department in 2012. Clinical records and telephone interviews were used for data collection from the 394 enrolled patients. Survival analysis taking competing risks into account was performed. RAHF was taken as the event of interest and death without RAHF as the competing event.

**Results:** In the year after discharge, 113 patients (28.7%) died; 131 patients (33.3%) experienced a hospital admission after discharge and 67 (17.0%) died without RAHF. The remaining 196 patients (49.7%) were still alive without RAHF one year after discharge. Multivariable models, adjusting for age, gender and ejection fraction, showed that risk of RAHF was increased for patients with atrial fibrillation (SHR=1.58,  $p=0.02$ ), and for those with higher creatinine (SHR=2.00,  $p < 0.001$ ) or taking a betablocker at discharge (SHR=1.61,  $p=0.01$ ). Risk of death without RAHF was increased in males (SHR=1.72,  $p=0.04$ ), those aged 80 years or older (SHR=1.87,  $p=0.03$ ), patients with dementia (SHR=2.68,  $p < 0.001$ ) or RDW in the fourth quartile at admission (compared to the first, SHR=2.54,  $p=0.03$ ). Taking a betablocker at discharge and higher Platelet Distribution Width at admission reduced the risk of death without RAHF (SHR=0.552,  $p=0.04$  and SHR=0.886,  $p=0.009$ , respectively).

**Conclusions:** In this one year follow-up study, we identified patients more prone to RAHF, namely those with atrial fibrillation and renal dysfunction. Death without readmission is clearly an event competing with readmission. A simple laboratory value such as RDW at admission can alert clinicians to the risk of dying before RAHF. Betablockers seem to be special drugs to the patients able to tolerate them, leading to readmission and reducing the risk of death before RAHF. If confirmed by larger studies, these results may aid clinicians to select better intervention strategies in the most efficient way for these patients.

### P1075

#### Epidemiology of atrial fibrillation and flutter in Northern Italy: a cohort of hospitalized subjects

Unconditional grant by Medtronic Italia SpA

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**Introduction:** The prevalence of atrial fibrillation (AF) is rapidly rising in the developed world, while only few studies have investigated atrial flutter. Both conditions have been associated with an increased risk of more serious cardiovascular and cerebrovascular disorder and death.

**Purpose:** We conducted a large retrospective observational study, using healthcare administrative databases (HAD), with the aim of describing the characteristics of the population hospitalized for AF and flutter, and the adverse outcomes associated with both conditions, within a cohort of the general population of Lombardy, a region in Northern Italy.

**Methods:** From DENALI, a data warehouse that organizes HAD of the Lombardy Healthcare System, we extracted all hospitalizations for AF and flutter occurred between 2000 and 2010. We then identified the cohort of residents who underwent a first hospitalization with a diagnosis of AF or flutter between 2003 and 2009, after a wash-out period of 3 years. We followed each subject until 2010, death or emigration, extracting from DENALI all hospitalizations for outcomes of interest. Based on the diagnoses reported on the claims, we classified the cohort into three groups: people who during follow-up received only AF diagnosis ("AF" group), only flutter diagnosis ("Flutter" group), or both diagnoses ("AF and Flutter" group). We estimated mean annual mortality rates, as well as rates of hospitalization (x 100 person-years) for AF, flutter and ischemic stroke (IS), adjusting by age and gender.

**Results:** In the time period 2000 - 2010, the yearly average hospitalization rates (x10,000 person-years) for AF and flutter were respectively 46.15 (95% CI: 46.01; 46.28) and 4.33 (95% CI: 4.29; 4.37). We identified a cohort of 162,956 subjects (51% males), with a mean age of 75 years ( $\pm 12$  SD). The "AF" group absorbed 87.8% of the cohort, while "Flutter" and "AF and Flutter" groups accounted for respectively 5.6% and 6.6%. During a mean follow-up time of 3.2 years ( $\pm 2.3$  SD), the mean annual mortality rate was 12.43 (95% CI: 12.33 - 12.53), while mean annual hospitalization rates were: 16.89 (95% CI: 16.78 - 17.01) for AF diagnosis, 1.70 (95%

CI: 1.67 – 1.74) for flutter diagnosis and 3.26 (95% CI: 3.21 – 3.31) for IS. Hospitalization rates were highest within the "AF and Flutter" group, they decreased in the "AF" group and they were lowest within the "Flutter" group.

**Conclusions:** Our results confirm AF as a high healthcare impact disease, and they contribute to enhance the limited evidence regarding flutter, that emerges as a condition that should be carefully addressed.

#### P1076

##### Profile of the high coronary risk population

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**Introduction:** High blood pressure, lipid disorders, smoking, obesity are the group of major risk factors for heart disease. The risk of heart failure increases if they are not under control.

**Purpose:** The aim of this study is to analyse the prevalence of major risk factors and their control in Bulgarian high risk patients.

**Methods:** We analyse the data from Bulgarian cohort of high risk patients involved in EUROASPIRE IV survey (European Action on Secondary and Primary Prevention by Intervention to Reduce Events) held in 2014. The protocols of EUROASPIRE IV comprise standard questionnaires used by all participating countries to determine the patient health status.

**Results:** Only 36% of high risk patients in EUROASPIRE IV have blood pressure under target levels (SBP/DBP < 140/90 mmHg in patients using blood pressure lowering drugs and < 140/80 mmHg in diabetics). Among the patients in EUROASPIRE IV total cholesterol  $\geq$ 4.5 mmol/L is recorded in 70% of them. LDL cholesterol  $\geq$ 2.5 mmol/L is recorded in 83% of all patients. Therapeutic control of LDL-cholesterol < 2.5 mmol/L is achieved in 27% of the patients on lipid-lowering therapy. The total prevalence of diagnosed and undiagnosed diabetes (self-reported diabetes or fasting glucose  $\geq$ 7 mmol/L) in EUROASPIRE IV is 60%. Undiagnosed diabetes rate (fasting glucose >7 mmol/L and/or HbA1c >6.5%) among non-diabetic patients is 40%. 65% of the patients with self-reported diabetes have HbA1c <7.0% and 45% of them have HbA1c <6.5%. The prevalence of obesity in EUROASPIRE IV is 50.0% and this of central obesity is 86.0%. The prevalence of smoking among high risk patients in EUROASPIRE IV is 21.8% (an increase of 17.2% compared to EUROASPIRE III) and 40% of the current smokers have no intention to quit smoking (equal as in EUROASPIRE III).

**Conclusions:** We find a poor global control of blood pressure in high risk patients in Bulgaria. The lipid control in high risk patients is still insufficient - less than 2/3 of the patients do not reach target levels according ESC guidelines. We also find very high prevalence of obesity. Despite the physicians' activities, smoking rate increases in the group of high risk patients.

#### P1077

##### Improving the validity of general practice heart failure registers in Scotland through collaborative clinical audit

NHS Greater Glasgow & Clyde

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**Background:** Heart failure (HF) appears under-represented in Scottish general practice disease registers compared with accepted prevalence figures. Scottish general practices are required to enter two codes to add patients to a register and also distinguish between HF with reduced ejection fraction (HF-REF) and HF with preserved ejection fraction (HF-PEF).

**Purpose:** To improve the validity of general practice HF registers in a Scottish regional health authority, including the distinction between HF-REF and HF-PEF.

**Methods:** General practices undertook an audit from 01.10.14 to 31.03.15 to improve register accuracy. Practices conducted an individual review of the medical records of each patient on existing HF registers to confirm or refute diagnosis. Practices also undertook a case-finding exercise to identify patients with confirmed HF who were missing from registers. Case-finding was achieved by reviewing the medical records of patients taking possible HF medications (e.g. loop diuretics) and/or those with codes for left ventricular systolic dysfunction (LVSD) without HF codes. Validity for inclusion on a register was judged by reviewing the results of previous diagnostic imagery (e.g. echocardiograph) and clinical history in primary and secondary care medical records. Specialist advice was sought where needed.

**Results:** 143 / 241 general practices (59% of regional health authority) took part in the audit and submitted data (763,112 patients, ~14% Scotland). 5843 patients were on HF registers pre-audit (0.77% prevalence). 516 patients (8.8%) were miscoded as HF (false positives) and were removed from HF registers. 561 patients (9.6%)

were deemed to have a historic diagnosis that was no longer clinically relevant (e.g. acute events, LV recovered, reversible causes) and were re-coded to highlight this. 214 patients (3.7%) on HF register had been incorrectly coded as HF-REF despite having normal ejection fraction. 2066 patients (35.4%) on HF registers had a missing HF-REF code. 1659 additional HF patients were identified that were not on the HF register (false negatives); 1105 patients were identified with sole LVSD codes but were judged to also have clinical HF, and 554 patients were identified from medication case-finding. Post-audit HF registers increased to 7022 patients (0.92% prevalence). This figure also accounts for new diagnoses and deaths during audit period.

**Conclusion(s):** Clinical audit significantly improved the accuracy and validity of general practice HF registers, with coding problems identified in over half (57.5%) of the patients on baseline registers. Case-finding added 1659 patients that were inappropriately missing from registers. More research is needed to understand the reasons why baseline HF registers in general practice are significantly inaccurate. Work is under way nationally in Scotland to improve the communication of new HF diagnosis information between secondary care and general practice.

#### P1078

##### Acute heart failure in colombia

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Acute heart failure syndromes poses unique diagnostic and management challenges for clinicians, although much has been accomplished in the management of chronic HF, the absence of evidence-based clinical practice guidelines for acute heart failure is striking. There is a few information about the clinical characteristics of heart failure patients discharged from Colombian hospitals. ROCI project is a pilot registry designed to characterize this population in our country.

**Objective:** To describe the clinical characteristics of a population of patients discharged from 9 Colombian hospitals in a period of 4 months with diagnosis of acute heart failure and to compare this with the information available from ADHERE and ESC HF AHF arm registry.

**Methodology:** A prospective cohort study was designed

**Results:** 250 patients were included in 9 Colombian hospitals in four months. 37% were male, 66% of the population had more than 60 years, 67% had heart failure with reduced ejection fraction. Ischemic cardiomyopathy was the cause of heart failure in 38% of the patients, and 29% had diabetes. There was a high use of medical therapy recommended by the guidelines: beta blockers in 95%, ACE/ARB in 84%, aldosterone antagonist in 73% and ivabradine in 14,7% of the population the comparison of this clinical variables with those reported in international registries is shown in table 1

**Conclusion:** The ROCI registry showed that the population of acute heart failure patients from Colombia is younger than the reported in ADHERE and ESC HF AHF pilot arm, with a high proportion of women, a low prevalence of ischemic cardiomyopathy and most of our patients had heart failure with reduced ejection fraction. Diabetes was less prevalent in our population. This information is very important to face the challenge of giving a better care to our patients.

Table 1 roci vs adhere vs esc

CLINICAL CHARACTERISTIC	ROCI	ADHERE	ESC HF AHF pilot arm
Age	60	72 ± 14	70 ± 13
Male	37%	48%	63%
CORONARY HEART DISEASE	38%	57.4%	50,7%
HFREF	67%	54%	66%
DIABETES	29%	44%	35,1%

HFREF: heart failure with reduced ejection fraction

#### P1079

##### Risk of first myocardial infarction in a population-based cohort of incident heart failure patients.

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**Background:** There is considerable data available on the risk of developing heart failure (HF) following a myocardial infarction (MI), but only very few studies evaluated the reverse constellation in a systematic way, which means following-up a cohort of incident heart failure patients without past MI history until occurrence of first MI. While clinical trials usually represent selected patient populations with limited follow-up time, a longitudinal, large and population-based healthcare database may allow long-term follow-up of a large heart failure inception cohort.

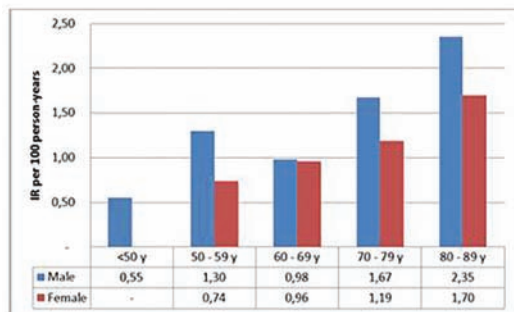
**Purpose:** To estimate the incidence and case fatality of first MI in a population-based cohort of incident heart failure patients without previous MI.

**Methods:** A retrospective cohort study was conducted in the UK general practice setting. Patients with a first diagnosis of HF during 2000-2005 and without prior MI or cancer (n = 14,373) were identified from The Health Improvement Network database (a longitudinal primary care database of electronic medical records, representative of the UK population) and followed-up until end of 2011 to ascertain first occurrences of MI. Validation of the HF cohort and the MI cases took place via review of the patient's electronic medical record, including free text comments review. Incidence rates (IR) and corresponding 95% confidence intervals (CI) were calculated.

**Results:** 858 patients (6% of the initial cohort) developed a first myocardial infarction during a mean follow-up of 2.26 years (incidence 1.49 cases per 100 person-years, CI 95%: 1.39-1.59). Incidence rates stratified by age and sex are displayed in figure 1. The risk was highest in the first year of follow-up after HF diagnosis (incidence rate 3.11 cases per 100 person-years (CI 95%: 2.81-3.44), where nearly half of the MI cases occurred (n=375). Incidence was generally higher in men than in women. Among the 858 patients with MI during follow up, 282 patients (33 %) died within 30 days after MI diagnosis.

**Conclusions:** Occurrence of a first MI in patients with incident heart failure is not uncommon and this combination is associated with high case fatality. Further analysis of the risk factors and possible preventive factors of MI in this population is warranted.

Figure 1. Incidence rate of myocardial infarction among newly diagnosed HF patients by age and sex



## P1080

### Beta-thalassemia minor is associated with decreased arterial stiffness and favourable LV diastolic profile

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**Background:**  $\beta$ -thalassemia minor ( $\beta$ - $\tau$ m) is associated with rheological and biochemical alterations that can affect cardiovascular function.

**Purpose:** To evaluate systolic and diastolic cardiac function and the elastic arterial properties in a large population of patients with  $\beta$ - $\tau$ m.

**Methods and Results:** 202 asymptomatic individuals with cardiovascular risk factors, 75 with  $\beta$ - $\tau$ m and 127 controls were prospectively enrolled. All participants underwent comprehensive echocardiographic evaluation. Arterial parameters were quantified noninvasively using applanation tonometry of the radial and femoral artery. Pulse wave analysis revealed that augmentation pressure, augmentation index, and heart rate-corrected augmentation index were significantly lower [median (interquartile range) 8.75 (4.625-13) vs. 11 (6.5-14.5),  $p=0,017$ ; 26.5 (17.5-33.375) vs. 30.5 (20.75-37.5),  $p=0,014$ ; and 22.25 (15.125-29.5) vs. 27 (20.5-33),  $p=0,008$ , respectively) in the  $\beta$ - $\tau$ m group compared with controls. Evaluation of myocardial diastolic function revealed that left atrial active emptying volume was significantly lower in  $\beta$ - $\tau$ m group in comparison with the control group 10.2 (7.4-14.4) vs. 12.0 (8.6-15.8),  $p=0,040$  and isovolumic relaxation time was more prolonged ( $80 \pm 19$

vs.  $87 \pm 24$ ,  $p=0,034$ ) in the control group compared with  $\beta$ - $\tau$ m individuals. Left atrial maximal volume index and kinetic energy were also lower in the  $\beta$ - $\tau$ m [20.2 (16.4-24.1) vs. 22.2 (17.8-26.4) and 30.1 (19.4-55) vs. 39.3 (23.1-59.5), respectively], although the differences were not statistically significant ( $p=0,062$  for both comparisons).

**Conclusion:**  $\beta$ - $\tau$ m is associated with decreased arterial stiffness and a favourable left ventricular diastolic function profile in asymptomatic individuals with cardiovascular risk factors. These findings provide support to a possible cardiovascular protective effect of the  $\beta$ -thalassemia heterozygosity that needs further evaluation.

## P1081

### Alterations of the left ventricular end-diastolic pressure-volume relationship are associated with higher mortality in non-heart failure individuals: data from a large-scale, population-based cohort.

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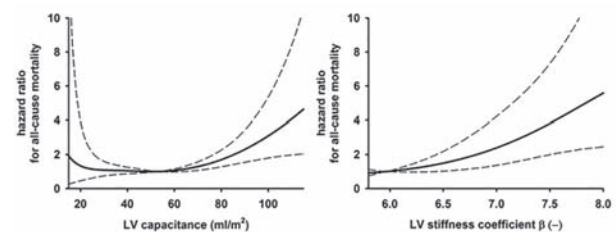
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**Background:** Left ventricular (LV) remodeling impacts on the LV end-diastolic pressure-volume relationship (EDPVR), which is different in heart failure (HF) with reduced ejection fraction (HFrEF) and HF with preserved ejection fraction (HFpEF). In a large-scale, population-based cohort (Gutenberg Health Study) we aimed to investigate alterations of the EDPVR in HF patients and their association to risk factors and all-cause mortality in non-HF individuals.

**Methods:** Based on clinical and echocardiographic data, participants were divided into "No HF" (n = 14511), HFrEF (n = 215) and HFpEF (n = 79). We estimated LV capacitance (i. e., the position of the EDPVR) and the EDPVR's stiffness-coefficient  $\beta$  from echocardiographic data using a single-beat method. LV capacitance was defined as the LV end-diastolic volume at an LV end-diastolic pressure of 20 mmHg indexed to body surface area. Values are given as median and interquartile range.

**Results:** The EDPVR was shifted rightward in HFrEF indicating higher LV capacitance compared to "No HF" (69.7 [53.3 - 85.3] vs 53.5 [45.2 - 63.0] ml/m<sup>2</sup>,  $p < 0,001$ ) and leftward in HFpEF indicating lower capacitance compared to "No HF" (51.0 [42.7 - 62.3] vs 53.5 [45.2 - 63.0] ml/m<sup>2</sup>,  $p=0,027$ ), while the stiffness-coefficient  $\beta$  was increased in both HFrEF and HFpEF (HFrEF: 5.99 [5.94 - 6.11], HFpEF: 6.16 [6.11 - 6.29], No HF: 5.94 [5.92 - 5.98], both  $p < 0,001$  vs No HF). In "No HF", a higher stiffness-coefficient  $\beta$  was associated with age, female gender, hypertension, diabetes and obesity, while age and female gender were associated with a leftward shift of the EDPVR, whereas dyslipidemia, obesity, smoking and impaired renal function were associated with a rightward shift of the EDPVR. Both changes of the EDPVR were associated with increased all-cause mortality in "No HF" (both  $p < 0,001$ , see figure).

**Conclusion:** In a large-scale, population-based cohort, we show distinct alterations of the EDPVR in HFrEF and HFpEF. Already in non-HF individuals, alterations of the EDPVR are associated with increased mortality.



## PSYCHOSOCIAL / ETHICAL CONCEPTS / EDUCATION

## P1082

### Patients' perspectives of communication about heart failure, prognosis and end-of-life care

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**Background:** Improving heart failure (HF) patients' understanding about their condition, including discussing the progression of HF and establish goals for end-of-life care, is an important outcome in patient-professional communication.

**Purpose:** To explore HF patient's perspectives regarding communication with health care professionals about HF, prognosis and end-of-life care.

**Methods:** A qualitative study with four focus-group interviews including 15 patients with HF was performed. The patients were in NYHA I-IV, and were not diagnosed with any other major life threatening disease. The participants consisted of 12 men and 3 women with an age range between 63 and 84 years of age. Data was analysed using thematic analysis to identify and interpret patterns in the data.

Preliminary

**Results:** One essential theme identified was: "Patients' approach to information about the illness and the prognosis" with the sub-themes: "Ignorance is bliss", "Truth gives freedom" and "Unawareness gives insecurity".

Patients used different approaches to discussions about their illness, prognosis and end-of-life care in. The sub-theme "Ignorance is bliss" expresses how some patients prefer to ignore the fact that they might die from their HF. They do not want to talk about the future and might get worried or offended by the topic. They want to decide themselves whether they want to talk about the future with professionals or not. If they choose to talk, they will ask about it themselves.

The second sub-theme "Truth gives freedom" illustrates that some patients believe that knowing "the truth" about their illness and its trajectory is crucial to live as good as possible. The truth for these patients are that they are probably going to die from HF. Patients ask from professionals to be honest with them about the future and help the patient to be able to plan ahead and be prepared for a time when the HF is deteriorating.

The third sub-theme "Unawareness gives insecurity" does not describe an active approach, rather it describes patients who claim that they do not know that they are suffering from a life-limiting illness. They meet professionals who provide little or no information about the illness progression, leaving the patients with an often lacking understanding of what HF is and how it might affect their lives. Patients believe that the professionals are responsible to initiate a communication about the future. But before doing so, they need to be sensitive and read the patients' body language, emotions and feelings to understand if they are ready to talk.

**Conclusions:** The different approaches patients use when discussing prognosis and end-of-life care might be ways for the patients to cope living with a serious illness. Having knowledge about patients' different approaches to communication is important for professionals in clinical practice who wants to initiate a conversation about prognosis and end-of-life care.

#### P1083

##### Predictors of therapeutic adherence in cardio-respiratory failure patients

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**Background:** The acquisition of harmful habits are the main causes of cardiovascular and respiratory diseases. Currently no cure for this condition is available and, although there is growing therapeutic strategies to achieve good control and improve the quality of life of patients, the reality is different. Lack of adherence fluctuates between 40 to 75%. Adherence is a multidimensional phenomenon which must also consider the thoughts, feelings and social interactions of patients. From this need to understand and explain this process the socio-cognitive models emerge. This work takes three models: a) Health Belief Model; b) Theory of Planned Behavior, c) Wallston's model.

**Objective:** To identify factors that predict the therapeutic adherence of patients with cardio-respiratory failure. **Material:** A clinical transversal and not experimental study was conducted. 134 patients from the cardiology outpatient service and heart failure and respiratory clinic were assessed with the following instruments: a) MBG Questionnaire to evaluate therapy adherence, b) Health Belief Model and Therapeutic Adherence Questionnaire, c) Theory of Planned Behavior Questionnaire, and d) Wallston's Model for Therapeutic Adherence Scale.

**Results:** Using a stepwise multiple linear regression, a predictor of adherence model, which includes factors of two of the proposed cognitive models, was obtained ( $r^2 = 0.217$ ,  $F = 8.931$ ,  $p < 0.01$ ): perceived benefits ( $t = 2.361$ ,  $\beta = -0.199$ ,  $p < 0.01$ ) of Health Belief Model; attitudes ( $t = 1.464$ ,  $\beta = 0.140$ ,  $p < 0.01$ ), self-efficacy ( $t = 2.386$ ,  $\beta = 0.214$ ,  $p < 0.01$ ) and social norms ( $t = 2.386$ ,  $\beta = 0.214$ ,  $p < 0.01$ ) of Theory of Planned Behavior.

**Conclusion:** It is important to have patient information about how to think, feel and relate to his disease, treatment and social context. These aspects can intervene to improve the prognosis and health status of the patient. These results hint some factors such as perceived benefits and social norms that are usually not taken into account during treatment and may affect adherence to it. It is necessary to continue

in this line of research to have a holistic model that explains the adherence behavior of the patient and modify them promptly if necessary.

#### P1084

##### Measures of health-related quality of life for adults with chronic heart failure: usefulness of the MacNew questionnaire

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**Background:** Health-related quality of life (HRQL) is an increasingly well-recognized measure of health outcome in cardiology. The administration of the MacNew questionnaire has been proposed as a routine investigation for patients suffering from chronic heart failure (CHF), with the goal of reducing unnecessary hospitalizations, which really can be avoided with the optimization of therapy and lifestyles, in case of detection of worrying low scores on occasion of the assessment of the questionnaire. The purpose of this study was to assess whether relatively high scores found with the MacNew questionnaire can be associated with a significantly decreased risk of unplanned hospitalizations due to relapses of cardiac decompensation during follow-up.

**Methods:** The study consisted in a retrospective analysis that involved 210 patients with CHF due to various etiology (ischemic, idiopathic, valvular, etc) followed up for one year after the first episode of acute decompensated heart failure (ADHF). According to customary practice that applies in our Institute, all of the patients underwent an evaluation by means of the MacNew questionnaire, in the context of the practices of psychological and psychosomatic assessment that are routinely implemented in CHF outpatients who are followed-up after a previous hospitalization for ADHF.

**Results:** At univariate analysis, a high value (namely, located above the median of the ensemble of the calculated values of MacNew score in the entire patient population) of the global score was shown to be associated with a significantly decreased risk of rehospitalization [HR (hazard ratio): 0.0903; 95% CI: 0.0324 to 0.2518;  $p < 0.0001$ ]. After adjustment for age, gender, myocardial infarction as initiating event, reduced left ventricular ejection fraction, baseline renal function and diabetes, that is, by incorporating the above-mentioned covariates within a multivariate Cox proportional hazards' regression model, the protection exerted by a high MacNew score against the risk of hospitalizations remained significant (HR: 0.0885; 95% CI: 0.0317 to 0.2472;  $p < 0.0001$ ).

**Conclusions:** High HRQL assessed by means of the MacNew questionnaire in outpatients with CHF appears to be associated with a reduced risk of rehospitalization over a one-year follow-up.

#### P1085

##### The relationship between acceptance of illness and quality of life in chronic heart failure patients

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**Background:** This study provided an in-depth insight into relationships between illness acceptance and quality of life (QoL) of chronic heart failure (CHF) patients. While QoL is well-established endpoint in CHF, little is known on illness acceptance in this group.

**Aims:** To analyse a relationship between QoL and illness acceptance in CHF patients.

**Methods:** The study included 204 patients (160 men and 44 women, mean age 63. ± 11 years) with at least 6-month clinical evidence of CHF corresponding to NYHA classes I-IV. All the patients were examined with Minnesota Living with Heart Failure Questionnaire (MLHFQ) and Acceptance of Illness Scale (AIS).

**Results:** Univariate analysis showed that the level of illness acceptance correlated inversely with patient age, and the level of QoL decreased with the severity of CHF (NYHA class). A relationship between illness acceptance and QoL was analysed by structural equation modelling. Model 1 was based on the assumption that QoL is modulated by AIS, Model 2 tested the opposite relationship. Both models included patient age and NYHA class as extrinsic determinants of AIS and MLHFQ scores, respectively. Model 2 proved to be well fitted ( $\chi^2(df:2) = 3.22$ ,  $p = 0.20$ , RMSEA = 0.055). AIS correlated inversely with age (bAge → AIS = -0.15, SE = 0.05,  $p = 0.002$ ) and QoL (bQoL → AIS = -0.15, SE = 0.02,  $p < 0.001$ ), and an increase in NYHA class was reflected by an increase in QoL scores (bNYHA → QoL = 5.75, SE = 1.97,  $p = 0.004$ ).

**Conclusion:** CHF patients may not accept their disease due to deteriorated QoL. As a result, they might be not involved in the therapeutic process, which leads to exacerbation of CHF, further deterioration of QoL and inability to accept the illness.

## P1086

**Validation of health belief model and therapeutic adherence questionnaire in cardio-respiratory failure patients**

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**Background:** Cardiovascular risk factors cause 16.7 million deaths per year worldwide. Efforts to improve the diagnostic and therapeutic processes of these diseases have been carried out. Non-adherence remains an obstacle to achieve this goal. In this sense, the cognitions of the patients about their disease and treatment play an important role. The Health Belief Model explains the influence of these cognitions on adherence, so it is important to evaluate them.

**Objective:** Evaluate the factorial structure and reliability of the Health Belief Model and Therapeutic Adherence Questionnaire in patients with cardio-respiratory failure. Method. 134 patients (74% women, mean age 47 years) from the cardiology outpatient service and heart failure and respiratory clinic were assessed with the Health Belief Model and Therapeutic Adherence Questionnaire (Likert scale 1 to 5). Reliability analysis was performed using Cronbach's alpha and a factor analysis was made using the principal axis factor analysis with varimax rotation.

**Results:** The final inventory was composed of 15 items with a Cronbach's alpha of 0.803. Four factors were obtained: perception severity, perceived susceptibility, perceived benefits and perceived barriers personal. These explain the 57% of the variance of the construct.

**Conclusion:** The scale is valid to assess the Health Belief Model factors. The results support the use of the instrument in cardio-respiratory failure patients. Have tools like this help to design intervention strategies to increase therapeutic adherence and effectiveness of medical treatment in these patients, improving their health and quality of life.

## P1087

**Validation of Self-efficacy of Caregivers of Chronic Patients Scale in caregivers of heart failure patients**

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**Background:** As construct self-efficacy mediates the relationship between knowledge and behavior. Therefore the belief that the caregiver has about his ability and self-regulation to give care to the patient without abandon his own life are decisive for the tasks of their role. The caregiver is the responsible for the patient and, in most cases, he supervise the pharmacological and nonpharmacological treatment of patient. However, despite its importance, self-efficacy is a variable that has not been studied in this population.

**Purpose:** Evaluate the psychometric properties of Self-efficacy of Caregivers of Chronic Patient Scale in a sample of caregivers of patients with heart failure.

**Methods:** A sample of 125 caregivers (75.2% female, age 54.8 ± 13.8) of heart failure patients attending the Instituto Nacional de Enfermedades Respiratorias "Ismael Cosío Villegas" was evaluated. Reliability analysis and factor was performed using Cronbach's alpha, the variability was calculated using t-student and a factor analysis was made using the method of principal components analysis with varimax rotation.

**Results:** The final inventory was composed of 19 items with a Cronbach's alpha of 0.895. The variability was statistically significant ( $p < 0.05$ ). Three factors were obtained: personal self-efficacy ( $\alpha = 0.828$ ), socio-affective self-efficacy ( $\alpha = 0.857$ ) and self-efficacy to the patient ( $\alpha = 0.809$ ). These explain the 56.81% of the variance of the construct.

**Conclusion:** The scale is valid to measure perceived self-efficacy in this population, so the results support the use of the instrument in caregivers of heart failure patients. Design strategies aimed to assess all variables around the caregivers to design intervention strategies to train and take care of them is needed.

## P1088

**Anxiety and coping based on emotions may contribute to reduced quality of life in patients with mild systolic heart failure**

National Science Centre (Cracow, Poland), grant no.: UMO-2011/03/N/NZ5/00243 A E Agnieszka Siennicka<sup>1</sup>; J Krzysztofik<sup>1</sup>; EA Jankowska<sup>1</sup>

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The perception of quality of life (QoL) may result from individual psychological characteristics of the patient. We investigated selected, potentially modifiable psychological features among patients with heart failure (HF) in relation to physical and emotional dimensions of QoL. 169 patients with stable HF (88% men, age: 63 ± 10 years, NYHA (I/II/III): 7/63/30%, ejection fraction: 31 ± 7%), completed:

- (1) Coping Inventory for Stressful Situations;
- (2) Generalised Self Efficacy Scale;
- (3) Acceptance of Illness scale;
- (4) Revised-Life Orientation Test;
- (5) State-Trait Anxiety Inventory and
- (6) Minnesota Living with Heart Failure Questionnaire.

Emotion-oriented coping was related to overall QoL ( $r = 0.37$ ) & somatic and emotional QoL ( $r = 0.24$  and  $r = 0.62$ , respectively, all  $p < 0.05$ ). More reduced QoL (overall in both dimensions) was significantly ( $p < 0.05$ ) but weakly ( $r = -0.21$ ,  $r = -0.20$  and  $r = -0.26$ , respectively) related to lower acceptance of the illness. Higher anxiety was related to more reduced QoL (overall & both dimensions): for anxiety-state:  $r = 0.28$ ,  $r = 0.22$  and  $r = 0.54$ , respectively; for anxiety-trait:  $r = 0.29$ ,  $r = 0.25$  and  $r = 0.46$ , respectively, all  $p < 0.05$ . Emotional QoL was related to avoidance-oriented coping ( $r = 0.26$ , including a subtype based on distraction,  $r = 0.34$ ) & lower self-efficacy ( $r = -0.20$ ) and lower optimism ( $r = -0.20$ , all  $p < 0.05$ ).

We showed that particular, measurable and modifiable psychological features are related to the way how the patients perceive their QoL. Further studies are needed to confirm if psychological support aimed at promoting adequate styles of coping, increasing illness acceptance, self-efficacy and optimism and/or reducing anxiety would result in an improvement of the QoL.

## EXERCISE TESTING &amp; TRAINING

## P1089

**Self-efficacy mediates the relationship between motivation and physical activity in patients with heart failure**

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**Background/Introduction:** Motivation to be physically active is needed, but may not sufficient to initiate physical activity in patients with heart failure (HF). Self-efficacy might explain the relationship between motivation and physical activity.

**Purpose:** This study aims to examine the role of exercise self-efficacy in the relationship between exercise motivation and physical activity in patients with HF.

**Methods:** Data of 101 stable HF patients (and 88% in NYHA II/III, mean age 67 ± 13, 62% men) were analyzed. Exercise self-efficacy was measured with the exercise self-efficacy scale; exercise motivation with the exercise motivation index and physical activity with a self-report questionnaire. Moderation and mediation are used for refining and understanding causal relationships. Logistic regression analyses were made to examine the moderation and mediation effect of exercise self-efficacy on the relation between exercise motivation and physical activity.

**Results:** In total 42% of the patient reported to be physically active less than 60 minutes per week. No moderation of exercise self-efficacy was found on the relation between exercise motivation and physical activity. Self-efficacy mediated the relation between exercise motivation and physical activity. Motivation predicted physical activity ( $b = .58$ ,  $p < .05$ ). After controlling for self-efficacy, the relation between motivation and physical activity was no longer significant ( $b = .76$ ,  $p = .06$ ), indicating full mediation. Sex, age and NYHA class did not have a significant association with the level of physical activity ( $b = .55$ ,  $p = .36$ ;  $b = -.03$ ,  $p = .22$ ;  $b = -.41$ ,  $p = .46$ ), but increased the R-square of the model and therefore contributing to explaining physical activity in patients with HF.

**Conclusion:** In addition to a high motivation to be physically active, it is important that patients with HF to have a high exercise self-efficacy. Motivation leads patients with HF to have higher self-efficacy and therefore are more confident in overcoming barriers to exercise, which in turn leads them to have higher physical activity.

## P1090

**Observation point in chronic heart failure after training program**

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**Objective:** To explore the possibility of the effect of an educational program in a municipal medical institution on the survival of patients, the functional state of the cardiovascular system (CVS), and psychological status.



**Material and methods:** in the municipal hospital for 4 years as a school health (SHZ) for patients with CVD. A total of 46 cycles of 5 sessions each. Patients aged 40-70 years, and visited more than 3 classes amounted monitoring group - 222 (1 oz.). 39 patients of the same age who are not engaged in the SZ included in the control group (2g.). At the beginning of the study groups were comparable in age: 58,8 ± 7,0 (1g.) Vs 59,1 ± 6,9 years (2g.) (P = 0,774). The patients before discharge from the hospital completed the survey of hospital assessment scales of anxiety and depression (HADS); the functional state of the CAS was assessed using the six-minute walk test (TSHH) and index ehokardiografaii - ejection fraction (EF). Patients in Group 1 were observed periodically. Re-examination was carried out in 2 years.

**Results:** during the 1st examination: the level of anxiety in both groups was at a subclinical level (7,33 ± 3,56 and 7,62 ± 5,09 points, p = 0.694); symptoms of depression were not in both groups. The average distance traveled in TSHH, did not differ between groups (1g. 439,09 ± 95,88 m in 2 m. 430,77 ± 86,13 m, p = 0,630), I corresponded functional class NYHA, value EF has been satisfactory in the 1st and 2nd groups (58,13 ± 8,51% and 56,71 ± 9,38%, p = 0.376). After 2 years in group 1 remained 211 patients: a 3 person there is no information, 8 - died (1 - from cancer pathology, by CVD -7 (overall mortality rate - 3.69% of the pathology CCC - 3.21%). In the control group left 35 people, and 4 died from CVD (mortality rate - 10.26%). In 2 years studied parameters were evaluated separately in each group. In group 1 significantly reduced the level of anxiety and depression (p = 0.000). Distance TSHH increased from 437,02 ± 104,08m to 466,34 ± 86,96 (p = 0,000), ejection fraction increased slightly to 59,35 ± 7,68% (p = 0.623). A different pattern was observed in the control group: indicators of anxiety and depression has not improved (p = 0.465 and p = 0.583, respectively). At the insignificant decrease of PV up to 53,27 ± 12,07% (p = 0.859) in the distance TSHH declined from 405,00 ± 65,65 m to 300 17 ± 50,91m (p = 0.028).

**Conclusions:** The active participation of patients with CVD in the educational programs in order to maintain communication with your doctor allows you to have a positive effect on a surrogate point (improvement in functional status and psychological status), and the final result (reduction in mortality).

#### P1091

##### Linear correlation between cardiac output and oxygen uptake at peak exercise in patients with heart failure with reduced ejection fraction

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**Background:** Oxygen uptake (VO<sub>2</sub>) during exercise is among the most reliable parameters to assess heart failure (HF) severity and prognosis. According to Fick law, VO<sub>2</sub> = cardiac output (CO) × arteriovenous O<sub>2</sub> differences [Δ(Ca-Cv)O<sub>2</sub>]. Therefore, an increase of peak exercise CO is associated with an increase of peak VO<sub>2</sub>, provided that Δ(Ca-Cv)O<sub>2</sub> does not decrease. During progressive exercise (ramp protocol), VO<sub>2</sub> is independent from CO up to the anaerobic threshold and becomes CO-dependent above it. Several factors can indeed influence the Δ(Ca-Cv)O<sub>2</sub> value at peak exercise in HF, either increasing or decreasing it, including exercise-induced haemoconcentration, muscle metabolic efficiency and peripheral blood flow distribution. Consequently, in HF, a constant peak exercise Δ(Ca-Cv)O<sub>2</sub> is not a definite event and non-invasive measure of CO is still a challenge.

**Purpose:** We tested the hypothesis of effective correlation between CO and VO<sub>2</sub> at peak of exercise in heart failure patients.

**Methods:** We analysed clinical data from 170 consecutive heart failure patients with reduced ejection fraction (HFrEF) who underwent full clinical evaluation at our HF unit. Patients' age was 65 ± 11 years, 86% were males. Average LVEF was 31 ± 8%. All patients were in stable clinical condition, in New York Heart Association (NYHA) functional class I-III. They underwent Cardiopulmonary Exercise test with non-invasive measurement of CO (CPET-CO) by inert gas rebreathing (IGR) at rest and peak exercise. The IGR technique uses an oxygen-enriched mixture of an inert soluble gas (0.5% nitrous oxide) and an inert insoluble gas (0.1% sulphur hexafluoride) inflated into a bag by the machine.

**Results:** CO increased from 3.23 ± 0.97 L/min at rest to 6.57 ± 2.52 L/min at peak exercise, and VO<sub>2</sub> at peak exercise was 1178.32 ± 410.42 mL/min, which corresponds to 61.20 ± 18.09 % of predicted. We found a linear correlation between CO and VO<sub>2</sub> peak, described by the equation: CO = 5,1246 × VO<sub>2</sub> + 0,5566 (R<sup>2</sup> = 0,6671). [image 1]

**Conclusions:** The concomitant measurement of CO and VO<sub>2</sub> at peak exercise in a large population of HF patients allowed us to obtain a predictive equation, which can be simply used to derive CO from VO<sub>2</sub> peak values measured at CPET. This equation has only been validated in HFrEF patients.

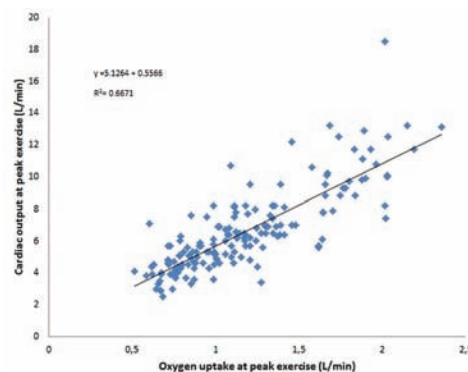


Image 1

#### P1092

##### Amount or intensity? Potential targets of exercise interventions in patients with heart failure with preserved ejection fraction.

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**Background:** Heart failure (HF) with preserved ejection fraction (EF) is a common condition where no pharmacological therapy has yet been identified. Physical activity prevents the development of HF with reduced EF and improves symptoms and quality of life (QoL) in prevalent HF irrespective of EF. The aim of this study was to determine the association of physical activity (amount and intensity) on phenotype including exercise performance in patients with HF with preserved EF.

**Methods:** 422 patients (Aldo-DHF trial) with stable HF with preserved EF were investigated (52% women, age 67 ± 8 years). All patients underwent detailed cardiopulmonary exercise testing (CPET) and echocardiography. Daily physical activity and physical function in QoL were assessed by self-reporting questionnaires (KöBet, SF-36). Exercise performance was measured by 6-minute walk test and CPET (peak oxygen uptake, peak VO<sub>2</sub>). Patients were classified according to the amount and intensity of physical activity and the association of physical activity and submaximal/maximal exercise capacity, diastolic function and QoL was analysed.

**Results:** Total physical activity (MET hours per week) was positively correlated with 6-minute walking distance (p < 0.002) and QoL (p < 0.05), but not with peak VO<sub>2</sub>. 6-minute-walking distance and peak VO<sub>2</sub> values were significantly higher in patients who performed high intensity exercise > 8 hours per week (p < 0.001 and p = 0.02, respectively). Time of high physical exercise was also positively correlated with 6-minute walking distance (r = 0.21, p < 0.001), with peak VO<sub>2</sub> and QoL (both r = 0.13, p = 0.01), whereas low physical exercise did not show significant associations. Interestingly, type or amount of exercise was not significantly related to any measure of diastolic function.

**Conclusion:** The total amount of daily physical activity is related to submaximal exercise capacity and QoL, whereas only daily high intensity exercise is associated with maximal exercise capacity in patients with HF with preserved EF.

#### P1093

##### Outcome of advanced heart failure patients with restrictive diastolic echocardiographic filling pattern (RDEFP) undergoing exercise based residential cardiac rehabilitation (EBCR)

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**Background:** EBCR is recommended and useful in chronic stable heart failure patients.

**Purpose:** We aimed to evaluate safety and outcome of EBCR in patients with RDEFP (early mitral deceleration time [DT] ≤ 140ms) and severe left ventricular dysfunction after recent episode of acute heart failure.

**Methods:** from June 2010 to May 2013, 20 consecutive patients (90% male, age 63 ± 15 years) with RDEFP and severe left ventricular dysfunction were admitted to a 3-weeks EBCR program (twice cycling or treadmill daily sessions with progressive increase as tolerated up to 14 Borg Rating of Perceived Exertion Scale, respiratory training) after a recent (1-3 weeks) episode of acute heart failure. Echocardiography on admission, Six minute walking test distance (6MWT), NT-proBNP on admission

and at discharge were assessed. Patients able to attend two daily sessions (30 minute each) at a workload of more than 30W Cycling or more than 2.5 Km/h at Treadmill by the end of rehabilitation program were categorized as Fit. Primary outcome was the occurrence at 1 year follow up of death (D), heart transplantations (HTx) or left ventricle assist device implantation (LVAD).

**Results:** All patients completed the rehabilitation program without complications related to exercise. At follow up primary outcome occurred in 9 patients; compared to alive at follow up (11 patients), these patients tolerated lower training workload and had lower 6MWT performance at admission and discharge; moreover they had higher NT-proBNP value at admission and discharge (Table)

**Conclusions:** In patients with RDEFP and severe left ventricular dysfunction after a recent acute heart failure EBCR is feasible and safe; exercise workload tolerance and submaximal exercise capacity by the end of EBCR program can help to predict outcome as well as NT-proBNP value.

PATIENTS	ALIVE	D/LVAD/HTx	p	
Indexed End diastolic volume (ml/m <sup>2</sup> ) (M ± SD)	120 ± 36	122 ± 28	119 ± 47	0.69
Left Ventricle Ejection Fraction (M ± SD)	27 ± 5	27 ± 4	27 ± 7	0.9
DT (M ± SD)	125 ± 12	121 ± 11	129 ± 11	0.07
NT-ProBNP at admission pg/ml (M ± SD)	6723 ± 8292	3344 ± 3795	10853 ± 10508	0.02
NT-ProBNP at discharge pg/ml (M ± SD)	7606 ± 8170	3837 ± 3811	12214 ± 9847	0.02
FIT	0.5	0.8	0.11	0.008
6MWT at admission m (M ± SD)	184 ± 156	279 ± 111	67 ± 122	0.0005
6MWT at discharge m (M ± SD)	312 ± 191	445 ± 119	150 ± 104	0.0005

M = mean SD = standard deviation

**P1094**

**The efficacy of EECP therapy to improve quality of life in chronic heart failure patients**

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**Backgrounds:** Depression is associated with a 5 fold increased risk of all cause mortality in patients with Chronic Heart Failure (CHF). The Enhanced external counter-pulsation (EECP) treatment can improve exercise tolerance in CHF patients. Regular exercise relieve depression and improve quality of life (QoL).

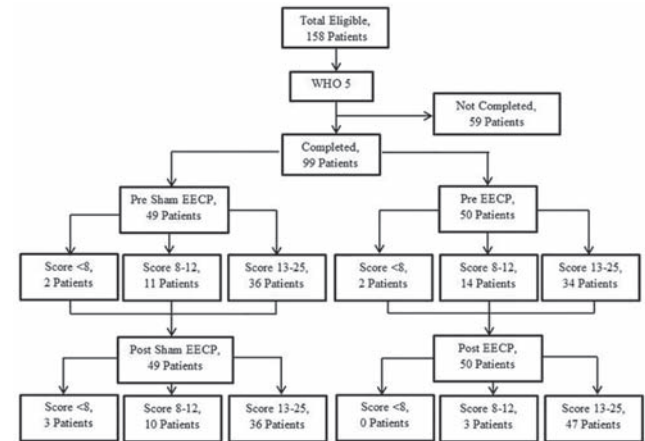
**Purpose:** to evaluate the risk of depression level before and after EECP therapy to improve quality of life in CHF patients.

**Methods:** A double blind randomized clinical trial was performed in 99 patients with CHF who had received EECP therapy in a clinic in Indonesia between January 2014 and June 2015. Subjects were categorized into 2 groups, i.e. 49 subjects had sham EECP therapy and 50 subjects had EECP therapy. All subjects were patients with

CHF who filled WHO5 (World Health Organization) questionnaire before and after receiving EECP therapy.

**Results:** There was no significant different between two groups regarding the baseline characteristic of CHF patients. There was no significant difference from the questionnaire results in sham group before and after EECP therapy, but in EECP group it showed statistically significant different (p < 0.05). The WHO5 questionnaire attributes result were found significantly improvement of felt cheerful and good spirit (p = 0.003) and woke up feeling fresh (p = 0.030) in EECP group compare with sham group.

**Conclusion:** EECP therapy is effective to reduce depression so that improve QoL in patients with CHF



Disposition of Patients

**P1095**

**Older patients and cardiac rehabilitation: indication or limitation**

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**Introduction:** Coronary artery disease (CAD) is an important cause of morbidity and death. Cardiac rehabilitation programs (CRP) have proven benefits over cardiovascular (CV) risk factors and exercise capacity. Among individuals with CAD, older patients (pts) are less likely to be referred to CRP.

**Purpose:** We aimed to compare pts aged ≥65 years with those <65 years regarding baseline clinical profile and exercise performance and their response to a CRP.

**Methods:** This study was based on a prospective analysis of 433 consecutive pts who underwent CRP after acute coronary syndrome (ACS) in a tertiary centre from January 2009 to October 2015. Pts were divided into two groups, G1: age ≥65 years and G2: age <65 years. Exercise performance was assessed using both duration and metabolic equivalents (METs) achieved in standard exercise test (ET) using Bruce protocol.

**Results:** Only 68 pts (15.7%) were aged ≥65 years. Mean age was 69.3 ± 4.1 in G1 and 51.8 ± 7.8 in G2. Older pts were less educated (p = 0.005). Hypertension (60.3% vs. 43.0%, p = 0.009) and diabetes (38.2% vs 15.7%, p < 0.001) were more frequent in older pts, whereas active smoking and family history of CAD were more often in younger pts. CAD was different between both groups. Lesion of 3 coronary arteries (CA) was more common in G1 (22% vs 9.0%, p = 0.002) with also higher prevalence of significant residual stenosis in those pts (42.2% vs. 23.2%, p = 0.001). Echocardiography showed normal or near-normal left ventricular (LV) systolic function with

1094. Table 1

Post EECP WHO-5	Subjects	Responses	p value	
All time	Most	More	Some	None
Study	Control	Study	Control	Study
Felt cheerful & good spirit	18	0	18	19
Felt calm & relaxed	9	3	28	22
Felt active & vigorous	11	3	21	17
Woke up feeling fresh	11	1	24	19
Filled with interesting	13	3	21	17

The comparison of WHO-5 questionnaire after EECP between groups

similar fractional ejection in both groups (G1:  $51 \pm 12\%$  vs G2:  $52 \pm 11\%$ ). Absolute functional capacity was significantly different between groups (G1:  $7.5 \pm 1.6$  METs vs. G2:  $8.8 \pm 2.3$  METs,  $p < 0.001$ ; G1:  $6.9 \pm 1.6$  min vs. G2:  $8.3 \pm 2.4$  min of ET duration,  $p < 0.001$ ). At the end of CRP both groups similarly improved their performance (G1:  $9.2 \pm 1.8$  METs vs. G2:  $10.8 \pm 2.1$  METs; G1:  $8.8 \pm 1.7$  min vs.  $10.3 \pm 2.2$  min of ET duration). After comparing the results of CRP, we found no statistically significant difference between two groups (more 25.8% METs in G1 vs. 27.6% METs in G2,  $p = 0.641$ ).

**Conclusion:** Older pts remain largely underrepresented in CRP cohorts. Although older pts had worse functional capacity, the relative improvement in exercise performance is similar in both younger and older pts. Age should not be considered, per se, criteria for referral/non-referral to CRP.

### P1096

#### After acute coronary syndromes - who are we rehabilitating

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**Purpose:** Cardiac rehabilitation (CR) has been shown to improve quality of life and reduce recurrent events and mortality. Still, rates of participation in CR programs are low, a problem which seems to particularly affect specific groups. We aimed to evaluate the rate of referral for CR after acute coronary syndromes (ACS) and significant determinants in daily practice.

**Methods:** We reviewed the clinical files of all patients (pts) admitted to our Cardiology Department with an ACS in 2014 and excluded those transferred to or with follow up in other departments or hospitals. Logistic regression was used to compare those referred for CR with those who weren't, regarding several sociodemographic and clinical characteristics; results are presented as odds ratio (OR) and p-value.

**Results:** We identified 639 pts hospitalized for ACS during 2014, 278 with follow up in our outpatient clinic. Mean age in the latter group was 63 years, with 206 (74%) male pts; 106 (38%) were referred for CR while the remaining 172 (62%) had follow up in the Ambulatory General Cardiology Clinic.

On univariate analysis, women (OR 0.49,  $p = 0.018$ ), older pts (OR 0.92 for a one year increase,  $p < 0.001$ ), those with a previous ACS (OR 0.35,  $p = 0.002$ ) or other important morbidities, namely cerebrovascular disease, peripheral artery disease or chronic kidney disease (OR 0.20,  $p = 0.001$ ), and those not in Killip I class (OR 0.18,  $p = 0.001$ ) were less likely to be referred to CR. In contrast, a diagnosis of myocardial infarction (MI) compared to unstable angina (OR 2.66,  $p = 0.014$ ), the presence of one vessel disease on coronary angiography (OR 2.93,  $p < 0.001$ ) and performance of percutaneous angioplasty (OR 3.50,  $p < 0.001$ ) were associated with bigger rates of CR referral. The number of cardiovascular risk factors, left ventricular systolic dysfunction and other ACS complications didn't have a statistically significant association with the outcome.

In a stepwise multivariate model, excluding previous ACS and one vessel disease for concerns of collinearity, older age (OR 0.93,  $p < 0.001$ ), Killip class (OR 0.19,  $p = 0.003$ ), comorbidities (OR 0.36,  $p = 0.041$ ), diagnosis of MI (OR 2.57,  $p = 0.031$ ) and coronary angioplasty (3.55,  $p < 0.001$ ), kept their statistically significant association with CR referral.

**Conclusions:** Our study shows more "linear" subjects have a higher rate of CR referral, while older patients, with more comorbidities and complicated clinical course tend to be left out. This referral bias is not totally unexpected, still we believe it should move us towards a more inclusive CR paradigm; most of all, those who could benefit the most should not be left out. Further research into this topic is warranted, comparing these results with variables influencing CR outcomes and testing strategies to overcome such barriers.

### P1097

#### The long term effects of high intensity exercise; a 5 years follow-up of a randomized controlled trial in heart transplant recipients

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**Background:** High-intensity interval training (HIT) has repeatedly proven to be superior to moderate continuous exercise regarding improvement of aerobic capacity in normal subjects and patients with established heart disease. Heart transplanted (HTx) patients has traditionally not been exposed to HIT because of chronotropic incompetence, but we have recently shown that HIT is safe and efficient also in this group. We now report 5 yr long-term effects of this intervention.

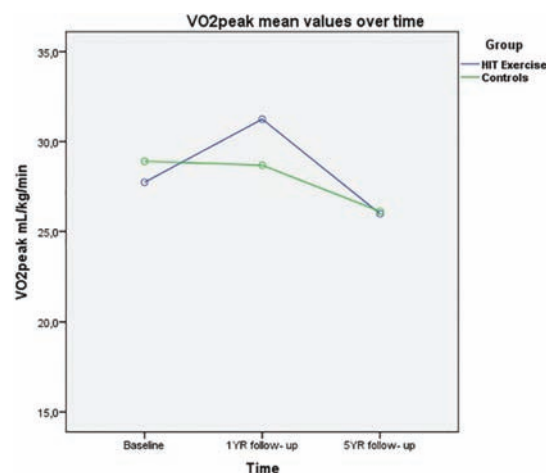
**Purpose:** To evaluate the long-term effects of HIT.

**Method:** 48 HTx patients completed a randomized control trial at our hospital in 2009-2011, comparing a 12-month HIT intervention with usual care. Four years after completed intervention, 41 patients were eligible for follow-up testing, to evaluate long-term effects of HIT. The patients underwent cardiopulmonary exercise

testing, blood sampling, echocardiography, intravascular ultrasound (IVUS) in coronary arteries, health-related quality of life questionnaires (QoL), measurement of body composition and isokinetic testing of muscle strength.

**Results:** Mean age (SD) of the patients at baseline was 49 (16) yr, 68 % men and mean years after HTx was 4 (2) yr. During 12 months of HIT, VO<sub>2</sub>peak increased significantly from 27.7 (5.7) to 31.2 (5.3) and thereafter decreased to 26.0 (6.2) ml/kg/min at 5 yr follow-up, while it remained slightly decreased during the whole period in the control group: 28.9(6.7), 28.7 (6.3) and 26.1 (7.1) ml/kg/min at baseline, 12 mo and 5 yr respectively. The HIT-group also had significantly higher muscular capacity and less coronary artery vasculopathy (CAV) at 12 mo. Analysis of variance (baseline, 12 mo, 5 yr) showed no changes between groups in VO<sub>2</sub>peak, muscular capacity, body composition, weight, chronotropic responses during exercise, glucose tolerance or lipid profile. The indifferences in aerobic performance between groups, was in line with the similar everyday activity frequency and intensity measured by senseWear armband at 5 yr follow-up.

**Conclusion:** Patients who had completed a 12 month HIT-intervention were not able to maintain their high post-exercise VO<sub>2</sub>peak levels and muscle capacity during long-term follow up. There were no significant differences in VO<sub>2</sub>peak levels between the two groups at 5 yr follow-up and they reported similar activity frequency and intensity. Despite the reduced VO<sub>2</sub>peak other positive effects may have sustained: for example the reduced CAV progression, which currently is being analyzed. However, our findings so far suggest that moderate levels of exercise and intensity are insufficient in order to maintain the achieved VO<sub>2</sub>peak levels. Intermittent periods of HIT are probably necessary to maintain high VO<sub>2</sub>peak levels.



### P1098

#### Exercise-induced changes of pulse wave in chronic heart failure patients with reduced ejection fraction

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**Purpose:** Arterio-ventricular coupling plays an important role in the pathophysiology of heart failure with reduced ejection fraction (HFREF). A decreased augmentation index (Alx) is found in HFREF patients. The changes in central hemodynamic parameters of these patients during exercise are still not well known. We investigated the changes in parameters of pulse wave analysis during cardiopulmonary exercise testing (CPET) in HFREF patients.

**Methods:** We compared 26 patients with chronic HFREF characterized by ejection fraction (EF)  $\leq 40\%$ , NYHA class  $\geq 2$  and absence of atrial fibrillation (CHF) to 26 control subjects without a history of heart failure (CON) matched according to sex, age and renal function. Pulse wave analysis was assessed before and immediately after CPET and for ten minutes during the recovery period with an oscillometric device. The regression models were adjusted for history of hypertension and coronary artery disease, smoking status, body mass index, use of ACE inhibitors and calcium antagonists and heart rate.

**Results:** In supine position at rest the Alx was significantly lower in CHF compared to CON ( $19.85 \pm 2.82$  vs.  $28.43 \pm 3.39$ ,  $p = 0.05$ ). After CPET, the Alx increased in CHF significantly compared to baseline ( $19.73 \pm 2.37\%$  vs.  $30.36 \pm 2.59\%$ ,  $p < 0.001$ ) and to CON four minutes after exercise cessation ( $28.90 \pm 2.21\%$  vs.  $22.81 \pm 2.52\%$ ,  $p = 0.05$ ). Furthermore, the amplitude of the reflected wave was reduced after exercise in CON but not in the CHF ( $13.3 \pm 6.04$  mmHg vs.  $16.4 \pm 7.2$  mmHg,



$p < 0.001$ ). In addition, the pulse wave velocity after exercise was significantly lower in CHF compared to CON ( $8.45 \pm 0.29$  m/s vs.  $9.09 \pm 0.25$  m/s,  $p < 0.05$ ).

**Conclusion:** This study provides new insights into the complex hemodynamic changes and the importance of arterio-ventricular coupling in patients with HFREF under exercise conditions. We observed an increased augmentation index in heart failure patients which might be one of the reasons for exercise intolerance observed in these subjects. The clinical utility of these findings, e.g. for individualized treatment adjustment, has to be evaluated by future studies.

### P1099

#### Left atrial function dynamics during exercise in heart failure of both reduced and preserved ejection fraction: pathophysiological implications on the right heart

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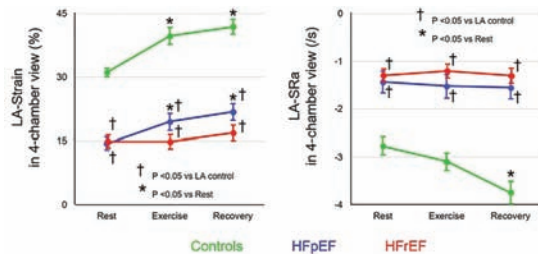
**Background:** Left atrial (LA) function plays a key role in the hemodynamics of heart failure (HF) of reduced (rEF) and preserved (pEF) ejection fraction. Extensive investigation of LA dynamics, however, has been performed exclusively at rest.

**Purpose:** We hypothesized that LA dynamic impairment during exercise may trigger right ventricular (RV) to pulmonary circulation (PC) uncoupling and ventilation inefficiency.

**Methods:** 49 patients with HFREF, 20 with HFpEF and 32 healthy subjects with normal LA size and reservoir function (LA volume index  $< 34$  ml/m<sup>2</sup>, and peak LA strain during LA relaxation  $> 23\%$ ) underwent cardiopulmonary exercise testing and contemporary Echo-Doppler assessment of LA-Strain and strain rate (SRa) and of RV to PC coupling (pulmonary arterial systolic pressure (PASP)/tricuspid annular peak systolic excursion (TAPSE) ratio), measured at rest, at 40% of predicted peak oxygen consumption, and during recovery.

**Results:** In controls, LA-Strain increased during exercise and recovery. HFpEF patients showed some LA-Strain increase during exercise and recovery whereas no changes occurred in HFREF. Baseline LA-SRa was greater in controls and only in this group a significant enhancement during recovery was observed (figure). LA-Strain at rest, exercise, and recovery significantly correlated with PASP/TAPSE and ventilation vs carbon dioxide slope in a continuous fashion across groups ( $r = -0.63$  and  $r = -0.59$ ;  $r = -0.65$  and  $r = -0.50$ ;  $r = -0.70$  and  $r = -0.53$  for controls, HFpEF, and HFREF, respectively,  $P < 0.05$ ).

**Conclusions:** In HF, an impaired LA-Strain response is a key hemodynamic trigger for RV to PC uncoupling and exercise ventilation inefficiency with some overlap between HFpEF and HFREF phenotypes. Reversibility of LA dynamic appears an unmet target of specific therapeutic interventions.



Changes in LA-strain and LA-SRa

### P1100

#### Peak VO<sub>2</sub> is still a valuable prognostic marker in the current era. A subanalysis of the Mecki score group

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**Background:** Cardiopulmonary exercise testing (CPET) is used to define prognosis of HF and for heart transplant (HT) listing, but its role has witnessed changes as well the prognostic profiles of HF

**Objectives:** To evaluate the changes in prognosis between different decades and the changing role of the CPET in advanced heart failure (AHF) patients enrolled in the MECKI score database

**Methods:** We selected, from a multicenter Italian HF database, 715 ambulatory patients with AHF, as defined by peakVO<sub>2</sub> criteria for HT, to evaluate long-term follow-up using death+urgent HT as end-point. Clinical, laboratory, echocardiographic and cardiopulmonary-exercise-test data were analyzed for the entire

population and for patients grouped according to the time of CPET performed, before 2005 (n=354) or after 2005 (n=361)

**Results:** The average peakVO<sub>2</sub> and follow-up were  $10.2 \pm 1.7$  ml/kg/min and  $941 \pm 600$  days. Overall survival rates were 91%-62% at 1-5 years. Survival rates at 1-5 years were significantly lower in patients before 2005 (85.5%- 62.3 %) with respect to the population studied after (94.3 %-79.1 %) ( $p = 0.002$ ), when adjusted for age and gender. The difference was maintained even when the analysis was unadjusted. With respect to the old decades (before 2005) the AHF population after 2005 is older ( $65.4 \pm 10.5$  vs  $63.1 \pm 10.4$  yr,  $P < 0.001$ ), presents higher left ventricular ejection fraction ( $30.9 \pm 9.0$  vs  $26.8 \pm 9.3$  %,  $P < 0.0005$ ), lower ventilatory response to exercise (VE/VCO<sub>2</sub> slope,  $36.2 \pm 8.5$  vs  $38.2 \pm 8.8$  ,  $P < 0.01$ ), higher percentage of not ischaemic aetiology (41.0 vs 32.7 %,  $P < 0.001$ ), CRT ( $14.6$  vs  $5.0 \pm$  %,  $P < 0.0001$ ), ICD ( $24.6$  vs  $11.8$  %,  $P < 0.0001$ ). The following variables were significantly related to prognosis in both old and actual decades (Peak VO<sub>2</sub>, LVEF) while Beta-blockade therapy was protective only in the older group and the renal function only in the actual group.

**Conclusions:** PeakVO<sub>2</sub> maintains its prognostic value in patients also in current era, of older, but better treated patients.

## PROGNOSIS

### P1101

#### Impact of the number of leukocytes on admission in patients with takotsubo syndrome

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**Background:** Several studies have reported that Takotsubo syndrome have a good outcome in hospital. However, it is proposed that male gender and underlying disease are independent prognostic factors Takotsubo syndrome. The aim of our study was to evaluate prognostic factors in patients Takotsubo syndrome.

**Method:** Patients were consisted with consecutive 97 cases in our institute. We retrospectively corrected clinical characteristics from medical record. We defined major adverse cardiac event (MACE) as in-hospital cardiovascular death, cardiac shock, severe heart failure and fatal arrhythmia. Patients were divided into the MACE group and non-MACE groups. We compared clinical characteristics between the two groups.

**Results:** Patients were consisted with 47 MACE and 50 non-MACE. Although there was no significant difference in age between the two groups, male was significantly higher in the MACE group than the non-MACE group (27.7 vs. 12.0 :  $p = 0.052$ ). The number of leukocytes on admission ( $8,918 \pm 3,417$  vs.  $10,216 \pm 4,051$ ;  $p = 0.059$ ), underlying disease (70.5 vs. 39.6 %;  $p = 0.003$ ) and physical stress (44.2 vs. 28.9 %;  $p = 0.01$ ) are significantly higher in the MACE group than in the non-MACE group. Multivariate logistic regression analysis revealed that the high leukocytes on admission (odds ratio=1.00; 95%CI=1.00-1.00; $p = 0.046$ ), underlying disease (7.67;95%CI=2.38-24.7; $p = 0.001$ ) and physical stress (1.00; 95%CI=1.000-1.003; $p = 0.007$ ) were independent predictors of MACE.

**Conclusion:** High leukocytes on admission, underlying disease and physical stress were independent predictors for major adverse cardiac event. Not only underlying disease and physical stress but also the number of leukocytes on admission is important prognostic factors in patients with Takotsubo syndrome.

### P1102

#### Serum lipoprotein levels and survival in patients with advanced cancer

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**Background:** We set out to evaluate a cohort of patients with advanced cancer and to assess the prognostic impact of lipoproteins, which are known as markers of cardiovascular disease.

**Methods:** From 2005 through 2010, we enrolled 137 patients with histologically confirmed cancer (age  $59 \pm 10$  yrs, 54% men, body mass index [BMI]  $24.5 \pm 4$  kg/m<sup>2</sup>, tumour stage I/II/III/IV 9/9/31/50%) and 56 healthy controls (age  $61 \pm 11$  yrs, 55% men, BMI  $26 \pm 4$  kg/m<sup>2</sup>). Patients were followed until censoring in February 2014 or until death. The cancer group consisted of 35 patients with colorectal, 65 patients with pancreatic, and 37 patients with non-small cell lung cancer. At baseline, a thorough cardiology assessment was performed including a full blood chemistry in the morning hours, before which patients were allowed a small breakfast.

**Results:** With respect to the metabolism we compared cancer patients with control subjects. In cancer patients, triglycerides (TG) levels were  $146 \pm 73$  mg/dL, low-density lipoprotein (LDL)  $108 \pm 43$  mg/dL, high-density lipoprotein (HDL)  $55 \pm 17$  mg/dL, LDL/HDL ratio  $2.2 \pm 1.4$ , and total cholesterol (TC)  $193 \pm 50$  mg/dL. Controls showed TG levels of  $149 \pm 75$  mg/dL, LDL  $124 \pm 36$  mg/dL, HDL  $58 \pm 16$  mg/dL, LDL/HDL ratio  $2.3 \pm 0.9$ , and TC  $211 \pm 41$  mg/dL. The difference between cancer patients and controls was significant for LDL ( $p = 0.017$ ) and TC ( $p = 0.018$ ). During a mean follow-up of 27 months, 82 patients (57%) died from any cause. In general, we found that tumour stage, metastases, BMI, surgery, anticoagulation and haemoglobin all predicted survival (all  $p < 0.05$ ). With respect to the lipid metabolism TG, HDL and LDL/HDL ratio predicted survival in continuous analysis (TG – hazard ratio (HR) 0.996 [0.993-0.999]  $p = 0.018$ ; HDL – HR 1.014 [1.000-1.028]  $p = 0.045$ ; LDL/HDL ratio – HR 0.79 [0.63-0.99]  $p = 0.040$ ). C-reactive protein did not predict survival. TG lower than 160 mg/dL (8.9 mmol/L) increased mortality significantly (HR 2.0 [1.2-3.3]  $p = 0.0097$ ). The effect for TG lower than 160 mg/dL stayed significant in a multivariable model (HR 2.3 [1.4-3.8]  $p = 0.0009$ ), which was adjusted for all before mentioned univariate predictors. In a second model we additionally included sex and age and the effect remained significant (HR 2.3 [1.4-3.7]  $p = 0.0012$ ).

**Conclusion:** Once colorectal, pancreatic or lung cancer have developed the prognostic factors shift into a state where low TG and LDL/HDL ratio and high HDL predict poor survival independently. This phenomenon has been described for heart failure and termed cholesterol paradox.

### P1103

#### Prognostic assessment in heart failure: what is the role of risk scores?

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**Background:** The prognostic stratification of risk in heart failure (HF) is crucial for therapeutic guidelines with devices and heart transplant. Therefore, the use of risk scores that incorporate several variables with prognostic impact can be an advantage. We evaluated the performance of 3 risk scores in a specialized HF consultation.

**Methods and Results:** Retrospective and observational study that included 147 patients with HF: mean age  $57 \pm 15$  years; 68% men and mean left ventricular ejection fraction  $36\% \pm 15\%$ . We calculated the scores: Seattle Heart Failure (SHF), MAGGIC Heart Failure Risk Calculator (MHFRC) and EMPHASIS-HF risk score (EHFRS) with patients basal values. The predictive value of mortality by risk scores and NT-proBNP was evaluated by c-statistics (AUC – Area Under the Curve). The mortality on follow-up period (median of 5 years) was 21,8%. The predictive value of mortality by risk scores and NT-proBNP are presented on table 1.

**Conclusions:** In a specialized HF consultation representative of real world, the predictive value of mortality by risk scores was weak. The performance demonstrated by the NT-proBNP in our population suggests a lightly superior potential benefit in comparison with the scores - which are composed by several variables and difficult to apply in clinical practice.

Table 1

	Median (interquartile interval)	AUC e CI 95%
SHF	18 [13; 29]	0,63 (0,41-0,86)
MHFRC	17 [13; 24]	0,55 (0,43-0,68)
EHFRS	4 [3; 6]	0,54 (0,43-0,65)
NT-proBNP (pg/ml)	782 [283; 3464]	0,67 (0,55-0,79)

### P1104

#### Predictors of LV dyssynchrony worsening in the presence of normal EF

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**Aim:** To reveal the predictors of electrical and mechanical dyssynchrony worsening in patients with LBBB and normal EF during a prospective study.

**Methods:** 68 consecutive patients (mean age  $55,8 \pm 9,0$  years; M47%) with LBBB revealed during annual check-up were enrolled into the study. History of CAD had 35 (51,5%) patients, hypertension - 64 (94,1%), 4 patients had no overt heart diseases after thorough examination. There were no patients with EF below 45%, and NYHA class > II. Fifty two (76,5%) of 68 patients had taken the recommended medication, mainly ACE-inhibitors and beta-blockers; however, 16 patients refused the recommendations. Follow-up period duration was  $32 \pm 13$  months (6-58 mths). Logistic regression (SPSS 11.5) was used to identify characteristics that might have the greatest impact on the dynamics of dyssynchrony. Twenty six parameters were analyzed altogether.

**Results:** QRS duration during the FU period has increased in 33,9% of patients, mostly in women: 41.9% vs. 25.8% among men; but overall QRS duration has not changed during FU ( $149 \pm 13$  ms vs.  $152 \pm 14$  ms,  $p = 0.66$ ). An independent predictor of its progression was end-diastolic volume index (EDVI; OR = 1,24; 95% CI: 1,00-1,52).

In the beginning of the study only 19 (21,1%) patients had signs of atrio-ventricular (AV) dyssynchrony. During the FU period 10 (14,7%) new cases of AV-dyssynchrony have occurred. Multivariate analysis showed the influence of chronic heart failure (CHF; OR 6,91; 95% CI: 1,95-24,50;  $p = 0.003$ ), and heart rate (HR; OR = 1,84; 95% CI: 1,18-2,87;  $p = 0.026$ ).

According to the univariate analysis interventricular (IV) dyssynchrony deterioration was related to the signs of previous myocarditis on cardiac MRI with gadolinium (OR = 3,5; 95% CI: 1,8-10,6;  $p = 0.013$ ), medical treatment by ACE-inhibitors and beta-blockers (OR = 1,9; 95% CI: 1,3-3,8;  $p = 0.02$ ), age (OR = 0,93; 95% CI: 0,87-0,99;  $p = 0.041$ ), BNP level (OR = 0,53; 95% CI: 0,28-0,99;  $p = 0.046$ ), IVS thickness (OR = 0,03; 95% CI: 0,01-0,82;  $p = 0.04$ ). Multivariate analysis revealed the influence of previous myocarditis (OR = 5,0; 95% CI: 1,5-16,68;  $p = 0.009$ ) and medical treatment (combination of ACE-inhibitors and beta-blockers) (OR = 2,6; 95% CI: 1,4-5,8;  $p = 0.008$ ). Interestingly, during FU period IV-dyssynchrony has decreased among those patients who followed the recommendations on medical treatment ( $68,29 \pm 15,63$  ms vs.  $61,95 \pm 15,85$  ms;  $p = 0.005$ ). However, it worsened in patients who refused them ( $55,62 \pm 18,96$  ms vs.  $64,38 \pm 15,04$  ms;  $p = 0,032$ ).

**Conclusions:** In patients with LBBB and normal EF EDVI was responsible for the increase of QRS complex duration during FU period of  $32 \pm 13$  months. Presence of CHF and HR was associated with AV dyssynchrony worsening. Predictors of IV-dyssynchrony were the signs of previous myocarditis on cardiac MRI with gadolinium and poor adherence to medical treatment.

### P1105

#### Influence of music therapy on patients with heart failure and early post-infarction angina; a substudy of the MUSIC-HF study

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Most studies have shown that early post-infarction angina (EPA) implies an unfavorable long-term prognosis among patients with acute myocardial infarction (AMI). 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 for reduction of anxiety and pain in patients with heart failure (HF) and EPA.

**Material and methods:** The effectiveness of music in reducing anxiety and pain during EPA attacks was tested using a two-group pretest-posttest experimental design with 230 patients with HF and EPA. Patients were randomly assigned to receive 30 min of sedative music ( $n = 115$ ) or treatment as usual ( $n = 115$ ). Anxiety, pain sensation, and pain distress were measured with visual analogue scales at start of chest pain episodes and 30 min later.

**Results:** Repeated measures MANOVA indicated significant group differences in anxiety, pain sensation, and pain distress from pretest to posttest ( $p = 0.0124$ ). Post hoc dependent t-tests and univariate repeated measures ANOVA ( $p = 0.0162$ ) indicated that in the sedative music, anxiety, pain sensation, and pain distress all decreased significantly ( $p = 0.0101$ ), while in the treatment as usual group, no significant differences occurred. Independent t-tests indicated significantly less posttest anxiety, pain sensation, and pain distress in the sedative music group than in treatment as usual groups ( $p = 0.0284$ ).

**Conclusion:** Sedative music was more effective than treatment as usual in decreasing anxiety and pain in patients with HF and EPA. Patients with HF should have beneficial of using sedative music as an adjuvant to medication during EPA episodes.

### P1106

#### The readmission in de novo heart failure patients within 30 days, either cardiovascular or non-cardiovascular causes, affecting the prognosis

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**Background/Introduction:** Heart failure (HF) readmission results in heavy expenditure on HF management. In a Medicare database study, HF is the most frequent reason of readmission within 30 days of discharge in both medical and surgery populations

**Purpose:** This study aimed to evaluate the readmission rate, outcome, and predictors of HF readmission.

**Methods:** Patients with de novo reduced left ventricular ejection fraction (LVEF <40%) who were admitted for acute decompensation of de novo HF were enrolled for analysis of readmission rate, mortality and predictors of readmission.

**Results:** A total of 688 de novo HF patients with LVEF <40% were enrolled. The in-hospital and 6-month mortality rates were 3.7% and 13.2%, respectively. In the patients surviving the index HF hospitalization, the 30-day and 6-month readmission rates were 11.9% and 28%, respectively. At the end of 6-month follow-up, the readmission group had higher mortality than the non-readmission group (27.4% vs. 10.2%;  $p = 0.001$ ). The survivors of the 30-day readmission had similar mortality rates at 6 months, regardless the causes of the readmission (cardiovascular vs. non-cardiovascular: 23% vs. 30.2%,  $p = 0.634$ ).

**Conclusion(s):** The HF patients suffered from 30-day readmission had worse prognosis at 6-month follow-up. Regardless of the readmission causes, the patients surviving the 30-day readmission had similar mortality rates at 6-month follow-up. These results underscored the importance of reducing readmission as a means to improve HF outcome.

### P1107

#### Validation of a new very simple score for outcome prediction in patients with chronic left ventricular systolic heart failureheart failure with reduced ejection fraction

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**Aim of this study** was to develop and validate a prognostic score for patients with chronic heart failure (CHF), simple to calculate using only easily obtainable parameters exclusively through collection of past and present medical history. 376 consecutive outpatients with left ventricular systolic CHF (ejection fraction -EF- <45%) were recruited through the Outpatient Heart Failure Clinic of San Raffaele Hospital (OSR). Twelve variables, collected at baseline, were individually correlated with 5-year mortality risk by univariate Cox regression analysis. They were: gender; age; presence of coronary artery disease, previous acute myocardial infarction (AMI), previous acute decompensated heart failure (ADHF), left ventricular ejection fraction (EF) <30%, NYHA class IV, diabetes mellitus, atrial fibrillation (AF), chronic renal failure (CRF), not taking beta-blockers (BB); not taking ACE-inhibitor (ACE-I). The variables that resulted significantly associated with increased mortality were then used to build a model of cardiac and overall risk of death through multivariate Cox regression analysis. The score thus obtained was subsequently validated on a different sample of 325 patients previously enrolled in other clinical studies. Previous ADHF, AF, EF <30%, not taking BB, CRF resulted significant predictors of cardiac and overall mortality. The model provides a maximum score of 14 points, subdivided as 3 points each for previous ADHF, AF, EF <30%, not taking BB and 2 points for CRF. The OSR risk score was validated on a different validation sample for cardiovascular (CVD) death by tertiles of score (1st tertile: 0-2; 2nd tertile: 3-5; 3rd tertile: > 5). Log Rank test showed a significant difference in 5-year CVD mortality risk ( $p = 0.004$ ). A significant difference in survival time by tertiles of OSR risk score was also observed for all-cause mortality (log-rank test:  $p = 0.003$ ). Compared to the first tertile of OSR score, the second tertile had an increasing risk for CVD admission (HR: 2.7; 95% CI: 1.5-4.9) and for admission due to HF worsening (HR:4.3; 95%CI: 1.3-14.5). In the third tertile the risk for CVD admission and for admission due HF worsening was also increased (HR: 3.2; 95%CI: 1.7-6.1 and HR: 3.8; 95%CI: 1.03-14.1.). In conclusion, the OSR Heart Failure Risk Score, derived and validated in chronic HF outpatients with left ventricular systolic dysfunction, is a simple, quick, inexpensive and readily-available tool for predicting patient outcome in 5-year time, in terms of cardiac and global mortality and morbidity. This prognostic model is exclusively based on patient's past and present medical history.

### P1108

#### High levels of galectin-3 is associated incremental risk of all-cause death in chinese patients with heart failure

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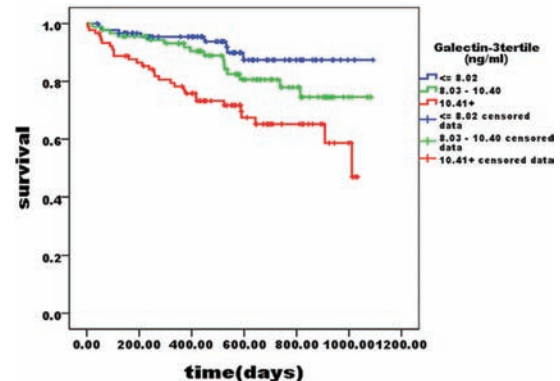
**Background:** Galectin-3, a novel biomarker associated with fibrosis and inflammation, has been used to stratify and prognosticate heart failure (HF). However, the usefulness of value in prognosis is controversial and data in Chinese HF population are sparse.

**Purpose:** To evaluate the prognosis value of galectin-3 in chinese HF patients.

**Methods:** Galectin-3, N-terminal pro B-type natriuretic peptide (NT-proBNP) levels and other clinical related variables were measured on admission in consecutive patients with HF in cardiology department of our hospital. Specifically, galectin-3 was detected by an enzyme-linked immunosorbent assay method. The primary end point was all-cause mortality and/or readmission at end of follow-up. The adjusted hazard ratio (HR) was determined by Cox regression model.

**Results:** We studied 272 patients with median age of 77 years and 55.9% were male. During a median follow-up period of 558 days, 53 patients (19.5%) died and 103 patients (37.9%) died and/or required re-hospitalization. Plasma galectin-3 levels by tertiles were associated with increased risk for main adverse cardiac events ( $p = 0.00$ ). Kaplan-Meier survival curves show the third tertile of galectin-3 were associated with incremental rate of primary end point (compared to second and first tertiles, the log rank  $p = 0.001$  and  $0.000$ , respectively). Multivariable Cox regression model show the highest tertile of galectin-3 was associated with increased risk of all-cause death or readmission for HF (HR=2.13, 95% confidence interval [CI]:1.24-3.68,  $P = 0.006$ ) compared with the lowest tertile after adjustment of age, NT-proBNP, creatinine, uric acid, albumin, hemoglobin and estimated glomerular filtration rate(eGFR).

**Conclusion:** Plasma galectin-3 is a novel independent predictor of all-cause mortality and/or readmission in Chinese patients with HF.High levels of galectin-3 is associated incremental risk of death in chinese HF patients.



kaplan-meier survival curve for death

### P1109

#### Predictors of outcome in outpatients with chronic heart failure during a long term follow-up

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**Background:** despite progress in the treatment and management of Heart Failure (HF), the prognosis of HF patients (pts) remains poor. Therefore an accurate prognostic stratification remains crucial to identify pts at high risk of mortality and hospitalizations who need a tailored treatment and closer follow-up.

**Purpose:** we aimed to assess the different predictive value of clinical, laboratoristic and instrumental parameters in outpatients with stable chronic HF.

**Methods:** we analyzed pts with reduced left ventricular ejection fraction (LVEF ≤45%) with optimized medical therapy according to current guidelines, clinically stable for at least 3 months, followed in our 'HF clinic'. All pts underwent clinical evaluation, laboratory exams, electrocardiogram and echocardiography. Median follow-up was 43 months. The composite end-point was: mortality and hospitalization for HF and for cardiovascular causes. Univariable analysis was performed using the t test for continuous variables and chi-square for categorical variables; multivariable analysis using Cox regression method.

**Results:** from 1st January 2011 to 31th December 2012 we evaluated 570 consecutive pts (mean age  $67 \pm 12$  years, 83% male); 486 pts (85.3%) were in NYHA class I-II, ischemic etiology was in 53% and idiopathic 44.7% of pts, 34.7% were diabetics and 26.3% were in atrial fibrillation. The average values of the main variables considered were: LVEF  $35 \pm 7\%$ ; eGFR  $64.1 \pm 36$  ml/min/1.73 m<sup>2</sup>, creatinine  $1.35 \pm 0.9$  mg/dl, hemoglobin  $13.3 \pm 1.6$  g/dl, HR  $67.9 \pm 12.34$  bpm. During the follow-up events occurred in 294 (52%) pts (121 death). Table 1 show the main prognostic parameters at univariable and multivariable analyses.

**Conclusion:** in our study population of outpatients with chronic HF and left ventricular systolic dysfunction, age, LVEF, diuretic dose and clinical congestion status remain the most powerful predictors of adverse outcomes during a long term follow-up.

### P1110

#### Hypokalemia and long-term outcomes in patients hospitalized for heart failure: a propensity-matched study

DZHK travel grant

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Table 1

Univariable analysis		Multivariable analysis			
Prognostic variables	p value	Prognostic variables	p value	Prognostic variables	p value
Age	<0,001	eGFR (ml/min/1,73 m <sup>2</sup> )	<0,001	Furosemide (mg)	0,026
NYHA classes III-IV	<0,001	Creatinine (mg/dL)	<0,001	Age	0,001
Atrial fibrillation	<0,001	Hemoglobin (g/dl)	<0,001	LVEF (%)	0,005
HR (bpm)	0,004	Mitral regurgitation	<0,001	Clinical congestion	<0,001
Clinical congestion	0,001	Furosemide (mg)	<0,001		
Ischemic etiology	<0,001	LVEF (%)	<0,001		

eGFR: Glomerular filtration rate, NYHA: New York Heart Association, LVEF: Left Ventricular Ejection Fraction, HR: heart rate

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**Background:** Low serum potassium is associated with higher risk of long-term mortality in ambulatory patients with heart failure (HF). The objective of the current study is to examine this association in patients hospitalized for worsening HF using propensity score matching design.

**Methods:** Of the 8049 patients hospitalized with a principle discharge diagnosis of HF, 1052 patients had hypokalemia (serum potassium <4.0 mmol/L) and 3142 had normokalemia (4.0 to 5.5 mmol/L), both on admission and at discharge. Propensity scores for hypokalemia were estimated for each of the 4194 patients and used to assemble a matched cohort of 995 pairs of patients with hypokalemia and normokalemia.

**Results:** Matched patients (n=1990) had a mean age of 75 years, 60% were women, and 28% African American. During 8 years of follow-up, all-cause mortality occurred in 66% and 62% of matched patients with hypokalemia and normokalemia, respectively (hazard ratio [HR], 0.94; 95% confidence interval [CI] 0.84-1.05; P=0.3). Similarly, no significant association between hypokalemia and all-cause mortality was found among different subgroups of patients. Hypokalemia had no association with all-cause hospitalization (HR, 0.99; 95% CI, 0.87-0.1.13; P=0.9) or HF hospitalization (HR, 0.95; 95% CI, 0.81-1.10; P=0.5).

**Conclusion:** Unlike in younger ambulatory patients with HF, hypokalemia was not associated with long-term mortality among real-world hospitalized HF patients.

#### P1111

##### Growth differentiation factor-15 is associated with poor prognosis in chinese patients with heart failure

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**Background:** Growth differentiation factor-15 (GDF-15), a novel biomarker associated with remodeling, oxidative stress and inflammation, has been used to stratify and prognosticate heart failure (HF). However, the prognostic value of GDF-15 in Chinese HF population is still unknown and related data are sparse.

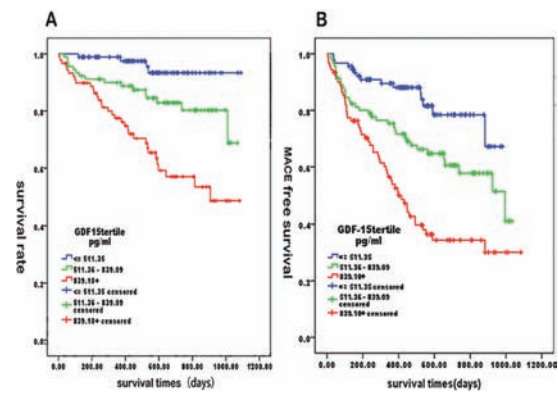
**Purpose:** To evaluate the prognostic value in chinese HF patients.

**Methods:** GDF-15 and other clinical related variables were examined on admission in 272 consecutive patients with HF in cardiology department of our hospital. GDF-15 was detected by a commercial enzyme-linked immunosorbent assay method. The primary end point was all-cause mortality; the secondary end point was main adverse cardiac events(MACE) including all-cause mortality and/or readmission for heart failure. The adjusted hazard ratio (HR) was determined by multivariate Cox regression model.

**Results:** A total of 272 patients with median age of 77 years and 55.9% were male. 53 patients (19.5%) died and 103 patients (37.9%) had MACE during a median follow-up time of 558 days. The third tertile of GDF-15 was associated with incremental rate of primary endpoint (compared to middle and low tertiles of GDF-15, the log rank p=0.001 and 0.001, respectively) and secondary endpoint (compared to middle and low tertiles of GDF-15, the log rank p=0.002 and 0.000, respectively). The incidence of primary endpoint and secondary endpoint also increased significantly when comparing the middle tertile to the low tertile of GDF-15 (the log rank p=0.02 and 0.01 respectively). Multivariate Cox regression model show the highest tertile of GDF-15 was associated with increased risk of all-cause death for HF [hazard ratio(HR)=5.95, 95% confidence interval(CI):1.88-18.78, P=0.002]

compared with the lowest tertile after adjustment of interference of related coexisted clinical factors including age, renal function or NT-proBNP.

**Conclusion:** Plasma GDF-15 is a novel independent predictor of all-cause mortality and/or readmission in Chinese patients with HF. It may potentially be used to stratify, prognosticate HF patients.



Survival analysis for mortality or MACE

#### P1112

##### Recovered heart failure: a different class of heart failure according to outcome?

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**Background:** Advances in drug therapy, devices, coronary revascularization and valvular repair are responsible for systolic function improvement (even sometimes to normal or almost-normal values) in a non-negligible number of patients with heart failure (HF) and reduced left ventricular ejection fraction (LVEF). The existence of a third class of HF beyond HF with reduced LVEF (HFrEF) and with preserved LVEF (HFpEF) has been proposed. Objective: Outcomes analysis of patients with recovered HF (baseline LVEF <45% that improve after one year of follow-up to a LVEF ≥ 45) compared to HFpEF and HFrEF. All-cause, cardiovascular, HF-related and sudden death were the specific end-points.

**Patients and Method:** LVEF at first visit and at one-year follow-up were assessed by echocardiography in 1063 patients (72.7% men; mean age 65.6 ± 11.9 years, range 30-96 years). Aetiology of HF was mainly ischemic heart disease (52.2%), followed by dilated cardiomyopathy (14%), valvular disease (8.7%) and hypertensive cardiomyopathy (8.6%). Mean LVEF was 32% ± 12. Most patients were in NYHA functional class II (68.3%) and III (25%). Patients were classified into three groups: 1) Recovered HF (LVEF <45% at baseline and ≥ 45% at one year; n=237); 2) HFpEF (LVEF ≥ 45% at baseline; n=145); and 3) HFrEF (LVEF <45% both, at first and at one-year visits; n=681). Mean follow-up was 4.7 ± 3.1 years after the second echocardiography (up to 10 years).

**Results:** Four hundred thirty-four patients (40.8%) died during follow-up. In Cox regression analysis (taking as reference recovered HF) outcomes for HFpEF and HFrEF patients were: all-cause mortality (HR 1.68 [95%CI 1.19-2.38], p=0.003; and HR 1.65 [95%CI 1.26-2.16], p<0.001, respectively); cardiovascular mortality (HR 2.30 [95%CI 1.40-3.60], p=0.001 and HR 2.41 [95%CI 1.61-3.60], p<0.001, respectively). Sudden death was only significantly higher in HFrEF (HR 3.62 [95%CI 1.45-9.07], p<0.001) and not in HFpEF (HR 1.40 [95%CI 0.38-5.22], p<0.66).

**Conclusion:** Recovered HF patients showed a better prognosis than HFpEF and HFrEF patients, mainly due to lower hazard of HF-related and sudden death.

**P1113**

**Prognostic value of prothrombin activity percentage measurement in patients with acute decompensated cardiac failure**

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**Background:** Abnormal liver function tests (LFTs) is a common feature in heart failure. It has been previously shown that abnormal LFTs predicts poor outcome in follow up. Prothrombin Activity Percentage (PA%) correlates with prognosis in patients with acute liver failure in settings such as acetaminophen intoxication, however prognostic implications of PA% in acute decompensated heart failure (ADHF) has not been evaluated previously. The present study was conducted to investigate the impact of PA% on cardiovascular outcomes in patients with ADHF in our institution.

**Objective:** To evaluate the relation between PA% and death/heart transplantation and hospital readmission due ADHF at 180 days in patients (pts) hospitalized with ADHF.

**Methods:** 223 consecutive pts admitted with ADHF between January-2013 and August-2014 were selected; patients on vitamin k antagonists were excluded (n=94). Heparin was not administered to any patient before blood collection. Blood samples were obtained at hospital admission; PA% was measured with an automatic coagulation analyzer (CA-500, Sysmex). Patients' basic characteristic data including sex, age, past medical history, medications, as well as blood exam results, were analyzed. The primary endpoint was a composite of all-cause death or readmission for heart failure at 180 days of follow up.

**Results:** There were 117 pts analyzed, mean age was 78 years old (+/- 11) and 68 pts (58%) were male, 49 pts (42%) had preserved ejection fraction (>50%); median PA% was 62,5% (IQR 25-75: 25-81,) and median creatinine was 1,22 mg/dl (IQR 25-75: 0,95-1,66). There were 40 (34%) death/heart transplantation and hospital readmission due ADHF and 22% (26) death at 180 days; PA% was significantly lower in the event group: 71 % versus 80% (p < 0.013), cox proportional hazards regression analysis showed that decreased prothrombin activity (< 70%) is an independent predictor of event (OR=3.82 CI95: 1,47-9,8, p=0.006) among variables including serum creatinine, hs- troponin and glucose at 180 days of follow up. (Figure)

**Conclusion:** decreased PA% at admission is a novel powerful predictor of death/heart transplantation in non-anticoagulated pts hospitalized due to ADHF suggesting the impact of liver dysfunction on disease process of heart failure. This variable could be included in a future as a part of risk stratification in acute heart failure setting.

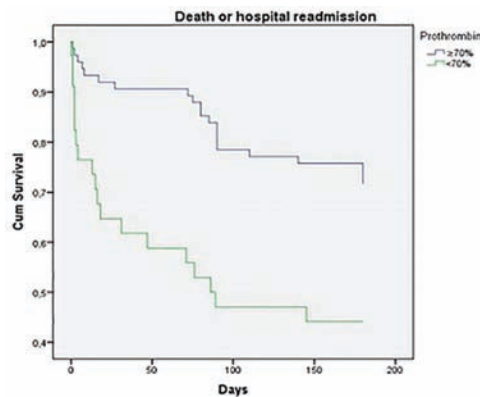


Figure. Primary endpoint

**P1114**

**Systolic blood pressure target: a new challenge in cardiovascular prevention in community-based population?**

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**Background:** Arterial hypertension (AH) is one of the most known risk factor for cardiovascular disease (CVD). Until now, systolic blood pressure (SBP) level ≤ 140mmHg has been considered the optimal SBP to reduce blood pressure-related adverse outcomes. Nevertheless, in SPRINT trial, SBP goal < 120mmHg resulted in lower CVD risk.

**Objectives:** To determine prevalence, characteristics and outcome in a group of hypertensive patients without known CVD compared to an increased cardiovascular risk (ICR) subgroup taking into account SBP goal < 120 mmHg.

**Methods:** We enrolled patients with AH and one other cardiovascular risk factor from 11/2009 to 10/2014. Patients with diabetes, known ejection fraction (EF) < 35%, New York Heart Association (NYHA) class III-IV and age < 50 years were excluded. Of these, we also identified an ICR subgroup defined by clinical or subclinical cardiovascular disease, chronic kidney disease (eGFR of 20 to < 60 ml min per 1.73 m2), or an age ≥ 75 years. All patients were in optimized medical therapy. Clinical variables of study population were derived from the E-data chart for Outpatient Clinic collected in a Cardiovascular Observatory.

**Results:** Of all 3003 cases, after exclusion of diabetes and known EF < 35% (1239 pts, 41%), we identified a cohort of 1764 patients ≥ 50 years old (71 ± 9 years old, 51% males). Current smoking status was in 250 patients (14%), dyslipidemia in 1072 (61%) and obesity in 452 patients (26%). Median value of SBP was 138 ± 19mmHg and of diastolic blood pressure (DBP) was 81 ± 9mmHg. Medical therapy was consistent in renin-angiotensin receptor blocker (ARB) for 1028 patients (58%), calcium antagonist (CA) therapy for 321 (18%), beta blockers (BB) for 777 (45%) and diuretics for 457 (25%). Atrial fibrillation (AF) was in 575 patients (32%), of whom, 353 (20%) was persistent or permanent AF. Anticoagulant therapy was present in 376 patients (21%). We also identified a subset of 1156 ICR patients (65%, 80 ± 4 years old, 52% males). In this latter group SBP was 140 ± 20mmHg (< 120mmHg in 234 patients, 20%) and medical treatment was ARB for 670 patients (58%), CA for 196 (17%), BB for 497 (43%) and diuretics for 266 (23%). In a median follow up of 22 months, 236 patients (13%) of the first group died or were admitted for HF, conversely 17% showed an event in the ICR subgroup. Taking into account SBP different goals, we had 3% (in SBP < 120mmHg) vs 3.8% (in SBP ≥ 120 mmHg) of total events in the first group (p=NS), and 13.2% (SBP < 120mmHg) vs 14.4% (SBP ≥ 120 mmHg) of total events in the ICR group (p=NS).

**Conclusions:** In the subset of hypertensive patients, obtaining an effective blood pressure control is crucial. Nevertheless recent studies have proposed a more aggressive control, our results showed that SBP target < 120 mmHg didn't influence outcome, also in a high risk subgroup (ICR). Clinical characteristics of our population (as the older age) could explain these results, discouraging the SBP target < 120mmHg as driver to medical therapy.

**P1115**

**Prognostic impact of left atrial function by 2D speckle-tracking echocardiographic analysis in patients with chronic systolic heart failure.**

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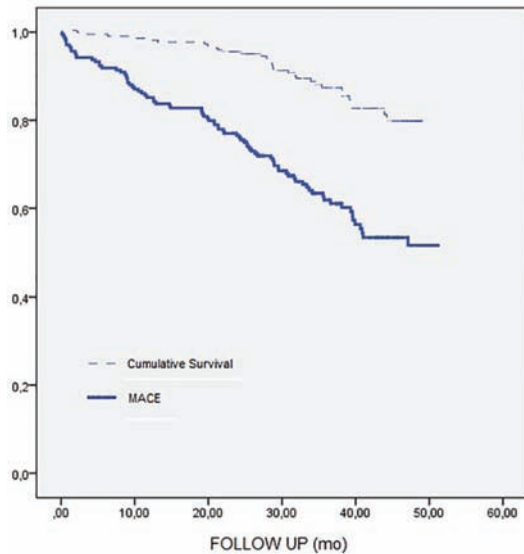
**Introduction:** The size of the left atrium (LA) have been proposed as a powerful predictor of major adverse cardiac events (MACEs) in patients with heart disease. The prognostic impact of the LA function is still widely debated. Speckle-tracking two-dimensional strain echocardiography (2DSE) analysis is considered a feasible and reproducible approach to quantify LA dynamics.

**Purpose:** Accordingly, the purpose of this study was to assess the prognostic impact of the LA intrinsic myocardial function using 2DSE analysis in patients with chronic systolic heart failure (HF).

**Methods:** From October 2011 to December 2014, 427 consecutive outpatients were referred to our HF-center. Eligible patients were 18 to 85 years of age, with left ventricular ejection fraction (LVEF) < 40% and sinus rhythm. Exclusion criteria were refractory atrial arrhythmias to medical therapy, pregnancy, primary valvular disease, mechanical valve prosthesis, recent myocardial infarction or coronary intervention, severe obstructive pulmonary disease or severe renal failure (creatinine clearance < 30 ml/min). The final study population included 209 outpatients (80% male, mean age 68.2 ± 11.0 years) with either idiopathic or ischemic etiology. Peak atrial longitudinal strain (PALS) were measured in all enrolled subjects. PALS values were obtained by averaging all segments (global PALS), and by separately averaging segments measured in the 4-chamber and 2-chamber views. Primary endpoint was MACEs.

**Results:** After 39.8 ± 9.0 months of follow-up (range, 22-51 months), 84 patients (40.2%) met the primary endpoint (Figure 1). Global PALS, LA volume, LV end-systolic volume and LVEF differentiated patients with MACEs at the univariate regression analysis. According to the multivariate Cox regression analysis, reduced global PALS results the only predictor of MACEs [hazard ratio (HR) 0.946, 95% CI 0.917-0.976, P = 0.001].

**Conclusions:** In patients with chronic systolic HF, global PALS is an independent predictor of prognosis useful to stratify patients at high risk.



### P1116

#### Prognostic value of ultrasound lung artefacts (comet tail sign) in acute heart failure.

Health Research Project (FIS) P112/00694

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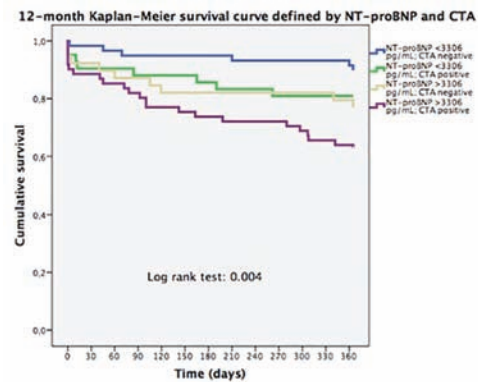
**Introduction:** Assessment of interstitial oedema at the bedside with lung ultrasound (LUS) produces a pattern known as comet-tail artefact (CTA), as the sonographic equivalent of Kerley-B lines.

**Purpose:** We investigated the prevalence of CTA in patients admitted to hospital with a diagnosis of acute heart failure (AHF) and evaluated their relationship with HF biomarkers and prognosis.

**Methods:** From 2013 to 2014, consecutive patients with AHF were prospectively enrolled. During the first 24 hours, a bedside thoracic ultrasound was performed (V-SCAN; GE) to identify CTA. Cumulative mortality over 12 months according to the presence or absence of CTA was recorded. Patients were classified according to LUS and plasma NT-proBNP (defined by median) into four groups. Multivariable adjusted risk for mortality was generated.

**Results:** Of 204 patients, median age was  $81 \pm 9$  years, 51% were men and median hospital stay was  $8 \pm 7$  days. The prevalence of CTA on admission was 51% and persisted for a mean of  $3 \pm 2.5$  days. Patients with positive CTA had higher median NT-proBNP ( $p=0.006$ ) and lower haemoglobin ( $p=0.08$ ). Forty-six patients (23%) died by 12 months. Patients who died were older ( $p=0.001$ ), had had a longer hospital stay ( $p=0.027$ ) and higher plasma urea ( $p=0.000$ ), creatinine ( $p=0.034$ ), NT-proBNP ( $p=0.000$ ) and Cystatin C ( $p=0.014$ ). CTA was associated with higher mortality (OR=2.19;  $p=0.011$ ; KM Log Rank 0.01). Compared to patients without CTA, those with CTA had a higher 12-month mortality if NT-proBNP was greater than median ( $>3,300$ pg/mL) (38% vs 23%) and for patients with NT-proBNP below median, 12-month mortality was 19% and 10% for those with and without CTA ( $p=0.004$  amongst the four groups, figure 1). The strongest univariate predictors of 12-month mortality were Cystatin C [Exp(B)=3.3,  $p=0.009$ ], NT-proBNP [Exp(B)=2.1,  $p=0.000$ ] and CTA [Exp(B)=2.2,  $p=0.013$ ]. Multivariable analysis demonstrated that age, length of hospital stay, Cystatin C, NT-proBNP and plasma urea and creatinine were independent predictors of prognosis at one year. When NT-proBNP was taken out of the model, CTA also predicted outcome.

**Conclusion:** CTA identified with LUS may be used to stratify mortality risk in daily clinical practice for patients with AHF, either alone or combined with NT-proBNP.



KM defined by CTA and NT-proBNP

## PULMONARY HYPERTENSION

### P1117

#### Prognostic value of MMP/TIMP imbalance at follow up assessment in idiopathic pulmonary arterial hypertension

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**Introduction:** Pulmonary arterial hypertension (PAH) is a progressive pulmonary disease which is caused by remodeling and vasoconstriction of the small pulmonary arteries resulting in right heart failure. Despite treatment mortality remains high in PAH patients and 1- and 3-year survival is estimated at 88% and 68%. Many biomarkers have been tested for clinical assessment of PAH, but up to now, only brain natriuretic peptide (BNP) and NT-proBNP are widely used in routine practice to estimate disease prognosis. Extracellular matrix accumulation and remodeling processes in lung and heart are of particular interest for the progression of PAH. Matrix metalloproteinases (MMPs) and their endogenous inhibitors TIMPs are involved in this pathological condition.

**Purpose:** The aim of this study was to investigate MMP/TIMP ratios of selected biomarkers (MMP2, MMP9, TIMP1, TIMP4) at follow up examination (V2) and their prognostic value in patients with idiopathic PAH (IPAH).

**Methods:** Blood samples were taken from patients with IPAH during right heart catheterization at diagnosis and follow-up examination (V2). Coincident with sample collection hemodynamic, laboratory and clinical parameters were acquired. In this sub-study MMP2, MMP9, TIMP1, and TIMP4 plasma levels at V2 were measured as duplicates by ELISA as instructed by the manufacturer. Data analysis was performed with SPSS.

**Results:** Ratios of MMP2/TIMP1 and MMP9/TIMP1 did not correlate with the hemodynamic data, whereas MMP2/TIMP4 and MMP9/TIMP4 ratios showed good correlations with mPAP and MMP2/TIMP4 ratio additionally with PVR. No correlations were found for BNP. Furthermore, MMP2/TIMP4 plasma ratio shows good correlation with tricuspid annular plane systolic excursion (TAPSE). Additionally, biomarker ratios correlate with markers of renal dysfunction. For clinical worsening and survival analysis, patients were divided into two groups, according to their MMP2/TIMP4 plasma level ratios. Log rank test showed significantly reduced mortality rates and clinical worsening events, respectively, for patients below the cut off value.

**Conclusion:** A strong correlation of MMP2/TIMP4 ratio was found with hemodynamic parameters for disease progression as well as with TAPSE, a marker of right ventricular function and prognostic marker in PAH. Moreover, MMP2/TIMP4 ratio is a good predictor for survival and clinical worsening in our patient cohort.

### P1118

#### Pulmonary endarterectomy across borders - an ongoing effort for chronic thromboembolic pulmonary hypertension management

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**Introduction:** Pulmonary endarterectomy (PE) remains the gold standard treatment for chronic thromboembolic pulmonary hypertension (CTEPH). Most patients (pts)



present substantial clinical and haemodynamic improvement after surgery, while pts who are not submitted to PE have an unfavourable prognosis.

**Purpose:** Characterization of a population of pts with CTEPH submitted to PE across borders and assessment of the postoperative course.

**Methods:** Retrospective analysis of 16 pts with CTEPH followed in a referral center for the treatment of pulmonary hypertension (PH) and submitted to PE in a specialized surgical center abroad.

**Results:** Sixteen pts with mean age  $54 \pm 10$  years and female predominance (75%) were included. In the preprocedure evaluation 63% presented with WHO functional class III, the mean distance in the 6-minute walk test (6MWT) was  $376 \pm 130$  meters and the median NT-proBNP was 510 pg/ml (interquartile range 122-2456 pg/ml). TTE revealed preserved RV function in 36% (average TAPSE  $18 \pm 5$  mm), dilated RV in 64% and RA in 70%, mean PASP of  $90 \pm 17$  mmHg and mild pericardial effusion in 20%. Right heart catheterization showed a cardiac index (CI) of  $2.52 \pm 0.97$  l/min/m<sup>2</sup>, mean pulmonary artery pressure (PAPm) of  $44 \pm 14$  mmHg and pulmonary vascular resistance (PVR) of  $11.1 \pm 5.9$  WU. Before surgery 63% were treated with phosphodiesterase type 5 (PDE5) inhibitors, 25% with endothelin receptor antagonists and 6% with prostacyclin analogues. In the postoperative evaluation, performed  $285 \pm 247$  days after surgery, there was a substantial improvement in the WHO functional class (79% in class I), mean distance in the 6MWT (mean increase of  $104 \pm 58$  meters) and NT-proBNP (mean reduction of 339 pg/ml). TTE showed normalization of RV dimensions in 63% of pts and of the RA dimensions in 33%, as well as marked reduction in PASP (mean reduction  $50 \pm 22$  mmHg) and absence of pericardial effusion in all pts. Haemodynamic evaluation demonstrated reduction in PAPm to  $28 \pm 11$  mmHg and in PVR to  $5.3 \pm 1.7$  WU. Nevertheless, 79% maintained residual PH (defined as PAPm  $\geq 25$  mmHg and/or PVR  $> 3$  WU). Regarding postoperative therapy, 89% of pts suspended PDE5 inhibitors and all suspended endothelin receptor antagonists and prostacyclin analogues, while 29% started riociguat. There was also a significant reduction in the number of hospital admissions and duration of hospitalizations due to cardiovascular causes in the 12 months following PE, comparing with the 12 months before surgery ( $0.14 \pm 0.36$  vs.  $0.44 \pm 0.51$  admissions per patient,  $p = 0.025$ ;  $2 \pm 8$  vs.  $12 \pm 17$  days,  $p = 0.027$ ).

**Conclusion:** Although a significant proportion of pts submitted to PE maintains residual PH, we documented a substantial improvement in clinical, laboratory echocardiographic and haemodynamic parameters, as well as improvement in quality of life and long term prognosis. This study highlights the role of international cooperation in the management of pts with CTEPH.

## P1119

### Pulmonary hypertension as an independent predictor of cardiovascular mortality in patients with renal replacement therapy

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**Introduction:** Hemodialysis patients are at increased risk of cardiovascular (CV) mortality. Pulmonary hypertension (PH), has been recently reported as unrecognized threat in dialysis patients. The aim of the present study was to determine the incidence and the value of PH in predicting CV mortality in dialysis patients.

**Methods:** We studied 80 stable hemodialysis patients (females 37.5%, mean age  $50.36 \pm 12.34$  years) and 45 peritoneal dialysis patients (females 40%, mean age  $55.07 \pm 13$  years) on renal replacement therapy (RRT) for more than 3 months. All patients had been followed up for 2 years and the endpoint was CV mortality. PH was defined as systolic pulmonary artery pressure (SPAP)  $\geq 35$  mmHg as determined by Doppler echocardiographic evaluation. To rule out secondary PH, patients with pulmonary disease, collagen vascular disease, and volume overload at the time of echocardiography were excluded.

**Results:** According to the echocardiographic findings, PAH was found in 35 (28%) in overall patients. Cardiovascular mortality during follow up was 15.5% (19 events). The main causes of CV death were sudden deaths (31.5%), deaths from ischemic heart disease and stroke with 26.4% respectively. Significant higher value of SPAP was found in patient with CV mortality in comparison with patients alive in therapy:  $40.27 \pm 9.145$  vs  $33.29 \pm 6.37$  ( $p = 0.011$ ). Binary regression logistik analysis showed an increase of 14% of cardiovascular mortality for each unit increase of PAH [OR = 1.14 (1.00-1.30)  $p = 0.05$ ].

**In conclusion:** Our study showed that PH is frequent in patients treated with RRT. It is an independent predictor of CV mortality.

## P1120

### A new index for risk stratification in patients with pulmonary hypertension.

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**Introduction:** In patients with systemic sclerosis a ratio between Forced-Vital-Capacity (FVC) and diffusing capacity of carbon-monoxide (DLCO, FCV%/DLCO%)  $> 1.5$  could be a predictor of pulmonary hypertension (PH). The aim of this study was therefore to evaluate whether this index could be used in patients with PH, regardless of etiology.

**Methods:** 83 consecutive outpatients with suspected PH at non-invasive work-up underwent spirometry and DLCO test before right heart catheterization (RHC); FVC%/DLCO% ratio was then calculated and compared with mean pulmonary-artery-pressure (mPAP) and mortality at 5-year follow up.

**Results:** Significant correlations between FVC%/DLCO% and PAsP and mPAP levels were found ( $p < 0.05$ ). After ROC curve analysis and definition of best cut-off values for PAsP and FVC%/DLCO%, increased mPAP values at RHC were observed comparing subjects with both PAsP and FVC%/DLCO% values below cut off values (-/-), either PAsP or FVC%/DLCO% above cut off values (+/-), or both above (+/+) ( $p < 0.05$ ). Poorer survival rates were observed at follow up with higher FVC%/DLCO% values (0% for  $< 1$ , 17.4% for 1-3, 33.3% for  $> 3$ ,  $p < 0.05$ ), and comparing subjects with either increased PAsP and FVC%/DLCO% values or both with those with lower (Log-Rank  $p < 0.05$ ).

**Conclusions:** FVC%/DLCO% values are related to mPAP in subjects with suspected PH and may further stratify the risk of mortality in addition to PAP.

## P1121

### First collaborative registry of pulmonary hypertension in Argentina (RECOPIAR Registry): a clinical snapshot from a developing country

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**Purpose:** Epidemiology of pulmonary hypertension (PH) might have regional differences based on several modifiers, including socioeconomic, geographic and ethnic factors as well as prevalent diseases. The aims of RECOPIAR Registry were to evaluate epidemiology, clinical profile, management and therapeutic strategies, of a broad population with PH under collaborative effort of five medical scientific societies.

**Method:** Between Jul-14/Jul-15, 305 incident and prevalent patients with PH were prospectively included by 60 investigators from 20 provinces from Argentina. The inclusion criteria were: 1-patients over three months of age; 2 -mean pulmonary arterial pressure (mPAP) at rest  $\geq 25$  mmHg by right heart catheterization (RHC) and 3 - clinical stability in the absence of hospitalization in last month.

**Results:** Mean age was  $49 \pm 18$  years and 73% were women. A half of patients were referred from other centers, 34% were incident cases and 19% did not have social security. Classification of PH in groups 1 to 5 (Nice) was the following: 68%; 14%; 7%; 8% and 3%. The clinical manifestations were dyspnea 93%, fatigue 64%, syncope 12%, chest pain 19%, palpitations 24% and heart failure in 21% with previous hospitalization in 33%. The diagnostic work-up included ECG (95%), chest X-ray (91%), echocardiogram (95%), general lab (93%), serological test for connective tissue disease (59%), natriuretic peptides measurement (53%), V/Q scan (76%), pulmonary function test (71%), 6-minute walking test (83%), cardiopulmonary exercise test (5), angio CT (31%) and vasoreactivity test (77%). Treatment included diuretics (59%), mineralocorticoid receptor antagonist (57%), digoxin (26%), anticoagulants (49%), ACE-I/ARB (20%), betablockers (21%) and calcium antagonist (14%). Oxygen supplementation was used in 20% and cardiopulmonary rehabilitation in 12%. In patients with pulmonary arterial hypertension (PAH) vs other groups, the use of specific therapy was 79 vs 87% ( $p = NS$ ), without differences in the prescription of sildenafil in 73 vs 75% ( $p = NS$ ), iloprost 9.6 vs 5.3% ( $p = NS$ ), bosentan in 32 vs 35% ( $p = NS$ ), ambrisentan in 14.2 vs 19% ( $p = NS$ ), treprostinil in 7.4 vs 8% ( $p = NS$ ), macitentan (4 vs 6.7%). The follow-up was available in 197 patients (65%), with an overall mortality of 11.2% in PAH vs 11.1% in other groups ( $p = NS$ ).

**Conclusion:** In this Argentinean registry, two thirds of patients had pulmonary arterial hypertension. The diagnostic work-up was consistent with current recommendations according to guidelines. Therapeutic interventions included a high proportion of specific therapy, in PAH as well as in other groups. These findings remark the need of multidisciplinary approach and expert centers in the management of PH.

## P1122

### Vasoreactivity testing with intravenous sildenafil in patients with pre-capillary pulmonary hypertension associated with connective tissue disease

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**Aims:** The aim of the study was to investigate whether vasoreactivity testing (VRT) with intravenous sildenafil (SIL) is effective and predictive of the response to oral therapy in patients with pre-capillary pulmonary hypertension associated with connective tissue disease (CTD-PAH). Methods and

**Results:** Ten patients with CTD-PAH (9 female, mean age 62 y) without specific pretreatment were diagnosed by right heart catheterization, and VRT was performed by infusion of SIL 10 mg. Comprehensive evaluation of hemodynamic parameters before and after SIL included measurements at rest and during exercise. In terms of mean changes in the entire cohort, the mean pulmonary artery pressure (mPAP) decreased by 4.8 mmHg, the cardiac index (CI) increased by 0.28 l/min/m<sup>2</sup>, and pulmonary vascular resistance (PVR) decreased by 71 dyn-s-cm<sup>-5</sup>, with the largest effect being observed after 30 min. The largest individual decrease in mPAP was 8 mmHg. Exercise hemodynamics showed similar changes with reduction of the total pulmonary resistance (TPR = mPAP/CO) during exercise. The parameters of the systemic circulation were changed to a similar extent as the pulmonary circulation. After a treatment period (3 x 20 mg SIL p.o.) of 90 days, a multitude of parameters (NTproBNP measurement, cardiopulmonary exercise testing, repeated hemodynamic measurements) did not change significantly in the entire cohort. Only echocardiographic RV peak free wall strain showed a trend to improvement after therapy (median - 4.37, p = 0.059). Four individual responders were identified due to strict criteria derived from the pulmonary hypertension guidelines. The individual reaction of the responders upon VRT was not distinct from the others, but the parameter PAC (pulmonary artery compliance = stroke volume / PA pulse pressure, a measure of pulmonary artery stiffness) during exercise was markedly lower (i.e. worse) in nonresponders than in responders (p = 0.01). This difference showed to be more pronounced after intravenous administration of SIL (median 1.9 vs. 1.57).

**Conclusions:** In our small pilot study, VRT using i.v. SIL reduced mPAP and PVR and increased CI but failed to fulfill the Sitbon criteria for a positive test result. Intravenous administration of SIL was safe, and the effects were not selective for the pulmonary circulation. Responsiveness in VRT did not correlate with the clinical outcome, but PAC during exercise correlated with the success of an oral therapy.

#### P1123

##### The role of electrical cardiometry in non-invasive assessment of hemodynamic parameters in patients with pulmonary arterial hypertension

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**Background:** The electrical cardiometry (EC) technique could estimate cardiac output (CO), cardiac index (CI) and other parameters related to cardiac contractility and fluid status by measuring the thoracic electrical bioimpedance. It has been validated and is utilized in patients with left ventricular dysfunction, however its diagnostic performance in patients with pulmonary arterial hypertension (PAH) is unclear. In PAH patients, right-sided heart failure is very common cause of deterioration of patients' state and often leads to death. EC could be an opportunity to assess hemodynamic state of patient in non-invasive way.

**Purpose:** To investigate the usefulness of electrical cardiometry in assessment of hemodynamic status in PAH patients in comparison results obtained during RHC and echocardiography.

**Methods:** EC parameters were assessed by hemodynamic monitor in 21 patients diagnosed with PAH shortly after RHC and echocardiography. Statistical analysis was done to indicate the correlation between parameters obtained using both invasive and non-invasive techniques.

**Results:** All subjects with PAH (54.1 ± 17.2 years old, 11 females (52%)) were in II-IV functional class according to WHO. The etiology was idiopathic (71.4%, n = 15) and PAH associated with connective tissue diseases (28.6, n = 6). Patients with congenital heart diseases were excluded from the study. Mean weight of patients was 72.83 ± 17.35 kg and mean body surface area 1.81 ± 0.21 m<sup>2</sup>.

We observed a significant correlation (r = 0.64; p = 0.002) between thermodilution cardiac output measurement results (4.19 ± 1.13 l/min) and CO results obtained by ICON (4.72 ± 1.04 l/min). The mean difference between the two methods was 0.89 l/min.

Furthermore, EC monitor provides information about left ventricle afterload represented by systemic vascular resistance (SVR). There was a significant correlation between SVR calculated by EC monitor and SVR obtained during RHC (r = 0.66; p = 0.001). On the other side this technique could also indirectly predict right-sided cardiac function e.g. index of contractility (ICON) significantly correlated with parameters assessed by echocardiography like tricuspid annular plane systolic excursion (r = 0.57; p = 0.01). ICON also correlated with inferior vena cava diameter (r = 0.54; p = 0.014).

**Conclusions:** Electrical cardiometry method provides non-invasive insight into hemodynamic function of the heart. When compared to the thermodilution method during RHC, EC provides satisfactory CO measurements. RHC cannot be replaced but electrical cardiometry may provide fast assessment of patient's state at bedside or in outpatient care.

## LEFT VENTRICULAR FUNCTION

#### P1124

##### Pediatric heart transplantation recipients: echocardiographic evaluation of left ventricular mechanics

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**Introduction:** Recently some studies dealing with assessment of cardiac function by Speckle Tracking Imaging (STI) in heart transplant (HTX) recipients have been published, an integrated assessment of all myocardial properties of deformation is lacking.

**Purpose:** The aim of this study is to perform, by using Speckle Tracking Imaging, an integrated study of LV mechanics (longitudinal, radial, circumferential regional deformation, twist, untwist onset and diastolic function) in HTX recipients with preserved ejection fraction and good clinical conditions (NYHA I).

**Methods:** We enrolled 20 HTX subjects without symptoms (NYHA I) and with preserved ejection fraction (HTX group), and 40 normal subjects as control group (CTRL group).

**Results:** HTX patients were characterized by an early diastolic dysfunction, detectable by an increased value of E/E' ratio (HTX 10.58 ± 2.94; CTRL 5.3 ± 1.5; p < 0.0001). Compared to control group our HTX recipients showed: a) impaired longitudinal and radial strain values with normal circumferential strain values b) LV rotation was preserved at apex and impaired at basal level (bas rot CTRL -7.35 ± 1.6; HTX = -5.05 ± 2.89 p < 0.001; ap rot CTRL 6.92° ± 2.56°; HTX = 9.73 ± 4.38 p < 0.0001) with normal LV twist (CTRL 14.22 ± 3.4; HTX = 14.78 ± 5.58; p value not significant); c) delayed untwisting due to prolonged twist (time to peak twist/systolic time: CTRL 80.48 ± 13.69, HTX 103.45 ± 18.42 p < 0.0001).

**Conclusions:** Of interest "healthy" HTX patients, even in presence of widespread impairment of regional myocardial deformation, normal apical rotation, which account for normal amplitude of twist and in turn global ejection fraction. In addition delayed untwisting (after aortic valve closure) due to prolonged twist could be responsible of an early impaired LV diastolic filling.

#### P1125

##### Changes of ventricular-arterial coupling may reflect early cardiac remodeling in patients with myocardial infarction treated with percutaneous coronary intervention

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**Objective:** Ventricular remodeling may occur following myocardial infarction (MI) of the left ventricle (LV) and such remodeling has been shown to be correlated with increased patient morbidity and mortality. It is important to estimate the likelihood of remodeling from the state of the infarcted LV. The aim of the study was to assess the ventricular-arterial coupling (VAC) in patients with ST segment elevation (STEMI) and non ST segment elevation MI (NSTEMI) treated with percutaneous coronary intervention (PCI).

**Methods:** In 93 patients with acute coronary syndrome and PCI (70% male, age 61.5 ± 10.1 years (M ± SD), 57 (61.3%) with STEMI, smokers 25%, arterial hypertension 20.4%, blood pressure (BP) 129 ± 6/82 ± 7 mmHg, LVEF 47.4 ± 4.3%) 2-dimensional echocardiography was performed to assess arterial elastance (Ea) and end-systolic LV elastance (Ees) on admission and in 4 weeks. VAC was assessed as the ratio Ea/Ees.

**Results:** Baseline LVEF was 47.4 ± 4.3, E/A 0.95 ± 0.18, Ea 1.9 ± 0.3 mmHg/ml/m<sup>2</sup>, Ees 2.1 ± 0.4 mmHg/ml/m<sup>2</sup>, VAC 0.89 ± 0.1. At baseline all patients had LVEF > 40% and VAC in optimal range. In 4 weeks after PCI VAC > 1.2 (upper optimal level) was revealed in 19% of patients with STEMI and 44% with NSTEMI. In patients with achieved VAC > 1.2 Ees (2.1 ± 0.4 vs 1.6 ± 0.2 mmHg/ml/m<sup>2</sup>, p < 0.001), stroke work (SW) (6254 ± 1516 vs 6112 ± 1059 mmHg\*ml/m<sup>2</sup>, p > 0.05), potential energy (PE) (62.8 ± 4.3 vs 56.3 ± 5.4 mmHg\*ml/m<sup>2</sup>, p < 0.001), pressure-volume area (PVA) (6317 ± 2136 vs 6179 ± 1060 mmHg\*ml/m<sup>2</sup>, p < 0.001), LV work efficiency (SW/PVA) significantly decreased (p < 0.001) while Ea (1.9 ± 0.3 to 2.1 ± 0.4 mmHg/ml/m<sup>2</sup>, p > 0.05) did not change. In patients with VAC in optimal range in 4 weeks Ees decreased from 2.3 ± 0.3 to 2.1 ± 0.4 mmHg/ml/m<sup>2</sup> (p < 0.001), Ea (p < 0.001) and VAC (p < 0.001) did not change.

**Conclusions:** Impairment of functioning of cardio-vascular system assessed by increased value of VAC > 1.2 was revealed in 27% of patients with acute coronary syndrome. Increase of VAC is associated predominantly with decrease of Ees and LV work efficiency (SW/PVA). Increased in the VAC index > 1.2 indicating LV-arterial

uncoupling may be an early marker of cardiovascular remodeling in MI or systolic dysfunction.

**P1126**

**Heterogeneous response of ventricular-arterial coupling and left ventricular efficiency to afterload increase in untreated hypertensive subjects**

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**Aim:** to evaluate cardiovascular adaptation to increased afterload during handgrip isometric exercise (HIE) in untreated hypertensive patients.

**Methods:** 75 untreated hypertensive patients (age 54 ± 7 years, 44 males, BP 153/93 mmHg) underwent simultaneous EchoCG and blood pressure (BP) acquisition at rest and during HIE. End-systolic pressure was determined as 0,9 x brachial systolic BP (SBP). Arterial elastance (Ea) and LV elastance (Ees) were calculated as end-systolic pressure (ESP) /stroke volume (SV) and ESP/end-systolic volume (ESV). Ventricular-arterial coupling index was assessed as Ea/Ees. Efficiency of left ventricle (ELV) was evaluated by stroke work (SW)/pressure-volume area (PVA) ratio. SW=ESP×SV, PVA=SW+PE (ESP×ESV/2-end diastolic pressure ×ESP/4). p < 0,05 was considered significant.

**Results:** Ea/Ees < 0,5 was found in 76% (n=57, 18 female) before HIE. In 38% (n=22, 4 (23%) female) Ea, Ees, Ea/Ees and SW/PVA did not change significantly. In 11% there was further decrease of Ea/Ees associated with significant increase of ELV. In 51% (n=29, 14 (49%) female) Ea/Ees increased due to increase of Ea from 1,98 ± 0,32 to 2,35 ± 0,41 (p < 0,05) while Ees increased from 5,95 ± 2,2 to 4,58 ± 1,0 (p < 0,05). Ea/Ees increase was associated with decrease of ELV from 0,89 ± 0,02 to 0,84 ± 0,02 (p < 0,05) indicating cardiovascular misadaptation to HIE.

In subjects (n=18, 3 female) with normal Ea/Ees 0,5-1,2 before HIE Ea/Ees and ELV did not change in 8 (49%, all males). In 10 subjects (3 female) Ea/Ees decreased due to significant increase of Ees (from 3,15 ± 0,68 to 5,02 ± 1,34 (p < 0,05), and ELV increased from 0,81 ± 0,03 to 0,88 ± 0,01 (p < 0,05).

**Conclusion:** Cardiovascular misadaptation to afterload is the most prevalent type of reaction to HIE in subjects with decreased baseline Ea/Ees and may be also observed in subjects with normal baseline ventricular-arterial coupling. This misadaptation in subjects with baseline ventricular arterial uncoupling is associated with female gender.

**P1127**

**Ventricular-arterial uncoupling may be an early sign of cardiovascular remodeling in hypertensive men**

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**Objective:** To evaluate ventricular-arterial coupling (VAC), left ventricular hypertrophy (LVH), diastolic function and arterial stiffness in young and middle-aged men with uncomplicated arterial hypertension

**Methods:** 97 young men aged 18-27 years (21,2 ± 1,9 years, BP 156,5 ± 14,0/98,5 ± 9,1 mmHg) and 68 middle-aged men aged 40-60 years (n=68, age 53,9 ± 7,2 years, BP 152,7 ± 9,6/94,8 ± 7,8 mmHg) (M) underwent simultaneous EchoCG, blood pressure (BP) and pulse wave velocity measurement. VAC index was calculated arterial elastance (Ea) and left ventricular elastance (Ees) ratio. Ea=end-systolic pressure/stroke volume, Ees=end-systolic pressure/end-systolic volume. LVH was diagnosed if LV mass index was > 115 g/m<sup>2</sup>. Increased arterial stiffness -if PWV > 10 m/s, diastolic dysfunction - if E/A < 1,0 and E/E' < 7 m/s.

**Results:** In young men Eea 1,86 ± 0,32 and index VAC (0,52 ± 0,10) was similar to that in middle-aged (1,9 ± 0,47 and 0,48 ± 0,19, respectively), despite that Ees in young men was significantly lower (3,67 ± 0,85) than in middle-aged men (4,6 ± 2,1, p < 0,01). VAC index < 0,5 was found in 34% young men and in 57% middle-aged men (p < 0,05), LVH in 7,4% and 67% (p < 0,05), diastolic dysfunction 4,1% and 62%, respectively. VAC index was similar in those with and without LVH or diastolic dysfunction in the both age groups. In young men with LVH VAC index was 0,63 ± 0,26, without LVH 0,54 ± 0,12, in middle-aged patients with LVH - 0,45 ± 0,16, without LVH - 0,49 ± 0,21. In young men with diastolic dysfunction VAC index was 0,61 ± 0,13, without diastolic dysfunction - 0,58 ± 0,16. In middle-aged men 0,45 ± 0,14 and 0,48 ± 0,16, respectively. PWV > 10 m/s was found in 22,7% of young men and in 80,1% of middle-aged (p < 0,05). No significant correlation between VAC index and BP, LVMI, PWV, E/A, E/E' was found.

**Conclusion:** Decrease in the VAC index < 0,5 indicating LV-arterial uncoupling may be an early marker of cardiovascular remodeling in hypertensive men that may be observed before development of LVH, diastolic dysfunction or increased arterial stiffness.

**P1128**

**Patients with acute coronary syndromes without left ventricular function evaluation represent a special high risk population: a single centre observation.**

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**Introduction:** According to the guidelines left ventricular (LV) function should be routinely assessed in patients with acute coronary syndromes (ACS). Nevertheless and for multiple reasons this recommendation is not always followed.

**Objective:** In a single centre, authors (AA) sought to characterize the group of patients with ACS in that LV function was not evaluated, regardless of the reason. Methods and

**Results:** A series of 963 patients with ACS (unstable angina - 165; non ST elevation acute myocardial infarction - AMI - 404; ST elevation AMI - 394) were split in four groups according to LV function: Gr.A - LV function not evaluated (n=87); Gr.B - normal LV function (n=661); Gr.C - moderate impairment (ejection fraction > 30% < 50%) (n=161); Gr.D - severe impairment (ejection fraction < 30%) (n=54). Groups were compared regarding clinical and laboratorial characteristics at admission and also in-hospital management. Main differences are showed in the Table.

**Conclusions:** According to the current data the group of patients not investigated for LV function showed a specially high risk profile and, paradoxically, an invasive strategy and revascularization were less used when compared with the group of patients with normal LV function.

60442. Table - Main differences between groups

	Gr A n=87	Gr B n=661	Gr C n=161	Gr D n=54	P value
Age (mean+DP)	67+13	64+12	68+11	74+10	<0,001
GFR (ml/min)	78,6+29,6	84,2+27,4	76,2+25,5	68,7+24,3	<0,001
KK Class > 1	11 (12,6%)	56 (8,5%)	42 (26,1%)	30 (55,6%)	<0,001
Invasive strategy	27 (31,0%)	387 (58,5%)	72 (44,7%)	14 (25,9%)	<0,001
Multivessel disease (*)	11 (40,7%)	160 (41,3%)	38 (52,8%)	7 (50,0%)	0,03
KK Class max. > 1	30 (35,5%)	122 (18,5%)	61 (37,9%)	41 (75,9%)	<0,001
High risk GRACE score	63 (72,4%)	433 (65,5%)	135 (83,9%)	51 (94,4%)	<0,001
Revascularization	21 (24,1%)	277 (41,9%)	56 (34,8%)	10 (18,5%)	<0,001

(\*) estimation based on the number of patients selected for an invasive strategy

GFR - glomerular filtration rate; KK - Killip Kimbal

**P1129**

**Left ventricle diastolic function impairment in patients with arterial hypertension and no LV hypertrophy**

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**Objective:** The mechanisms of formation of left ventricular diastolic dysfunction (LV DD) remains unclear. One of the main reasons for LV DD is arterial hypertension (AH). Blood vessels are the first target organ that is affected by AH. However, whether the arterial stiffness may impair left ventricle diastolic function (DF LV) has been insufficiently studied. We tried to correlate the arterial stiffness, ventriculararterial coupling (VAC) and indicators of DF LV.

**Design and methods:** We examined 67 patients with essential AH stage 2 (mean SBP 157,57 ± 5,46 mmHg, mean DBP 92,13 ± 2,87 mmHg; BMI 28,99 ± 0,99; age 52,77 ± 3,59), 33 men and 34 women with no symptoms of heart failure. The following diagnostic procedures were performed: office BP measurement, measurement of central BP (cSBP) and adjusted augmentation index (AIx75%), carotid-femoral (cfPWV) pulse wave velocity, Doppler echocardiography according to local full protocol, LV DD was determined by measuring velocity of the peak E and peak A of transmitral flow with determination of E/A, velocity of peak E' by tissue Doppler with determination of E/E', deceleration time (Dt) and isovolumic relaxation time (IVRT) measurement. LV myocardium mass index (LVMMI) was evaluated using ASE formula. To assess the relationship between these values we used Spearman correlation analysis.

**Results:** As we can see according to the office measurement peripheral BP of patients was high, respectively central SBP level was also elevated (142,78 ± 5,85 mmHg). Systolic function (EF 64,07 ± 1,45%) was preserved, indicators of DF LV were also within normal limits, but there was a slight tendency to their impairment (E/A 1,07 ± 0,1; E/E' 9,07 ± 2,59; Dt 236,58 ± 14,74; IVRT 87,78 ± 6,03), maybe,



due to mild LV hypertrophy (LVMMI  $97.50 \pm 5.42$ ). However we have found a worsening of arterial stiffness (cfPWV  $12.02 \pm 0.78$ ) and ventriculararterial coupling (VAC  $1.59 \pm 0.05$ ). E/A correlated with Alx75% ( $r=0.433$ ;  $p<0.001$ ) and cfPWV ( $r=0.32$ ;  $p=0.1$ ). E/E' correlated with VAC ( $r=0.292$ ;  $p=0.026$ ), LVMMI ( $r=0.55$ ;  $p<0.001$ ), Alx75% ( $r=0.469$ ;  $p<0.001$ ), cfPWV ( $r=0.303$ ;  $p=0.02$ ). Dt correlated with LVMMI ( $r=0.268$ ;  $p=0.035$ ), Alx75% ( $r=0.317$ ;  $p=0.011$ ). IVRT correlated with LVMMI ( $r=0.290$ ;  $p=0.025$ ), Alx75% ( $r=0.430$ ;  $p=0.001$ ) and cfPWV ( $r=0.270$ ;  $p=0.035$ ). But we have found no significant correlation between VAC and cfPWV, however VAC was correlated with LVMMI ( $r=0.342$ ;  $p=0.006$ ).

**Conclusions:** We found significant correlation between arterial stiffness and all the indicators of DF LV, but there was no correlation between cfPWV and VAC. The strongest correlation was between Alx75% and all of indicators of DF LV.

## HFpEF - HEART FAILURE WITH PRESERVED EJECTION FRACTION

### P1130

#### Predictors of preclinical left ventricular diastolic dysfunction in type 2 diabetes mellitus

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Some studies have shown that diabetes may be an independent risk factor for left ventricular (LV) diastolic dysfunction (DD).

**Purpose:** To determine the prevalence of preclinical diastolic dysfunction (DD), and risk factors associated with this entity in type 2 diabetes mellitus (T2DM) patients with normal ejection fraction (EF), with or without hypertension (HT), no overt coronary artery disease, asymptomatic for heart failure.

**Methods:** Case-control study of 380 patients (256 DM, 124 DM+HT, mean age  $58.9 \pm 7.3$  years) and 100 age-matched control subjects, recruited from Mars 2008 through December 2012. LV diastolic function was evaluated by Doppler echocardiography (combined transmitral flow, TDI and propagation velocity).

**Results:** The prevalence of DD was 58.7% in DM vs 80% in DM+HT ( $p<0.001$ ). The multivariate analysis showed that the best predictors of DD were LV remodeling (OR=19.72, 95%CI 6.97-55.2), glycemic control (HbA1c) (OR=1.49, 95% CI 1.3-1.69) and diabetes duration (OR=1.14, 95% CI 1.06-1.22).

**Conclusions:** The prevalence of preclinical DD was high in type 2 diabetic patients. LV remodeling, glycemic control, and diabetes duration were the best predictors of preclinical DD.

### P1131

#### NYHA functional class is associated with diastolic pulmonary pressure and predicts outcome in patients with heart failure and preserved ejection fraction

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**Background:** Patients with heart failure (HF) and preserved ejection fraction (HFpEF) suffer from functional impairment resulting in reduced quality of life. Specific pathomechanisms underlying symptoms have not yet been defined.

**Methods and Results:** Between January 2011 and December 2014, 193 HFpEF patients were enrolled. Those in more advanced New York Heart Association (NYHA) functional classes (III/IV,  $n=136$ ) were older ( $p=0.008$ ), had higher body mass indices (BMI,  $p=0.004$ ) and higher levels of NT-pro-brain natriuretic peptide (NT-pro-BNP,  $p=0.001$ ) as compared with less symptomatic patients (NYHA II,  $n=57$ ). Furthermore, parameters reflecting left ventricular (LV) diastolic dysfunction were more pronounced in advanced NYHA classes (early mitral inflow velocity/early diastolic mitral annular velocity:  $p=0.023$ ) as well as parameters reflecting right ventricular (RV) afterload (diastolic pulmonary artery pressure (dPAP),  $p=0.001$ ). By multivariable regression analysis, age ( $p=0.007$ ), BMI ( $p=0.002$ ), NT-pro-BNP ( $p<0.001$ ) as well as early mitral inflow velocity/ mitral peak velocity of late filling ( $p=0.031$ ) and dPAP ( $p<0.001$ ) were independently associated with advanced NYHA classes. After 21.9  $\pm$  13.1 months of follow-up, 64 patients (33.2%) reached the combined endpoint defined as hospitalization due to HF and/ or cardiac death. By multivariate Cox analysis NYHA functional class was independently associated with outcome (HR 2.133,  $p=0.040$ ) as well as NT-pro-BNP (HR 1.655,  $p<0.001$ ) and a visually impaired RV function (HR 2.360,  $p=0.001$ ).

**Conclusion:** Symptoms of breathlessness in HFpEF are multi-factorial and largely related to BMI, LV diastolic function and the pulmonary vasculature. Clinically meaningful therapeutic interventions should target body weight, LV stiffness as well as concomitant pulmonary vascular disease.

### P1132

#### The prognostic value of EAS index and E/DT in heart failure patients with preserved ejection fraction

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**Objective:** Doppler-derived parameters assessed by trans thoracic echocardiography (TTE) have been proposed for predicting prognosis in Heart Failure patients with reduced Ejection Fraction (HFrEF). This prospective study investigates the prognostic value of two novel Doppler parameters EAS index and E/DT among other parameters in Heart Failure patients with preserved Ejection Fraction (HFpEF).

**Methods:** In this prospective cross sectional study, conducted in 2015, 100 consecutive HFpEF patients (left ventricular Ejection Fraction  $\geq 45\%$ ) were enrolled. The mean age was  $63 \pm 18.3$  years. Doppler-derived diastolic variables including two new parameters E/DT and EAS index were measured by TTE. The primary endpoint for six months follow up were cardiac death, heart failure hospitalization, need for inotropic agent infusion, and cardio renal syndrome. Cox regression test determine the predictors for poor prognosis.

**Results:** During the six months follow up, no death was reported. The E/DT was prolonged in patients who were hospitalized, had cardiorenal syndrome, or needed inotropic agent infusion. There was also correlation between higher EAS index and poor prognosis. In the univariable analysis, E/Em, E/DT, EAS index, and LAVI were significantly correlated with short term outcome ( $P$  value  $< 0.001$ ). In the multivariable analysis, E/DT and EAS index were independently predictor of short term prognosis (hazard ratio = 1.02,  $P = 0.001$ ).

**Conclusions:** E/DT and EAS index, easily measured by echocardiography, may have a useful incremental prognostic value in patients with HFpEF.

Table 1

	mean	STD
AGE (year)	63.1	8.2
HR (beat/min)	74.1	6.1
ESV (ml)	34.8	10.4
LVEDD (cm)	4.9	0.43
MPI	0.67	0.2
Tapse (cm)	9.8	1.4
Em (cm/sec)	4.9	1.2
Sm (cm/sec)	5.7	0.7
Am (cm/sec)	6	2.4

Table 1: Basic information study population

### P1133

#### Predictors of long-term prognosis of ambulatory patients with heart failure and preserved ejection fraction

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**Background:** Patients (pts) with heart failure and preserved ejection fraction (HFpEF) have been historically considered with better prognosis than those with reduced systolic function (HFrEF). However, actual prognosis of these patients is uncertain.

**Purpose:** To assess the prognosis of pts with HFpEF.

**Methods:** A cohort of 536 outpatients with HF was prospectively followed in a tertiary HF clinic during the 2010-2015 period. Clinical, ECG, echocardiographic and biochemical data were registered. Cox regression analysis was used to identify the predictors on mortality of patients with HFpEF.

**Results:** Mean age was  $68 \pm 13$  years and 67% were men. The etiology of HF was ischemic (35%), cardiomyopathy (25%), valvular (16%), hypertension (14%) and others (10%). Pts were in NYHA functional class I-II (61%) and III-IV (39%). HFrEF was found in 348 pts (65%) and the remaining 188 (35%) had HFpEF. Mean follow up was  $24 \pm 20$  months. Comparing HFrEF with HFpEF, the latest group had older age ( $74 \pm 12$  vs.  $65 \pm 13$  years;  $p<0.001$ ), more frequently were females (51 vs. 33%;  $p<0.001$ ), had higher hypertension rates (80 vs. 71%;  $p=0.02$ ), higher incidence of atrial fibrillation (56 vs. 33%;  $p<0.001$ ) and lower median of NT-ProBNP values (1369 [642-2499] vs. 2000 [857-4416];  $p=0.002$ ). Pts with HFpEF had higher mortality (32 vs. 16%;  $p=0.001$ ). Kaplan-Meier curves comparing 3-years survival of the two groups, showed that pts with HFpEF had a significant worse survival (60 vs 78%;  $p=0.003$ ) (figure 1). Multivariate analyses identify as independent predictors of worse prognosis in HFpEF: older age (1.068 [95% CI 1.031-1.106];  $p<0.001$ ), NT-proBNP  $> 1500$  ng/L (2.837 [95% CI 1.614-4.984];  $p<0.001$ ), Na+

<135 mmol/L (2.316 [95% CI 1.05-5.109];  $p=0.03$ ) and lower systolic pressure (0.767 [95% CI 0.655-0.899];  $p=0.001$ ). The discrimination ability of this model was 0.77 (c-statistics index), with a good internal validation after the boots trapping (0.75).

**Conclusions:** 1) In this cohort, patients with HFpEF had worse prognosis than HFrEF. 2) NT-proBNP >1500 ng/L may help to identify patients at higher risk of death. 3) Based on the worse prognosis of patients with HFpEF, more studies are needed to improve their survival.

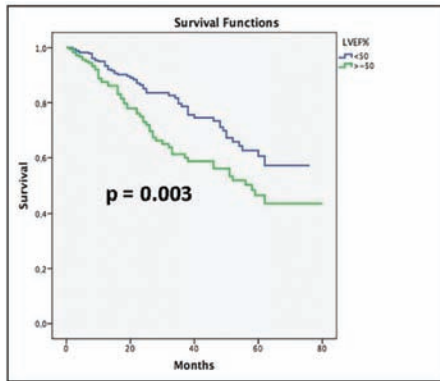


Figure 1. Kaplan-Meier curves.

**P1134**

**Predictive value of diastolic left ventricular function on exercise capacity in heart failure patients with preserved ejection fraction**

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**Background:** Limitation in exercise capacity (EC) is a one of the typical manifestation of heart failure with preserved ejection fraction (HFpEF) that is closely related to poor quality of life. Single pathophysiological mechanism governing exercise intolerance in HFpEF is unlikely to exist. The purpose of this study was to identify the role of diastolic left ventricular (LV) function echocardiographic variables, especially LV filling pressure in prediction of reduced EC in patients with HFpEF.

**Methods:** We assessed LV systolic and diastolic function in 171 patients (62.1 ± 9.9 y; 39.8% men and 60.2% women) who fulfill clinical and/or echocardiographic criteria of HFpEF presence using 2D echocardiography and tissue Doppler imaging. EC measured in units of metabolic equivalents (METs) was assessed using Bruce protocol treadmill stress testing. We defined reduced EC as <7 METs. Pulmonary function tests and complete blood cell count were also performed to exclude non-cardiac causes of exercise intolerance.

**Results:** HFpEF patients had preserved LVEF (66.1 ± 6.8%) and LV diastolic indexes in favor of diastolic dysfunction. Patients with reduced EC of <7 METs vs. those with capacity of ≥7 METs were older ( $p=0.007$ ), more frequently women ( $p=0.012$ ) with diabetes mellitus ( $p=0.018$ ), showed significantly higher body mass index ( $p=0.007$ ) and wider waist circumference ( $p=0.002$ ). As for diastolic echocardiographic parameters there was lack of significant difference between those with and without reduced EC. However, there was a significant positive correlation between reduced EC of <7 METs and reduced ratio of early and late transmitral filling velocities (E/A,  $r=0.237$ ,  $p=0.002$ ), along with significant negative correlation with elevated LV filling pressure measured as a ratio of peak early diastolic filling velocity to early diastolic mitral annular velocity (E/e') at septal point as well as an average ratio ( $r=-0.209$ ;  $p=0.006$ ;  $r=-0.171$ ,  $p=0.025$ ; respectively). On multivariate regression analysis of diastolic variables, reduced EC <7 METs was independently negatively related to E/e' septal ratio ( $\beta=-0.121$ ; 95%CI: -0.164 to -0.004;  $p=0.001$ ) and positively related to E/A ratio ( $\beta=1.05$ , 95%CI 0.186 to 1.917,  $p=0.018$ ).

**Conclusion:** LV diastolic dysfunction was strongly associated with exercise capacity in patients with HFpEF. Reduced E/A ratio and elevated LV filling pressure, as its markers, were identified as independent predictors of poor exercise capacity.

**P1135**

**Potential value of stress NT-proBNP assessment for the prediction of subclinical HFpEF in hypertensive patients**

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Our aim was to determine if, in asymptomatic hypertensive patients (HTs), NT-proBNP assessment obtained during physical stress could have diagnostic utility for detection of subclinical diastolic dysfunction.

112 ambulatory adequately-controlled asymptomatic HTs (62 females, 55.4%, aged 48-66 years, mean age 56.4 ± 6.8 years) with normal coronary angiography or myocardial perfusion scintigraphy results were enrolled into the study. Heart failure with preserved ejection fraction (HFPEF) was defined as LVEF ≥50% and E/Vp ≥2.5 (ratio of early peak diastolic transmitral E wave velocity to intraventricular flow propagation velocity Vp; E/Vp ≥2.5 significantly correlates with impaired myocardial relaxation). The levels of NT-proBNP were assessed at rest and within 3 minutes in the recovery during maximal stress testing (cycle ergometer, James protocol). Two clinical groups were formed according to the results of E/Vp ratio evaluation (E/Vp <2.5; n=58 and E/Vp ≥2.5; n=54).

There was no significant difference in rest levels of NT-proBNP in both groups (182 ± 80 ng/l vs 198 ± 60 ng/l,  $p<0.5$ ). HTs with E/Vp <2.5 had mean stress NT-proBNP concentrations of 226 ± 80 ng/l; those with E/Vp ≥2.5 had a significantly higher mean stress NT-proBNP levels of 889 ± 92 ng/l ( $p<0.05$ ).

The assessment of NT-proBNP in asymptomatic HTs during physical stress, but not in rest might be of potential value for identification of those with subclinical HFPEF. These patients should be considered for closer monitoring and appropriate treatment adjustment to avoid subsequent progression of this very common in hypertensive population type of heart failure.

**P1136**

**Relation between serum Parathyroid hormone and diastolic function in heart failure preserved ejection fraction**

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**Background:** The pathophysiology of heart failure with preserved ejection fraction is complex. Previous studies have suggested hyperparathyroidism in the pathogenesis of systolic heart failure, associated with cardiac hypertrophy, fibrosis and heart failure severity. In this prospective cross-sectional study, we evaluated the relation between serum PTH level and diastolic dysfunction severity in HFPEF.

**Methods:** 60 stable chronic heart failure patients with Left Ventricular Ejection Fraction >40% were enrolled. Patients with atrial fibrillation rhythm, significant valvular pathology and systemic diseases were excluded. Mean age was 67.15 ± 7.25 (71.7% women). Serum PTH, calcium and phosphate were measured in fasting state. Diastolic dysfunction grade were determined by transthoracic echocardiography based on E/A ratio, E deceleration time, E/Em ratio and LA volume index in the same day. Patients were divided to 3 subgroups grade 1, 2 and 3 diastolic dysfunction. The association of serum PTH, calcium and phosphate with the severity of diastolic dysfunction was assessed.

**Results:** Mean PTH level were 59.1 ± 34.21, 87.77 ± 30.3, and 119.75 ± pg/mL in grade 1, 2 and 3 of diastolic dysfunction respectively (P value: 0.0001). There was significant correlation between E/Em ratio and serum PTH level ( $r=0.737$ , P value <0.05). This study didn't show significant association of E/Em ratio (or diastolic grade) with serum Ca and P level.

**Conclusion:** Elevated PTH can be directly related to the severity of diastolic dysfunction in patients with heart failure preserved ejection fraction

Table 1

P value	SD	Mean PTH level(mg/dl)	Diastolic grade	
0.002	15.5	48.9	I	<60 years
	23.2	86.3	II	
	20.4	109.3	III	
0.001	26.8	66.6	I	>60 years
	39.3	88.9	II	
	36.4	130.2	III	

Correlation between of PTH level and diastolic grade in study population

**P1137**

**Quantifying the risk of repeated hospitalizations following an admission for acute heart failure: preserved versus reduced ejection fraction**

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**Background:** Heart failure with preserved ejection fraction (HFpEF) and reduced ejection fraction (HFrEF) share a comparable high mortality risk. However,

differences in rehospitalization burden over time between these two entities remains unclear.

**Methods:** We prospectively included 2013 consecutive patients discharged for acute heart failure (AHF). Left ventricular ejection fraction was assessed by echocardiography in all patients during index hospitalization. 1082 (53.7%) patients had HFpEF and 931 (46.2%) had HFrEF. Cox and negative binomial regression methods were used to evaluate the risk of death and repeated hospitalizations, respectively.

**Results:** At a median follow up of 2.36 years (IQR: 0.96-4.65), 1018 (50.6%) patients died and 3849 readmissions were registered in 1406 (69.8%) patients. Of them, 2233, 1571, and 1589 were cardiovascular (CV), non-CV, and HF-related, respectively. Overall, there were no differences between HFpEF and HFrEF in the rates of mortality (16.7 vs. 16.1 per 100 person-years, respectively;  $p=0.794$ ), and all-cause repeated hospitalizations (70.8 vs. 70.2 per 100 person-years, respectively,  $p=0.791$ ). After multivariable adjustment, and compared to patients with HFrEF, those with HFpEF exhibited a similar risk of all-cause readmissions (IRR: 1.04 CI 95%:0.93-1.17;  $p=0.461$ ). With regard to specific causes, HFpEF showed similar risks of CV and HF-related rehospitalizations (IRR: 0.93, CI 95%:0.82-1.06;  $p=0.304$ , and IRR: 0.96, CI 95%:0.83-1.13;  $p=0.677$ , respectively), but higher risk of non-CV readmissions (IRR: 1.24; CI 95%:1.04-1.47;  $p=0.012$ ).

**Conclusions:** Following an admission for AHF, HFpEF patients have a similar total rehospitalization burden compared to those with HFrEF. However, HFpEF patients are more likely to be readmitted for non-CV causes.

### P1138

#### Predictive value of left ventricular global longitudinal strain on exercise capacity in heart failure patients with preserved ejection fraction

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**Background:** Echocardiographic left ventricular (LV) global longitudinal strain (GLS) analysis using two-dimensional speckle-tracking (2D-STE) is an accurate contemporary method in detecting subclinical systolic dysfunction. It has been reported that diastolic function correlates better to exercise capacity than systolic function. We hypothesized that exercise capacity (EC) is more closely related to GLS than to ejection fraction (EF), especially in heart failure patients with preserved ejection fraction (HFpEF).

**Method:** In order to justify the hypothesis, we assessed LV systolic function in 180 pts (62.0±9.8 y; 54.0% men and 75.0% women) who fulfill clinical and/or echocardiographic criteria of HFpEF presence using 2D echocardiography and speckle tracking software for myocardial deformation assessment. EC measured in units of metabolic equivalents (METs) was assessed using Bruce protocol treadmill stress testing. We defined reduced EC as <7 METs.

**Results:** Out of 180 patients with HFpEF 56 pts (31.1%) had EC of <7 METs. Patients with reduced EC of <7 METs vs. those with capacity of >7 METs were older ( $p=0.013$ ), of female gender ( $p=0.006$ ) with diabetes mellitus ( $p=0.030$ ), showed significantly higher body mass index ( $p=0.001$ ) and wider waist circumference ( $p=0.001$ ). Unlike other systolic parameters which were insignificantly lower in pts with reduced EC of <7 METs, GLS was significantly lower ( $p=0.019$ ) vs. those with capacity of >7 METs (-16.46±5.12% vs. -17.95±3.25%, respectively) as it was the number of segments with LV strain <-12% (4.41±3.87 vs. 2.85±2.72%, respectively) ( $p=0.002$ ). On multivariate regression analysis of systolic parameters, the number of segments with GLS of <-12% ( $\beta=-0.204$ ; 95%CI: -0.317-(-0.094);  $p=0.0001$ ) and GLS of <-12% ( $\beta=1.349$ ; 95%CI: 0.080-2.617;  $p=0.037$ ) appeared as significant independent predictors of reduced EC of <7 METs.

**Conclusion:** The assessment of GLS with speckle-tracking echocardiography identified individuals with subclinical LV systolic dysfunction despite preserved LVEF. Greater impairment of GLS in patients with HFpEF appeared as significant independent predictor of reduced EC measured in METs.

## BASIC SCIENCE: CHRONIC HEART FAILURE

### P1140

#### Combination of platelet activation and membrane fragility signs for estimation of HF progression

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The activation of platelets at sites of vascular injury plays a key role in hemostasis. Although, the elevated levels of platelet activation markers have been demonstrated also in patients with severe-to-end stage heart failure (S-ESHF), which could followed by heart failure progression, thromboembolic complications (TEC) and adverse cardiac and non-cardiac events in follow up.

**Aim:** Local elastic properties (LEP) of platelets were investigated by atomic force microscopy (AFM) in patients with ischemic S-ESHF, whom were admitted for open heart surgery. Cohort of study included 6 male with HF NYHA class III (mean age 56,7 years, preoperative LVEF 29,7±6,4%) – group A and 4 male with HF NYHA class IV (mean age 52,4 years, preoperative LVEF 16,1±3,1%) – group B. All patients were operated in hyperpotassium blood cardioplegia condition: group A – coronary bypass grafting and mitral valve and/or left ventricular plasty, group B – implantation of left ventricular assist device (VAD). Blood sample volumes were taken before surgery, after bypass starting and after surgery in operation room. AFM images were captured in air using contact mode with commercially available silicon cantilevers CSC38 ("MikroMasch" Co., Estonia, spring constant of 0.03 N/m). Platelet (from 10 to 15 specimens) LEP were quantitatively determined on the basis of force spectroscopy (Young's modulus, kPa). Additionally, at least 10 singly located platelets of one patient were visualized for presence of activity (platelet lamellipodia, aggregates). The data were compared to healthy male volunteers, matched in age.

**Results:** Patients of group A had lower Young's modulus ( $p<0.02$ ) in spite of the presence of platelet lamellipodia, but not of the platelets aggregates. The visual analysis and multiple data measurement by AFM in both groups showed significant correlation ( $r=0.7$   $p=0.001$ ) between NYHA class, end point (stroke, death, heart transplantation) and AFM data (Young's modulus and lamellipodia presence). Moreover, patient of group B with TEC had significantly higher Young's modulus (319.7±37.2 kPa), if compare to group A (125.2±24.5 kPa,  $p=0.001$ ) and patients without TEC of group B (284.17±44.9 kPa,  $p=0.06$ ).

**Conclusions:** Platelet fragility has been increased in patients with HF progression. In patients with severe-to end stage HF signs of platelet activity (presence of lamellipodia) and high Young's modulus could be a composite predictor of end point. Platelet cytoskeleton dysfunction pattern of a combination of platelet fragility and its activation should be further investigated properly to effect HF progression pathways.

### P1141

#### The influence of the gut microbiota on heart failure so far

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**Background/Introduction:** The gut microbiota may play an influential role in the pathophysiology of Heart Failure (HF) through the generation of disease modifying metabolites. This could have an important part in developing new strategies inside HF treatments.

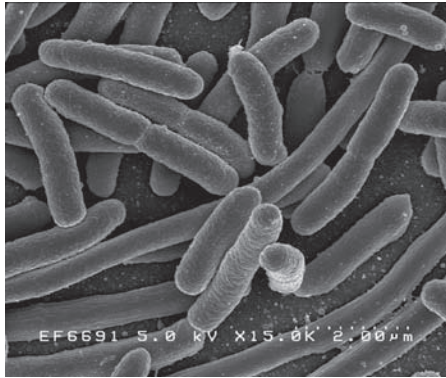
**Purpose:** The aim was to assess the association between the human gut microbiota and the underlying disease mechanisms in HF through the existing literature.

**Methods:** A search incorporating "gut microbiota & cardiovascular disease" was undertaken in PubMed.

**Results:** A total of 277 studies were found. Of these, 162 included humans, and 113 were reviews. Atherosclerosis is a keen predictor of HF and has been linked in human experiments to phosphatidylcholine (PC), choline and carnitine through trimethylamine-N-oxide (TMAO). PC and its intermediates are substantial parts of red meat, fish, egg yolk, and some vegetables. Overall, disease mechanisms leading to HF through the gut microbiota are separated into two theories. First, insufficient perfusion of the human gut may lead to dysfunction of the barrier of the intestines allowing inflammatory and bacterial metabolites to translocate into the systemic circulation. For instance, increased systemic bacterial DNA in patients with cardiovascular may be associated to higher inflammatory markers such as CRP. However, translation into the HF pathophysiology remains unsolved. Second, metabolites generated in the human gut microbiota may impact the HF pathophysiology through cardiorenal conversions. Patients with chronic kidney disease retain uremic toxins, which are produced by the microbiota. An example is indoxyl sulfate, which may induce hypertrophy and fibrosis in the heart. Diabetes type 2 has been associated to alterations of the gut microbiota through inflammatory proteins such as TNF, IL-1 $\beta$  and IL-6. This leads to hyperglycemia causing  $\beta$ -cell autoinflammation, which predicts a lower insulin production. However a connection between diabetes and HF through the microbiota remains unestablished.

**Conclusions:** So far, the role of the gut microbiota remains elusive in the HF pathophysiology, but further investigations will determine its importance. However, underlying diseases of HF such as atherosclerosis and hyperglycemia are associated with the human gut microbiota.





Escherichia coli

**P1142****Endothelial dysfunction, level of leptin and body mass index in patient with coronary heart disease with preserved systolic function in combination with hepatic steatosis.**

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**Objective:** To compare the relationship blood lipid spectrum, endothelial dysfunction, level of leptin and body mass index (BMI) in patient with coronary heart disease with preserved systolic function in combination with hepatic steatosis.

**Methods:** Examined 28 men (mean age  $57.2 \pm 1.21$  years) with coronary heart disease with preserved systolic function and hepatic steatosis. Allocated 3 groups according to BMI: group 1 consisted of 8 (32%) people who are overweight (BMI 25 to 29.9 kg/m<sup>2</sup>), group 2 - 13 (44%) with first degree of obesity (BMI 30 to 34.9 kg/m<sup>2</sup>), group 3 - 7 (24%) with second degree of obesity (BMI 35 to 39.9 kg/m<sup>2</sup>). Studied biochemical parameters: the levels of leptin, total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), triglycerides (TG), high density lipoprotein cholesterol (HDL-C), level of C-reactive protein. 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.

**Results:** Found that in the initial state increasing BMI in the range of 25 – 34.9 kg/m<sup>2</sup> was not associated with a significant difference in the lipid spectrum. According to the reactive hyperemia test data, endothelial dysfunction was found in 7 patients (77%) in a group 1, and in all patients in a group 2 and in a group 3. Vasospastic response observed in 2 patients (22%) in a group A. Reactive hyperemia index (RHI) was lower ( $4.0 \pm 5.3\%$ ) in the group B and in group C ( $4.4 \pm 1.7\%$ ) than in group A ( $7.8 \pm 5.2\%$ ) ( $p < 0.05$ ). The mean level of leptin were  $16.0 \pm 9.7$  ng/ml in a group 1,  $24.2 \pm 14.6$  ng/ml in a group 2 then in a group 3 -  $43.5 \pm 20.2$  ng/ml ( $p < 0.05$ ). There was correlation between the endothelial dysfunction and level of TC ( $r=0.94$ ,  $p=0.01$ ), level of LDL-C ( $r=0.92$ ,  $p=0.01$ ) in a group 1 and level of leptin ( $r=0.76$ ,  $p=0.01$ ) in a group 2 however in a group and 3 such connection was not observed.

**Conclusion:** Thus, in patients with coronary heart disease with preserved systolic function in combination with in combination with hepatic steatosis and overweight (BMI 35 to 39.9 kg/m<sup>2</sup>) level of leptin were more expressed in those who had first degree of obesity (BMI 25 to 34.9). RHI was lower in the group 2 and 3 than in group A. There was an association the endothelial dysfunction and level of TC, level of LDL-C and level of C-reactive protein in a group 1 and level of leptin in a group 2 however in a group and 3 such connection was not observed.

**P1143****Vagal deficiency in cardiac failure: role of deep breathing test**

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**Introduction:** Vagal stimulation, a new very promising management of cardiac failure is under investigation. Measuring vagal response as a daily practice in cardiac failure patients would be of interest. The objective of this study is to report vagal response, obtained by the deep breathing test, in cardiac failure patients.

**Materials and methods:** This prospective study is including a group of symptomatic cardiac failure subjects with ejection fraction EF <40% [group 1] with sinus rhythm, able to perform the deep breathing test, compared to a group of healthy subjects [group 2]. All of them had clinical examination, ECG, echocardiography and deep breathing test. Statistical study will use Student's test, P will be significant when <0.05.

**Results:** We included 34 patients, 10 patients [group 1] compared to 24 patients [group 2]. Preliminary results showed vagal response of  $7.8 \pm 1.7\%$  in group 1 versus  $27 \pm 7.4\%$  in group 2 [ $p < 0.05$ ].

**Conclusion:** This preliminary result showed a significant vagal deficiency response in cardiac failure patients when compared to normal subjects. This study is still going on and we intend to include more patients to validate this result

**P1144****MiR30-GALNT1/2 axis-mediated glycosylation at threonine 48 and 71 plays an essential role in the increased secretion of unprocessed pro-brain natriuretic peptide by failing hearts**

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**Background:** Plasma levels of biologically less active prohormone of brain natriuretic peptide (proBNP) is increased in patients with heart failure, as well as mature BNP-32. The underlying mechanisms of increased plasma proBNP levels in heart failure remain unclear, however.

**Purpose:** We investigated mechanisms underlying the increased plasma levels of proBNP in heart failure.

**Methods:** We assessed cardiac production and peripheral metabolism of proBNP in patients with heart failure by measuring plasma proBNP levels using human proBNP-specific assay system, which we have developed, and the conventional BNP assay system, which detects both proBNP and BNP-32. To elucidate the molecular mechanisms underlying the processing and secretion of proBNP, we generated lentivirus vectors carrying several mutations in glycosylation sites of proBNP. [Results] In samples from coronary sinus, plasma proBNP/BNP ratios were significantly elevated in heart failure patients in accordance with the disease severity. In conditioned medium of cultured ventricular myocytes expressing wild type human proBNP, proBNP/BNP ratio was 37%, while in those of myocytes expressing glycosylation-resistant mutant of proBNP, proBNP/BNP ratio was only 3%, demonstrating the essential contribution of glycosylation to the secretion of proBNP. Among 7 glycosylation sites, we found that glycosylation of Thr48 and Thr71 in proBNP is critical for the secretion of proBNP from ventricular myocytes by attenuating proBNP processing. We identified GalNAc-transferase (GALNT) 1 and 2 mediates the glycosylation-regulated increase in cardiac proBNP secretion by screening with siRNAs. Indeed, GALNT1 and 2 expression was increased in FCS-treated ventricular myocytes and failing hearts. We further found that GALNT1 and 2 expression is suppressed by miR-30 family, which is abundantly expressed in the myocardium, and that miR-30s expression is decreased in FCS-treated ventricular myocytes and failing hearts.

**Conclusions:** We have elucidated a novel miR-30-GALNT1/2 axis that mediates glycosylation at threonine 48 and 71 in proBNP, thereby increasing the proportion of proBNP secreted and impairing the compensatory actions of BNP during the progression of heart failure.

**P1145****Role of sarcoplasmic reticulum calcium leak in heart failure**

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**Background:** Increased diastolic sarcoplasmic reticulum (SR) Ca<sup>2+</sup> leak via the cardiac ryanodine receptor (RyR2) occurs in heart failure (HF) and has been suggested to have a mechanistic role in the development of HF.

**Objective:** We tested the hypothesis that inhibiting or inducing SR Ca<sup>2+</sup> leak modulates HF progression.

**Methods:** Wild-type C57BL/6J mice were subjected to transaortic constriction (TAC)-induced pressure overload (PO), treated with or without a selective, small chemical RyR2 stabilizing Rycal compound (S36). Moreover, knock-in mice with the patient mutation RyR2-R2474S (Ryr2RS/WT) were subjected to shunt-induced volume overload (VO).

**Results:** In TAC model, SR Ca<sup>2+</sup> leak was significantly reduced in S36- versus placebo-treated mice at 3 weeks post-TAC. However, both treatment groups developed comparable contractile dysfunction. Interestingly, S36-treated mice exhibited an improved survival after TAC (72.01 % vs. 49.12 %,  $P < 0.05$ ). Implanted ECGs showed a markedly decreased arrhythmia score by 42% after TAC ( $2.05 \pm 0.42$  vs.  $3.54 \pm 0.39$ ,  $P < 0.05$ ). Using optical imaging we observed significantly reduced arrhythmia susceptibility by 72% post-TAC ( $11.33 \pm 4.36$  vs.  $40.94 \pm 8.47$ ,  $P < 0.05$ ). In VO model, thought SR Ca<sup>2+</sup> leak dramatically increased in Ryr2RS/WT mice,

both WT and Ryr2RS/WT mice had a similar depressed pump function after shunt. **Conclusion:** These results suggest that SR Ca<sup>2+</sup> leak may not primarily influence contractile remodeling in two different HF models, whereas ventricular arrhythmias were significantly reduced and survival was improved by S36 treatment. We conclude that selective SR Ca<sup>2+</sup> leak inhibition via the new drug compound S36 might be a promising option for selective treatment of cardiac arrhythmias in HF due to increased PO.

#### P1146

##### Perfusion-metabolic scintigraphy for prognosis of recurrent left ventricular remodeling after the comprehensive surgical treatment of patients with ischemic cardiomyopathy

The study was supported by a grant from the Russian Science Foundation (No.15-15-10016)

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Purpose of the study was to study perfusion and metabolism of the left ventricular (LV) myocardium in patients with ischemic cardiomyopathy (ICMP) and to identify the scintigraphic predictors of the efficacy of comprehensive surgical treatment of the left ventricular dysfunction.

**Methods:** The study comprised 32 patients with ICMP who underwent comprehensive surgical correction of the LV dysfunction (myocardial revascularization, LV cavity reconstruction, and restoration of the obturator function of the mitral valve if necessary). Inclusion criteria: > 75% stenosis of coronary arteries; one and more myocardial infarctions in the past medical history; heart failure (HF) III-IV NYHA functional class; LV ejection fraction (EF)<45%; end systolic volume index (ESVI) > 60 mL/m<sup>2</sup>; and the presence of akinetic and dyskinetic areas of the LV according to data of echocardiography. Before surgical treatment, all patients received scintigraphy with 99mTc-MIBI and with 123I-BMIPP for evaluation of myocardial perfusion and metabolism, respectively. In early period (four weeks) and 12 months after the surgery, all patients underwent echocardiography study to estimate intracardiac hemodynamics.

**Results:** Twelve months after surgical treatment, patients were assigned to two groups: group 1 comprised patients (n=18) with beneficial outcome of the operation that stopped the process of LV remodeling (LVESVI ≤ 15% one year after surgery compared with the early postoperative period). Group 2 comprised patients (n=14) in whom LV remodeling was progressing despite successful performance of the surgery (LVESVI > 15% compared with the early postoperative period). Prior to surgery and in the early postoperative period LV pumping function (LVEF, LVESVI, LVEDV) didn't significantly differ between groups. Also groups didn't significantly differ in the following scintigraphic parameters: myocardial perfusion defect size and metabolic defect size. Groups differed significantly in size of perfusion-metabolic mismatch (13.23 ± 11.7% and 4.1 ± 11.5%, p < 0.01). The best cut of value 12% for perfusion-metabolic mismatch size can predicted the efficacy of comprehensive surgical treatment for the left ventricular dysfunction with the sensitivity and specificity of 100% and 56%, respectively.

**Conclusions:** The results of myocardial perfusion-metabolic scintigraphy can be used as a method for prediction of the progressing cardiac remodeling in the post-operative period of comprehensive surgical correction of LV dysfunction in patients with ICMP.

#### P1147

##### Development of recommendations for the improvement of palliative care of patients with chronic heart failure

Deutsche Herzstiftung (German Heart Foundation)

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**Background and Purpose:** Despite similar symptom burden patients with chronic heart failure (CHF) receive less palliative care (PC) than patients suffering from malignant diseases. Reasons are seen e.g., in the cyclic course of disease, lack of knowledge about possibilities and structures of PC, and insufficient interprofessional communication. However, research suggests that CHF patients benefit from PC as shown in fewer drug use and hospitalization rates as well as higher quality of life. Within a 3-round Delphi method this study purposes on the development of recommendations for the German healthcare system in order to improve availability of PC for CHF patients.

**Method:** Altogether 18 experts/practitioners agreed to participate within the Delphi method. In the 1st round 16 of them submitted suggestions for the improvement of access to PC of CHF patients by answering questions regarding overcoming barriers, improvement of treatment, and appropriate time for beginning of PC verbatim within an online platform. Questions were derived from results of an initial

questionnaire which was developed based on interviews with healthcare professionals regarding attitudes and experiences with PC for CHF patients. Participants were M=49.00 years old (SD=15.75) and had M=21.29 years of work experience (SD=7.51), 56.3% worked as physicians and 25% as nurses (18.7% other/not specified), 56.3% were male.

**Results:** Suggestions for improvement concentrated on better education regarding PC as well as CHF of patients, professionals, and public; need for more research regarding PC of CHF patients; and better visibility of PC for CHF. Sets of criteria (e.g., medical variables), definition of red flags, use of tools (e.g., surprise question, algorithms for electronically identifying and forwarding PC candidates) were recommended in order to better determine accurate time for initiation of PC. Further, closer cooperation between the different medical disciplines and professional groups involved in care of CHF as well as more intense involvement of nursing staff were suggested. In the next 2 rounds participants will judge the suggestions which will be complemented with research findings regarding their relevance and practicability. Delphi method will be finished at the end of February 2016.

**Conclusion:** Overall, a need for the improvement of CHF patients' access to PC was perceived by healthcare professionals. Barriers to PC might be able to overcome by better education, improvement of cooperation between the different groups involved, and definition of markers for better identification of PC need in CHF patients.

#### P1148

##### The evolution of functional parameters at patients with diastolic heart failure after cardiovascular rehabilitation

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**Purpose:** To determine the effect of the comprehensive rehabilitation program on functional parameters at patients with coronary heart disease (CHD) and diastolic heart failure after coronary revascularization.

**Methods:** The study included 45 patients, mean age 60,8 ± 0,7 years, 25 men and 20 women, with the CHD and diastolic heart failure (EF ≥ 45%, NYHA class III, stage C), which have undergone to coronary revascularization. Patients were divided into 2 groups: Gr. I - with cardiovascular rehabilitation (CVR); Gr. II - without CVR. All patients received secondary prevention treatment. Echocardiographic examination and exercise stress test (EST) was done initially, after 1, 3, 6 months.

**Results:** After 6 months of supervision at patients from Gr. I the left ventricle end-systolic volume (ESV) decreased by 14,87% (p < 0,05), the left ventricle end-diastolic volume (EDV) decreased by 15,92% (p < 0,05). At the patients from Gr. II ESV and EDV had a tendency to increased (10,90 % and 5,07%). The left ventricular ejection fraction (LV EF) increased by 10,89% in Gr.I and decreased by 4,34% in Gr.II, but insignificant statistically. The duration of the test increased in both groups (68.83 % vs 25.93 %). The total working volume (kgm/min) increased more in Gr. I than Gr. II (47.89 % vs 1.39 %). Double product at peak of EST (systolic blood pressure x heart rate/ 100) had a tendency to increased in both groups (12.39 % vs 5.84 %). The significant positive correlations have revealed between ESV and myocardial aerobic deficiency - r = 0.65 (p < 0,001), LV EF and duration of the test - r = 0.64 (p < 0,001), LV EF and double product - r = 0.68 (p < 0,001). The opposite correlation have revealed between ESV and the duration of the test - r = -0.63 (p < 0,01), ESV and double product - r = -0.69 (p < 0,001), EDV and double product - r = -0.60 (p < 0,01), LV EF and myocardial aerobic deficiency - r = -0.64 (p < 0,001).

**Conclusions:** 1. The cardiovascular rehabilitation program after coronary revascularization improved the functional parameters and diastolic heart failure profile of patients with ischemic heart disease; 2. A significant correlation was observed between volumetric parameters, LV ejection fraction and exercise test indices.

#### P1149

##### Short-to-mid term effects of Levosimendan on biochemical and clinical parameters in patients with congestive heart failure

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**Introduction:** The Levosimendan is a new calcium sensitizer with vasodilatory, antiapoptotic and inotropic actions in myocardial cells.

**Purpose:** The aim of this study was to evaluate the short-to-mid term effects of Levosimendan on biochemical and clinical parameters in patients with congestive heart failure chronic heart failure (HF), admitted to the Cardiac Intensive Care Unit.

**Materials and Methods:** Forty-eight patients with deregulation HF (aged 65 ± 12 years), an ejection fraction of 30% or less, and New York Heart Association (NYHA) functional class III or IV symptoms, participated in this study. All the patients received a 24-h infusion of Levosimendan and changes of hematological parameters (hematocrit, white blood cells, platelets), biochemical parameters (urea, creatinine, uric acid, creatine phosphokinase, Creatine phosphokinase-MB, lactate dehydrogenase), plasma NT-proBNP levels and clinical profile were assessed.

**Results:** There were a statistically significant reduction in NT-proBNP, white blood cells, urea, creatinine and lactate dehydrogenase and hematocrit levels. However, most of the other clinical parameters showed non-significant improvement. The clinical profile of patients improved significantly.

**Conclusions:** Levosimendan is a new positive inotropic agent for safe and effective treatment of advanced heart failure. Short-to-mid term intravenous treatment with levosimendan might improve the survival of HF patients. However, the predictive value of these cardioprotective effects requires further investigation in the form of larger, multicenter, randomized studies.

#### P1150

##### Longitudinal study of long-term effects of doxycycline on cardiac structure and functions using high-frequency, high-resolution ultrasound imaging in a mouse model of Marfan syndrome

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**Background:** Our previous study showed that treatment with doxycycline, a general inhibitor of matrix metalloproteinases (MMPs), is more effective than atenolol in preventing thoracic aortic aneurysm in Marfan mice by preserving elastic fiber integrity and normalizing aortic function. Our data also suggests that doxycycline reduces aortic dilation and stiffness in the aorta of Marfan mice.

**Purpose:** In this study we have investigated the effects of doxycycline on the cardiac structure and functions by performing longitudinal study on Marfan mice (3, 6, 9, & 12 months) using high resolution ultrasound imaging.

**Methods:** Marfan (n = 12) and control (n = 13) mice were given sub-antibiotic dose of doxycycline in their drinking water (0.24 g/L/day) starting at 6 weeks of age, when non-treated groups received plain drinking water. Various parameters including aortic diameter, pulse wave velocity, cardiac ejection fraction & stroke volume, left ventricular (LV) wall thickness, LV mass and mitral valve early and atrial velocities (E/A) ratio were measured in doxycycline and sham treated control and Marfan mice.

**Results:** Measurements of the normalized thickness of the interventricular end diastolic septum (IVSd) showed significant increase in Marfan compared to control mice starting at 6-month of age ( $p < 0.05$ ), however, with doxycycline treatment, Marfan mice no longer showed significant difference in IVSd thickness vs. controls. Likewise, Marfan mice showed significant increase in normalized LV mass compared to control mice, starting at 3-month of age ( $p < 0.01$ ), but no difference between treated Marfan and control mice from 6 months on. With respect to the cardiac function, a significant decrease in early filling velocity and E/A ratio was found in Marfan mice at all age groups compared to controls ( $p < 0.05$ ), regardless of doxycycline treatment. Both stroke volume and cardiac output did not show significant difference in Marfan vs. control mice, regardless of age and treatment. Of note, low dose of doxycycline was very effective in decreasing aortic dilatation and normalizing pulse wave velocity in treated Marfan groups. This is in agreement with our previous data showing improvements in elastin organization and structural integrity within the aortic wall in doxycycline-treated Marfan mice.

**Conclusions:** Our findings suggest that long-term doxycycline treatment may have protective effects in preventing both cardiac hypertrophy and aortic dilatation in Marfan mice, with no apparent beneficial effects on left ventricular diastolic dysfunction.

#### P1151

##### Alterations of plasma macrophage migration inhibitory factor (MIF) concentration in patients with chronic heart failure treated with cardiac resynchronization therapy

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**Introduction:** Inflammatory activation plays a pivotal role in a chronic heart failure with reduced ejection fraction (HF-REF). Cardiac resynchronization therapy (CRT) is a unique treatment method, that may reverse the course of HF-REF. Macrophage migration inhibitory factor (MIF) is a proinflammatory cytokine that has been shown to mediate both disease-exacerbating and beneficial effects.

**Purpose:** We aimed to evaluate the MIF concentration in HF-REF patients and its relationship with disease severity and CRT.

**Methods:** The study included 37 patients (64.1 ± 11.04 years, 6 females) with chronic stable HF-REF, EF < 35%, controlled at baseline and after 6 months of CRT. The control population without history of HF-REF included 27 healthy volunteers

(63.9 ± 8.1 years, 8 females). MIF serum concentrations was determined using multiplex method (Quantibody Array Human Chemokine, Ray-Biotech Inc.).

**Results:** HF-REF patients were characterized by higher MIF concentration comparing to healthy volunteers both at baseline (39.95 IQR: 23.6–89.8 vs 32.34 IQR: 16.27–43.15 pg/mL,  $p = 0.022$ , respectively) and after 6 months of CRT (42.94 IQR: 23.6–89.8 vs 32.34 IQR: 16.27–43.15 pg/mL,  $p = 0.045$ , respectively). In HF-REF population at baseline concentration of MIF correlated with serum level of chemokines: CCL28 ( $R = 0.67$ ,  $p = 0.001$ ), I-TAC ( $R = 0.65$ ,  $p = 0.002$ ) and IL-28A ( $R = 0.61$ ,  $p = 0.021$ ). Furthermore, MIF correlated directly with EF ( $R = 0.57$ ,  $p = 0.02$ ) and with the lung gas exchange parameters measured in cardiopulmonary exercise testing (CPET): maximal end-tidal CO<sub>2</sub> pressure (PETCO<sub>2</sub>) ( $R = 0.57$ ,  $p = 0.02$ ) and inversely with ventilatory equivalent for CO<sub>2</sub> (VE/VC<sub>02</sub> slope) ( $R = -0.55$ ,  $p = 0.02$ ). There were no differences in MIF concentration between patients who benefited from CRT (responders) and those who did not benefit (nonresponders) at baseline (34.98 IQR: 20.3–114.92 vs 42.32 IQR: 38.37–59.52 pg/mL,  $p = 0.6$ ) and 6 month follow-up (46.92 IQR: 24.15–124.6 vs 39.26 IQR: 23.18–75.17 pg/mL,  $p = 0.47$ ).

**Conclusions:** HF-REF patients present increased MIF concentration compared to healthy subjects, however its levels correlate with markers of better prognosis. The CRT-related improvement in patient's functional status is not associated with changes in MIF. The precise role of MIF in pathogenesis of HF-REF and its prognostic value remains to be established.

#### P1152

##### The role of clinical particularities and co-morbidities in the development of different types of left ventricular dysfunction after 12 months from coronary revascularization - retrospective analysis

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**Background:** The clinical manifestations and co-morbidities were crucial in the development of chronic heart failure and the prognosis life of patients. Purpose: comparative analysis of clinical parameters, comorbidities in different types of left ventricular dysfunction after coronary revascularization over 12 months.

**Methods:** 186 patients who have revascularization by coronary artery bypass grafting or percutaneous coronary angioplasty, mean age 59, 8 ± 0.7 years, the final stage (after 12 months from coronary revascularization) were divided into 3 groups (Gr.) depending on the value ejection fraction (EF), determined ultrasound Simpson's method: Gr.1 - EF ≤ 35% (n = 30), Gr.2 - EF between 35% and 45% (n = 36), Gr.3 - EF ≥ 45% (n = 121)

**Results:** Congestive heart failure (New York Heart Association classes III-IV) was recorded in Gr.1 = 75 %, Gr.2 = 70 %, Gr.3 = 10,74%. NT proBNP levels (pg/ml) it was higher in Gr.1 = 462,09 ± 60,3 compared to Gr.2 = 248 ± 52,5 and Gr.3 = 90,48 ± 21,36 ( $p < 0,01$ ). Charlson Comorbidity Index was comparable between Gr.1 and Gr. 2 (5,15 ± 0,43 vs 4,86 ± 0,43) and statistically significantly lower Gr.3 = 3,35 ± 0,35,  $p < 0,0001$ . There were significant differences in the presence of chronic pulmonary disease (Gr.1 = 58,33%, Gr.2 = 40%, Gr.3 = 33,06%,  $p < 0,05$ ), of moderate renal disease (respectively 62,5% ; 53,34% ; 31,4%,  $p < 0,05$ ), Q-Wave old myocardial infarction (91,67% , 83,33%, 39,67%,  $p < 0,05$ ), which were compared between Gr.1 and Gr.2 and significantly lower in Gr. 3

**Conclusions:** 1. The presence of Q-Wave old myocardial infarction, chronic obstructive pulmonary disease, moderate renal disease have negative impact on the development of left ventricular dysfunction after 12 months from coronary revascularization

2. The patients with mild systolic dysfunction are similar to patients with severe systolic dysfunction by the studied parameters

#### P1153

##### Relationship between renal function and age in patients with chronic heart failure and preserved ejection fraction

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**Background:** As known, heart failure with preserved ejection fraction is associated with age and renal dysfunction. functional disorders of the kidneys. Also? decreased glomerular filtration rate (GFR) is a bad prognostic factor among these patients.

**Objectives:** we aimed to evaluate relationship between renal function and age 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: 74 pts aged 59 years (1 group), 73 pts from 60 to 75 years old (2 group), and 51 pts aged older 76 years old (3 group). GFR was calculated by MDRD formula.

**Results:** The average GFR in the first group was 82,2 ± 12,7, the second – 65,5 ± 17,7 in the third and 64,0 ± 11,6 ( $p < 0,05$ ). Normal GFR was found in 6.8% (5 pts) of the first group, 17.8% (13 pts) of the second group and in 5.9% (3 pts) in the third group, mild reduction of 52.7% ( 39 pts) of the first group, 45.2% (33 pts) of the second group and in 37.3% (19 pts) of the third group, chronic renal failure in



20.2% (15 pts) of the first group of patients, 37% (27 pts) of the second group and in 56.9% (29 pts) of the third group ( $p < 0.05$ ).

**Conclusion:** Renal dysfunction was found in patients with chronic heart failure with preserved LVEF in all age groups. But it showed a reduction of GFR in patients with increasing age and increasing number of patients with moderate renal functional impairment and chronic renal failure depending on age. The development of renal dysfunction associated with age in patients with heart failure with preserved ejection fraction.

#### P1154

##### Anemia in chronic heart failure

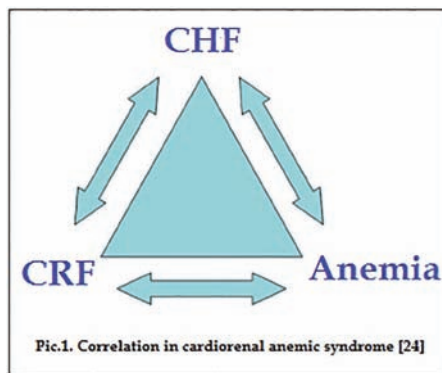
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**Background:** In recent decades, life expectancy has increased significantly in patients with chronic heart failure (CHF). In this regard, before the cardiologists and physicians got a number of new questions about the management of patients with a large number of related diseases and conditions, such as anemia and decreased renal function.

**Methods and Results:** The prevalence of anemia among patients with cardiovascular disease is relatively well studied. Anemia is a frequent co-morbidity in chronic heart failure [2-10], its prevalence varies in a wide range of 4 to 61% (average 18%) depending on the severity of the main disease (functional class by NYHA) and used criteria of anemia. The fact of increasing the overall and cardiovascular mortality in the presence of anemia in patients with chronic heart failure is confirmed in numerous studies. Thus, in a retrospective study SOLVD shown, reduction the hematocrit rate by 1%, increases the total mortality in patients with CHF by 2.7% [13]. OPTIME study showed, at the level of hemoglobin less than 12 g / dl, risk of death or rehospitalization increased by 12%[14].

**Conclusion:** Nowadays, there are reliable data on the need for active detection and correction of anemia in patients with CHF. Accumulated documentary base in these patients for the treatment of anemia with erythropoietin as a single agent or in combination with intravenous iron preparations does not allow unambiguously to determine the expedience and safety of this approach. These studies on the use of intravenous iron preparations as monotherapy in patients with CHF and iron deficiency, regardless of the presence of anemia could significantly expand the indications for their use in this pathology.



#### P1155

##### Impact of diabetes on epidemiology and treatment of patients with chronic heart failure

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**Introduction:** The prevalence of patients with concomitant heart failure (HF) and diabetes mellitus (DM) continues to increase with the general aging of the population. Patients with concomitant HF and DM have diverse abnormalities that potentially contribute to worse outcomes than those without comorbid DM. The purpose of our study is to re-evaluate the epidemiology and therapy of HF patients with concomitant DM.

**Methods:** We conducted a prospective study at the day hospital of HF in a university hospital where 430 patients were admitted for HF between January 2014 and April 2015. Only 145 had DM. We randomly selected a subset of 145 patients diagnosed as non-diabetic to ensure a significant statistical comparison between the diabetics and non diabetics HF patients.

**Results:** Patients with DM had a higher prevalence of ischemic cardiomyopathy

(74% vs 44,9%,  $p < 0.001$ ). The left ventricular ejection fraction was significantly lower in the group with DM (27, 1% vs 17, 5%,  $p < 0.001$ ). Age, cardiovascular risk factors, clinical symptoms and repolarization disorders did not significantly differ. 25% of the patients with DM were on insulin and 60,5% were controlled on oral antidiabetics only. Inhibitor of angiotensin converting enzyme (ACE inhibitor) and angiotensin II receptor blockers (ARBs) were more prescribed for patients with DM (78% vs 63,1% for ACE inhibitors and 18,3% vs 13,4% for ARBs).

**Conclusion:** Our paper discusses the impact of DM in HF patients and underscores the potential need for the development of targeted therapies.

#### P1156

##### The cost-effectiveness of sacubitril/valsartan in chronic heart failure with reduced ejection fraction

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**Background:** Chronic heart failure with reduced ejection fraction (HFrEF) represents a major public health issue and is associated with significant morbidity and mortality.

**Purpose:** We evaluate the cost-effectiveness of sacubitril/valsartan (formerly LCZ696) compared with an angiotensin-converting-enzyme (ACE) inhibitor in the treatment of HFrEF from a UK National Health Service perspective.

**Methods:** A cost-utility analysis was performed based on PARADIGM-HF, a large Phase III multicentre randomised controlled trial comparing sacubitril/valsartan with enalapril in HFrEF patients with New York Heart Association Functional Classification II-IV symptoms. We created a series of regression models which extrapolated health-related quality of life (EQ5D), hospitalisation rates and survival over a life-time horizon. A parametric survival model was used in the base-case to predict all-cause mortality from PARADIGM-HF. In an alternative analysis, cardiovascular (CV) mortality was modelled from PARADIGM-HF, and non-CV mortality taken from national life tables. Negative binomial and multilevel models were used to predict all-cause hospitalisation and EQ-5D over time, respectively. Adverse event rates were assumed to be constant. Costs and outcomes were discounted at 3.5%. The primary outcome was the incremental cost-effectiveness ratio (ICER). Deterministic (DSA) and probabilistic sensitivity analyses (PSA) were performed.

**Results:** Sacubitril/valsartan was associated with ICERs of approximately £17,900 (all-cause mortality) and £16,600 (CV mortality) vs enalapril. In the base-case scenario, compared with enalapril, treatment with sacubitril/valsartan was predicted to improve patient survival by 0.48 years and lead to 0.42 additional quality-adjusted life years and 15% fewer hospitalisations (0.06/year absolute reduction; 8% reduction in discounted lifetime hospitalisation costs). DSA showed that results were most sensitive to the extrapolation of mortality. Results were also sensitive to assumptions around duration of treatment-effect and time horizon, but were robust to other structural changes, with most scenarios associated with ICERs below £20,000. PSA suggested that the probability sacubitril/valsartan was cost-effective at thresholds of £20,000 and £30,000 was 66% and 95%, respectively.

**Conclusions:** Our analysis suggests sacubitril/valsartan is likely to be cost-effective vs an ACE inhibitor (the current standard of care) at conventional willingness-to-pay thresholds, in patients with HFrEF and NYHA class II-IV symptoms. This conclusion is consistent with the results of an independent analysis performed in the US setting.

#### P1157

##### Predictors of 12- and 36-month mortality in chronic heart failure

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**Background:** Despite good knowledge about predictors of long-term mortality in chronic heart failure (CHF) the comparable value of them in dependence of patient's follow-up duration is still non-well investigated. Aim: The purpose of study was to identify the predictors of 12- and 36-month mortality in CHF.

**Methods:** 95 clinical, echocardiographic and laboratory variables in 267 CHF patients with left ventricular ejection fraction LVEF < 40 % were analyzed. Predictors of 12- and 36-month mortality were determined in stepwise multiple logistic regression model.

**Results:** Table 1. Most important predictors of 12- and 36-month mortality in CHF patients.

**Conclusion:** HOMA index is a strongest predictor of CHF patients mortality irrespective of follow-up duration. Predictors related to left ventricular function (low LVEF, high LVEDVI) are valuable only in relation to 36-month mortality prognosis. The predictive value of elevated plasma UA and level SAP < 100 mmHg is the high in regard to both 12- and 36-months mortality. According to follow-up duration increases the predictive value of low BMI, size LA > 49 mm and HR > 75 beats p.m.

Table 1

	OR	36 month	OR
HOMA > 2,65	8.48	HOMA > 2,65	6.67
HR > 75 beats p.m.	7.9	BMI < 22kg/m <sup>2</sup>	5.99
SAP < 100mmHg	5.4	SAP < 100mmHg	3.95
BMI < 22kg/m <sup>2</sup>	3.59	LA > 49mm	3.01
UA > 500µmol/l	3.125	UA > 500µmol/l	2.78
Blood lymphocyte < 21%	2.69	LVEDVI > 133 ml/m <sup>2</sup>	2.68
6 min walk distance < 360m	2.43	Blood lymphocyte < 21%	2.65
LA > 49mm	2.18	LVEF < 30%	2.45

\* All predictors are significant (p < 0.05). HOMA – HOMA index; UA - uric acid; BMI - body mass index; LVEDVI - left ventricular end diastolic volume index; HR - heart rate; SAP - systolic arterial pressure; LA - left atria size; LVEF - left ventricular ejection fraction.

**P1158**

**Levels of adiponectin, leptin, inflammatory and anti-inflammatory cytokines in patients with systolic chronic heart failure in relation to insulin resistance state**

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**Background:** Insulin resistance (IR) is observed in 30-49% cases of systolic chronic heart failure (CHF). Nevertheless, the levels of adiponectin, leptin, inflammatory and anti-inflammatory cytokines in IR associated with CHF were studied insufficiently. Objective. To evaluate the levels of adiponectin, leptin, inflammatory and anti-inflammatory cytokines in relation to IR state.

**Methods:** The study involved 107 CHF patients (NYHA II – IV) with left ventricular ejection fraction ≤ 40% without diabetes. IR was defined as HOMA index ≥ 2,77. The levels of adiponectin, leptin, inflammatory and anti-inflammatory cytokines were determined by IFA method. The index of systemic inflammatory (ISI) was calculated as ratio of inflammatory to anti-inflammatory cytokine levels.

**Results:** The patients were divided in 2 groups in accordance to presence of IR. IR patients had a significantly higher level of insulin than the non-IR patients (< 0,05). CHF patients demonstrated significantly higher (< 0,05) adiponectin and leptin levels in comparison with the control age-matched persons. In CHF patients the levels of inflammatory and anti-inflammatory cytokines were significantly lower (< 0,05) than controls. There was no significant difference in cytokine levels between IR and non-IR groups. IR group demonstrated a significantly higher ISI in comparison with non-IR group.

**Conclusion:** HF patients are characterized by higher levels of adiponectin, leptin, inflammatory and anti-inflammatory cytokines. Simultaneously, CHF patients with IR demonstrated a higher inflammatory response than non-IR patients.

Table 1. The levels of adiponectin, lep

Index	Control group (= 15)	HOMA	
Group 1 Group 2			
Insulin, mklUO/ml	9,3 ± 1,1	7,6 ± 0,4	24,8 ± 3,5* **
Glucose, mmol/l	4,7 ± 0,2	5,0 ± 0,1	5,4 ± 0,1*
HO	1,5 ± 0,2	1,7 ± 0,1	6,0 ± 0,9* **
Leptin, ng/ml	3,7 ± 0,2	5,5 ± 3,0*	8,3 ± 3,1*
diponectin, mkg/ml	7,9 ± 0,7	10,8 ± 0,6*	11,6 ± 0,6*
TNF - £, pg/ml	32,8 ± 4,5	50,9 ± 32,9	144,8 ± 75,6
IL 6, pg/ml	1,8 ± 0,5	10,4 ± 2,4*	20,51 ± 1,1*
IL 10, pg/ml	1,3 ± 0,2	7,2 ± 1,7*	11,0 ± 4,8*
ISI	7,7 ± 1,6	59,4 ± 9,6*	127,61 ± 8,3* **

\* < 0,05 in comparison with controls; \*\* < 0,05 between group 1 and group 2.

**P1159**

**The relationship between the heart rate variability and poor outcome in patients with Q-myocardial infarction**

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**Objective:** To estimate the initial level of the heart rate variability (HRV) in patients with AMI complicated further by the sudden cardiac death (SCD).

**Materials and Methods:** We analyzed data 205 male patients Q- MI. All patients were hospitalized with Republican Specialized Center of Cardiology for the period 2006-2010, with a diagnosis of acute Q- wave myocardial infarction. Mean age was 51.7 ± 9 years. All patients on the 10-14 day of the disease Holter ECG monitoring was performed with an analysis of HRV. The observational period was 36 months. Depending of the outcome, the patients were divided into 2 groups: I group (n = 191) of survivors, II group (n = 14) who died suddenly.

**Results:** Comparative analysis of clinical and anamnesis data showed that the mean age of the groups were not statistically different. Analysis of the level of HRV showed that the average SDNN on II group of patients was 92.07 ± 12.9 ms. At the same time, the qualitative analysis showed that 9 (70 %) patients of the II group was below 100 ms. The SDNN less than 50 ms identified in 2 (22%), the mean value SDNN (50-100 ms) in 78 % of patients. The activity index of the parasympathetic system RMSSD was also significantly lower in patients who died suddenly. Thus, the average rate was 21.8 ± 3.8 ms. At the same time, the vast majority of patients (84.6 %) had on pre-discharged stage RMSSD below 36 ms. The pNN50% averaged 476 ± 20 while indices below 5.5 % have eight (81.5%) patients. Study of spectral parameters revealed that on patients with SCD the baseline total power spectrum at 72% consisted of ultra performance, low and very low frequencies. But the ratio LF/HF, which characterizes the relation of low and high frequencies averaged 3.0 ± 0.4. The analysis of the calculated HRV index computed by combining SDNN and HRVTi showed that in comparison groups on the initial stage, it was only moderately reduced on 2 patients (15%) and on 17 (10.7 %) patients, respectively, while 15% of patients with SCD at baseline HRV was reduced significantly, that significantly above the group with a favorable outcome. In addition, on 23% of patients with a poor outcome group revealed an independent predictor of fatal arrhythmias in the next 3 years, while in the group of survivors, it was detected in 8.3 % of cases.

**Conclusion:** patients with AMI complicated by SCD already in subacute stage of the disease characterized by a greatly reduced total HRV and spectral indices presented ultra-low and very low frequencies.

**P1160**

**The systolic function and heart rhythm variability at patients with myocardial infarction**

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**The purpose:** studying of interrelation between the left ventricular (LV) systolic function with vegetative regulation of heart rhythm at patients with Q-wave myocardial infarction (MI).

**Materials and methods:** 112 males (middle age 51,8 ± 13,6 years) with Q-wave (IT) are surveyed. To all patients for 10-14 day of disease were performed echocardiogram and Holter monitoring with the analysis of heart rhythm variability (HRV). LV systolic function was estimated on a parameter of ejection fraction (EF). According to EF patients have been divided into 3 groups: I – with normal of EF (55 % and more) – 36 person; II – moderate decrease of EF (55-35 %) – 45 person; III – with significant decrease of EF (less than 35 %) – 31 person.

**Results:** the dispersive analysis revealed the statistically significant shortening interval RR in process of deterioration LV systolic function. SDNN decreased in parallel with decreasing of EF. Besides attracted attention of distinction in values dRR and %HF with the maximal difference between groups I and III (=0,04). Results of the correlation analysis have shown, that HRV has been correlated with myocardium contractile functions: correlations LV EF with RR (r=0,7 p <0,05) and SD (r=0,6 p <0,01) are revealed. The correlation analysis has revealed interrelation between low EF and frequency of heart rate (r=0,7 p <0,05).

**The conclusion:** on 10-14 day of Q-wave MI the worsening of LV contractile abilities is associated with disturbance in heart rhythm regulation clinically determined as increasing of sympathetic activity and suppression of parasympathetic influences.

**BASIC SCIENCE: HEART FAILURE DIAGNOSIS**

**P1161**

**Assessment of RV function following percutaneous transvenous mitral commissurotomy (PTMC) for rheumatic mitral stenosis**

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**Objective:** Abnormal right ventricular function plays an important role in development of clinical symptoms and overall prognosis of patients with mitral stenosis. Hemodynamic and radionuclide studies have demonstrated long-term improvement in RV function after PTMC. However, exact quantification by conventional echocardiographic technique is difficult owing to complex 2D anatomy. This study evaluates the immediate and short term follow up impact of successful percutaneous transluminal mitral valve commissurotomy on RV function in patients with mitral stenosis using 2D Echo and Doppler tissue imaging echo.

**Methods:** 219 patients (mean age 26+6yrs) with rheumatic MS, all in sinus rhythm were studied before and 24-48hrs after PTMC. Parameters of global and longitudinal RV function were assessed by conventional and tissue Doppler imaging echo.

**Results:** Immediately following PTMC mitral valve area increased from baseline of  $0.71 \pm 0.15$  cm<sup>2</sup> to  $1.84 \pm 0.17$  cm<sup>2</sup> (P 0.0001), RV outflow tract fractional shortening (RVOT - FS) increased from  $33.94 \pm 7.55\%$  to  $37.33 \pm 7.67\%$  ( $< 0.001$ ). There was a significant decrease in systolic pulmonary artery pressure from  $48.93 \pm 13.08$  mmHg to  $29.56 \pm 7.71$  (P  $< 0.0001$ ). RV Tei-index decreased from  $0.47 \pm 0.12$  to  $0.32 \pm 0.11$  (P 0.001).

**Conclusion:** Long term evaluation of RV function and benefits using invasive and radionuclide methods post PTMC has shown incongruous results in improvement of right ventricular (RV) function immediately after PTMC. In this study, immediately after successful PTMC significant improvement in parameters of infundibular and global RV function as assessed by RVOT fractional shortening, Tei index and tissue Doppler velocities was observed

An Evaluation of study parameters

	Pre	Post	difference	t value	P value
LVIDD	4.80 ± 5.10	4.07 ± 0.45	0.733	2.115	0.036*
LVIDS	2.73 ± 0.36	2.70 ± 0.37	0.032	2.227	0.027*
RVDD	2.14 ± 0.37	1.62 ± 0.35	0.521	20.921	<0.001**
MVA	0.71 ± 0.15	1.84 ± 0.17	1.129	69.309	<0.001**
MVG	17.42 ± 3.69	5.54 ± 1.09	11.881	49.750	<0.001**
PASP	48.93 ± 13.08	29.56 ± 7.71	19.370	31.261	<0.001**
HR	77.84 ± 12.25	70.71 ± 8.82	7.128	11.289	<0.001**
LA	4.47 ± 0.41	3.70 ± 0.45	0.768	37.250	<0.001**
EF	59.31 ± 2.23	58.68 ± 1.63	0.630	5.004	<0.001**
TAM	16.99 ± 3.03	17.55 ± 2.62	0.551	4.273	<0.001**
RVMPI	0.47 ± 0.12	0.32 ± 0.11	0.152	24.428	<0.001**

## BASIC SCIENCE: CO-MORBIDITIES

### P1162

#### The role of biomarkers in risk stratification of kidney injury in patients with acute coronary syndrome

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The development of renal dysfunction in patient with acute myocardial infarction, especially in those who underwent angiography, is an actual problem, because it worsens the prognosis for those patients. In order to diagnose this condition in time the search for biomarkers is going. One of them is the Growth differentiation factor 15 (GDF 15).

**Purpose:** estimate the role of various markers in the development of cardiorenal syndrome in patients with acute coronary syndrome (ACS).

**Methods:** 73 patients were screened with different forms of ACS (55 male and 18 female), mean age was 61,  $8 \pm 1$ , 3 years. In anamnesis patients had: 23% - previous myocardial infarction, 51% - stable angina, 84% - hypertension, 16% - diabetes mellitus, 6% - chronic kidney disease. Based on the results of the examination glomerular filtration rate (GFR) was calculated by Modified diet renal disease method (MDRD). A group of patients has been selected (n=54), their creatinine level was determined during the first 24 hours and after 48 hours. All patients were divided into two groups according to acute kidney injury network classification (AKIN): 21 patient

in the first group with negative dynamic (1st stage AKIN and higher), 33 patient in the second group without creatinine dynamic. In addition, the levels of GDF 15, N terminal-pro B-type natriuretic peptide (NT-pro BNP) were determined during the first day of hospitalization (normal range of GDF 15  $< 1200$  pg / ml, NT pro-BNP  $< 200$  ng/ml). The follow-up period was 6 months.

**Results:** By comparing selected groups significant difference was found in creatinine level and GFR in both groups ( $< 0.001$ ;  $< 0.01$ , respectively). The analyses of biomarkers interconnection (NT pro-BNP, GDF 15) and GFR showed significant difference of estimated parameters in both groups as well ( $\leq 0.04$ ;  $\leq 0.02$ , respectively). Also, correlation of high and medium strength was found between biomarkers (GDF 15, NT pro-BNP) and GFR ( $\leq 0.0001$ ,  $p \leq 0.01$ ).

**Conclusions:** The biomarker GDF 15 can be used for risk stratification in development of acute kidney injury in patients with ACS, its as sensitive as the known marker NT-pro BNP. For high prognostic possibility we can use combination of biomarkers.

### P1163

#### Daily activity per minute slept drops with renal impairment in patients with chronic stable heart failure.

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**Background:** Optimal sleep may replenish energy levels and improve functional capacity. Daily activity levels per minute slept may reflect the efficiency of nocturnal energy storage. It is not known what factors may influence this relationship and whether it affects functional capacity.

**Objective:** We evaluated what factors were related to nocturnal energy storage in patients with chronic stable heart failure.

**Methods:** 105 consecutive patients with chronic Heart failure participated. We evaluated patients' activity and sleep levels using FitBit Activity trackers. From this it was possible to calculate the average number of steps taken daily per minute slept at night. We also assessed NYHA and 6 minute walk distances, body composition, diet and cardiac parameters.

**Results:** 76 men and 29 women, avg 67 years were enrolled. Steps per minute slept correlated significantly with age ( $r = -0.43^{***}$ ), eGFR ( $r = 0.36^{**}$ ), BNP ( $r = -0.36^{**}$ ), 6 min walk distance ( $r = 0.46^{***}$ ), NYHA ( $r = -0.23^*$ ), protein intake ( $r = 0.29^{**}$ ), Fat free Mass ( $r = 0.25^*$ ), Total body water ( $r = 0.25^*$ ), LV ejection fraction (ns) and LV diameter (ns). However estimated GFR (\*\*) was the only significant parameter in a multivariate analysis to correlate with nocturnal energy storage in these patients. N.B {ns = not significant)  $p < 0.05$  \*  $p < 0.01$  \*\*,  $p < 0.001^{***}$ }

**Conclusion:** Our results highlight that in patients with chronic stable heart failure, renal function may determine nocturnal muscle energy storage and subsequent functional capacity in patients with heart failure.

### P1164

#### Phenotype of a mouse model of type 3 cardio-renal syndrome

Inserm and Paris Diderot University  
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**Introduction:** Acute Kidney Injury (AKI) has been strongly associated with both short and long-term mortality in hospitalized patients. Reasons for such an association remain uncertain but damage on remote organs has been proposed as a cause of long-term morbidity and mortality. The Cardio-renal Syndrome type 3 (CRS-3) is characterized by an initial AKI that leads to an acute cardiac injury and/or dysfunction. Our first objective was to develop a mouse model of CRS-3 in order to better understand the mechanisms involved.

**Methods and Results:** In C57Bl6 mice we performed nephrectomy of the right kidney and 25 minutes ischemia of the left kidney followed by reperfusion. To get insights into the kinetics of the kidney-heart cross-talk after renal I/R, mice were sacrificed at different time points after reperfusion (3, 6, 12, 24, 48, 72h and 28 days, n=7 per time point). Renal tissue damage was detected within the tubulo-interstitial compartment as early as 3h post-I/R, leading to renal dysfunction at 24h (increased x10 serum creatinine and Blood Urea Nitrogen levels,  $p < 0.001$ ). All functional renal parameters returned to baseline levels at 2-3 days post-I/R. From a cardiac standpoint, renal I/R induced heart damage illustrated by the increase in different cardiac markers of injury (BNP, ANP and QSOX1-mRNAs,  $p < 0.01$ ), oxidative stress (DHE x3,  $p < 0.001$ ) and cardiac inflammation (CD68, MCP1, TGF $\beta$  and Galectin-3-mRNA x2) but cardiac function was normal. Similarly to the kidney, all stress markers returned to basal levels within 3 days post-I/R but markers of cardiac inflammation (CD68 and TGF $\beta$  x2:  $p < 0.01$ ) remained elevated at day 28 post-I/R. This sustained inflammation was accompanied by a cardiac dysfunction (-10% in fraction shortening,  $p < 0.001$ ) and fibrosis (x3,  $p < 0.001$ ) 28 days after renal I/R.



**Conclusion:** Altogether the data indicated that an acute renal I/R provokes an early cardiac injury and long-term cardiac dysfunction, therefore providing an innovative mouse model of CRS-3.

#### P1165

##### **IFN-gamma plays protective roles in the pathogenesis of cardio-renal syndrome type 1 through the induction of intracardiac ANP expression.**

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**Introduction:** The dysfunction of heart and kidney is frequently accompanied in patients, leading to increased morbidity and mortality. Dysfunction of heart often leads to that of the kidney - the so called cardio-renal syndrome (CRS) type 1. Although the growing evidences indicate that inflammation plays important roles in the pathogenesis of CRS, the pathogenic roles of cytokines in CRS is still not fully understood. In our study on cardiac hypertrophy induced by transverse aortic constriction (TAC) in IFN-gamma deficient (IFN-g-KO) mice, we found that IFN-g-KO mice were prone to CRS type 1. Thus, we investigated the involvement of IFN-gamma in the pathogenesis of CRS type 1 by using mice subjected to severe TAC.

**Methods:** Male BALB/c (WT) and IFN-g-KO mice (8-12 week-old) were subjected to TAC. TAC was achieved by tying around the transverse thoracic aorta against a 28-gauge needle using a 7-0 silk suture, and then removing the needle. Three days after TAC, cardiac function was examined by echocardiography. The intracardiac and intrarenal gene expression induced by pressure overload was evaluated by real-time RT-PCR. Acute renal injury was evaluated with blood urea nitrogen (BUN), serum creatinine (CRE), histological, immunohistochemical examination and TUNEL staining.

**Results:** Upon the evaluation of cardiac function by echocardiography at 3 days after TAC, there was no significant difference between WT and IFN-g-KO mice. However, 60% of IFN-g-KO mice died within 10 days after TAC, whereas 90% of WT mice survived. The gene expression for ANP significantly increased in the left ventricle of WT mice 3 days after TAC, which was not observed in IFN-g-KO mice. In WT mice, neither significant elevation of serum BUN and CRE levels and histopathological alterations of the kidneys was observed. On the other hand, TAC induced significant increase of BUN and CRE in IFN-g-KO mice. Consistently, IFN-g-KO mice exhibited significant histopathological alterations such as tubular dilatation as well as disappearance of brush borders in damaged tubules with massive infiltration of neutrophils. Moreover, extensive tubular cell apoptosis was found in IFN-g-KO but not WT mice. Furthermore, intrarenal gene expression of inflammatory cytokines was more up-regulated in IFN-g-KO mice compared with WT ones. Prior administration of neutralizing anti-IFN-gamma antibody to WT mice significantly suppressed TAC-induced ANP gene expression in the heart and increased serum BUN and CRE levels. On the contrary, ANP infusion into IFN-g-KO mice significantly reduced TAC-induced elevation of serum BUN and CRE levels.

**Conclusion:** IFN-gamma plays protective roles in the pathogenesis of CRS type 1 through the induction of intracardiac ANP expression.

#### P1166

##### **The role of adiponectin receptor 1 and tnf- $\alpha$ in the process of skeletal muscle adiponectin resistance, mitochondrial dysfunction and impaired myogenesis in chronic heart failure.**

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**Background:** Skeletal muscle metabolic alterations including adiponectin resistance and mitochondrial dysfunction are common features in chronic heart failure (CHF). We previously demonstrated that CHF patients are characterized by a functional adiponectin resistance at the level of the skeletal muscle.

**Purpose:** The aim of the present study was to examine the role of adiponectin receptor 1 (AdipoR1) and TNF- $\alpha$  on adiponectin signalling and mitochondrial function in skeletal muscle.

**Methods:** Myoblasts and myotubes cultures were initiated from muscle biopsies (m. vastus lateralis) of 10 CHF patients (LVEF;  $31.30 \pm 2.89\%$ ) and 10 age- and gender matched healthy controls. Cultures from healthy donors were transfected with siAdipoR1 and/or treated with TNF- $\alpha$  (10ng/ml; 72h).

**Results:** Primary CHF myotubes preserve the features of adiponectin resistance in vitro as evidenced by a tendency toward increased adiponectin expression ( $p=0.058$ ) and a downregulation of AdipoR1 ( $p=0.051$ ) and its underlying signalling pathway ( $p < 0.05$ ). Upon siRNA-mediated silencing of AdipoR1, phosphorylated AMPK and AMPK activation were reduced (pAMPK, pAMPK/AMPK,  $p < 0.01$ ). High-resolution assessments of myoblast proliferation were evaluated using the

xCELLigence RTCA and a delayed growth rate was observed ( $p < 0.0001$ ). Moreover, the expression of AdipoR1 was negatively correlated with the time needed to reach the maximal cell index ( $r=-0.7319$ ,  $p=0.003$ ). Incubation with TNF- $\alpha$  decreased the mRNA expression levels of genes involved in lipid (PPAR $\alpha$ , ACADM), glucose (AMPK, HK2) and mitochondrial (FOXO3) metabolism ( $p < 0.0001$ ), and led to impaired myogenesis (MyoD1, Myogenin;  $p=0.047$  and  $p=0.031$ ; respectively). In addition, an increased cellular senescence, as evidenced by SA- $\beta$ -gal activity and p53 acetylation ( $p < 0.05$ ) was apparent and accompanied by increased secretions of IL-1 $\beta$ , IL-6, IL-10 and IFN- $\gamma$  (Meso Scale Discovery;  $p < 0.05$ ). TNF- $\alpha$  treatment partially restored the siAdipoR1-induced delay in myoblast proliferation ( $p < 0.001$ ).

**Conclusion:** Primary CHF muscle cells exhibited characteristics typical to in vivo skeletal muscles of CHF patients including a conserved adiponectin resistance. Silencing of AdipoR1 attenuated the proliferation of muscle cells and the activation of AMPK. In contrast, inflammation induced impairment of adiponectin signalling, myogenesis and mitochondrial biogenesis, suggesting that an increased inflammatory constitution contributes to adiponectin resistance and skeletal muscle dysfunction in CHF patients.

#### P1167

##### **Metabolic reprogramming as therapeutic strategy to ameliorate skeletal muscle tissue engineering procedures**

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**Background:** Stem cells and regenerative medicine raise great expectations because of the promise to reconstitute aged, injured and diseased tissues. While success has been achieved for hematological and epithelial diseases, several hurdles remain for diseases affecting skeletal and cardiac muscle. Maximizing the survival and the myogenic activity of the engrafted cells used for tissue engineering by preconditioning with suitable bioactive molecules would allow better therapeutic outcomes. Notably, energy management and metabolic reprogramming seem to play a key role in stem cell differentiation. We, therefore, propose that myogenic precursors preconditioning by metabolic shift induction might potentiate and ameliorate the efficacy of reconstructive muscular tissue strategies.

**Methodology:** We will evaluate the effect of metabolic reprogramming on stem cell myogenic capabilities and survival and on 3D artificial muscle generation in vitro and in vivo.

**Results:** Our data show that TMZ exert a profound effect on stem cells, altering their gene expression profile. It stimulates differentiation of both C2C12 and satellite cells as shown by enhanced expression of muscle-specific genes and proteins and by higher myotube size and fusion index. Moreover we developed a biotechnology demonstrating the possibility to build in vitro and in vivo a complete and functional artificial muscle in mice.

**Conclusions:** We expect to select metabolic remodeling agents able to improve the generation and implantation of artificial muscles. We will also clarify the key metabolic changes occurring during muscle differentiation, and this will allow further specific therapeutic approaches for muscle replacement.

#### P1168

##### **Megestrol acetate improves cardiac function in a model of cancer-cachexia induced cardiomyopathy by autophagic modulation**

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**Background:** Cachexia is a complex metabolic syndrome associated with cancer. One of the features of cachexia is the loss of muscle mass, characterized by disbalance of protein synthesis and protein degradation. Muscle atrophy is due to hyperactivation of the main cellular catabolic pathways, including autophagy. Cachexia also affects cardiac muscle and the atrophy of the heart impairs cardiac function and is likely to contribute to mortality. Anti-cachectic therapy in patients with cancer cachexia is so far limited to nutritional support and anabolic steroids. The use of the appetite stimulant megestrol acetate (MA) has been discussed as a treatment for cachexia.

**Methods:** In this study the effects of MA were tested in cachectic tumour-bearing rats (Yoshida AH-130 ascites hepatoma). Rats were treated with 100mg/kg/d MA or placebo starting one day after tumor-inoculation for 16 days. Body weight and body composition were assessed at baseline and at the end of the study. Cardiac function was analyzed by echocardiography at baseline and day 11. Locomotor activity and food intake were assessed before tumor inoculation and at day 11. Autophagic markers were assessed in gastrocnemius muscle and heart by western blot analysis.

**Results:** Treatment with 100mg/kg/d MA significantly attenuated the loss of body weight ( $-9 \pm 12\%$ ,  $p < 0.05$ ) and the wasting of lean and fat mass ( $-7.0 \pm 6\%$  and  $-22.4 \pm 3\%$ ,  $p < 0.001$  and  $p < 0.05$  respectively). Administration of 100mg/kg/d MA significantly protected heart from general atrophy ( $633.8 \pm 30$  mg vs placebo  $776 \pm 10$  mg,  $p < 0.001$ ). Tumor-bearing rats displayed cardiac dysfunction, e.g. left ventricular ejection fraction (LVEF), left ventricular fractional shortening (LVFS), the stroke volume (LVSV), the end diastolic volume (LVEDV) and the end systolic volume (LVESV) were significantly impaired in tumour-bearing rats. MA significantly improved LVEF, LVFS and LVESV. Western blotting analysis showed an upregulation of the autophagic pathway in gastrocnemius and hearts of tumor-bearing rats. MA was able to modulate the autophagic markers (e.g. Beclin-1, p62, TRAF-6 and LC3) in the gastrocnemius and in the hearts of tumor-bearing rats. Most importantly, 100mg/kg/d MA reduced mortality (HR: 0.44; 95%CI: 0.20-1.00;  $p = 0.0486$ ).

**Conclusions:** MA improved survival and reduced wasting through a marked down-regulation of autophagy, occurring in both skeletal and heart muscle, the latter effect leading to a significant improvement of cardiac function. Our data suggest that MA might represent a valuable strategy to counteract the development of cancer cachexia-induced cardiomyopathy.

#### P1169

##### Mineralocorticoid receptor activation affects skeletal muscle development and metabolism.

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**Background:** It's known that Mineralocorticoid Receptor (MR) activation affects adipocytes differentiation and function and we showed that MR antagonism is able to improve insulin-stimulated glucose uptake in a mouse model of diet-induced obesity and insulin resistance. Adipose tissue secretome shows a paracrine effect on vascular system and cardiac function, as well as on skeletal muscle metabolism. Interestingly, MR blockade is able to affect skeletal muscle metabolism, improving insulin signaling. In addition, renin-angiotensin-aldosterone system (RAAS) activation, through MR-dependent mechanisms, leads to skeletal muscle atrophy in mice.

**Purpose:** Our aim is to evaluate a possible involvement of MR activation in regulating skeletal muscle differentiation and function in vitro and in vivo.

**Methods:** We investigated the involvement of MR in regulating murine skeletal muscle cells (C2C12) differentiation 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 characterized the ontogenesis of MR in a murine myoblast cell line (C2C12) by RT-PCR and western blot analyses in order to evaluate the expression of MR during myotubes differentiation in vitro. We observed an increase in MR protein expression in skeletal myotubes during differentiation (96h). To evaluate the effects of MR activity on C2C12 cells, we treated C2C12 myoblasts, after differentiation stimulus, with aldosterone (Aldo, 10<sup>-8</sup> mol/L) for 6h and 24h and we observed that Aldo significantly reduced 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, tyrosinephosphorylated IRS-1, GLUT4 levels mRNA expression and Akt phosphorylation. Interestingly, we observed improved soleus muscle insulin signaling 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 and insulin sensitivity, which suggest a potential application of MR antagonists to improve skeletal muscle function.

#### P1170

##### Myocardial iron content and mitochondrial function in heart failure

supported by GACR GA15-1400S  
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**Background:** Iron replacement improves clinical status in iron-deficient patients with heart failure (HF), but the pathophysiology is poorly understood. Iron is essential not only for erythropoiesis, but also for cellular bioenergetics. The impact of

myocardial iron depletion (MID) on mitochondrial function, measured directly in the failing human heart, is unknown. We hypothesized that myocardial iron content is decreased in HF patients and that HF with MID is associated with mitochondrial dysfunction.

**Methods:** LV samples were obtained from 91 consecutive HF patients undergoing transplantation and 38 HF-free organ donors (controls). Total myocardial iron was measured by inductively-coupled mass spectrometry in lyophilized samples. High-resolution respirometry, citric acid cycle and respiratory chain enzyme activities, respiratory chain components (complex I-V) and ROS-protective enzymes protein expression were measured in tissue homogenates to quantify mitochondrial function.

**Results:** Myocardial iron content was 22% lower in HF compared to controls ( $156 \pm 41$  vs  $200 \pm 38$   $\mu\text{g/g}$  dry weight,  $p < 0.001$ ). MID was present in 22% of HF patients and was associated with more extensive coronary disease, less beta-blocker usage and longer HF duration compared to non-MID HF patients. Compared to controls, HF patients displayed reduced myocardial O<sub>2</sub> respiration and reduced activity of all examined mitochondrial enzymes (all  $p < 0.001$ ). Myocardial iron correlated with aconitase and citrate synthase activity in HF patients. MID in HF was associated with reduced aconitase and citrate synthase (by -27% and -16%,  $p < 0.05$ ), preserved activity of respiratory chain oxidoreductases, but reduced expression of respiratory chain complexes III and V, catalase and glutathione peroxidase.

**Conclusions:** Myocardial iron content is systematically decreased in advanced HF. Myocardial iron deficiency is associated with mitochondrial dysfunction. These relations may lead to reduced substrate flexibility, impaired energy production and diminished ROS-defense in iron-deficient failing myocardium.

#### P1171

##### New oral anticoagulants in heart failure

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**Background/Introduction:** Anemia and iron deficiency is associated with a high risk of poor outcomes in patients with heart failure, especially those using oral anticoagulants. Anemia is common in heart failure but nevertheless is associated with poor outcomes.

**Purpose:** This study is aimed to evaluate whether the new oral anticoagulants (NOAC) – apixaban, rivaroxaban and dabigatran-, are less or more related to iron deficiency and anemia compared to classical oral anticoagulants: vitamin K antagonists(VKAs) and thus if they contribute to the patients outcomes?

**Methods:** A total 108 patients admitted consecutively in our clinic were evaluated during hospitalization and after discharge periodically. Patients included had the discharge diagnosis from our clinic: heart failure and anemia. The patients were divided into 3 groups, depending on whether they used NOAC or VKAs or none: 45 patients (41.66%) were using VKAs, 37 patients (34.26%) were on NOAC, while 26 patients (24.04%) used neither one. Among the first group, 8 patients (21.62%) used rivaroxaban, 12 patients (32.43%) used apixaban and 17 patients (45.94%) used dabigatran. A follow up time of 2 years proved that patients using NOAC versus VKAs had poor outcomes. The endpoint assessed in our study were: NYHA decompensation, iron deficiency, stroke, myocardial infarction, peripheral arterial disease, tromboembolism, renal failure and mortality.

**Results:** The use of NOAC(27.21%) are less related to iron deficiency and anemia compared to group using VKAs (43.64%). Two year mortality rate was significantly reduced in patients with NOAC versus VKAs (12.73% versus 31.42%,  $p < 0.001$ ). The other composit endpoints showed no significant differences between the compared groups. Anemia is an independent risk factor for heart failure. The role of anemia is controversial but it is linked to other risk factors /comorbidities.

**Conclusion(s):** NOAC are more safer and proven their efficacy better than VKAs which are more related with anemia and have poor outcomes. Patient using oral anticoagulants should be monitored often, every 2 months for iron deficiency and anemia.

#### P1172

##### Anemia in heart failure

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**Background/Introduction:** Anemia is an independent risk factor for heart failure patients. It is proven to be linked to other risk factors or to other comorbidities. Anemia is common in heart failure but nevertheless is associated with poor outcomes.

**Purpose:** Quality of life in heart failure patients is reduced compared with that of patients who suffer from other comorbidities like: hypertension, diabetes mellitus, stroke patients, parkinson disease, renal failure.

**Methods:** A total of 517 patients admitted consecutively in our clinic were evaluated during hospitalization and after discharge periodically. The patients included

had heart failure and anemia or iron deficiency. The follow-up periode of 4.2 years performed included surveillance and a quality of life questionnaire completed by the patient. Blood test were performed for a more accurate stratification (hemoglobin, hematocrit, iron level, red blood cells size and color, ferritin and transferin saturation).

**Results:** Patients expressed their physical symptoms and functional limitations associated with chronic heart failure through symptoms like: shortness of breath (21.64%), fatigue (22.61%), pulmonary rales (16.38%), leg oedema (19.23%) decrease in effort capacity (20.14%). The scores assessed (from the quality of life questionnaire) outline a depreciated life quality compared to patients with other comorbidities.

**Conclusion(s):** Anemia turned out to be an ominous sign in patients with chronic heart failure. Chronic heart failure patients strongly express their desire in improving: life, effort intolerance, physical and psychological capacity (score) and functional status.

**P1173**

**The reduction of central sleep apnea severity in the left lateral position is not due to an improvement in cardiac hemodynamics in patients with chronic heart failure**

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**Background:** Moderate-to-severe central sleep apnea (CSA) affects about one-third of patients with chronic heart failure (CHF) and systolic dysfunction. CSA severity markedly decreases moving from the supine to the lateral position, with no difference between the left and the right position, but the mechanisms have not been fully defined.

**Purpose:** We tested the hypothesis that CSA attenuation in the left lateral position is due, at least in part, to an improvement in cardiac hemodynamics.

**Methods:** 16 clinically stable CHF patients (male, age: 60 ± 7, NYHA class: 2.6 ± 0.5, EF: 30 ± 5 %) with CSA and an apnea-hypopnea index ≥ 15 events/h were studied. Each subject underwent two consecutive echo-Doppler examinations in random order, one in the left lateral (90°) and the other in the supine (0°) position. The following parameters were investigated: left ventricular end-diastolic volume, (LVEDV), left atrial volume (LAV), ejection fraction (EF), mitral regurgitation (0-4) (Mitr\_Reg), cardiac output (CO), deceleration time (DT), E/e' ratio, right atrial volume (RAV), tricuspid annular plane systolic excursion (TAPSE) and right ventricular-atrial gradient (Right\_VA\_grad). Results. As shown in the table below, we found a general trend, albeit of modest clinical relevance, towards worse hemodynamics in the left lateral position.

**Conclusions:** This study shows that the reduction of CSA severity from the supine to the left lateral position in patients with CHF is not due to an improvement in cardiac hemodynamics as assessed by echo-Doppler. Other factors, particularly position-induced changes in lung volumes, might be the main cause.

Table 1

	Supine position	Left lateral position	P
LVEDV (ml)	196 ± 66	202 ± 75	0.41
LAV (ml)	108 ± 39	117 ± 43	0.037
EF (%)	32.3 ± 5.9	29.6 ± 5.2	0.031
Mitr_Reg	1.0 ± 0.8	1.2 ± 0.9	0.041
CO (l/min)	4.4 ± 1.0	4.2 ± 1.1	0.71
DT (ms)	175 ± 49	171 ± 63	0.75
E/e'	13.3 ± 4.1	16.2 ± 5.3	0.023
RAV (ml)	60 ± 22	70 ± 23	0.003
TAPSE (mm)	21.8 ± 7.1	19.5 ± 5.1	0.035
Right_VA_grad	24.8 ± 12.6	26.5 ± 11.6	0.048

**BASIC SCIENCE: CYTOKINES AND INFLAMMATION**

**P1174**

**Acute exercise-induced response of monocyte subtypes and relation to endothelial function in heart failure with preserved ejection fraction**

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**Background:** Exercise intolerance is the main symptom of heart failure (HF) with preserved ejection fraction (HFpEF). Training improves symptoms, but underlying mechanisms are obscure. Recently, endothelial dysfunction was advocated as primum movens in HFpEF pathophysiology. Monocytes play a crucial role in low-grade vascular inflammation causing endothelial dysfunction, associated with prognosis in HF.

**Purpose:** In untrained HFpEF patients, we aimed to evaluate the effect of an acute exercise bout on (1) endothelial function and (2) levels of circulating monocyte subtypes.

**Methods:** Nine HFpEF patients were included. Before and after a maximal cardiopulmonary exercise test (CPET), microvascular endothelial function was measured using Framingham reactive hyperaemia index (FRHI). Also, monocyte subtypes were quantified by flow cytometry: CD14++CD16-CCR2+ (phagocytic Mon1), CD14++CD16+CCR2+ (intermediate Mon2), and CD14+CD16++CCR2- (patrolling Mon3). Data are reported as median (interquartile range).

**Results:** Patients were predominantly female (66,7%), elderly, obese and hypertensive. Peak oxygen uptake was 13,9 (12,1-16,8) ml/kg/min and maximum workload was 60 (60-75) watts, indicating severely impaired exercise capacity. FRHI, monocyte count and subtypes at baseline and after CPET are reported in Table 1. Endothelial function was impaired (FRHI ≤ 0,51) in 77,8% at baseline, and improved significantly after CPET. Baseline absolute monocyte count was normal (reference 200-1000 cells/μL) and showed a trend towards increase after CPET. Proportionally, Mon2 increased at the expense of Mon1, while Mon3 remained unchanged.

**Conclusion:** Endothelial dysfunction is a characteristic of HFpEF. After an acute exercise bout, endothelial function improves. This improvement is associated with a change to a less inflammatory profile in monocytes. These findings point towards a role for monocyte subtypes in vascular inflammation and endothelial dysfunction in HFpEF.

Results	Before exercise	After exercise	% Change	P value before-after comparison
Monocyte count (cells/μL)	380 (320 - 540)	490 (365 - 580)	+ 19,2 (-6,6 - 31,2)	0,078
Mon1 (% of monocytes)	83,9 (77,3 - 90,1)	82,1 (73,0 - 84,5)	-3,7 (-6,5 - 1,2)	0,012
Mon2 (% of monocytes)	6,2 (4,7 - 6,6)	8,4 (4,7 - 13,2)	+ 32,1 (4,5 - 79,2)	0,020
Mon3 (% of monocytes)	10,8 (5,5 - 16,2)	12,2 (6,8 - 13,9)	+ 13,1 (1,0 - 36,6)	0,164
FRHI	0,30 (0,07 - 0,53)	0,67 (0,36 - 1,00)	+ 134 (-3 - 214)	0,020
Mon1: CD14++CD16-CCR2+, Mon2: CD14++CD16+CCR2+, Mon3: CD14+CD16++CCR2-, FRHI: Framingham reactive hyperemia index.				

**P1175**

**Proinflammatory cytokines and heart rate variability in women with coronary heart disease**

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Examine the level of proinflammatory cytokines and time parameters of heart rate variability in coronary heart disease (CHD) due to minimal thyroid insufficiency, a comparative analysis of structural - functional parameters of heart disease in women with the content of thyroid stimulating hormone (TSH) 0.5-2.0 mU / l and 2,1-4,2 mU/l.

**Materials and methods:** Formed two groups (gr.) of women with CHD: 1 - 35 gr. with TSH 0.5-2.0 mU/l, 2 gr. -30 with TSH 2,1-4,2 mU/l, 52,4 ± 6,7 years. All surveyed, except for general clinical studies conducted ECG monitoring using complex 'Astrocard' (Moscow) with the same software; rate variability was determined by the daily ECG. And echocardiography with measurement of the basic structural and functional parameters. For the quantitative determination of tumor necrosis factor alpha (TNF-alpha), interleukin1 (IL-1) and interleukin6 (IL-6).

**Results:** In the group with TSH levels > 2,0mU/l compared with women with TSH 0.5-2.0 mU/l end-diastolic dimension (EDD) is 12% higher (p = 0.001), interventricular septum 14% thicker (p = 0.0034), the rear wall of the left ventricle at 10% thinner (p = 0.046). When comparing transmitral flow in women with high normal TSH levels (gr. 2), the median value of blood flow velocity in the late diastolic filling (peak



A) above by 10% ( $p=0.04$ ), time slowing blood flow early diastolic filling (DTE) is higher by 14% ( $p=0.04$ ), and left ventricular isovolumic relaxation time higher by 12% ( $p=0.001$ ) compared with 1 group of women. Revealed a weak correlation between the level of TSH and KDR ( $r=0.17$ ,  $p=0.049$ ), and between level svT4 and DTE ( $r=0.28$ ,  $p=0.038$ ). Violations of the autonomic regulation of the heart rate group 2 patients showed pronounced declines in SDNN and SDANN. All surveyed CHD patients with TSH  $> 2,0\text{mU/l}$  there was a significant increase in levels of circulating pro-inflammatory cytokines IL-1, IL-6 and TNF-alpha, compared to patients with ischemic heart disease  $0,5-2,0\text{mU/l}$  ( $p < 0,01$ ).

**Conclusions:** CHD with decreased thyroid activity is accompanied by disorders of the autonomic regulation of the heart rate with a reduction in the absolute values of the time parameters of heart rate variability, as well as overproduction of proinflammatory cytokines IL-1, IL-6, TNF-alpha. A structural and hemodynamic changes in heart begin with TSH levels  $> 2,0\text{mU/l}$ , which gives reason to believe such a minimum level of TSH thyroid insufficiency, affects the course of CHD in women and the development of measures to prevent the early development of heart failure.

#### P1176

##### Exposure to CXCL12 prolongs naive CD4+ T lymphocytes survival.

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**Background/Introduction:** Naive T lymphocytes recirculate through the body, traveling from secondary lymphoid organs through tissues and via lymphatic vessels and peripheral blood into other secondary lymphoid organs and into the bone marrow. In these tissues, lymphocytes are exposed to the chemokine CXCL-12 (also known as SDF-1) which is abundantly produced in bone marrow and in lymph nodes by stromal cells. CXCL12 is known to drive lymphocytes chemotaxis, and in other cells types such as stem cells an antiapoptotic effect has been described.

**Purpose:** Here we analyzed the effect of CXCL12 exposure on naive CD4+ T lymphocytes cultured in a nutrient poor medium.

**Methods:** CD4+ naive T cells were purified from peripheral blood by immunomagnetic negative isolation, and were cultured in 2% FBS for up to 9 days in presence or not of CXCL12.

**Results:** CXCL12 exposed cells survived longer than untreated lymphocytes, as at day 7 living CXCL12 treated cells were 52% versus 27% in untreated controls ( $p < 0.001$ ). This pro-survival effect was specific for resting naive lymphocytes, as in vitro activated lymphoblasts, both treated or not with CXCL12 died rapidly by day 3. The increased percentage of living cells observed was not due to proliferation, as we did not observe a costimulatory effect of CXCL12. The pro-survival effect seems to be mediated by PKA-dependent CREB activation, and consequent increased expression of the antiapoptotic factor Bcl2, that, together with BclXL, could account for the prolonged lifespan of CXCL-12 exposed naive T lymphocytes.

**Conclusion(s):** This previously unreported activity of CXCL12 could contribute in vivo to the maintenance of the naive T lymphocytes pool.

## BASIC SCIENCE: HYPERTENSION / LV HYPERTROPHY / RENAL DENERVATION

#### P1177

##### Inhibition of long noncoding RNA Chast prevents pressure-overload induced cardiac hypertrophy

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**Purpose:** Long noncoding 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 and to translate these findings into a therapeutic strategy.

**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 cardiomyocytes after transverse aortic constriction. Modulation of the pro-hypertrophic calcineurin-NFAT pathway and chromatin immunoprecipitation revealed that NFAT is a direct inducer of Chast expression. Further, overexpression of Chast was sufficient to enhance cardiomyocyte hypertrophy in vitro and in vivo, since this

transcript provokes cardiomyocyte growth and pro-hypertrophic gene expression. LncRNA-pulldown assays identified a number of cardiac hypertrophy relevant interaction partners that are likely to be involved in the pathological remodeling process. Consequently, pharmacological inhibition of Chast ameliorated pressure-overload induced hypertrophy and protected murine hearts from cardiac remodeling and heart failure. Structure-sequence alignments to the human genome indicated a central conserved sequence. Examining the expression in hypertrophic human heart tissue from aortic stenosis patients and healthy controls, this transcript revealed a strong upregulation in diseased hearts, indicating a conserved function of Chast.

**Conclusions:** Based on a genome-wide lncRNA profiling we identified the novel lncRNA Chast that promotes cardiomyocyte hypertrophy. Targeting this transcript in vivo represents a promising therapeutic approach for the treatment of heart failure.

#### P1178

##### Pivotal role of regulator of G-protein signaling 12 in pathological cardiac hypertrophy

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**Background:** Cardiac hypertrophy is a major predictor of heart failure and is regulated by diverse signaling pathways. As a typical multi-domain member of the regulator of G-protein signaling (RGS) family, RGS12 plays a regulatory role in various signaling pathways. However, the precise effect of RGS12 on cardiac hypertrophy remains largely unknown.

**Purpose:** This study aims to explore the role of RGS12 in the development of cardiac hypertrophy and heart failure.

**Methods:** We generated genetically engineered mice and neonatal rat cardiomyocytes (NRCMs) to investigate the effects of RGS12 in cardiac hypertrophy. Echocardiography as well as pathological and biochemical analyses were performed to determine the extent of cardiac adverse remodeling triggered by hypertrophic stimuli. Subsequently, western blots and rescue experiments were performed to explore the signaling pathways responsible for RGS12-mediated cardiac hypertrophy. Furthermore, co-immunoprecipitation experiments were performed to confirm the association between RGS12 and MEK1/2 in NRCMs.

**Results:** Four weeks after aortic banding, RGS12 deficiency prevented cardiac hypertrophy with preserved fractional shortening ( $43.0 \pm 3.4\%$  versus  $28.4 \pm 2.2\%$  in control mice;  $P < 0.05$ ), whereas RGS12-overexpressing mice exhibited exaggerated cardiac hypertrophy and reduced fractional shortening ( $20.8 \pm 4.1\%$  versus  $28.6 \pm 3.2\%$  in wild type mice;  $P < 0.05$ ). Similarly, after angiotensin II administration, the cell surface area was decreased in NRCMs infected with AdshRGS12 ( $1442.2 \pm 154.1 \mu\text{m}^2$  versus  $2389.0 \pm 220.4 \mu\text{m}^2$  in AdshRNA infected NRCMs;  $P < 0.05$ ), but further increased in NRCMs infected with AdRGS12 ( $3437.9 \pm 430.2 \mu\text{m}^2$  versus  $2524.0 \pm 337.8 \mu\text{m}^2$  in AdGFP infected NRCMs;  $P < 0.05$ ). Mechanistically, our data indicated that the activation of MEK1/2-ERK1/2 signaling may be responsible for the pro-hypertrophic action of RGS12. Furthermore, a physical interaction between RGS12 and MEK1/2 was identified by co-immunoprecipitation experiments.

**Conclusion:** We provide the first evidence that RGS12 contributes to pathological cardiac hypertrophy by augmenting MEK1/2-ERK1/2 signaling pathways. Therefore, RGS12 may represent a novel diagnostic and therapeutic target for pathological cardiac hypertrophy and heart failure.

#### P1179

##### EMAP II reduces arterial stiffness and end-diastolic myocardial stiffness in hypertension and diabetes

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Endothelial monocyte-activating polypeptide-II (EMAP-II) plays an important role in the development of inflammation, apoptosis and angiogenesis and is able to increase blood tissue barrier permeability. It studied as an antitumor agent. On the other hand, EMAP II is able to stimulate the expression of inducible NOS (iNOS) and increase endothelium- and NO-dependent dilatation, that increase the synthesis of NO. Continuous growth of hypertension and diabetes leads to an increased prevalence of Coronary artery disease.

The aim of work was to investigate whether EMAP II could improve heart function in spontaneously hypertensive rats (SHR) and streptozotocin-induced diabetic rats. Rats were divided into control, diabetic, and SHR groups. The functional cardio-hemodynamic indicators registered via Pressure-Volume System. The recombinant endothelial monocyte activating polypeptide II -EMAP II ( $0,85\text{mg}$  in  $10 \mu\text{l}$ ) was administered intravenously.

It was shown that after EMAP II end-diastolic pressure in streptozotocin-induced diabetic rats was decreased by 25,4%. End-systolic and end-diastolic pressure of SHR didn't change. After EMAP II the end-diastolic myocardial stiffness reduced in 4,7 times in SHR, the end-diastolic myocardial stiffness decreased by 25,5% in streptozotocin - induced diabetic rats. In SHR after treatment with EMAP II, arterial

stiffness decreased by 23.2%, in streptozotocin-induced diabetic rats, arterial stiffness was decreased by 26.3% ( $P < 0.05$ ).

Thus, EMAP II improves pathological features of heart function in SHR and streptozotocin-induced diabetic rats. The positive effect of EMAP II in hypertension and streptozotocin-induced diabetes was in the decrease of arterial stiffness and end-diastolic myocardial stiffness.

#### P1180

##### Cardiovascular remodelling in L-NAME-induced hypertension: effect of ivabradine

VEGA 1/0071/15, VEGA 2/0195/15, UK/96/2015

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**Introduction:** Ivabradine reduces heart rate via If channel-inhibition in the sinoatrial node. In the SHIFT study, ivabradine reduced CV morbidity and mortality in heart failure. Beside bradycardic effect, ivabradine may achieve part of its protective cardiovascular benefit by its potential antiremodelling action. The aim of the study was to show the effect of ivabradine on blood pressure, heart rate (HR), left ventricular (LV) remodelling and LV function in L-NAME-hypertension.

**Material and methods:** 30 male Wistar rats were divided into 4 groups: control (C), ivabradine (10 mg/kg/day, Iv), L-NAME (40 mg/kg/day, L-NAME) and L-NAME+ivabradine (L-NAME+Iv). Systolic BP and HR were measured once a week (tail-cuff method). After 4 weeks of treatment rats underwent echocardiography. Afterwards rats were killed and LV were removed and processed for biochemical investigation.

**Results:** L-NAME significantly ( $p < 0.05$ ) increased BP, LV weight and slightly increased LV hydroxyproline concentration and content, associated with deterioration of echocardiographic systolic and diastolic LV-function parameters. Ivabradine reduced HR (by 15%), systolic BP (by 8%) and attenuated systolic and diastolic dysfunction of the LV in L-NAME-hypertension. Hemodynamic benefits were associated with partial prevention of LV hypertrophy and fibrosis.

**Conclusions:** Ivabradine prevented LV dysfunction supposedly by reducing HR, BP and myocardial fibrosis.

#### P1181

##### Early diagnostic and correction of syndrome cognitive impairments in arterial hypertension in family doctor practice

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Recently, it was proved the impact of arterial hypertension (AH) on the development of cognitive impairment (CI), which lead to a decrease in quality of life, professional and social exclusion. So far unresolved issue of timely detection and correction of cognitive disorders in patients with hypertension. Objective. Improving the program management of patients with hypertension in the practice of the family doctor for early detection and correction of cognitive impairment syndrome. Methods and materials. The study involved 67 outpatients with controlled hypertension 1-2 stages and impaired cognitive function. The average age of the surveyed amounted to  $53.1 \pm 8.3$  years, the average - AH  $12.4 \pm 6.7$  years. All patients underwent a comprehensive examination protocol for cardiac patients, made additional diagnostic procedures, ambulatory blood pressure monitoring, neuropsychological examination, integrated assessment of cognitive functions on a scale MMSE, quality of life - by the method of "36 health status survey". Patients received a personalized mono- or combination antihypertensive therapy of four major classes of antihypertensive drugs first line, in addition to beta-adrenergic receptors, because the risk of bradycardia when combined with ipidakrin. Additionally, all patients were prescribed nootropic drug - phenibut, dose of 250 mg 3 times a day and 30 are added to the treatment of anticholinergic drugs - ipidakrin 10 mg x 2 times a day. Duration of treatment - 6 weeks. Results. In analyzing the course of hypertension steps 1 and 2 found that even in patients with controlled hypertension against a background of effective non-pharmacological therapy and emerging drug CI: In 34.4% - were light level, in 56.1% - moderate and in 9.5% - mild dementia. In analyzing the structure of CI found that their performance at various levels of higher brain functions meet all cognitive areas of human activity, but suffer neural processes of nature (the ability of concentration, psychomotor speed reactions) and verbal memory. In a further appointment ipidakrin and phenibut combination in patients with hypertension and syndrome of CI recorded significantly better performance integrated intelligence, the positive dynamics in the areas of attention, concentration, reaction speed, verbal memory, levels of reactive and personal anxiety, quality of life compared with patients which additionally used only phenibut. Conclusion. The long-term observation of patients with hypertension in the practice of the family doctor must conduct a

dynamic analysis of cognitive and neuropsychological examination, assessment of cognitive functions integrated on a scale MMSE. Combined therapy of hypertension and CI should include more than antihypertensive and effective nootropic (phenibut) and anticholinergic drugs (ipidakrin), which leads to the correction of cognitive disorders and emotional state, improve the quality of life and level of adaptation in society.

#### P1182

##### Hypertension patients: the cerebral circulation and impairment of cognitive functions

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**Background:** Recent findings were proved the impact of arterial hypertension (AH) on the development of cognitive impairment. Nevertheless, the cognitive disorders and cerebrovascular circulation are less studied in hypertensive patients. The aim of our study was to investigate cognitive function changes and cerebral circulation in hypertensive patients compared to the control group.

**Methods:** In study was included 245 patients with AH 1-2 stages (134 women and 111 men aged 34-69 years, median age -  $53.8 \pm 4.3$  years) and 47 age-matched healthy controls were enrolled. The cerebral blood flow velocities were evaluated by transcranial Doppler. Mean velocity of middle cerebral artery (MCA) was monitored at resting in patients and controls. All patients were examined according to the recommendations of European Society of Cardiology (2013); neuropsychological diagnostics included integrated assessment of cognitive functioning by MMSE scale; assessment of cognitive disorders by Frontal Assessment Battery (FAB) scale; memory - by Luria's method of "Remembering 10 words"; attention and speed of sensory-motor reactions were analyzed by Schulte and Rybakov's technique.

**Results:** We have not found significant differences in mean velocity of MCA in patients with AH compared to controls ( $75.5 \pm 7.2$  m/s vs  $71.2 \pm 6.4$  m/s,  $P > 0.05$ ). Cognitive disorders were revealed in 33.9% patients (49 women and 34 men). By MMSE method mild CD (27-26 points) were revealed in 28.9% of patients, and moderate CD (25-24 points) - in 68.7%. Two patients (2.4%) were diagnosed with mild dementia (23 points). Decrease in verbal memory, speed of sensory-motor reactions and impaired ability to concentrate was revealed in 63.8% of patients and in 12.8% of controls.

**Conclusion:** The patients with arterial hypertension 1-2 stages are characterized by the development of mild to moderate cognitive disorders, significantly affecting the quality of life, worsening of efficiency of certain types of work, reducing quality and volume of work performed. Cognitive impairment was more often in patients with arterial hypertension 1-2 stages even without changes in cerebral circulation.

## BASIC SCIENCE: MOLECULAR BIOLOGY / GENETICS

#### P1183

##### Rs2274273 from LGALS-3 locus and cardiac ventricular remodeling after first myocardial infarction: preliminary results

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**Purpose:** Post-myocardial infarction remodeling is characterized by acute loss of myocardium, which leads to changes in heart structure and function. A hallmark of this process is fibrosis formation. Galectin-3 (gal-3), a  $\beta$ -galactoside-binding lectin, promotes fibrosis in multiple organs. It has been suggested to play an important role in the pathophysiology of left ventricular (LV) remodeling after first acute myocardial infarction (AMI). The rs2274273 (C > T) has been most significantly associated with plasma gal-3 levels in the only GWAS of circulating gal-3. Our study aimed to assess the relationship between this SNP and echocardiographic parameters of cardiac remodeling after first AMI.

**Methods:** 167 patients (mean age,  $55.5 \pm 8.4$ ) who have suffered first AMI were prospectively included in the study. Doppler echocardiography was performed 3 to 5 days after AMI and repeated after 6 months. Genotyping was performed by Taqman real-time PCR.

**Results:** Our results showed that carriers of CC genotype, according to the T allele dominant model (CC vs. CT + TT), had significantly shorter LV diameter in long-axis, at the baseline ( $81.70 \pm 10.24$  vs.  $85.23 \pm 7.66$ , Mann-Whitney U test,  $p = 0.02$ ) and 6 months after ( $83.20 \pm 9.37$  vs.  $85.98 \pm 7.74$ , Mann-Whitney U test,  $p = 0.04$ ), and shorter LV diameter in short-axis, according to the T allele recessive model (CC + CT vs. TT) 6 months after ( $49.40 \pm 6.98$  vs.  $53.29 \pm 5.67$ , Mann-Whitney U test,  $p = 0.02$ ). Carriers of TT genotype, according to the T allele recessive model had larger right ventricle at the baseline ( $33.45 \pm 5.85$  vs.  $36.68 \pm 3.89$ , Student's t-test,  $p = 0.03$ ). Carriers of T allele, according to the T allele dominant model had higher end-diastolic volume at the baseline ( $105.45 \pm 31.27$  vs.  $116.16 \pm 33.28$ , Mann-Whitney U test,  $p = 0.03$ ).

**Conclusions:** Our preliminary results suggest that rs2274273, previously associated with plasma gal-3 levels, might be a significant predictive marker of cardiac ventricular remodeling, after first AMI. Further study on larger sample size should be conducted to replicate and estimate the validity of these preliminary results.

#### P1184

##### The non coding repressor of NFAT (NRON) and its role in heart disease

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Non-coding regulator of NFAT (NRON) inhibits NFAT activation by preventing nuclear export of transcription factor NFAT. In response to increased intracellular Ca<sup>2+</sup> levels, calcineurin dephosphorylates and activates NFAT, while NFAT proteins are rephosphorylated and inactivated by multiple NFAT kinases, such as glycogen-synthase kinase 3 (GSK3), CK1, and dual-specificity tyrosine-phosphorylation regulated kinase 1 (DYRK1) and DYRK2. NRON promotes phosphorylated (inactive) state of NFAT by forming a RNA-protein scaffold complex with NFAT, DYRK2, GSK3, CK1 and IQGAP1. Inhibition of NRON and its interacting partners is essential for efficient NFAT activation. Although the function of NFAT in heart diseases is well established, the role of NRON was never investigated in this context. NRON expression is suppressed in pressure over-loaded murine hearts. Conversely, inhibition of NRON in isolated rat primary cardiomyocytes and cultured mouse HL-1 cells has significantly increased cardiomyocyte size. Interestingly, bioinformatic analysis revealed that NRON and NFAT inhibitory kinases DYRK2 and GSK3 can be targeted by pro-hypertrophic microRNAs such as miR-212/132 implying that NRON's action on NFAT can be modulated by miR-212/132 directly by targeting NRON or indirectly by targeting NRON interacting kinases. During myocardial infarction (MI), intracellular Ca<sup>2+</sup> levels are elevated and NFAT is activated. Consistent with this, NRON expression changes when cytoplasmic Ca<sup>2+</sup> levels are manipulated by treating cells with reagents such as thapsigargin, ionomycin, CPA (cyclopiazonic acid) or PMA (phorbol myristate acetate). Interestingly, DYRK2 expression also paralleled NRON expression, which was significantly reduced in failing hearts, suggesting that NRON may also function of a decoy target for DYRK2 targeting miRNAs such as miR-212/132. To further validate the important role of NRON in heart disease, we generated a NRON knockout mice model. First experiments show that indeed NRON knockout leads to a deregulated NFAT action. The role of NRON needs to be further assessed in detail, by different models for heart failure induction and more sophisticated proteomic methods like SILAC in vivo.

#### P1186

##### Diabetes associated DNA variants relation with prevalent left ventricular hypertrophy and diastolic dysfunction

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**Purpose:** Although diabetes, hyperglycemia and insulin resistance increases risk of future cardiovascular disease (CVD), earlier genetic studies have failed to show associations between diabetes related SNPs and CVD-risk. Here we set out to examine if 43 single-nucleotide polymorphisms (SNPs) with earlier established genome wide association with increased risk of type 2 diabetes (T2D), hyperglycemia and insulin resistance were also associated with prevalent early signs of heart disease as measured by echocardiographical examination (UCG).

**Methods:** We genotyped 43 SNPs in 43 genes that reported genome-wide significant association with T2D, hyperglycemia and insulin resistance traits, in 1792 subjects from the population-based Malmö Preventive Project (MPP) with full UCG data (mean age 68 years; 29% women, 36% prevalent T2D). Logistic regression was used to adjust for covariates (age, sex, systolic and diastolic blood pressure, hypertensive treatment and diabetes status).

**Results:** In the fully adjusted logistic regression analysis common variants in 4 genes were associated (p < 0.05) with increased risk of prevalent diastolic dysfunction (DD) ADAMTS9 (Odds ratio (OR), 1.22, p=0.045), HNF1B (OR, 1.21, p=0.028), JAZF1 (OR, 1.18, p=0.044), TSPAN8 (OR, 1.25, p=0.023) and common variants in 4 genes were associated with decreased risk of prevalent DD HNF1A (OR, 0.77; p=0.011), KLF14 (OR, 0.85, p=0.044), TCF7L2 (OR, 0.81, p=0.018), NOTCH2 (OR, 0.72, p=0.021). The genetic risk scores (GRS) of the 4 SNPs associated with increased risk of DD and the 4 SNPs associated with decreased risk of DD association with prevalent DD were (OR=1.19, 95% CI 1.08-1.32, p=0.001) and (OR=0.82, 95% CI 0.74-0.91, p=1.4x10<sup>-4</sup>), respectively. Furthermore, common variants in 3 genes were associated (p < 0.05) with decreased risk of prevalent left ventricular hypertrophy (LVH) (HNF1A (OR, 0.67, p=0.001), ADAMTS9 (OR, 0.79, p=0.038), GIPR (OR, 0.74, p=0.018). The GRS of these 3 SNPs was also highly significantly associated with decreased LVH risk (OR=0.74, 95% CI 0.64-0.85, p=3.1x10<sup>-5</sup>).

**Conclusion:** Here we show that identified in GWAS T2D and glycemic traits susceptibility loci are associated with both increased and decreased risk of structural heart abnormalities as measured by UCG. Replication of these findings is presently ongoing in an independent Swedish cohort.

#### P1187

##### Impact of KCNJ11 gene polymorphisms of ATP-sensitive potassium channel on left ventricular end-diastolic volume and mass in chronic systolic heart failure

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**Background:** ATP-sensitive potassium channels play an important role in the normal functioning myocardium, especially under stress. Intense physical activity or systemic hypertension in animals with knockout of the KCNJ11 gene, encoding the Kir6.2 pore-forming subunit of these channels lead to the rapid development of heart failure and death. The same consequences can be for single nucleotide polymorphisms in KCNJ11, which can impair the function of the channel.

**Aim:** To investigate KCNJ11 gene polymorphisms of ATP-sensitive potassium channel in relation to echocardiographic parameters in chronic heart failure (CHF) patients (pts).

**Methods:** 98 stable (NYHA II-III) CHF pts of ischemic origin with left ventricular systolic dysfunction (ejection fraction (EF) ≤ 45%) on standard treatment were examined. Echocardiographic data (left ventricular (LV) end-diastolic volume (EDV), LV end-systolic volume (ESV), LV mass, LVEF, left atrium and right ventricle sizes, systolic pulmonary artery pressure) were measured by standard method. KCNJ11 polymorphisms (Val337Ile (rs5215) and Lys23Glu (rs5219)) was genotyped by polymerase chain reaction-restriction fragment length polymorphism analysis.

**Results:** The frequency of Val337Ile genotypes was: Ile/Ile – 40,8% (n=40), Ile/Val – 44,9% (n=44), Val/Val – 14,3% (n=14). The pts with Val/Val genotype had LV mass 362,3 [238,0;392,0] g, which was significantly lower vs Ile/Val pts – 400,2 [288,0;450,0] g, (p=0,037). The frequency of Lys23Glu genotypes was: Glu/Glu – 42,9% (n=42), Lys/Glu – 44,9% (n=44), Lys/Lys – 12,2% (n=12). The pts with Lys/Lys genotype had LV EDV – 170,0 [150,0;210,5] ml and LV mass 335,3 [268,5;365,3] g, these are significantly lower than Lys/Glu group: LV EDV-221,5 [154,5;270,0] ml (p=0,052) and LV mass-428,4 [306,3;460,1] g, (p=0,036).

**Conclusion:** In stable ischemic systolic CHF greater LV EDV is associated with Lys/Glu genotype of Lys23Glu, while greater LV mass is associated with Ile/Val genotype of Val337Ile and Lys/Glu genotype of Lys23Glu of KCNJ11 gene polymorphisms.

#### P1188

##### Gene expression profiling to predict and identify cardiac allograft acute cellular rejection: the GET-study

AREMCAR, Novartis

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**Aims:** Serial invasive endomyocardial biopsies (EMB) for histological grading remain the gold standard for acute cellular rejection (ACR) diagnosis.

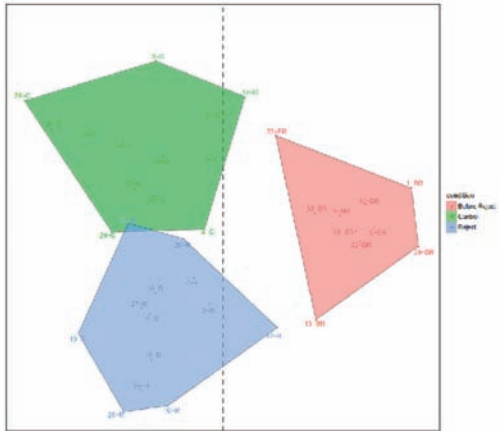
**Purpose.** We aimed to explore the myocardial Gene Expression Profiling (GEP) value for diagnosing and identifying predictive biomarkers of ACR.

**Methods and Results:** A case-control study nested within a retrospective heart transplant patients cohort included 126 patients with median (IQR) age 50.3 (41.2-57.2) years and 111 (88%) males. Among 1157 EBM performed, 467 were eligible (i.e. corresponding to either ISHLT grade 0 or ≥ 3A), among which 36 were selected for GEP according to the grading: 0 (CISHLT, n=13); rejection ≥3A (RISHLT, n=13); 0 one month before ACR (BRISHLT, n=10). We found 294 genes differentially expressed between CISHLT and RISHLT, mainly involved in immune activation, and inflammation. Hierarchical clustering showed a clear segregation of CISHLT and RISHLT groups and heterogeneity of GEP within RISHLT. All BEM presented immune activation, but some RISHLT BEM were strongly subject to inflammation, whereas others, closer to CISHLT, were characterized by structural modifications with lower inflammation level. We identified 15 probes significantly



different between BRISHLT and CISHLT, including the gene of the muscular protein TTN. This result consolidates the concept of structural alterations preceding inflammation in ACR. Using a Linear Discriminant Analysis based on these 15 probes, we identified the histological status of every 36 EMB.

**Conclusion:** Myocardial GEP is a helpful method to accurately diagnose ACR, and predict rejection one month before its histological occurrence. These results should be considered in cardiac allograft recipients' care.



LDA of C, R and BR samples (GET-study)

#### P1189

##### The right ventricle molecular changes associated with pulmonary arterial hypertension are attenuated by Urocortin-2 treatment

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Pulmonary arterial hypertension (PAH) leads to right ventricular (RV) failure and death. Urocortin (UCN)-2 is a peptide highly expressed in the cardiovascular system. It was previously shown, in an experimental model of MCT-induced PAH, that UCN-2 treatment is able to restore PAH-induced severe abnormalities in cardiac function and structure. This study investigated the underlying molecular mechanisms to the beneficial effects of UCN-2 in myocardial function, in the same experimental model. Male Wistar rats randomly received monocrotaline (MCT, 60mg/Kg) or vehicle. After 14 days, 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). RV sample collection, for RT-PCR and western blot, was performed 24-25 days after MCT administration. Only significant results (mean ± SEM, p < 0.05) are given.

Molecular analysis showed that expression of UCN-2 and its receptor CRHR2 are altered in MCT animals. In the RV, the UCN-2 levels are increased in MCT animals (MCT vs. CTRL: 2.5 ± 0.9 vs 1.0 ± 0.3AU), while CRHR2 levels are decreased (0.5 ± 0.1 vs 1.0 ± 0.1AU). These values are reversed with UCN-2 treatment (0.5 ± 0.1 and 0.9 ± 0.1AU, respectively). Pathology markers are increased in MCT animals, namely BNP (15.3 ± 2.5 vs 1.0 ± 0.1AU), ET-1 (3.4 ± 0.4 vs 1.0 ± 0.2AU) and HIF-α (1.6 ± 0.3 vs 1.0 ± 0.2AU) and are attenuated or reversed with UCN-2 treatment (6.9 ± 2.1, 1.8 ± 0.6, 1.0 ± 0.1AU, respectively). At the metabolic level, the MCT group showed higher expression of GLUT1 (3.8 ± 0.8 vs 1.0 ± 0.1AU) and lower expression of GLUT4 (0.5 ± 0.1 vs 1.0 ± 0.1AU) when compared to control animals, while in MCT+UCN-2 group, GLUT1 expression is reversed (1.5 ± 0.4 vs 1.0 ± 0.1AU) and GLUT4 expression remained lower (0.6 ± 0.1 vs 1.0 ± 0.1AU). Caspases 3 and 8, two apoptotic markers, are elevated in the MCT animals (3.9 ± 0.6 vs 1.0 ± 0.1AU and 2.8 ± 0.3 vs 1.0 ± 0.2AU, respectively) and are attenuated by UCN-2 treatment (2.0 ± 0.4 and 1.3 ± 0.2AU, respectively). Moreover, we have found decreased expression levels of STAT3, ERK and p38 protein phosphorylation in MCT animals (0.6 ± 0.1, 0.5 ± 0.1 and 0.5 ± 0.2AU), values which were also reversed with UCN-2 treatment (1.0 ± 0.1, 0.9 ± 0.1, 1.1 ± 0.2AU).

In conclusion, we show that UCN-2 treatment is able to restore the changes in expression of markers of cardiac overload, hypertrophy and hypoxia induced by PAH. The beneficial effects of UCN-2 treatment appear to be associated with the modulation of different signaling pathways, namely apoptotic, metabolic, and survival/proliferation pathways.

#### P1190

##### Clinical and prognostic profile of patients with dilated cardiomyopathy caused by mutations in MYBPC3 gene

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**Background:** MYBPC3 mutations are frequent in patients (pts) with hypertrophic cardiomyopathy (HCM), representing 40–50% of all HCM mutations. Mutations in this gene are also found in pts with dilated cardiomyopathy (DCM), accounting for approximately 2% of the cases, where knowledge of genotype-phenotype correlations remains sparse.

**Purpose:** We aimed to describe the clinical course of pts with DCM carrying mutations in MYBPC3 gene.

**Methods:** We evaluated 107 pts with idiopathic DCM (age ≤ 50 years) or familial DCM (irrespective of the age). Detailed clinical data were obtained. Echocardiographic, resting and 24h-ECG and CMR parameters were collected. Molecular analysis included LMNA/C, MYH7, MYBPC3, TNNT2, ACTC1, TPM1, CSRP3, TCAP, SGCD, PLN, MYL3, TNNI3, TAZ and LBD3 genes. Pts with mutations in MYBPC3 gene were comprehensively analyzed.

**Results:** Ten variants in MYBPC3 gene were found in 9 (8.4%) pts (4 men, mean age 52 ± 12 years, 6 cases of familial DCM). None of the variants had been previously described in association with DCM, but six were associated with HCM (Asp75Asn, Gly278Glu, Gly279Ala, Glu441Lys, Arg495Gln and Glu619Lys). Mean age at diagnosis was 44 ± 10 years and symptoms of heart failure (HF) were the initial manifestation in 7 pts. Five pts had previous hospitalization (2 from HF and 3 from arrhythmic causes), two received an ICD and one a CRT device. In 3 pts there was history of heart transplant in a family member and in 2 there was family history of sudden death. Mean LVEDD was 67 ± 3 mm, LVEF 32 ± 10% and in 3 pts there was right ventricular function impairment. Three pts had AF, 5 LBBB and episodes of nonsustained VT (NSVT) were documented in 2. LGE was present also in 2 pts. Three pts exhibited a particular dismal clinical course: a woman with c.1226+6T > C mutation, LVEDD 71 mm and LVEF 18%, AF, LBBB and NSVT, presented 3 HF-hospitalizations, had ICD implantation and eventually died of HF; a man with Arg495Gln mutation, had LVEDD 67 mm and LVEF 32%, extensive LGE, a previous hospitalization from arrhythmic cause, presented aborted cardiac arrest and subsequent ICD implantation; a woman with Ala433Gly mutation presented in NYHA class III, LVEF 15%, LVEDV 212 mL/m<sup>2</sup> and 10 previous HF-hospitalizations. On the other hand, one pts had two MYBPC3 variants (Glu441Lys+Gly279Ala) and another an additional mutation in TNNT2 gene (Ser275Phe) beyond MYBPC3 mutation (Arg44His): both were in NYHA class I and had no congestion; LVEF/LVEDD were 49%/61mm and 45%/51mm and neither had right ventricle impairment; the latter had AF and a previous arrhythmia-related hospitalization.

**Conclusions:** In our population, mutations in MYBPC3 gene appear to be more common than in previous series. Although most of the variants found were previously associated with HCM, a causative role also in DCM seems plausible. Carriers of mutations in MYBPC3 gene present a variable, but in general dismal, clinical course, with very severe outcome in some instances.

#### P1191

##### Grapevine microRNAs in an in vitro model of cell line: new potential insight on their role in the setting of human health.

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**Introduction:** microRNAs, the most abundant class of small-non coding RNA involved in post-transcriptional regulations, are emerging as the next generation "smart" biomarkers and could be helpful in further improving the diagnostic and therapeutic processes of cardiovascular diseases, the major causes of morbidity and mortality of industrialized countries. Growing evidence has indicated that diet-derived miRNAs, might be considered as a nutraceutical compound able to have an active role in human health. However, studies on the potential action of plant miRNAs at cardiac level are still lacking. To date, few experimental models have been built to evaluate the role of plant miRNA administered either in vivo or in vitro in mammalian cell lines.

**Purpose:** aim of this study was to evaluate the effect of miRNA extracted from selected Tuscany Vitis vinifera grapevine on an in vitro model of murine cardiac endothelial cell line (MCEC-1).

**Methods:** small RNAs were extracted from Vitis vinifera berries, cultivar Sangiovese, at last developmental stage (harvest), by a two steps extraction and evaluated for purity and integrity. MCEC-1 line were maintained in DMEM-low glucose supplemented with 10% FBS and seeded for 24 hours. The cells were then transfected with grapevine small RNAs at different doses (5, 20, 50 ng) in triplicate. After 48 hours

of treatment the MTT system was used to evaluate the effects of different doses of small RNA on MCEC-1 cell line. As control MCEC-1 untreated cell line were used. Bioinformatics analyses were carried out to identify putative mammalian targets to the most abundant miRNAs of grapevine berries.

**Results:** grapevine small RNAs treatment increased cells viability in comparison with the control untreated cells. The result showed a significantly viability increased in MCEC-1 treated with a dose of 50 ng small RNA. Even though MCEC-1 treated viability was higher than untreated cells, any statistically significant difference at 5 ng and 20 ng doses were observed. The bioinformatics analysis, supported by manual annotation, identified 36 more abundant grapevine miRNAs in mature Sangiovese berries, for which 141 putative target expressed in MCEC-1 cell line were obtained.

**Conclusion:** in this study we evaluated for the first time the effect of grapevine small RNAs on a model of murine cell line. The experiment allowed observed a positive effect of grapevine small RNAs administration to MCEC-1 viability and to identify the best effective dose. We also reported a preliminary bioinformatics analysis for the identification of putative murine targets to grapevine miRNAs. Our observation reinforce the hypothesis that grapevine miRNAs could represent a novel avenue for nutraceutical approach in the cardiovascular diseases.

#### P1192

##### The ageing and high arterial pressure change IGF-1/miRNA-1 regulation in hypertrophied myocardium of SHR and Wistar rats

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**Purpose:** The miRNA-1 has inhibitory effect on IGF-1, which is known as a potent stimulator of cardiac hypertrophy. The aim of the study was to determine the features of IGF-1/miRNA-1 regulation of the cardiac hypertrophy development under high arterial pressure and in ageing.

**Methods:** The experiments were performed in male Wistar rats and SHR 6 or 18 months in age. In young rats, left ventricular (LV) hypertrophy was induced by low dose isoprenaline (ISO) injections for 7 days. Control rats treated NaCl saline. In all groups, parameters of heart function were investigated using the ultra-small catheter 2F ("Millar Instruments", USA). The samples of heart LV tissue were collected from narcotized rats in the dynamics of the experiments, and were assayed using morphological methods. The levels of mRNA, miRNA or protein expression were estimated by real time PCR and WestBlot.

**Results:** After ISO injections, the progressive LV hypertrophy was revealed in both lines of young animals. The parameters of heart function and structural rebuilding in rats were typical for heart remodeling and these changes were strongly pronounced in SHR. The old rats, especially SHR, showed the development of the first stage of a pathological heart remodeling including myocardial hypertrophy, fibrosis and diastolic and pumping dysfunction. Furthermore, it was found that initial IGF-1 protein expression was higher in SHR than in Wistar rats. Maximal induction of IGF-1 protein was found in third day of ISO application. In opposite, IGF-1 mRNA expression was prevailing in Wistar rats, and it was reduced in third day of the treatment. The expression of miRNA-1 was also changed showing the dynamic of its reciprocal regulation with IGF-1. During ISO treatment, SHR demonstrated a lower levels of IGF-1 mRNA and protein than Wistar rats that indicates the presence of inhibitory effect of miRNA-1. In old rats, the decrease of miRNA-1 expression levels was found.

**Conclusions:** The data obtained indicate that significant changes in miRNA-1 expression occur in heart due to pressure afterloading and senescence. These changes lead to reciprocal modulation of IGF-1 mRNA and protein level followed by cardiac remodeling. Dynamic of these changes during LV hypertrophy development confirms the presence of phase regulation of IGF-1 by miRNA-1 at the translation level. High arterial pressure in SHR leads to intensification of inhibitory translational regulation of IGF-1 in LV. In ageing, reduction of miRNA-1 level and its inhibitory effect on IGF-1 may be a factor of the progression of heart failure, especially in SHR.

#### P1193

##### Polymorphisms of GSTT1 is associated with higher risk of chronic heart failure among smokers

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**Background:** Chronic heart failure (CHF) secondary to ischemic heart disease belongs to oxidative disease. Glutathione transferase T1 enzyme (GSTT1) is involved in detoxification of byproducts of tobacco smoke. Around 15-30% of white population doesn't exhibit GSTT1 enzyme activity (GST1 null genotype) because of GSTT1 gene deletion polymorphism. Smoking is a potent source of free radicals and well

known risk factor for coronary disease. Aim: To examine influence of different risk factors and GSTT1 polymorphism on the risk of development CHF.

**Material and methods:** One hundred and twenty patients suffering from CHF were included in the study. The criterion for admission was left ventricular ejection fraction (LVEF)<45%. Sixty nine healthy controls matched for sex and age served as control group. Age, sex, smoking history, hypertension, dyslipidemia, diabetes mellitus and obesity were evaluated as risk factors. GST genetic polymorphism was determined by PCR. Both patients and controls were dichotomized into GSTT1 null and GSTT1 active genotype. Independent factors on CHF risk were evaluated by multiple logistic regression model.

**Results:** Distribution of GSTT1 gene polymorphism did not differ between patients and controls. It corresponded to the results obtained in white population, with 24.2% of participants having GSTT1 null genotype. Among controls, GSTT1 null was found in 23.2%. Hypertension (OR=6.65; CI:2.75-16.30; p<0.05), diabetes (OR=8.88; CI:1.76-14.89; p<0.05), old age (more than 50 year) (OR=5.78; CI:1.35-24.67; p<0.05) and obesity (OR=2.62; CI:1.13-6.08; p<0.05) were independent risk factors for CHF. Smoking wasn't independent risk factors for CHF (OR=1.63; CI:0.79-3.39; p>0.05). GSTT1 null genotype alone wasn't independent risk factor for CHF (OR=1.06; CI:0.52-2.12; p>0.05), but GSTT1 null genotype in smokers was independent risk factor (OR=3.68; CI:1.05-12.89; p<0.05).

**Conclusion:** We conclude that presence of GSTT1 null genotype increases the risk of CHF in smokers.

#### P1194

##### The prognostic value of different allelic distribution of aldosterone synthase receptor in a congestive heart failure caucasian population.

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Blockade of the aldosterone receptor has shown to improve congestive heart failure (CHF) outcomes. Aldosterone synthase is on chromosome 8q22 and exists as a common single nucleotide polymorphism C to T transition for position -344. The C allele determines an increased in aldosterone production more efficiently than T allele.

**Purpose:** to assess the -344T/C polymorphism of the aldosterone synthase promoter in a Caucasian CHF population.

**Methods:** CHF consecutive patients were enrolled. The DNA from peripheral blood was isolated and genotyping for the -344 T/C SNP in the aldosterone synthase gene was performed.

**Results:** on 175 CHF patients (114 male; age 69.9 ± 10.2 years) 61 had a TT genotype (34.9%), CT in 80 (45.7%) and finally a CC in 34 (19.4%). CHF patients were divided into C-group (-CT/CC genotype, 114 subjects) and T-group (-TT genotype, 61 subjects). The two groups did not differ in term of age, non-invasive cardiac output at rest (4 ± 1.4 vs 4.1 ± 0.9 l/min, p=0.7), creatinine plasma level (1.34 ± 0.8 vs 1.24 ± 0.5 mg/dl, p=0.8) or end-systolic or diastolic left ventricle diameter (p=0.6 and p=0.29 respectively), left ventricle ejection fraction (LVEF) (p=0.29) and plasma BNP (p=0.3). C-group patients had a higher degree of disability than T-group (Barthel Index, p=0.004), NYHA class (p=0.02) and a lower cardiac index (p=0.01) (Table 1). The two groups showed a similar clinical outcome at

Table 1. Main clinical features.

	CT/CC genotype (n = 114)	TT genotype (n = 61)
NYHA on admission/ discharge	3 ± 0.7 / 2.1 ± 0.5	2.7 ± 0.7* / 1.8 ± 0.4*
Left Ventricle Ejection Fraction [%] LV end systolic/diastolic diameter[mm](n = 105)	33.3 ± 12 / 46.2 ± 15.1 / 56.4 ± 12.5	35.4 ± 12.5 / 48.2 ± 10.1 / 59.7 ± 10.6
BNP on admission / discharge [pg/ml] (n = 92)	1576.6 ± 1973.8 / 23.6 ± 1171.2	1156.5 ± 1665.4 / 1019.9 ± 795.9
Cardiac Index [l/min/mq] (n = 55)	2.1 ± 0.6	2.4 ± 0.6*
6min walk test discharge[meters](n = 82)	317.3 ± 126.1	315.2 ± 127.4
Barthel index admission / discharge	82.3 ± 25.4 / 88.5 ± 19.5	93.3 ± 10.9* / 98.3 ± 4.9**

\*p < 0.05; \*\* p < 0.01 Pearson Chi2.

48-months follow-up (Kaplan Meier survival curves  $p=0.16$ ; log-rank 1.99) with 22 dead patients (12.6%), no cardiac transplantation and 15 (8.6%) readmission to hospital for an acute decompensated heart failure.

**Conclusions:** in Caucasian patients the C allele (CC or CT) at -344T/C SNP in aldosterone synthase gene does not significantly influence clinical prognosis of CHF.

#### P1195

##### Molecular characterization of portuguese patients with dilated cardiomyopathy

PTDC/BIM-MEC/0650/2012

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**Introduction:** Dilated cardiomyopathy (DCM) affects 1:2500 adults. Familial forms account for 30-50% of all the cases and autosomal-dominant inheritance is the dominant pattern of transmission. Mutations were identified in several genes and molecular diagnosis appears to have implications for clinical practice, genetic counseling and risk stratification.

**Purpose:** We intend to estimate the frequency and molecular basis of familial and idiopathic cases of DCM in Portugal.

**Methods:** Multicentric study of unrelated familial and idiopathic DCM patients (pts). Detailed clinical data were obtained. Search for mutations in LMNA/C, MYH7, MYBPC3, TNNT2, ACTC1, TPM1, CSRP3, TCAP, SGCD and PLN, MYL2, MYL3, TNNI3, TAZ, LDB3 genes was performed, using PCR technique with direct-sequencing (NGS with at-least a 30-fold coverage combined with Sanger sequencing). Pathogenicity was assessed by comparisons with mutations previously described, functional tests and segregation studies.

**Results:** 107 pts were included, 59% men, mean age at diagnosis  $38 \pm 13$  years, with 45% of familial cases. Mean LVTD was  $64 \pm 9$ mm and LVEF  $31 \pm 11$ %. Most pts were in NYHA class I (48%). Atrial fibrillation, left bundle branch block and non-sustained VT were present in 11%, 26% and 26% pts, respectively. ICD was implanted in 27%, CRT in 11% and conventional pacemaker in 6%. Previous hospitalization from heart failure was documented in 39% and from arrhythmic cause in 20% of pts, and heart transplantation was performed in 10% of pts. Familial history of sudden death was present in 24%. In total, 34 rare variants, in 8 genes, were identified in 28 (26%) pts, most in MYBPC3, TNNT2 and LMNA genes. Four pts had 2 mutations (in same or different genes) and one pts had 3 mutations in LMNA. Diagnosis yield was higher in familial cases (33% vs 22%). Only one variant had been previously associated with DCM (LMNA) and 8 with hypertrophic cardiomyopathy (2 in MYH7 gene and 6 in MYBPC3 gene). There were no significant differences in age, gender, previous cardiac-related hospitalizations, use of devices, heart transplantation and major ECG, echocardiographic and CMR parameters, between pts with and without genetic mutations.

**Conclusion:** Our results reflect the complexity and diversity of DCM genetics and the difficulty in determine a clear phenotypic pattern of pts with rare variants. Studies with larger number of pts/family members and longer follow-up period, will elucidate the causative role of the variants found and allow further insight in genotype-phenotype correlations and risk stratification in DCM pts.

#### P1196

##### Does the gene expression differentiate patients with ischaemic heart failure from healthy individuals?

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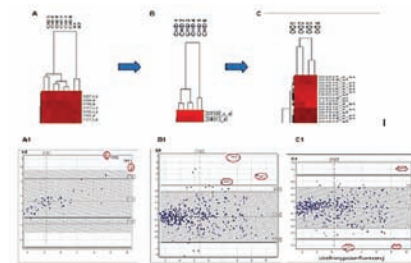
**Introduction:** Cardiovascular diseases are leading cause of death surpassing even those of malignancies. Heart failure (HF) is not only a major cause of mortality but also frequent reason for hospitalization, disability, sickness absence and as a consequence generates significant economic costs. The main cause of HF is coronary artery disease (CAD).

**Purpose:** The aim of the study was to compare genetic similarities and differences between groups of healthy and affected (both ischaemic and non-ischaemic HF) subjects as well as to determine distinctive genes.

**Methods:** Semi-quantitative analysis using oligonucleotide microarray HG-U133A (Affymetrix) technique: from the group of patients with ischaemic HF (n=52) 6 and from the group of patients with CAD without coexisting HF (n=23) 2 persons were randomly selected for further analysis. The control group were healthy individuals

(n=2) in who exclusion of CAD was confirmed by coronary angiography and 64-row computed tomography with coronary artery calcium score assessment (CACs=0). Mean age of studied subjects was 69 yrs. Material for the molecular tests was RNA extracted from peripheral blood mononuclear cells. Results Increased transforming growth factor beta-1 (TGF- $\beta$ 1) and tissue inhibitor of metalloproteinase type 1 (TIMP-1) differentiated patients from healthy individuals. Patients with ischaemic HF were characterized by increased gene expression of TGF- $\beta$ 1, TIMP-1 and TIMP-2 as compared to patients with CAD without coexisting HF. Reduced TGF- $\beta$ 1 and TIMP-1 as well as increased TIMP 9 expression was associated with HF progression and lower left ventricular ejection fraction. Results of cluster analysis for gene transcripts directly connected with HF and CAD are presented in figure 1 (A, B and C): A - all studied group, B - patients with ischaemic HF and those with CAD without HF, C - patients with different clinical stage of ischaemic HF (CHD 1-2 - LVEF <20%, CHD 3-4 - LVEF 20-40%, CHD5-CHD6 patients with CAD without HF, K1-K2 - controls). Typing, using Bland-Altman method, differentially expressed genes (A1, B1 and C1). Hatched boxes' area - genes with non-discriminative value:  $\pm 1$  minimum double decrease or increase of transcript expression (biological criterion);  $\pm 1.3$  time change of fluorescence level providing utility of designated transcript differentiating in quantitative RT-PCR (statistical criterion).

**Conclusions:** Evaluation of cluster analyzes identified TGF- $\beta$ 1 gene to be most differentiating patients with advanced ischaemic HF from patients with CAD without coexisting HF. Statistically significant decline of TGF- $\beta$ 1 transcriptional activity and its receptor III in patients with HF and its further reduction during decompensation of HF suggest important role of these genes in development and decompensation of HF. Transcriptional activity of TGF- $\beta$ 1 could be useful diagnostic and prognostic marker identifying patients with CAD and high risk of HF developing and decompensation.



Cluster analysis and genes' typing

## BASIC SCIENCE: VASCULAR BIOLOGY

#### P1197

##### The eye, a window to the heart - Retinal vessel analysis in heart failure

Funded by the Swiss Heart Foundation.

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**Background:** Endothelial dysfunction appears to play an important pathophysiological role in heart failure. Previous studies focused on the relevance of brachial endothelial dysfunction in disease pathogenesis. Less is known about the extent of endothelial dysfunction in other vascular beds, the retinal microcirculation in particular. Retinal vessel analysis (RVA) is a new method allowing study of the retinal microcirculation in a standardized way using high-resolution caliber measurements of retinal vessels.

**Purpose:** The primary goal of this study was to evaluate the extent of retinal microvascular endothelial dysfunction as assessed by flicker-induced dilatation of retinal vessels in heart failure patients compared to age- and sex matched healthy controls.

**Methods:** In this prospective, observational, single-center study, patients with a diagnosis of heart failure on stable pharmacological therapy and currently compensated status and healthy controls were recruited for the assessment of vascular function. RVA was conducted using an Imedos retinal vessel analyzer (Jena, Germany) with the assessment of retinal flicker-induced vasodilatation (FID) using an established stimulation protocol and the measurement of retinal arteriovenous ratio (AVR) calculated from retinal vessels using fundus photographs.

**Results:** 45 heart failure patients (mean age  $60.3 \pm 10.4$  years, 24 % female, mean left ventricular ejection fraction  $36.9 \pm 14.2$  %) and 31 healthy controls (mean age  $57.4 \pm 15.3$  years, 26% female) were included in this analysis. Heart failure patients showed significantly reduced FID of retinal arterioles and venules compared to



healthy controls (mean arteriolar FID  $1.2 \pm 1.9\%$  vs.  $3.2 \pm 2.0\%$ ; mean venular FID  $2.8 \pm 1.8\%$  vs.  $4.8 \pm 2.1\%$ , both  $p < 0.0001$  respectively). No significant difference in retinal AVR was found between both groups (mean AVR  $0.84 \pm 0.07$  in heart failure patients and  $0.85 \pm 0.06$  in healthy controls,  $p = 0.32$ ).

**Conclusions:** Heart failure patients are characterized by a profound alteration in retinal microvascular endothelial function as assessed by FID of retinal arterioles and veins. RVA may be a useful tool for the non-invasive assessment of microvascular function in heart failure.

#### P1198

##### Stress-induced vascular dysfunction: Evaluation of sympathetic activity and endothelial function in patients with takotsubo syndrome

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**Background:** Transient left ventricular apical ballooning syndrome or Takotsubo cardiomyopathy is an acute cardiac syndrome mimicking ST-segment elevation myocardial infarction. This syndrome is typically observed in patients experiencing sudden physical or emotional stress. The precise etiology and pathophysiology of this syndrome as well as its prognosis remains unclear.

**Purpose:** Aim of this study was to evaluate the vascular function and structure as well as sympathetic nervous activity in patients with Takotsubo syndrome and matched controls.

**Methods:** 22 patients with Takotsubo syndrome and 21 controls, matched for age, cardiovascular risk factors and medications were included in this prospective observational study. Flow-mediated vasodilatation (FMD) of the brachial artery at baseline and during stress tests was used as a marker for endothelial function. Arterial stiffness was evaluated by tonometric measurement of pulse wave velocity. Carotid atherosclerosis was assessed using ultrasound measurement of intima-media thickness and total plaque area. Sympathetic activation was measured using microneurography and quality of life was assessed using EQ-5 questionnaires.

**Results:** Compared to controls, patients with Takotsubo syndrome had a significantly reduced endothelial function (FMD  $3.0 \pm 1.7\%$  vs.  $5.0 \pm 1.7\%$ ;  $p = 0.016$ ) and an increased sympathetic nervous activity (MSA  $49.7 \pm 27.5$  vs.  $28.7 \pm 15.1$  Burst/100HB,  $p = 0.04$ ). Cardiovascular risk factors (age, weight, glucose, lipid profile and physical activity), pharmacological therapies, pulse wave velocity, intima-media thickness, total plaque area and quality of life were similar between both groups.

**Conclusions:** Our findings highlight the potentially important role of sympathetic activation and endothelial dysfunction in patients with Takotsubo syndrome.

#### P1199

##### CD34 positive bone marrow derived cells inhibit intimal hyperplasia in mouse model of vascular injury

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**Introduction:** Vascular progenitor cells contribute to repair of injured vasculature. In this study, we aimed to investigate the role of bone marrow derived cells in the intimal formation after arterial injury.

**Methods and Results:** Balloon injury of wild type mice femoral artery was followed by local delivery of bone marrow-derived cells from GFP transgenic mice. The arteries were collected 1, 4, 7 and 14 days after injury and studied for morphology, localization and phenotypes of delivered cells. Bone marrow-derived cells were present in the intima only at the early stages of arterial injury and expressed endothelial progenitor cell markers (CD31, CD34, VEGFR-2). In the areas where intima was thicker, bone marrow-derived cells differentiated to intimal smooth muscle cells but they did not fuse with intimal cells. Delivery of CD34+ cells contributed to a 1.4 fold inhibition of intimal hyperplasia.

**Conclusion:** Bone marrow-derived endothelial cells differentiated but not fused with vascular smooth muscle cells at the early stages of intimal formation and inhibited intimal hyperplasia.

# RAPID FIRE 3 – CHRONIC HEART FAILURE MANAGEMENT

Monday 23 May 2016 08:30–10:00

Location: Agora

## 1236

### Morbidity, mortality, and cost impact of stage b and stage c heart failure: comparative analysis to underline the clinical and economic need for heart failure prevention strategy.

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**Introduction:** Heart failure (HF) has hit the epidemic proportion and is incurring significant cost to the health care system. Given the major morbidity, mortality and economic burden of this condition, a prevention strategy needs careful assessment to determine its role in the future health care policy. The STOP-HF Programme has underlined the clinical and cost effectiveness of a biomarker driven risk stratification and intervention strategy in those at risk for HF. Supportive data to establish the widespread application of this prevention strategy would come from a comparative analysis of patients at risk for HF and those of a new community diagnosis of HF followed in a disease management programme. To assess the importance of HF prevention, we report the morbidity, mortality and economic costs of an at-risk cohort compared to established community HF.

**Method:** 1517 patients attending the HF prevention unit and rapid access clinic for possible new onset HF from 2002 up to end of 2012 were selected for this analysis. The demography, medical diagnoses, biomarkers, echocardiographic parameters and medications were recorded. Defined by Doppler echocardiography, patients were categorised to stage A, stage B, and stage C HF. Follow-up time for events was until the end of 2014. Hospitalisations were collected, confirmed by HIPE records and categorised as HF event, non-HF cardiovascular (non-HF CV) event, non-cardiovascular (non-CV) event and death. In the pre-specified cost analysis, direct costs associated with emergency hospitalisations and total costs were analysed using a case-mix approach from the perspective of the healthcare provider. Result: 1071 patients were in stage A, 146 in stage B, and 300 in stage C (184 C-PEF and 116 C-REF). Mean follow-up years were 3.3 years. BNP increased through the stages at 18.7pg/mL (stage A), 62.2pg/mL (stage B), 232pg/mL (stage C), 183pg/mL (stage C-PEF) and 382pg/mL (stage C-REF). The HF events rate is 8.1% in stage C. The unadjusted annual death rate increased across the spectrum (0.6% in stage A, 2.1% in stage B and 11% in stage C). The non-HF CV events were significantly higher in stage C (7%). The non-CV events were 42% in stage C, a significant 3-fold increase compared to stage B (12.4%). The non-CV events were similar both in stages C-REF and C-PEF (41.9% vs 42%). The HF, non-HF CV and death events were higher in the stage C-REF group. In the costing sub-study, emergency hospitalisation costs per patient per annum were €439 (stage A), €1114 (stage B) and €8803 (stage C). The total costs per patient per annum were €903 (stage A), €1748 (stage B) and €9763 (stage C).

**Conclusion:** The clinical and costs impact of HF care escalate significantly with the development of the symptomatic phase of HF syndrome. These data along with the positive clinical and cost effectiveness analysis of the STOP-HF Programme data underline the importance for focused HF prevention strategies.

## 1237

### Effects of 5 years treatment with nebivolol, carvedilol and bisoprolol in heart failure patients

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**Background:** Beta blockers improve left ventricular (LV) systolic function and prognosis in patients with chronic heart failure (CHF). Aim. This study compared the effects of long term treatment with nebivolol versus carvedilol or bisoprolol on

LV ejection fraction (EF) in CHF patients. Secondary end points were to assess the effect of the 3 beta blockers on exercise capacity and clinical outcome.

**Methods and Result:** A total of 150 CHF patients with EF <40% and NYHA class I, II or III were randomly assigned to receive nebivolol or carvedilol either bisoprolol for 5 years. At baseline and at the end of treatment all patients underwent clinical evaluation, echocardiography and 6 minutes walking test. The target doses were 5 mg/d for nebivolol, 50 mg/d for carvedilol and 10 mg/d for bisoprolol. At the baseline there were not significant different between 3 groups for NYHA class, EF and walking test distance. Compared with baseline values, EF increased by a similar extent in the carvedilol (C), nebivolol (N) and bisoprolol (B) groups (C from 33,1% to 37,9%,  $p < 0,001$ ; N from 34,6% to 38,5%,  $p < 0,001$ ; B from 34,3% to 38,2%,  $p < 0,001$ ). NYHA class decreased significantly in all groups and the 6 minutes walking distance increased (C from 415 m to 478 m,  $p < 0,001$ ; N from 431 m to 490 m,  $p < 0,001$ ; B from 422 m to 483 m,  $p < 0,001$ ). During 60 months 16 carvedilol patients (32%), 14 nebivolol patients (28%) and 16 bisoprolol patients had cardiac event including 5,4 and 6 deaths, respectively.

**Conclusion:** In very long term, nebivolol, carvedilol and bisoprolol appear to be similar effective in the treatment of patients with CHF.

## 1238

### MTP-131, a cardiolipin-targeting peptide, improves mitochondrial activity in the failing human heart

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**Background:** Mitochondrial dysfunction contributes to myocellular abnormalities in the failing human heart. We have previously shown significant abnormalities in cardiolipin content and electron transport chain complexes in failing human heart. MTP-131 (elamipretide) is a mitochondria-targeting peptide currently being investigated in several Phase 2 clinical trials for heart failure. In animal models of heart disease, MTP-131 improved cardiac and mitochondrial function through a mechanism involving stabilization of cardiolipin-dependent respiration.

**Purpose:** To determine whether MTP-131 treatment of the human failing heart improves mitochondrial function, assessed at different sites along the respiratory chain.

**Methods:** Ventricular tissue was rapidly harvested at the time of cardiac transplantation for end-stage heart failure secondary to idiopathic dilated cardiomyopathy (F), or from age-matched donor hearts (NF) not implanted for technical reasons. Tissue was either immediately used for respirometry or rapidly frozen at -80C. In fresh tissue, mitochondrial Complex I- and II-dependent respiration was determined using high-resolution respirometry. Total Complex IV activity was determined using spectrophotometric assays. From frozen samples, Complex IV in-gel activity assays were performed in Blue Native (BN)-PAGE to determine activity attributed to within the supercomplex (SCIV) or from uncomplexed, free Complex IV (FCIV).

**Results:** State 3 respiration (in pmol/(s\*mg)) was lower in F than NF when mitochondria were respiring via Complex I- or II-dependent substrates (glutamate/malate:  $40 \pm 11$  vs  $75 \pm 6$ ; succinate:  $64 \pm 16$  vs  $108 \pm 11$ ). MTP-131 treatment improved state 3 respiration in F mitochondria at both complexes I and II (glutamate/malate:  $74 \pm 6$ ; succinate:  $125 \pm 13$ ), but did not alter respiration in NF mitochondria under any substrate conditions. In BN-PAGE studies, SCIV activity was 30% lower ( $P < 0.05$ ) in F compared to NF-samples, but unchanged in the FCIV fraction. MTP-131 treatment increased SCIV activity ( $P < 0.05$ ) but did not change FCIV activity, suggesting that MTP-131-mediated improvements in respiration occur in mitochondrial supercomplexes. MTP-131 treatment of freshly-isolated F mitochondria increased Complex IV activity by 50% ( $P < 0.01$ ).

**Conclusion:** MTP-131 treatment improves mitochondrial function at the level of the individual complex, supercomplex and intact mitochondria in the failing human

heart. These findings suggest that stabilizing cardioplin-dependent respiratory complexes represents a novel treatment for improving mitochondrial function in heart failure.

### 1239

#### Is the cohort of paradigm-hf representative of the real world population of patients with systolic heart failure?

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**Background:** Neuro-hormonal blockade is the main-stem of the management of systolic heart failure (HF). In a recent trial, a combination of valsartan+sacubitril showed a greater benefit than enalapril. The relevance of such findings may be hampered by a strict protocol. Aim: To evaluate the representativeness of this trial in a real world population of patients with systolic HF.

**Methods:** We reviewed the records of 196 patients of a heart failure outpatient clinic between January 2013 and December 2014. We excluded 44 patients with preserved ejection fraction (EF), and applied the inclusion and exclusion criteria of the PARADIGM-HF study to the remaining population.

**Results:** From 152 patients with systolic heart failure, 106 patients (69.7%) lacked  $\geq 1$  inclusion criteria and 37 (24.3%) have  $\geq 1$  exclusion criteria. In the patients with an EF  $\leq 35\%$  (n=88), 43 patients (48.9%) lacked  $\geq 1$  inclusion criteria and 27 patients (30%) had  $\geq 1$  exclusion criteria. Combining inclusion and exclusion criteria, 26.9% (n=41) of patients with systolic HF and 39% (n=34) of patients with an EF  $\leq 35\%$  were eligible for the PARADIGM-HF trial (Table1). Conclusion: One of every four patients with systolic HF would be considered for treatment with the novel angiotensin receptor-neprilysin inhibitor.

Table1. Inclusion and exclusion criteria

Inclusion criteria, n(%) missing	Systolic HF (n = 152)	EF $\leq 35\%$ (n = 88)
NYHA > 1	30 (19,7%)	10 (11,3%)
EF $\leq 35\%$	64 (42,1 %)	0
NT-proBNP $\geq 600$ pg/ml	42 (27,6%)	18 (20,4%)
ACEI/ARB equivalent to enalapril 20mg	47 (30,9%)	25 (28,4%)
$\beta$ -blocker	4 (2,6%)	1 (1,1%)
Exclusion criteria, n(%)		
Hypotension	15 (8,2%)	9 (10,2%)
Systolic blood pressure < 95 mmHg	6 (3,9%)	6 (6,8%)
eGFR < 30 mL/min/1.73m <sup>2</sup>	11 (7,2%)	9 (10,2%)
K <sup>+</sup> > 5,4 mmol/L	7 (4,6%)	4 (4,5%)
Severe pulmonary, GI or liver disease	7 (4,6%)	3 (3,4%)
Severe valvular disease	3 (1,3%)	1 (1,1%)
Life expectancy < 5 years	12 (7,9%)	8 (9,1%)

Table1. Values are expressed in percentages (%); HF - heart failure; EF - ejection fraction; NYHA (New York Heart Association); ACEI - Angiotensin converting enzyme inhibitor; ARB - angiotensin receptor blocker; eGFR - estimated glomerular filtration rate;

### 1240

#### Evidence-based medications in multi-ethnic Asian patients with heart failure are associated with better outcomes in spite of lower doses

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**Background:** Evidence-based medical therapy (EBT) is the cornerstone of heart failure (HF) management. However data are scarce regarding the effect of EBT and their doses on outcomes in Asian patients with HF and reduced or preserved ejection fraction (HFrEF or HFpEF). Aims: To determine the effect of EBT on outcomes in Asian patients with HF

**Methods:** A prospective nationwide cohort (n=1087, 62 $\pm$ 12 years old, 75.5% men, 61% Chinese, 27% Malay, 11% Indian) of HF was followed for 1 year for all-cause mortality or HF hospitalizations as a composite outcome.

**Results:** In 706 HFrEF (EF<40%), baseline EBT included ACEI/ARB (74%),  $\beta$ -blockers (90%) and aldosterone antagonists (56%). Corresponding proportions in 345 HFpEF (EF $\geq$ 40%) were 63%, 83% and 21% (all p<0.05 vs HFrEF). Diuretic use was high in both HFrEF (92%) and HFpEF (84%). Median EBT doses (over 1-year) were lower than guideline recommended target doses e.g. enalapril 10mg mg/day, bisoprolol 2.5 mg/day, carvedilol 12.5 mg/day, spironolactone 25 mg/day. At 1-year follow-up, there were 360 composite events (111 deaths). There was continued use of ACEI/ARBs,  $\beta$ -blockers and aldosterone antagonists at 1 year in 60%, 83% and 44% of surviving HFrEF and 51%, 75% and 12% in surviving HFpEF. Baseline use of  $\beta$ -blockers was related to continued use at 1 year (p<0.001) and associated with reduced adjusted hazards of the composite outcome [HR=0.70 (95% CI 0.52-0.94) overall; HR=0.65 (95% CI 0.45-0.94) in HFrEF]. There was a protective effect (but not statistically significant) in HFpEF. Baseline use of ACEI/ARBs was related to continued use at 1 year (p<0.001) and associated with reduced hazards of the composite outcome in HFrEF [HR=0.73 (0.55-0.96)] but not the overall cohort or HFpEF alone. Aldosterone antagonists and diuretic use were not associated with reduced risk of the composite outcome. Dose of EBT was not related to outcomes. There was no interaction by ethnicity.

**Conclusions:** In Asian patients with HFrEF, use of ACEI/ARBs and  $\beta$ -blockers at baseline presentation is related to continued use during follow up and better outcomes, even at lower than guideline recommended-targeted doses.

### 1241

#### Improving the quality of heart failure care: secular trends at a regional center of excellence

Federal Ministry of Education and Research

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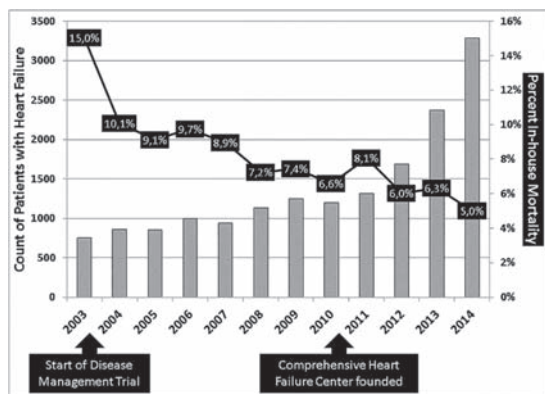
**Background:** Heart failure (HF) is the leading cause of hospitalization and a major cause of death in Germany. Cardiac societies, health policy makers and funding agencies strive to design and implement appropriate means to improve the quality of HF care, but quality control of such efforts has rarely been attempted. The University Hospital of Würzburg has a long research track in HF management. E.g., in 2003, a large multicentre intervention trial was started, revealing major positive effects of a dedicated HF management program executed by dedicated HF nurses (Circ Heart Fail. 2012;5:25-35). In Nov 2010, the Comprehensive Heart Failure Center (CHFC), sponsored by the Federal Ministry for Education and Research, was founded as an Integrated Center for Research and Treatment serving the aim to improve "Prevention of Heart Failure and its Complications". Since then, the CHFC has implemented several tools which allow to assess the quality of intra- and extra-hospital HF care and to analyse in detail clinical outcomes over time.

**Methods:** A dedicated data warehouse system was installed allowing reliable estimation of the true number of HF patients and their characteristics treated at the Center. The data warehouse exploits multiple information sources from standard clinical reports including the International Classification of Diseases (ICD) coded discharge diagnoses. We here analyse subjects with either of the 2 principal HF diagnoses I50 ("heart failure") and I11.0 ("hypertensive heart disease with heart failure") from years 2003 to 2014. Each subject was counted only once per year regardless of rehospitalization frequency.

**Results:** We observed a pronounced increase in the absolute number of HF in- and out-patients attending the Medical Department of the University Hospital in the reported period for both principal HF diagnoses (Figure); in 2003: n=52 (I11.0), and n=699 (I50); in 2014: n=780 (I11.0), and n=2508 (I50). The proportion of women remained fairly stable over time at about 40% (45-50% for I11.0, and about 40% for I50, respectively). The proportion of patients aged > 65 years continuously dropped from about 82% in 2003 to 74% in 2014, while the proportion of patients aged > 79 years remained fairly constant about 30% over time. In the same period, median hospital-length of stay in HF patients decreased from 10 days to 7 days, and in-house mortality decreased from 15% in 2003 to 6% in 2012 and 5% in 2014 (Figure).

**Conclusions:** The deliberate implementation of research and care structures was paralleled by major changes in patient populations treated at our tertiary care center. Improved awareness facilitating more adequate diagnostic coding is likely to affect mortality percentages (in particular in years 2013/2014). Improved measures for intra-hospital care and discharge management seem to help diagnosing HF earlier, attract more patients, and are associated with improved quality indicators.





Secular trends in heart failure patients

1242

Statins attenuate but not eliminate the reverse epidemiology of total serum cholesterol in patients with non-ischemic chronic heart failure

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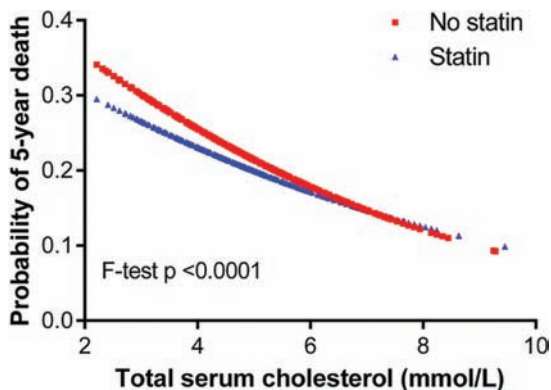
**Background:** As opposed to general cohorts, in patients with heart failure (HF) increasing levels of total serum cholesterol are associated with improved survival – termed reverse epidemiology. The potentially confounding impact of statin treatment thereon is unclear.

**Purpose:** To investigate the impact of statin treatment on the reverse epidemiology of cholesterol in patients with HF.

**Methods:** 2,992 consecutive patients with non-ischemic systolic HF were studied from three European HF registries. 1,736 patients were individually double-matched on both cholesterol levels and the individual propensity scores for statin treatment. All-cause mortality was analysed as a function of baseline cholesterol and statin use in both the general and the matched sample.

**Results:** 1,209 patients (40.4%) received a statin. During a follow-up of 13,740 patient-years, 360 statin users (29.8%) and 573 (32.1%) statin non-users died. When grouped according to cholesterol levels as low ( $\leq 3.6$ mmol/L), moderate (3.7-4.9mmol/L), high (5.0-6.2mmol/L), and very high ( $\geq 6.3$ mmol/L), we found improved survival with very high as compared with low cholesterol levels. This association was present in statin users and non-users in both the general and matched sample ( $p < 0.05$  for each group comparison). The negative association of TC and mortality persisted when cholesterol was treated as a continuous variable (HR 0.83, 95%CI 0.77-0.90,  $p < 0.001$  for matched patients), but it was less pronounced in statin users than in non-users (HR 0.85, 95% CI 0.77-0.95,  $p = 0.004$  and HR 0.81, 95%CI 0.73-0.90,  $p < 0.01$  for matched statin users and non-users, respectively).

**Conclusion:** Statins attenuate but not eliminate the reverse epidemiology of total serum cholesterol in patients with non-ischemic HF.



Probability of 5-year death plot

1243

Heart failure therapy in patients over 90 years diagnosed with left ventricular systolic dysfunction

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**Introduction:** Heart failure due to left ventricular systolic dysfunction (LVSD) is a very common condition in the elderly. Medical therapy increases survival, but very little data is available regarding its utility and efficacy in nonagenarian patients.

**Methods:** Between January 2008 and December 2013 we prospectively enrolled all patients diagnosed with LVSD (ejection fraction  $< 35\%$ ), and aged over 90 years. Clinical characteristics, electrocardiographic and echocardiographic results were collected, and a prospective follow-up was carried out via medical record review or telephone interviews.

**Results:** Out of the 60 patients who were enrolled, 51.7 % of them were male, and the mean age was 92.6 ( $\pm 6.1$ ) years. 85 % had high blood pressure, 38.3 % chronic kidney disease, 20 % cerebrovascular disease, 6.7 % chronic obstructive pulmonary disease, and 18.3 % were diabetic. 73.3 % were independent for their daily activities and only 5 % had a moderate-to-severe cognitive impairment. The mean left ventricular ejection fraction (LVEF) was 27.2 % ( $\pm 6.1$ ) but etiologic study of the LVSD was not carried out in almost the half of the study population (46.7%). Ischemic origin was identified in 36.7 % of the cases, nevertheless 68.1 % of this subgroup did not undergo coronary angiography. NYHA class I or II was present in 63.3% of the patients. Regarding the medical therapy, 46.7% were on betablockers, and the most common reason of not taking it, was bradycardia, but in more than the half of the cases the reason remained unknown. 70 % of the study population took either ACE inhibitor or ARAll blocker and 25 % was on aldosterone antagonist. Until the end of the mean follow-up of 14.3  $\pm$  11.9 months, 83.3 % of the patients died. The multivariate survival analysis with Cox regression showed that betablocker therapy was the only protective predictor (OR 0.23, IC95% 0.08-0.64) related to mortality.

**Conclusions:** According to our results, there is an underuse of the medical treatment in nonagenarian patients with LVSD. This could be related with a relatively high comorbidity rate or a probably less rigorous application of the current clinical guidelines in this study population. The single independent variable related to a higher survival was beta blocker therapy in nonagenarians.

1244

Liberal vs. restrictive oral fluid intake in patients with heart failure. Results of a metaanalysis that addresses the respective associations with rehospitalizations or with all-cause mortality

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**Background:** The guidelines of the Scientific Societies of Cardiology suggest limiting fluid intake in the diet as one of the non-pharmacological measures for the management of chronic heart failure. However, many patients with heart failure may suffer from severe thirst, even irrespective of a possible restricted fluid intake, and this has received relatively little attention in clinical studies. Therefore, we decided to perform a meta-analysis of studies that evaluated the efficacy and safety of the strategy of reducing the intake of water and other beverages in the diet of patients with chronic heart failure.

**Methods:** The studies included had to have the characteristics of randomized controlled trials that compared patients with heart failure undergoing limitation in fluid consumption with patients who had free access to water or other beverages. Primary outcomes of interest were heart failure hospitalizations and all-cause mortality. The effect size was expressed as pooled odds ratio(OR) in the case of binary variables, and as weighted mean difference (WMD) in the case of continuous variables.

**Results:** Six studies were incorporated into the meta-analysis. Significant heterogeneity was detected for the majority of investigated outcomes. Patients subjected to restricted fluid intake compared with patients admitted to free intake of beverages showed a similar rehospitalization rate (5 studies, pooled OR = 1.52; 95%CI: 0.67 to 3.43;  $p = 0.32$ ) and a similar mortality rate(5 studies, pooled OR = 1.55; 95% CI:0.87 to 2.75;  $p = 0.14$ ). Likewise, there were no differences in regards to patients' sense of thirst (4 studies, WMD = -0.7; 95% CI: -2.58 to 1.17;  $p = 0.46$ ), the duration of intravenous diuretic treatment(2 studies, WMD = 0.17 days; 95% CI: -1.26 to 1.6 days;  $p = 0.81$ ), the serum creatinine levels(5 studies, WMD = 0.05 mg/dl; 95% CI: -0.16 to 0.26 mg/dl;  $p = 0.12$ ), and serum sodium levels(5 studies, WMD = -0.86 mmol/L; 95% CI: -2.92 to 1.2 mmol/L;  $p = 0.41$ ). By contrast, serum BNP levels were significantly higher in the group with free water intake(4 studies, WMD=223.76 pg/ml ; 95% CI: 158.8 to 288.72 pg/ml;  $p < 0.001$ ).

**Conclusions:** In patients with heart failure, liberal fluid consumption does not seem to exert an unfavorable impact on heart failure rehospitalizations or all-cause mortality. However, larger randomized controlled trials are recommended in the future in

order to achieve definitive confirmation of the present findings, which substantially disavow any useful role of fluid intake restriction as a non-pharmacological measure to be adopted in heart failure management.

#### 1245

##### The effect of a multidisciplinary outpatient heart failure rehabilitation program on the rate of rehospitalization and cost of care in a tertiary Australian center.

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**Background:** Decompensated congestive cardiac failure is one of the most common causes of hospital admissions in the elderly population. It is associated with a significant financial burden on healthcare budgets worldwide. Objective: To determine the effectiveness of the existing multidisciplinary outpatient heart failure rehabilitation program at decreasing the rate of readmissions.

**Methods:** We included 155 heart failure patients who were referred to our heart failure rehabilitation program between November 2009 and December 2013. 41 patients were females. We conducted a retrospective analysis comparing rates of all-cause and heart failure related admissions in the same cohort before and after participation in the outpatient multidisciplinary heart failure rehabilitation program. Then we calculated the difference in healthcare spending utilizing the hospital admission coding system used for service reimbursement in the state public health system.

**Results:** Of 155 patients included, 110 patients had, at least, one hospital admission due to any cause before participation compared to 40 after enrollment (OR 0.1423, CI 0.0863 – 0.2345,  $p < 0.0001$ ). The all-cause admissions and days spent in hospital were significantly lower after enrollment (186 vs. 53) and (715 vs. 120) respectively. Similarly, admissions due to heart failure were lower after participation. 46 patients were admitted due to decompensated heart failure before participating in the program while only 5 needed inpatient treatment after (OR 0.079, CI 0.030 – 0.205,  $p < 0.0001$ ). There were 53 admissions with heart failure as the primary diagnosis before participation and only seven after. The calculated cost of all-cause admissions before enrollment was 1.345897.46 \$ compared to 469739.46\$ after enrollment.

**Conclusion:** Participating in structured multidisciplinary heart failure rehabilitation program was associated with significant reduction in all-cause hospital admissions, heart failure related admissions, and healthcare cost.

#### 1246

##### First-in-man trial of Beta-3-adrenoceptor agonist in chronic heart failure - effect on diastolic function

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**Introduction:** Cardiac myocyte Na<sup>+</sup> overload contributes to systolic and diastolic dysfunction in heart failure (HF).  $\beta_3$ -adrenoceptor ( $\beta_3$ -AR) stimulation activates the cardiomyocyte Na<sup>+</sup>-K<sup>+</sup>-pump, and has been shown to increase contractility in animal models of HF. In addition, since Ca<sup>2+</sup>-efflux via the Na<sup>+</sup>-Ca<sup>2+</sup>-exchanger and thus myocardial relaxation depends on the transmembrane Na<sup>+</sup>-gradient, we hypothesized that  $\beta_3$ -AR agonist treatment may improve diastolic function.

**Methods:** In a double-blind trial, we randomly assigned 70 patients with HF (NYHA class II-III) and ejection fraction (LVEF) <40% by 2D-echocardiography to receive the  $\beta_3$ -AR-agonist, Mirabegron (target dose 300 mg daily) or placebo for 6 months, on top of recommended HF therapy. Patients were assessed with 2D-echocardiography and CT at baseline and follow-up.

**Results:** Baseline and follow-up echocardiographic data were available in 59 patients (59 ± 12 yrs, 88 % male, 46% ischemic cardiomyopathy). LVEF at baseline was 34 ± 8% and the majority of patients (93%) were in NYHA class II. As for the LVEF, no difference in change of the grade of diastolic dysfunction based on e' lateral and deceleration time was seen between the treatment arms at follow-up (figure). Neither was there any difference between the groups in change from baseline to follow-up of any single measure of diastolic function (e' lateral for Mirabegron 6.9 ± 2.4 to 7.5 ± 2.5 cm/s and for placebo 6.7 ± 2.0 to 6.5 ± 2.8 cm/s, mean difference 0.9 cm/s [95% CI -0.3 to 2.0 cm/s],  $p = 0.14$ , E/e' ratio for Mirabegron 11.2 ± 5.5 to 10.5 ± 6.7 and for placebo 11.8 ± 5.8 to 11.4 ± 4.8, mean difference

0.8 [95% CI -1.6 to 3.2],  $p = 0.51$  or left atrial volume by CT for Mirabegron 68 ± 15 to 68 ± 18 and for placebo 60 ± 24 to 58 ± 23, mean difference 3 mL/m<sup>2</sup> [95% CI -4 to 9 mL/m<sup>2</sup>],  $p = 0.40$ ).

**Conclusion:** In this first-in-man, double-blind trial of  $\beta_3$ -AR stimulation in patients with chronic HF and moderately reduced LVEF in addition to recommended heart failure therapy, we did not identify an improvement in diastolic function with Mirabegron compared to placebo. Additional studies are needed to assess the effect in patients with severely reduced LVEF.

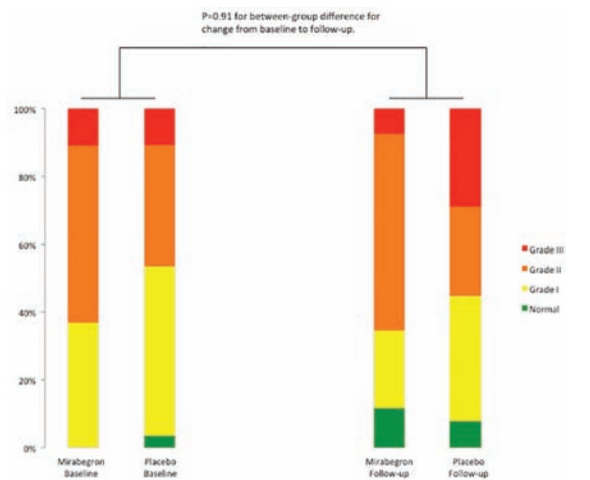
Figure. Diastolic dysfunction at baseline and follow-up.

Normal diastolic function: e' lat >10cm/s and deceleration time 140-240

Grade I dysfunction: e' lat <10cm/s and deceleration time < 140

Grade II dysfunction: e' lat <10cm/s and deceleration time 140-240

Grade III dysfunction: e' lat <10cm/s and deceleration time >240



Diastolic function

#### 1248

##### Survival in HFpEF vs HFrEF patients after beta-blocker titration: New insights from the CIBIS-ELD trial

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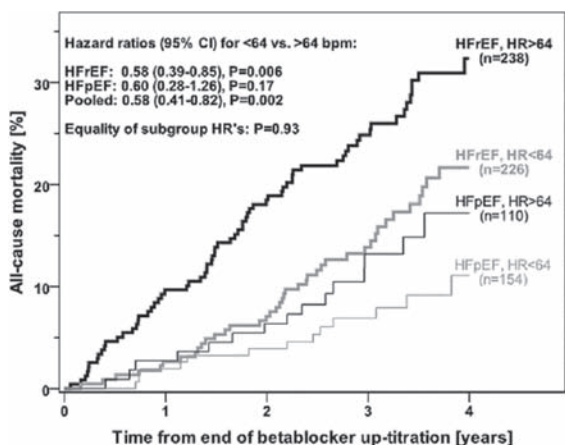
**Background:** Heart failure (HF) is a leading cause of mortality worldwide. Half of HF patients have preserved ejection fraction (HFpEF), and the other half reduced (HFrEF). Current guidelines provide no disease-specific drug regimen for HFpEF patients, but beta-blockers (BB) are considered excellent candidates.

**Purpose:** To compare the effects of BB titration on all-cause mortality in HFpEF vs HFrEF.

**Methods:** In the CIBIS-ELD trial, elderly HF patients were randomized to bisoprolol or carvedilol. BB dose was doubled every two weeks up to the target or maximum tolerated dose within 12 weeks. The long-term follow-up was performed after 4 years. This pre-defined secondary analysis compared HFpEF and HFrEF patients with regards to all-cause mortality during the 4 year follow-up period, according to heart rate (HR) achieved at the end of 12 weeks.

**Results:** During the 4 year follow-up, 134 patients died and data from 728 patients were available for this analysis (246 HFpEF and 464 HFrEF). Long-term survival was better in HFpEF patients. HFrEF patients with HR <64 bpm had significantly better survival compared to HR >64 bpm (hazard ratio = 0.58, 95% confidence interval: 0.39-0.85;  $p = 0.006$ ). Per contra, HFpEF patients with HR <64 bpm did not have significantly better survival compared to those with HR >64 bpm (hazard ratio = 0.60, 95% confidence interval: 0.28-1.26;  $p = 0.17$ ). Yet, a trend towards lower all-cause mortality in HR <64 bpm was observed (Figure).

**Conclusions:** HFrEF patients with lower HR had significantly better long-term survival. Due to certain limitations of our trial, results regarding HFpEF are still unclear. Therefore, a larger trial of a longer duration is needed to better understand the effects of BB titration on mortality in HFpEF.



Hazard ratios for all-cause mortality

1249

**Reduction in early recurrent hospitalisations after discharge for worsening heart failure with ivabradine: a post-hoc analysis of SHIFT**

Servier, France

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**Background and Purpose:** Despite use of recommended therapy, readmission rates of patients hospitalised for heart failure (HF) 1 and 3 months after discharge approach 15% and 30%, respectively. This early postdischarge period has been termed the “vulnerable phase”, and represents a major burden for patients, doctors, and society. Therefore an urgent need exists for novel approaches to improve early postdischarge outcomes. Data from the SHIFT study showed that ivabradine reduces the burden of hospitalisations for worsening HF, with a significant reduction of 25% of total (first and recurrent) HF hospitalisations versus placebo during a median follow-up of 22.9 months. Here, we examined the effect of ivabradine on the vulnerable phase after HF hospitalisation, by analysing the incidence of early readmission rate up to 90 days after discharge.

**Methods and Results:** In SHIFT 6505 patients with stable systolic chronic HF, in sinus rhythm, heart rate  $\geq 70$  bpm, and treated with guideline-recommended therapy were randomized to placebo or ivabradine (2.5 to 7.5 mg bid). The incident rate ratio (IRR) and associated confidence intervals for all hospitalization events in the ivabradine group vs. the placebo group were estimated from a Poisson regression (with correction of overdispersion), and adjusted for beta-blockers or pre-specified baseline prognostic factors. 1186 patients experienced at least one hospitalisation for worsening HF during the study. Within 3 months after the first hospitalization for worsening HF, 131 patients (25%) in ivabradine group vs 203 patients (30%) in placebo group had at least one recurrent hospitalization for any cause. The total number of readmissions was significantly reduced in the ivabradine group versus placebo from the first month.

**Conclusions:** In patients hospitalised for worsening HF in the SHIFT study, ivabradine reduced the number of recurrent hospitalisations during the vulnerable phase from the first month. This suggests that continuation or early introduction of ivabradine postdischarge will improve early outcomes in HF patients.

60758. Table 1.

	Number of all-cause readmissions		Incident rate ratio (95% CI) p value	
	Ivabradine (n = 514)	Placebo (n = 672)	Adjusted for beta-blockers	Adjusted for prognostic factors
1 month	54	102	0.69 (0.49-0.97) p = 0.03	0.70 (0.50-1.00) p < 0.05
2 months	115	201	0.75 (0.58-0.97) p = 0.03	0.75 (0.58-0.98) p = 0.03
3 months	166	278	0.78 (0.63-0.98) p = 0.03	0.79 (0.63-0.99) p = 0.04

1250

**Intramyocardial injections of the continuous erythropoietin receptor activator (CERA) in patients with chronic ischemic cardiomyopathy. Results of the randomized study**

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**Background:** Recent stem cell trials have uniformly shown that paracrine mechanisms are responsible for effects on LV function and angiogenesis rather than integration of transplanted cells into muscular tissue or capillaries. We previously found monthly subcutaneous injections of low-dose erythropoietin to improve LV remodeling following PCI. Here we tested the hypothesis, that intramyocardial-guided delivery of C.E.R.A., a long-acting erythropoietin analogue, attenuates LV remodeling in patients with ischemic cardiomyopathy.

**Methods:** A total of 59 patients with symptomatic heart failure due to ischemic heart disease and left ventricle ejection fraction of less than 45% were randomly assigned to receive either monthly subcutaneous administration of 30U of C.E.R.A. over 6 months (n=29) or intramyocardial application of one 180 U dose (n=30) of C.E.R.A. guided by the NOGA system to ischemic regions defined by unipolar voltage between 6 and 12 mV. Outcome variables were measured at baseline and at 6 months follow up. Primary outcome measure was individual change in ejection fraction as measured by echocardiography. Secondary outcomes included NYHA functional class, 6 minute walk test, end diastolic diameter, end diastolic diameter, left ventricular wall motion, heart failure hospitalization. Patients were followed for 6 month to access primary and secondary outcomes, Results None of the patients developed periprocedural complications following C.E.R.A. injections. Intramyocardial-guided delivery of C.E.R.A. significantly improved left ventricle ejection fraction compared with subcutaneous injections (intra-individual  $\Delta EF + 4.2 \pm 1.2\%$  vs  $+ 0.7 \pm 0.9\%$ , respectively,  $p = 0.042$ ). Intramyocardial delivery resulted in a more pronounced improvement of NYHA class compared to subcutaneous injections ( $-0.6 \pm 0.1$  vs  $-0.2 \pm 0.1$ , respectively,  $p = 0.014$ ). No significant differences regarding 6 minute walk test, end diastolic diameter, end diastolic diameter and left ventricular wall motion were observed. 4 (13%) patients from intramyocardial C.E.R.A. group and 6 (21%) patients from subcutaneous group required hospitalization due to worsening of heart failure ( $p = 0.5$ ).

**Conclusions:** Intramyocardial delivery of C.E.R.A. is safe and has positive impact on left ventricle ejection fraction and clinical status in patients with chronic ischemic cardiomyopathy. Extended follow up and larger patient numbers warrants further assessment of the C.E.R.A. effect in this category of patients.

1251

**Hemodynamic effects of Levosimendan in patients with reactive pulmonary hypertension**

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**Purpose:** Reactive pulmonary arterial hypertension (RPH) has a severe impact on survival of patients with acute decompensated heart failure (ADHF). The aim of our work is to study the hemodynamic effects of Levosimendan (L) in patients with ADHF and RPH.

**Methods:** 25 patients with ADHF and RPH were enrolled. At baseline and after 6, 12, 24 hours of L treatment we assessed: heart rate (HR); systolic and diastolic blood pressure (SBP,DBP); systolic, diastolic and mean pulmonary arterial pressure (sPAP,dPAP, mPAP); right atrial pressure (RAP); pulmonary wedge pressure (PWP); cardiac output (CO); cardiac index (CI); arterial oxygen saturation (SaO<sub>2</sub>), mixed venous oxygen saturation (SvO<sub>2</sub>), arterial-venous O<sub>2</sub> difference ( $\Delta AVO_2$ ); systemic vascular resistance (SVR); total, pre-capillary and post-capillary pulmonary vascular resistance (PVR). A p-value < 0.05 was considered significant.

**Results:** As shown in table 1, mPAP decreased at 6, 12, 24 hours ( $p < 0.07$ ;  $p < 0.06$ ;  $p < 0.01$  respectively) compared to baseline. SVR had a significant decline ( $p < 0.02$ ) after 24h L infusion. Total PVR were significantly reduced at 6h ( $p < 0.04$ ), 12h ( $p < 0.04$ ) and 24h ( $p < 0.02$ ); pre-capillary PVR significantly decreased at 24h



60623. Table 1

Hemodynamic parameters	Baseline (mean ± DS)	6h (mean ± DS)	p	12h (mean ± DS)	p	24h (mean ± DS)	p
sPAP mmHg	55 ± 13	552 ± 11	ns	53 ± 14	ns	51 ± 20	ns
dPAP mmHg	26 ± 6	24 ± 6	ns	24 ± 4	ns	21 ± 7	0,08
mPAP mmHg	37 ± 6	31 ± 7	0,07	30 ± 9	0,06	31 ± 12	0,01
Δ AV O <sub>2</sub> vol%	5,87 ± 1,87	4,91 ± 0,91	ns	5,32 ± 0,86	ns	4,32 ± 1,43	0,05
Sa O <sub>2</sub> vol%	93 ± 6,4	94,37 ± 2,18	ns	94,74 ± 2,93	ns	95,42 ± 3,46	ns
Sv O <sub>2</sub> vol%	57 ± 11,02	62,2 ± 5,64	ns	60,18 ± 6,26	ns	68,18 ± 5,31	0,01
SVR Wood Units	16,03 ± 7,77	11,61 ± 4,28	0,06	13,20 ± 3,51	ns	10,37 ± 3,21	0,02
Total PVR Wood Units	9,19 ± 4,13	6,75 ± 1,86	0,04	6,66 ± 2,14	0,04	5,56 ± 2,09	0,02
pre-capillary PVR Wood Units	5,49 ± 3,23	3,63 ± 1,29	ns	3,88 ± 2,20	ns	2,85 ± 2,10	0,04
post-capillary PVR Wood Units	3,69 ± 2,69	3,12 ± 1,63	ns	2,78 ± 1,92	ns	2,70 ± 1,56	ns

( $p < 0.043$ ). We observed a significant improvement of  $\Delta\text{AVO}_2$  ( $p < 0.05$ ) and of  $\text{SvO}_2$  ( $p < 0.01$ ) after 24h infusion. There were no significant differences in HR, SBP, DBP, RAP, WP, CO CI. Conclusion: 24h of L infusion has positive hemodynamic effects in

patients with ADHF and RPH, as confirmed by the improvement of  $\Delta\text{AVO}_2$  and the reduction of mPAP, total and pre-capillary PVR. These data suggest the benefit of L in ADHF patients and RPH.

## MODERATED POSTER SESSION 4 – BASIC SCIENCE

Monday 23 May 2016 10:00–11:00

Location: Poster Area

1252

**Long-term administration of ranolazine attenuates diastolic dysfunction and adverse myocardial remodeling in a model of heart failure with preserved ejection fraction**A De Angelis<sup>1</sup>; D Donato Cappetta<sup>1</sup>; E Piegari<sup>1</sup>; LP Ciuffreda<sup>1</sup>; G Esposito<sup>1</sup>; A Rivellino<sup>1</sup>; R Russo<sup>1</sup>; F Rossi<sup>1</sup>; K Urbanek<sup>1</sup>; L Berrino<sup>1</sup><sup>1</sup>Second University of Naples, Department of Experimental Medicine - Section of Pharmacology, Naples, Italy

**Background:** Although significant advances have been made in understanding the characteristics of heart failure with preserved ejection fraction (HFpEF), a lot of information is still missing. At the same time none of the pharmacological treatments has shown to be effective in reducing mortality in patients with HFpEF, and most clinical trials have disappointing results. There is a general agreement that extracellular matrix changes, myocyte hypertrophy and altered intracellular calcium homeostasis contribute to diastolic dysfunction by impaired relaxation and increased stiffness of the left ventricle. One of the potential mechanisms involved in HFpEF pathophysiology is an increase late Na<sup>+</sup> current in cardiac myocytes. This has created the background for experimental and clinical studies that suggested the benefits of ranolazine (RAN) justifying the need of additional studies.

**Purpose:** To investigate the effects of chronic administration of RAN on experimental model of HFpEF.

**Methods:** Seven-weeks old Dahl salt-sensitive rats were fed a high salt diet (8% NaCl) for 5 weeks to induce hypertension. Afterwards, rats continued with a high salt diet and were administered either with vehicle or RAN (20 mg/kg/die, ip) for the following 8 weeks. Control rats were maintained on a low salt diet (0.3% NaCl).

**Results:** While systolic parameters were not altered, diastolic parameters were changed in high salt animals. Hemodynamic analysis showed a decreased dP/dt min, increased LVEDP, longer time constant and steeper slope of the end-diastolic pressure-volume relationship. Treatment with RAN attenuated these alterations and determined a reduction in mortality. Additionally, the magnitude of myocardial hypertrophy and activation of PI3K/Akt pathway were reduced. Alteration in diastolic compliance as a consequence of elevated myocardial stiffness was confirmed by an increase of collagen deposition and activation of pro-fibrotic TGF- $\beta$ /SMAD3 signaling. These effects were counteracted by RAN. High salt rats had a decrease in SERCA2 and an increase in Na<sup>+</sup>/Ca<sup>2+</sup> exchanger (NCX). Treatment with RAN reduced NCX expression and determined an increment of SERCA2. Moreover, the levels of nitrotyrosine and oxidized dihydroethidium were higher in high salt rats. RAN induced a decrement of oxidative stress, supporting the concept that reduction in ROS may mediate beneficial effects.

**Conclusions:** Our findings support the possibility that diastolic dysfunction can be attenuated by RAN, indicating its ability to affect active relaxation and passive diastolic compliance.

1253

**Raf kinase inhibitor protein modulates interstitial and replacement cardiac fibrosis**

Deutsche Forschungsgemeinschaft, Bonn, Germany (KA 4024/3-1)

T Meier<sup>1</sup>;A Kazakov<sup>1</sup>; R Hall<sup>2</sup>; F Lammert<sup>2</sup>; M Bohm<sup>1</sup>; U Laufs<sup>1</sup><sup>1</sup>Saarland University, Department of Internal Medicine III, Cardiology, Homburg, Germany; <sup>2</sup>Saarland University, Department of Internal Medicine II, Gastroenterology, Homburg, Germany

**Background:** Genetic determinants of cardiac fibrogenesis are not completely understood. Quantitative Trait Loci (QTL) analyses in BxD recombinant inbred mouse lines and subsequent characterization of the identified target was applied to identify novel regulators of myocardial fibrosis.

**Methods and Results:** For genome-wide QTL analysis, 26 BxD lines representing a genetically mosaic but homozygous for all loci genetic reference population were treated with CCl<sub>4</sub> (0.7 mg/kg, 12i.p. injections, 6 weeks) to induce cardiac and systemic fibrosis. The cardiac QTLs linked to collagen accumulation

were screened for potential candidates by expression QTL analyses, availing of transcriptomic data of CCl<sub>4</sub>-treated BxDs (Affy 1.0 ST arrays). Cardiac fibrosis in the left ventricle (LV) of BxD lines assessed by picrosirius red staining correlated with LV RKIP mRNA (R=0.4; p=0.05). 10-week-old male C57/Bl6 wildtype (WT) and C57/Bl6-RKIP-deficient mice (RKIP<sup>-/-</sup>) were subjected to transverse aortic constriction (TAC, 360  $\mu$ m) or sham-operation or treatment with CCl<sub>4</sub> for 6 weeks, untreated mice served as controls (n=12 per group). RKIP<sup>-/-</sup> reduced both CCl<sub>4</sub>-induced interstitial- and TAC-induced replacement-LV fibrosis to 75  $\pm$  9% in CCl<sub>4</sub>-treated RKIP<sup>-/-</sup> and to 61  $\pm$  12% in RKIP<sup>-/-</sup>-TAC compared with the respective control groups. Collagen I $\alpha$ 2 mRNA was reduced by approximately 50% both in RKIP<sup>-/-</sup>-TAC and RKIP<sup>-/-</sup>-CCl<sub>4</sub>. RKIP<sup>-/-</sup> increased the number of CD31+ endothelial cells to 118  $\pm$  4% in CCl<sub>4</sub>-treated and to 157  $\pm$  18% in RKIP<sup>-/-</sup>-TAC per mm<sup>2</sup>, decreased the number of fibroblasts per mm<sup>2</sup> in TAC mice by 20  $\pm$  5%, the percentage of cycling Ki67+ fibroblasts in CCl<sub>4</sub>-treated mice to 23  $\pm$  18% and the percentage of CXCR4+ fibroblasts in TAC mice to 74  $\pm$  8%. RKIP<sup>-/-</sup> adult cardiac fibroblasts demonstrated decreased migration capacity and fibronectin production. Expression of pro-angiogenic mediators (angiogenin, DLL4, FGFs, leptin) was increased in RKIP<sup>-/-</sup>-TAC. RKIP-deficiency diminished cardiomyocyte apoptosis in CCl<sub>4</sub>-treated mice to 39  $\pm$  13% and in TAC mice to 31  $\pm$  10%. Heart weight to tibia length ratio, cardiomyocyte cross-sectional area, oxidative stress in cardiomyocytes and fibroblasts and the percentage of Ki67+ cardiomyocytes were decreased in RKIP<sup>-/-</sup> TAC. All effects were significant with p < 0.05.

**Conclusions:** These data identify Raf Kinase Inhibitor Protein as an important regulator of interstitial and replacement cardiac fibrosis.

1254

**Aortic tissue proteomic profiling identifies the osmosignaling pathway components aquaporin-1 and tonicity binding protein as molecular biomarkers and mediators of vascular disease in diabetes**R Madonna<sup>1</sup>; V Doria<sup>1</sup>; P Confalone<sup>1</sup>; R De Caterina<sup>1</sup><sup>1</sup>Institute of Cardiology, "G. d'Annunzio" University, Italy

Macro- and microvascular complications are important causes of morbidity and mortality in patients with type 1 (T1DM) and type 2 diabetes (T2DM), but an understanding of their mechanisms is far from being complete. The hyperosmolar component of hyperglycemia is an important biophysical candidate to mediate glucotoxicity and vascular dysfunction. We hypothesized that the hyperosmotic stress in overt diabetes may contribute to endothelial dysfunction through activation of osmosensing structures, such as aquaporin-1 (AQP-1) and its transcription factor Tonicity Binding Protein (TonEBP), and downstream target such as cyclooxygenase (COX)-2 in human endothelial cells. The current study investigated whether levels and activity of key molecules, such as AQP-1, TonEBP and COX-2, previously shown as causally linked to diabetic microangiopathy, are differentially expressed in human aortic endothelial cells (HAECs) exposed to hyperglycemia-induced hyperosmotic stress and in aortas of a type 1 diabetic mice developing atherosclerosis. We incubated HAECs with glucose or mannitol for 24 h, and tested them for protein levels and in vitro angiogenesis. We used the Ins2Akita mice cross-bred with apolipoprotein E-null (ApoE) mice as a model of type 1 diabetes developing atherosclerosis (along with nondiabetic/nonatherosclerotic and nondiabetic/atherosclerotic controls), to test the in vivo relevance of in vitro observations (n=8). Compared with incubations with normal (5 mmol/L) glucose concentrations, cells exposed to both high glucose and high mannitol (at 30.5 or 50.5 mmol/L) increased expression of the water channel AQP1 and COX-2. This was preceded by increased activity of the osmolarity-sensitive transcription factor TonEBP, and enhanced endothelial migration and tubulization in Matrigel, both reverted by treatment with AQP1 and TonEBP siRNA. Compared with nondiabetic/nonatherosclerotic controls, aortas of Ins2Akita, ApoE<sup>-/-</sup> and Ins2Akita/ApoE<sup>-/-</sup> mice showed increased levels of a glycosylated AQP1 isoform, while higher levels of COX-2 and TonEBP were found in Ins2Akita and Ins2Akita/ApoE<sup>-/-</sup> mice (COX-2), and Ins2Akita (TonEBP), respectively (Figure).

The concerted up-regulation of COX-2, which is known to be implicated in excessive angiogenesis characterizing unstable plaques, and the upregulation of hypertonicity stress proteins AQP1 and TonEBP suggest that glucose-related hyperosmolarity may play a role as a biomarker and mediator of the excessive angiogenesis that characterizes diabetic vascular disease, and might constitute a promising new target for therapeutic interventions.

Table: Aorta proteomic profiling

	C57	Ins2AKITA	ApoE <sup>-/-</sup>	Ins2AKITA/ApoE <sup>-/-</sup>
Gly-AQP1	86±57	126±71**	138±70**	125±73**
nonGly-AQP1	56±25	92±57**	81±59	73±54
TonEBP	99±57	148±49*	127±70	81±37
COX-2	105±36	141±52*	100±34	146±54*

Legend: C57, nondiabetic/nonatherosclerotic controls; Gly, glycosylated; apoE<sup>-/-</sup>, apolipoprotein E null mice; N=8 mice per group, values expressed as mean ± SD; \* p < 0.05 vs C57; \*\* P < 0.01

Aorta proteomic profiling

## 1255

### Elamipretide (Bendavia, MTP-131) normalizes cGMP levels in left ventricular myocardium of dogs with advanced heart failure

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<sup>1</sup>Henry Ford Hospital, Detroit, United States of America

**Background:** The second messenger cyclic guanosine monophosphate (cGMP) is reduced in heart failure (HF) and is implicated in the progressive deterioration of both LV systolic and diastolic function that characterizes the HF state in patients with reduced ejection fraction (HFrEF). cGMP is also reduced in patients with HF and preserved ejection fraction (HFpEF) and can contribute to progressive worsening of LV relaxation. cGMP generated by guanylyl cyclases (GC) produces its effects by activation of several downstream effectors that include cGMP-dependent protein kinase and cGMP-regulated phosphodiesterases (PDEs). It is well known that the nitric oxide (NO)/soluble GC (NO-sGC) system, once activated, results in the formation of cGMP. In HF, NO generated by endothelial nitric oxide synthase (eNOS) is reduced leading to reduced activation of NO-sGC and, hence, reduced formation of cGMP. Limited activation of eNOS as a result of reduction in cGMP can also negatively impact mitochondrial biogenesis. We previously showed that elamipretide (Bendavia, MTP-131), a novel mitochondria-targeting peptide, improves LV systolic and diastolic function in HF dogs with reduced EF (HFrEF), normalizes maximum rate of ATP synthesis and levels of eNOS.

**Purpose / Hypothesis:** This study tested the hypothesis that chronic therapy with elamipretide normalizes cGMP levels in LV myocardium of dogs with HFrEF (LV EF ~30%).

**Methods:** Studies were performed in LV tissue of 14 HF dogs randomized to 3 months therapy with subcutaneous injections of elamipretide (0.5 mg/kg once daily, n = 7) or saline (HF-Control, n = 7). LV tissue from 6 normal (NL) dogs was used for comparisons. cGMP level (pmol/mg protein) was determined using commercially available Elisa kits. Protein level of eNOS was assessed in LV tissue homogenate by Western Blotting and bands quantified in densitometric units (du).

**Results:** cGMP level in NL dogs was  $1.02 \pm 0.1$  pg/ml and decreased significantly in HF-Control dogs to  $0.47 \pm 0.05$  pg/ml ( $p < 0.05$ ). Treatment with elamipretide restored tissue levels of GMP to near normal ( $0.77 \pm 0.05$  pg/ml) ( $p < 0.05$  vs. HF-Controls). eNOS level in NL dogs was  $0.68 \pm 0.07$  du and decreased to  $0.19 \pm 0.02$  du in HF-Controls ( $p < 0.05$ ). Treatment with elamipretide significantly increased protein levels of eNOS to levels closer to normal ( $0.38 \pm 0.03$  du) ( $p < 0.05$  vs. HF-Controls).

**Conclusions:** cGMP and eNOS levels are reduced in LV of dogs with advanced HF. Chronic therapy with elamipretide restores cGMP and eNOS levels to near normal. These findings suggest that elamipretide, in addition to being potentially useful for the treatment of HFrEF, may also be useful in the treatment of patients with HFpEF.

## 1256

### Role of intercellular adhesion molecule 1 in mediating pro-atherogenic and pro-fibrotic effects of mineralocorticoid receptor activation

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**Background:** In clinical trials, mineralocorticoid receptor (MR) antagonists decrease cardiovascular ischemia and mortality suggesting a beneficial role of MR inhibition in the vasculature. In endothelial cells (ECs) MR activation by aldosterone promoted transcription of Intercellular Adhesion Molecule 1 (ICAM-1) and leukocyte adhesion, an effect that was inhibited by spironolactone and ICAM-1 blocking antibody. These data support that MR activation in human ECs promotes ICAM-1-mediated leukocyte-EC adhesion, an important step in early atherosclerosis lesion formation.

**Results** To further explore the mechanisms through which MR is able to regulate endothelial ICAM-1 expression, we performed transient transfection experiments in HUVEC. We observed that aldosterone is able to activate (2 fold) a 3 Kb promoter region upstream the transcription start site of human ICAM-1 gene. Such effect was inhibited by co-incubation with spironolactone, confirming the presence of elements responsive to signaling pathway(s) activated by MR. Bioinformatics analysis of this region revealed the presence of three different highly conserved regulatory elements: one NF- $\kappa$ B binding site, one AP1 binding site and one glucocorticoid/mineralocorticoid responsive element (GRE/MRE). Blocking of either c-Jun or NF- $\kappa$ B pathway resulted in a marked reduction of the aldosterone effect on ICAM-1 promoter activity, suggesting the involvement of these transcription factors. Selective deletion of the putative MRE/GRE completely abolished promoter activity induced by aldosterone. In order to verify if the development of atherosclerosis and fibrosis induced by MR activation, could be prevented by deletion of ICAM-1, we generated a double knock out ApoE<sup>-/-</sup>/ICAM-1<sup>-/-</sup> mouse. In these mice, we examined the aortic root after infusion of aldosterone and administration of atherogenic diet for 4 and 8 weeks. At level of aortic root, we observed a significant reduction in lipid content and activated inflammatory cell area in plaques from ApoE<sup>-/-</sup>/ICAM-1<sup>-/-</sup> mice compared to ApoE<sup>-/-</sup> mice. Moreover, expression of type I and III collagen was reduced in ApoE<sup>-/-</sup>/ICAM-1<sup>-/-</sup> mice, after 8 weeks of treatment.

**Conclusion(s):** These results suggest: - ApoE<sup>-/-</sup>/ICAM-1<sup>-/-</sup> mice, fed an atherogenic diet for 4 weeks, are resistant to early atherosclerosis and plaque inflammation induced by aldosterone. - ApoE<sup>-/-</sup>/ICAM-1<sup>-/-</sup> mice, fed an atherogenic diet for 8 weeks, are resistant to aldosterone-induced fibrosis - MR-induced ICAM-1 expression requires NF- $\kappa$ B and c-JUN transcriptional activity. - ICAM-1 has a central role in the development of atherosclerosis induced by aldosterone.

## 1257

### Mechanical stretching on cardiac adipose progenitors upregulates sarcomere-related genes

A Aida Lucia-Valldeperas<sup>1</sup>; C Soler-Botija<sup>1</sup>; C Prat-Vidal<sup>1</sup>; C Galvez-Monton<sup>1</sup>; S Roura<sup>1</sup>; I Perea-Gil<sup>1</sup>; R Bragos<sup>2</sup>; A Bayes-Genis<sup>3</sup>  
<sup>1</sup>Health Science Research Institute Germans Trias i Pujol, Badalona, Spain;  
<sup>2</sup>University Polytechnic of Catalunya, Barcelona, Spain; <sup>3</sup>Germans Trias i Pujol University Hospital, Badalona, Spain

**Background:** The cardiac tissue is an unfriendly environment for the implantation of therapeutic cells due to its unavoidable contractility. Cardiac cells respond to mechanical stimuli and adjust their performance accordingly. It is also known that mechanical stimulation of tissue-engineered constructs improves their organization and contraction force.

**Purpose:** We hypothesize that mechanical conditioning of therapeutic cells could improve their retention and cardiovascular potential, to help in cardiac tissue restoration.

**Methods:** Cardiac adipose tissue-derived progenitor cells (ATDPCs) were mechanically stretched for 7 days at 1 Hz in 3 different surfaces (vertical, horizontal and smooth) (Figure 1). Gene and protein analysis were carried out for each cell type and condition. Secretome analysis after stimulation was also performed.

**Results:** A device was designed and validated to effectively apply a ~10% stretch. Mechanically stimulated cardiac ATDPCs increased the expression of cardiac transcription factors (GATA-4 and Tbx5) and structural genes (cTnI and  $\alpha$ -actinin) after 7 days of mechanical stimulation. This gene modulation was different depending on the patterned surface, however the secretome analysis revealed that the vertical pattern was the most convenient for cardiac ATDPCs conditioning. Indeed, the secretome of cardiac ATDPCs stretched on vertical patterned surfaces was significantly associated to myocardial infarction, left ventricular extracellular matrix remodelling and the regulation of myoblast differentiation.

**Conclusions:** Mechanical conditioning of cardiac ATDPCs enhances the expression of early and late cardiac genes related with the cardiac sarcomere, and it is strongly dependent on the culture surface pattern.

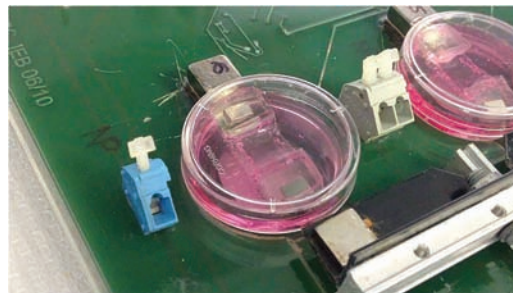


Figure 1. Mechanical stimulation device.



1258

**Cardiac specific deletion of crif1 results in vulnerable heart function through mitochondrial damage in mice.**

This research was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education S A Seon Ah Jin<sup>1</sup>; JK Oh<sup>1</sup>; MJ Kim<sup>1</sup>; UL Choi<sup>1</sup>; SW Seong<sup>1</sup>; KT Ahn<sup>1</sup>; SW Choi<sup>1</sup>; JO Jeong<sup>1</sup>

<sup>1</sup>Chungnam National University Hospital, Daejeon, Korea Republic of

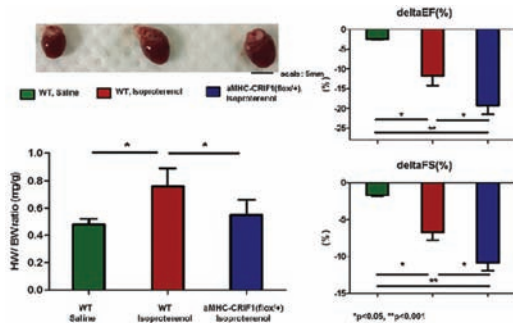
**Background/Introduction:** Mitochondria are key organelles for cellular energy production. Mitochondrial dysfunction is associated with various diseases such as neurodegeneration, neuromuscular disease and diabetes. Although cardiac tissues which require high energy metabolism are most vulnerable, the mechanisms underlying mitochondrial cardiomyopathy are largely unknown. CRIF1 is a critical mitochondrial protein for the synthesis and formation of the OxPhos complex in the inner mitochondrial membrane.

**Purpose:** We investigated the physiologic role of CRIF1 in the heart and mitochondrial cardiomyopathy through it.

**Methods:** The CRIF1<sup>flx/flx</sup> mice were crossed with Myh6-Cre transgenic mice, which harbor cardiac-specific murine alpha myosin-heavy chain (Myh6, heavy polypeptide 6, cardiac muscle, alpha) promoter drives expression of Cre in this transgenic strain. To investigate the physiologic role of CRIF1 in the heart, we used wild type and Myh6-Cre;CRIF1<sup>flx/+</sup>. Western blot analysis was performed according to standard methods with commercially available antibodies. Oxygen consumption rates (OCR) in cardiomyocytes were measured using a Seahorse XF-24 flux analyzer. Histological and echocardiographic examinations were done before and after isoproterenol infusion with mini-osmotic pump.

**Results:** Cardiac-specific deletion of CRIF1 leads to mitochondrial dysfunction. In the mutant cardiac muscles, mitochondrial inner structure was altered with lack of cristae. The basal OCR in the CRIF1<sup>flx/+</sup> cells showed no significant gap compared to wild type, but was reduced more after oligomycin treatment ( $p < 0.001$ ). It was not recovered after maximal respiration ( $p < 0.001$ ). The mutant cardiomyocytes showed also decreased pSTAT3 and increased pERK. Although mutant cardiomyocytes showed decreased oxygen consumption rates and ATP production, there were no distinguished cardiac phenotyping showing normal cardiac function. To evaluate cardiac phenotyping after injury, the ratio of heart weight-to-body weight was measured at each week after isoproterenol infusion. At 2 weeks, the heart weight-to-body weight ratios of Crif1<sup>flx/+</sup> were low significantly ( $p < 0.05$ ). Consistently, the values of deltaEF and deltaFS (difference of ejection fraction or fractional shortening between before and after isoproterenol infusion) at 4 weeks were markedly decreased in the mutant mice ( $p < 0.001$ ).

**Conclusions:** In conclusion, mutant cardiomyocytes showed decreased rates of oxygen consumption and ATP production, suggesting that CRIF1 plays an essential role in the maintenance of both mitochondrial structure and respiration in cardiomyocytes. Mutant CRIF1 mice showed decreased cardiac hypertrophy and vulnerable heart function after isoproterenol infusion in mice.



1259

**Serelaxin effect on cardiac remodeling in an acute myocardial infarction animal model**

Study funded by Novartis and fully realized, as a blind study, in Cariology Department of Virgen de la Arrixaca University Hospital, Murcia, Spain MC Asensio-Lopez<sup>1</sup>; A Lax<sup>1</sup>; J Jesus Sanchez-Mas<sup>1</sup>; MJ Fernandez-Del Palacio<sup>2</sup>; L Caballero<sup>1</sup>; MT Perez-Martinez<sup>1</sup>; M Navarro<sup>1</sup>; I Garrido-Bravo<sup>1</sup>; FJ Pastor-Perez<sup>1</sup>; DA Pascual-Figal<sup>1</sup>

<sup>1</sup>University Hospital Virgen De La Arrixaca, Murcia, Spain; <sup>2</sup>Department of Animal Medicine and Surgery, Murcia, Spain

**Introduction.** Relaxin-2 is a natural reproductive hormone that has been associated with anti-inflammatory, anti-fibrotic and angiogenic effects in cardiac ischemia

models. Serelaxin (RLX030), a recombinant form of the relaxin-2 human hormone, has been able to relieve dyspnea and congestion in patients with acute heart failure and to reduce mortality. To date, the effects of RLX030 on cardiac remodeling and function in acute myocardial infarction (AMI) have not been evaluated. Purpose. The objective of the study was to characterize the dose effects of serelaxin on cardiac remodeling and heart function in an animal model of AMI. Methods. Sprague-Dawley rats were subjected to AMI by permanent ligation of the left anterior descending coronary artery. Infarcted animals were divided into an untreated group or a group treated with RLX030 (30 μg/kg/day, i.v.) for 72 h from the time of ligation. The control group was subjected to the same surgery but without ligation. Animals were sacrificed 7 days after surgery. By RT-PCR levels of markers were measured in the infarcted zone including: fibrosis (collagen I, collagen III, TIMP-1, α-SMA and TGF-β), inflammation (IL-6, TNF-α and MCP-1), angiogenesis (VEGF-A and VEGF-B) and remodeling (sST2 and galectin-3). Each value is referred to the control group and is expressed as mean ± standard error. Results. In the histological analysis, the AMI group showed high levels of expression of all fibrosis and inflammation markers and decreased angiogenesis markers compared to the control group. Compared with AMI group, treatment with RLX030 showed lower expression values of IL-6 (16.1 ± 3 vs. 7.4 ± 3.8, AMI vs. AMI + RLX030,  $p = 0.04$ ) and MCP-1 (15.1 ± 2.5 vs. 7.7 ± 1.3,  $p = 0.01$ ) and higher values of VEGF-A (0.73 ± 0.09 vs. 1.1 ± 0.1,  $p = 0.02$ ) and VEGF-B (0.58 ± 0.09 vs. 0.9 ± 0.07,  $p = 0.02$ ). RLX030 treatment did not prevent fibrosis markers increase induced by the AMI, but it reduced sST2 levels (1059 ± 219 vs. 412 ± 163, AMI vs. AMI + RLX030,  $p = 0.018$ ) and galectin-3 levels (98 ± 25 vs. 26 ± 5, AMI vs. AMI + RLX030,  $p = 0.04$ ), suggesting a favorable effect on myocardial remodeling in the longer term.

**Conclusions:** Our results suggest an early protective effect of RLX030 on AMI by reducing inflammation, promoting angiogenesis and favorably modulating galectin-3 and sST2 remodeling markers

1260

**Synchronous electromechanical conditioning of adult cardiac adipose tissue-derived progenitor cells within a fibrin construct drives recovery of cardiac function after myocardial infarction**

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**Purpose:** 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) to study the viability of a tissue engineered construct with cardiac adipose tissue-derived progenitor cells (cardiac ATDPCs); and 2) to examine the effect of electromechanically stimulated cardiac ATDPCs embedded in a fibrin patch within a myocardial infarction (MI) model in mice.

**Methods:** Cardiac ATDPCs were electromechanically stimulated mimicking the physiological heart environment: 2 ms pulses of 50 mV/cm at 1 Hz and 10% stretching during 7 days. Cell viability was evaluated through a Life&Dead assay. The cells were harvested, labelled, embedded in a fibrin hydrogel, implanted over the infarcted area of the murine heart and animals were sacrificed at 21 days post-implantation. 39 mice were randomly distributed: without cells and with stimulated or non-stimulated cells. Echocardiography, gene and protein analysis were also carried out.

**Results:** Physiologically stimulated ATDPCs showed increased expression of cardiac transcription factors, structural genes and calcium handling genes. After 3 weeks of in vitro culture in the fibrin construct, cells exhibited high viability and remained labelled. 21 days post-implantation, cardiac function (measured as left ventricle ejection fraction between pre-sacrifice and post-MI) increased in animals treated with stimulated ATDPCs constructs by 5% - 12% relative to unstimulated cells and non-treated animals, respectively. Constructs containing stimulated cells presented vascularization and integration with the host blood supply, resulting in an increased vessel density in the infarct border region. Histology analysis showed cell proliferation and cardiac markers expression of implanted cardiac ATDPCs, but also scarce migration to the mouse myocardium.

**Conclusions:** Trained cells within the implanted fibrin patch expressed main cardiac markers, and migrated into the underlying ischemic myocardium. Thus, synchronous electromechanical conditioning prior to cell implantation emerges as a promising therapeutic strategy for cardiac regeneration after myocardial infarction.

1261

**Perinatal adaptation to the extrauterine life involves a gradual decrease in the sensitivity for oxidative titin modifications in cardiomyocytes of the rat**

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<sup>1</sup>University of Debrecen, Division of Clinical Physiology, Debrecen, Hungary

**Purpose:** During the first weeks of postnatal life cardiomyocytes undergo a maturation process whereby embryonic proteins are gradually replaced by those of the adult myocardium. Along this process, the N2BA titin isoforms are switched for N2B titin isoforms leading to an increase in sarcomeric passive force ( $F_{\text{passive}}$ ) to coordinate left ventricular (LV) diastolic function. Here we attempted to reveal how titin isoform composition and oxidative insults (SH oxidation, carbonylation) influence  $F_{\text{passive}}$  of LV cardiomyocytes following birth.

**Methods:** Experiments were performed at different stages of postnatal development (at 0, 7 and 21 days) of control Wistar rats.  $F_{\text{passive}}$  was measured in single permeabilized LV cardiomyocytes. The effects of SH oxidation and carbonylation of the two titin isoforms on  $F_{\text{passive}}$  were evaluated following in vitro exposures to an oxidative agent, dithiodipyridine (DTDP, 10 mM) or Fenton reagents (50  $\mu\text{M}$   $\text{FeSO}_4$ , 1.5 mM  $\text{H}_2\text{O}_2$ , 6 mM ascorbic acid) in cardiomyocytes followed by the application of the antioxidant dithiothreitol (DTT, 10mM). Titin isoform composition was analyzed by SDS-gel electrophoresis, while Western-blot analyses were carried out for the semiquantitative determination of SH groups (by biotinylation) and carbonyl groups (by OxyBlotTM) in titin isoforms.

**Results:**  $F_{\text{passive}}$  was significantly increased with age in a range of sarcomere lengths (SL, 1.9-2.5  $\mu\text{m}$ ) along with an antiparallel change in the N2BA/N2B ratio ( $80 \pm 1\%/20 \pm 1\%$ ,  $41 \pm 1\%/59 \pm 1\%$ ,  $10 \pm 1\%/90 \pm 1\%$  in 0-, 7-, and 21-day-old rats, respectively,  $n = 5-7$ ). DTDP and Fenton reagents significantly increased  $F_{\text{passive}}$  in 0- and 7-day-old rats, but to a lesser extent in 21-day-old animals (DF $F_{\text{passive}}$  of DTDP:  $99 \pm 26\%$ ;  $65 \pm 23\%$  vs.  $39 \pm 21\%$ ; DF $F_{\text{passive}}$  of Fenton:  $138 \pm 33\%$ ;  $55 \pm 13\%$  vs.  $27 \pm 8\%$   $P < 0.05$  in 0-, 7-day-old vs. 21-day-old groups. SL: 2.3 $\mu\text{m}$ ,  $n = 7-8$ ). The effects of oxidative insults were completely reverted by the application of DTT in the same age groups. The relative extents of DTDP-evoked SH oxidations and Fenton-evoked carbonylations declined with cardiomyocyte age for both titin isoforms (N2BA(DTDP):  $80 \pm 1\%$ ,  $71 \pm 1\%$ ,  $64 \pm 1\%$ , N2B(DTDP):  $74 \pm 1\%$ ,  $62 \pm 2\%$ ,  $53 \pm 2\%$ ; N2BA(Fenton):  $157 \pm 6\%$ ,  $134 \pm 4\%$ ,  $35 \pm 3\%$  N2B(Fenton):  $190 \pm 10\%$ ,  $158 \pm 4\%$ ,  $74 \pm 4\%$  in 0-, 7- and 21-day-old rats, respectively,  $P < 0.05$ ,  $n = 4-20$ ).

**Conclusion:** Cardiomyocyte differentiation is accompanied by a gradual decrease in the oxidative sensitivity of  $F_{\text{passive}}$  due to the sarcomeric maturation of N2BA and N2B titin isoforms.

## CLINICAL CASE CORNER 4: WHEN THE HEART IS BURNING: CASES OF INFLAMMATORY CARDIAC INVOLVEMENT – PART I

Monday 23 May 2016 10:00–11:00

Location: Poster Area

1262

### A heart with no legs to run: giant cell myocarditis in a patient with bilateral leg amputation after giant cell vasculitis.

A Alberto Aimò<sup>1</sup>; A D'ascanio<sup>2</sup>; A Pucci<sup>2</sup>; A Giannoni<sup>3</sup>; G Vergaro<sup>3</sup>; A Barison<sup>3</sup>; L Innocenti<sup>3</sup>; C Passino<sup>1</sup>; M Emdin<sup>1</sup>

<sup>1</sup>Sant'Anna School of Advanced Studies, Pisa, Italy; <sup>2</sup>University of Pisa, Pisa, Italy; <sup>3</sup>Gabriele Monasterio Foundation, Pisa, Italy

A 23-year old woman with a history of dystimia and drug abuse developed ulcerative skin lesions in her lower limbs. Such lesions which were excruciatingly painful, spread out, merged, and became rapidly infected. The histological findings led initially to a presumptive diagnosis of granulomatous slack skin disease, an extremely rare subtype of T-cell cutaneous lymphoma. A temporary treatment with steroids and cyclophosphamide was therefore undertaken, but the response was partial, partly because of poor patient compliance. One year later, a bilateral above-knee amputation was mandatory.

Several months after the amputation, the patient presented with progressive oedema, complained of dyspnoea at rest, orthopnoea, and paroxysmal nocturnal dyspnoea. After admission to an Emergency Department, cardiac function deteriorated rapidly until cardiogenic shock supervened; she was treated with aortic counterpulsation, combined norepinephrine and levosimendan infusion, and non-invasive mechanical ventilation. An ischaemic aetiology was excluded by coronary angiography. Cardiac magnetic resonance documented 25% left ventricular ejection fraction (LVEF), diffuse hypokinesia, and myocardial oedema; this last finding, together with a marked increase of the inflammatory markers, suggested an acute myocarditis. Discharged with a low-dose bisoprolol, valsartan, with furosemide and spironolactone treatment, she underwent repeated hospitalizations, till, after 3 months, she was transferred to our Cardiology Department with pulmonary congestion, bilateral pleural effusion, anasarca, and fever. At echocardiogram, a 18% LVEF was estimated. After unloading treatment with levosimendan and intravenous furosemide, left heart catheterization was undertaken, and a myocardial biopsy allowed to diagnose giant cell myocarditis. Methylprednisolone and cyclosporine were then started.

In the following two months, bisoprolol, ramipril, and aldosterone antagonist were up-titrated. serial echocardiograms documented a slow but steady recovery of systolic function. Meanwhile, the former skin lesion biopsy was re-evaluated, and the evidence of macrophages with the appearance of giant cells in the context of skin granulomas, allowed a diagnosis of small vessel vasculitis. At discharge, the patient did not display any signs or symptoms of heart failure, and had a 25% LVEF. One month later, the reverse remodeling was further advanced, with 35% LVEF, while NT-proBNP had dropped from 20728 to 3684 ng/L. This case confirms the association between giant cell myocarditis and other autoimmune manifestations. Furthermore, the evidence of giant cells in both skin and heart biopsies suggests common pathogenesis for cutaneous and cardiac lesions, a concept that has never been proposed so far. With regard to treatment, our case demonstrates that a relatively rapid recovery of cardiac function can be achieved by integrating an immunosuppressive strategy with optimal heart failure management.

1263

### An 18 year old man with severe left ventricular systolic dysfunction and mysterious intracardiac masses. What is the diagnosis?

G Georgiana Tamasescu<sup>1</sup>; S Iancovici<sup>1</sup>; M Dan<sup>1</sup>; A Aexandrescu<sup>1</sup>; M Dorobantu<sup>1</sup>

<sup>1</sup>Emergency Clinical Hospital Floreasca, Cardiology, Bucharest, Romania

The imaging of left ventricular masses can be very spectacular but establishing the aetiology and choosing a right treatment can be challenging. We present the case of an 18-year-old man admitted to our clinic for new acute heart failure. The patient had a history of recent respiratory tract infection with high fever followed by

persistent cough and shortness of breath for which he underwent empiric antibiotic treatment. On admission, the patient was severely dyspnoea at rest and ineffective cough. Chest X-ray revealed cardiomegaly and bilateral confluent opacities in the inferior lung fields. ECG showed sinus tachycardia without other changes. Blood tests revealed marked leucocytosis, inflammatory syndrome and very high natriuretic peptides. Transthoracic echocardiography (TTE) showed a very dilated left ventricle (LV) with severe systolic dysfunction (LVEF 10%) and multiple large and mobile masses with a hypo echogenic core, occupying the whole LV apex. No spontaneous contrast was seen in the LV. Moderate functional mitral regurgitation was observed. The CT scan confirmed bronchopneumonia and intracardiac masses. The patient was admitted in the intensive care unit and received standard heart failure treatment. The sputum samples were repeatedly negative, blood serology was positive for acute cytomegalovirus infection. The differential diagnosis was between extensive intracardiac thrombosis in a dysfunctional dilated LV, newly discovered cardiac tumours, atypical vegetations in a patient with pulmonary infection and Löffler's syndrome, but no eosinophilia was detected. The MRI, initially postponed due to patient's clinical status, confirmed diagnosis of acute myocarditis and intraventricular thrombosis with no criteria of non-compaction cardiomyopathy. The cardiac imaging performed didn't give a straight answer about the aetiology of these masses and a clinical decision had to be made before having a clear diagnosis in order to avoid embolic complications and unfractionated heparin treatment was initiated. Several days after starting Heparin, subsequent echocardiographic evaluation showed complete resolution of these masses under anticoagulant treatment proving it was LV thrombosis. We concluded it is a rare case of acute myocarditis with severe LV dilatation and systolic dysfunction and signs and intraventricular thrombi following a respiratory infection with CMV. Sometimes, in the acute setting, multimodality imaging cannot be performed completely and the treatment decisions have to be made before having a clear diagnosis in order to avoid complications. In this particular case the evolution under anticoagulant treatment revealed better the aetiology than the cardiac imaging alone.

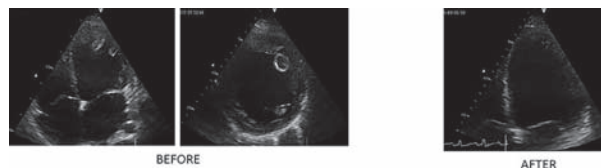


Fig 1 Apical 4 chambers and SAX

1264

### Exercise induced pulmonary hypertension in unexplained dyspnea due to scleroderma left heart diastolic dysfunction

V Valentina Labate<sup>1</sup>; F Bandera<sup>2</sup>; G Generati<sup>2</sup>; V Donghi<sup>2</sup>; M Guazzi<sup>2</sup>

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**Introduction-Case report description:** Almost half of patients with heart failure have preserved ejection fraction (HFpEF). According to consensus recommendations, a diagnosis of HFpEF can be obtained when signs and symptoms of HF, normal left ventricular (LV) systolic function and impaired LV relaxation and compliance are met simultaneously. Some HFpEF patients, however, may be misclassified, because they have virtually normal diastolic function and filling pressure at rest, compared with controls. We report a case of a patient with unexplained dyspnea



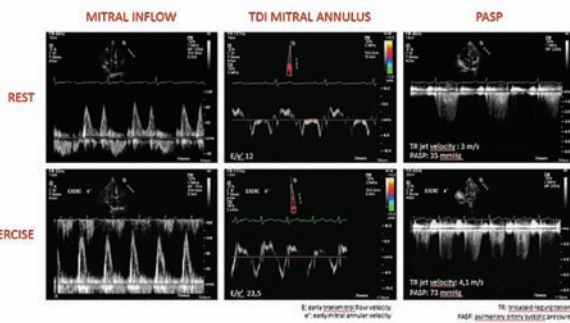
and suspected HFpEF evaluated by a combined approach using cardiopulmonary test (CPET) simultaneously with exercise stress echocardiography (ESE).

A 76-year-old mild hypertensive woman was referred to our center for evaluation of exertional dyspnea. She referred a rapid progression of dyspnea during effort (NYHA II class). Raynaud's phenomenon was also referred. Rest echocardiography revealed normal biventricular structure and function and initial diastolic dysfunction (LV ejection fraction 77%, E/e' 12, TAPSE 24mm, PASP 35 mmHg).

Description of the problem, procedures, techniques and/or equipment used Dyspnea is a common unspecific symptom and can be caused by many different conditions. Not only multiple systems are involved and interact synergistically in the complex pathophysiology of dyspnea but dynamic changes in cardiac function and pulmonary pressure can play a key role in the genesis of this symptom. Based on these considerations a dynamic evaluation by means of CPET combined with ESE using a tiltable ergometer was performed (incremental ramp of 12 W/min). CPET showed a reduced peak  $\text{VO}_2$  (12.2 ml/kg/min, 61% of predicted), characterized by the flattening of  $\Delta\text{VO}_2/\Delta\text{Work Rate}$  relationship (mean slope 7.2). The ventilatory efficiency was normal (VE/VCO<sub>2</sub> slope of 29.2). During exercise rapid increase of LV filling pressure (E/e' 25.3) associated with severe dynamic pulmonary hypertension (PH) (PASP 73 mmHg) and dynamic mitral regurgitation (MR) was detected.

**Answers-Discussion:** In patients with early stage HFpEF with diastolic dysfunction that has not yet caused an increase in left atrial pressure, E/e' could be normal at rest, whereas it could increase only during a 'diastolic stress', such as exercise. Additional effort abnormalities, i.e. reduced exercise capacity, exercise-induced PH, dynamic MR a steeper VE/VCO<sub>2</sub> slope can support the diagnosis of HFpEF.

**Conclusions-Implications for clinical practice:** Traditional echocardiographic indices may be insensitive for the diagnosis of HFpEF because they try to identify patients with breathlessness during exercise, using only resting diagnostic criteria. Diagnosis may therefore remain challenging, especially in the earlier stages when symptoms occur just during exercise. Exercise appears the ideal physiological condition to monitor simultaneously cardiac filling pressure by ESE and symptoms by CPET making early diagnosis of HFpEF more likely.



dynamic echocardiographic evaluation

## 1265

### Heart failure, heart rate and myasthenia gravis

E Elio Venturini<sup>1</sup>; L Magni<sup>1</sup>; R Testa<sup>1</sup>

<sup>1</sup>Department of Cardiology - Civic Hospital, Cecina (LI), Italy

**Introduction:** Myasthenia gravis (MG) is an autoimmune neuromuscular disorder causing muscle weakness and fatigue. The treatment of cardiac disorders that affect patients with MG can be a challenge because many drugs induce or worsen symptoms of the disease. Case report description: we report the case of a 76-year-old male with late-onset MG who developed systolic heart failure. The patient (P) was referred by her general practitioner for tachycardia and effort dyspnea (NYHA IIb class). At the age of 71 years he had bilateral ptosis, hyposthenia and weakness of upper limb muscles. A diagnosis of MG was made. Physical examination showed arterial blood pressure of 150/85 mmHg, heart rate (HR) of 116/min, regular a holosystolic murmur (2/6 Levine scale) and a III sound (ventricular gallop). There were ankle edema and rales at lung bases bilaterally. The ECG showed sinus tachycardia, a first-degree atrioventricular block and left bundle branch block and the echocardiogram a reduction of ejection fraction (EF: 30%) with diffuse hypokinesia. The brain natriuretic peptide was increased (BNP 878 pg/mL; normal value 0-100) and the chest X-ray confirmed cardiomegaly. Due to the concomitant MG was started treatment with ACE inhibitors and diuretics. After about one month, exertional dyspnea improved (NYHA IIa) and also HR was reduced (90 /min) as well as the BNP (638). Therefore ivabradine (IVA) was added and the dose was gradually increased to 7.5 mg x 2. Was tolerated with no worsening of MG symptoms. At a 6 months follow up the p is asymptomatic with no signs or symptoms of HF, in normal sinus rhythm (HR 70/min). The BNP is 218. Also the EF (40%) is improved. Discussion and implications for clinical practice: ryanodine and titin receptors are expressed in striated muscles and in the heart. This may cause a cross immunogenicity and lead to the

HF sometimes preceded by an autoimmune myocarditis. Also serum antibodies against adrenergic receptors present in P with MG can be involved. Beta-blockers are a cornerstone in the treatment of heart failure, but are contraindicated in MG. The clinical case confirmed another observation that IVA is a good alternative to reduce the HR in patients with systolic HF and sinus rhythm. Its efficacy is also demonstrated by the improvement in EF and the reduction of the BNP. IVA is effective in improving clinical outcome in HF (cardiovascular death, hospitalizations, worsening HF) in P without MG. Is a HR-lowering agent which acts specifically on the sino-atrial node and inhibits the If current of cardiac pacemaker cells, with no effects on other cardiac ionic currents, like those of the neuromuscular junction. The HF is rare in MG and the overlapping of symptoms between the two conditions may delay the diagnosis. The echocardiogram and the BNP are valid diagnostic tools. IVA is a useful, effective, and well-tolerated drug for systolic HF in MG in sinus rhythm.

## 1266

### Non-infective endocarditis in a patient with fever

D Daniela Teferici<sup>1</sup>; A Lloji<sup>2</sup>; A Idrizi<sup>3</sup>; Y Themeli<sup>4</sup>; M Luzati<sup>5</sup>

<sup>1</sup>University Hospital Center Mother Theresa, Tirana, Albania; <sup>2</sup>University Hospital Center Mother Theresa, Internal Medicine, Tirana, Albania; <sup>3</sup>University Hospital Center Mother Theresa, Service of Nephrology, Tirana, Albania; <sup>4</sup>Diagnostic Center Med.al, Tirana, Albania; <sup>5</sup>University Hospital Center Mother Theresa, Cardiology - Cardiac surgery, Tirana, Albania

**Introduction:** Libman Sacks endocarditis (LSE) is present in 1 on every 10 patients with systemic lupus erythematosus (SLE). The diagnosis of LSE becomes challenging in differentiating it from infective endocarditis (IE). Case: This is a 16 year old female who presents with fatigue, fever, shortness of breath. History of present illness stated 2 weeks ago. On physical examination she presented increased central venous pressure, tachypnea, tachycardia, temperature 38.8°C, BP150/90mmHg, a grade V/VI pansystolic mitral murmur. 3 pairs of blood culture samples were collected from different sites and all had negative results. A cardiac ultrasound revealed large pericardial effusion (PE) and the decision of pericardiocentesis was made. The patient's laboratory work up revealed high creatinine levels, proteinuria, abnormal LFTs, hemolytic anemia, thrombocytopenia, WBC 10900, CRP 33.8g/L. Work up showed positive antinuclear antibody (ANA), anti-dsDNA, anti-ENA screen and slightly depressed serum complement levels. According to the diagnostic criteria the diagnosis of SLE was made and the patient started treatment with methylprednisolone and cyclophosphamide. A transthoracic echo (TTE) revealed: diffuse infiltration of anterior mitral leaflet and a nodular thickening on it, sized 20x10mm (Fig. 1), severe mitral regurgitation, concentric hypertrophy of LV, normal size and systolic function of both ventricles. A small amount of PE was detected. Considering a possible IE, elevated CRP and WBC levels, ampicillin and gentamycin for 2 weeks was added. As the urea and creatinine levels raised up and the patient became oliguric, she was transferred to nephrology ward; hemodialysis was started. Under the above mentioned treatment, her symptoms improved; afebrile, creatinine level after reaching 7mg/dl went down up to 3mg/dl. TTE studies have yet to be repeated as of writing this article. Discussion: This is a case report of a young patient with SLE, who presented with progressive dyspnea, (caused by PE) and fever. The patient had an aseptic vegetation in the mitral valve with severe MR. The most commonly involved valve in LSE, is the mitral valve. The vegetation seen on TTE, was on the anterior mitral valve leaflet, with infiltration of the entire leaflet. Laboratory parameters can be useful in distinguishing IE from LSE. 3 laboratory data are important: white blood cell count, c-reactive protein (CRP) and blood cultures. The leukocytes tend to decrease during lupus activity and the opposite occurs in IE. Very high CRP levels suggest an infectious cause; for a definitive differential diagnosis, the blood cultures are more important. In the present case, a diagnosis of LSE was more probable, as the leukocyte count was slightly elevated, the CRP was not highly elevated and blood culture samples had negative results. **Conclusion:** Patients with SLE will be more likely to develop cardiac manifestations of lupus, such as valvular regurgitation and possible LSE.



1267

**Infiltrative cardiomyopathy: a novel aetiology**TG Moon<sup>1</sup>; K O'gallagher<sup>1</sup>; D Sado<sup>1</sup><sup>1</sup>King's College Hospital, Department of Cardiology, London, United Kingdom

**Introduction and case report description:** Cardiomyopathy is a common condition encountered by the cardiologist but clinicians should be vigilant to rarer causes. We present the case of a 52-year-old gentleman presenting with pulmonary oedema secondary to an infiltrative histiocyte cardiomyopathy caused by Rosai-Dorfman Disease (RDD).

**Description of the problem, procedures, techniques and/or equipment used**

A 52-year-old Afro-Caribbean male presented with a 6-month history of dyspnoea, decreasing exercise tolerance and paroxysmal nocturnal dyspnoea. Clinically he was in pulmonary oedema. He had a history of RDD and chronic hepatitis B. There was no previous cardiac history. Transthoracic echocardiography (TTE) demonstrated biventricular hypertrophy with suggestion of a right atrial mass. At this point the cardiac diagnosis was unclear.

**Questions, problems or possible differential diagnosis**

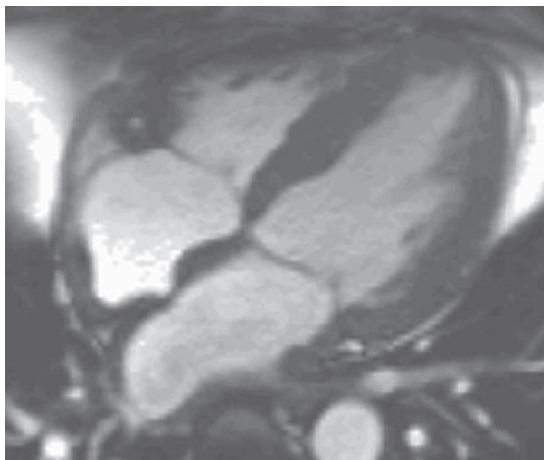
What are the differential diagnoses for biventricular hypertrophy with a right atrial mass? What technique would you use to confirm the diagnosis? How would you manage this patient?

**Answers and discussion**

The differential diagnoses included amyloidosis, sarcoidosis or hypereosinophilic syndrome but subsequent cardiovascular magnetic resonance (cMR) imaging was not consistent with any of these. cMR imaging revealed thickening of all four cardiac chambers. No right atrial mass was seen, however the right atrial wall was grossly thickened. There was normal gadolinium kinetics and no late enhancement. The patient proceeded to an endomyocardial biopsy. Histological assessment demonstrated a lymphocytic and histiocytic infiltration with emperipolesis and positive S100 staining. These findings are characteristic of RDD. To our knowledge this is the first case describing infiltration of all four cardiac chambers secondary to RDD. The patient received cisplatin, etoposide and dexamethasone as medical therapy for RDD. Serial cMR demonstrated improvement in myocardial infiltration and a reduction in cardiac mass, but progressive infiltration of the aortic valve and initially moderate, then severe aortic regurgitation. An intended aortic valve replacement has not been possible due to ongoing gastrointestinal and respiratory complications of immunosuppression.

**Conclusions and implications for clinical practice**

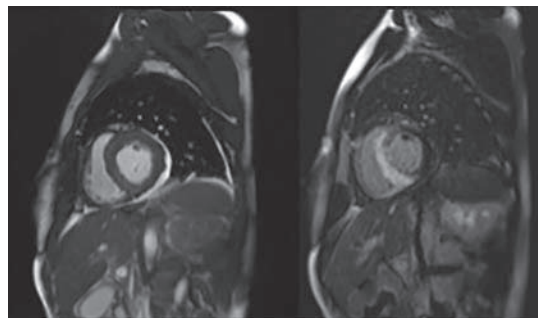
Originally described in 1969, RDD is a rare, non-clonal proliferative disorder of histiocytes of unknown aetiology which typically causes bilateral painless cervical lymphadenopathy. Extra-nodal involvement most commonly involves the skin, nasal cavity, paranasal sinuses, orbit, upper respiratory tract and bone. Cardiac involvement is rare, occurring in <1% of cases. To our knowledge, this is the first description of RDD involving all four cardiac chambers. This case highlights the need to be vigilant to rare causes of cardiomyopathy and the role of endomyocardial biopsy in diagnosing cardiomyopathies of uncertain aetiology.



cMR- Rosai Dorfman Cardiomyopathy

**Introduction:** Myocarditis is an inflammatory disease of the myocardium with a wide range of clinical presentations, from subclinical disease to sudden death. Viral infection is the main aetiology and its treatment may require immune therapy when an unstable presentation occurs. Case report: A 39-year old white female without previous cardiovascular history was admitted to the coronary unit because of chest pain. A stage IVA follicular lymphoma was diagnosed six months before admission. The patient completed a first line regimen with rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone. No completed remission was achieved after treatment, starting a second line regimen with rituximab, etoposide, methylprednisolone, cytarabine and cisplatin. The patient developed pericardial chest pain, hypotension and fever a few hours after the second cycle. On examination, blood pressure was 72/50 mmHg and heart rate was 92 bpm. Heart sounds were rhythmic without murmurs. An electrocardiogram showed an ST-segment elevation in the inferior leads and an echocardiogram was performed revealing a mild left ventricular systolic dysfunction with inferoseptal akinesia. Troponin I levels raised up to 50,1 ng/ml. A computerized tomography coronary angiogram was performed, showing normal coronary arteries. A cardiovascular magnetic resonance found the presence of late gadolinium enhancement involving the inferoseptal epicardium and mid myocardium. Left ventricular ejection fraction (LVEF) was 39%. PCR for detection of enterovirus was positive in pharyngeal and blood samples. According to these results an acute enterovirus myocarditis was suspected. After stabilizing the patient with inotropic agents, immune therapy consisting of intravenous methylprednisolone and immunoglobulin was initiated. A new echocardiogram revealed a deterioration of the LVEF down to 34% and severe functional mitral regurgitation. The patient developed dyspnoea, starting treatment with diuretics with an initial good response. Ten days after diagnosis the patient suffered a ventricular fibrillation, return of spontaneous circulation (ROSC) was achieved after thirty minutes of cardiopulmonary resuscitation. Cardiogenic shock resistant to inotropic agents and intraaortic balloon pump occurred and the patient was deceased after 48 hours.

**Discussion and conclusion:** Acute myocarditis may associate in a minority of patients a poor prognosis. The differential diagnosis includes ischemic heart disease, valvular heart disease, congenital heart disease, other cardiomyopathies and pulmonary disease. Rituximab is a monoclonal antibody directed against the CD20 antigen on B-lymphocytes, which modifies the humoral immune response increasing viral infections. Lethal enterovirus myocarditis associated with rituximab is an extremely unusual condition described in the medical literature and its treatment should include haemodynamic support, immune therapy and mechanical support in unstable patients.



Cardiovascular magnetic resonance

1269

**A rare cause of polyserositis with constrictive pericarditis**PD Pitic<sup>1</sup>; PI Petre<sup>1</sup>; DM Dan<sup>1</sup>; DM Dorobantu<sup>1</sup><sup>1</sup>Emergency Clinical Hospital Floreasca, cardiology, Bucharest, Romania

Constrictive pericarditis is a rare cause of chest pain. The patients present usually with signs and symptoms of right heart failure, without any history of heart disease and with normal systolic function. The etiology remains the most important challenge.

We present the case of a 47 years old man, smoker who came in the emergency department complaining in the last month of cough and constrictive chest pain, improved by leaning forward. He associated also a pharyngeal infection, self-treated with nonsteroidal anti-inflammatory drug and antibiotic therapy; under this medication the symptoms were solved briefly.

At the emergency room a fast echocardiography was done, revealing circumferentially pericardial fluid. The patient was admitted in the cardiology department for further investigation. A CT (computed tomography) scan of the chest and abdomen with intravenous contrast was done. The result was polyserositis- thickening of the pericardium with a small amount of pericardial fluid, bilateral pleural effusion and peritoneal fluid. Also moderate increased volume of the liver was found; no pathological masses were detected. The blood work revealed the presence of a

1268

**Lethal enterovirus myocarditis associated with rituximab**O Oscar Gonzalez Fernandez<sup>1</sup>; T Lopez Fernandez<sup>1</sup>; C Alvarez Ortega<sup>1</sup>; R Mori Junco<sup>1</sup>; P Meras Colunga<sup>1</sup>; V Rial Baston<sup>1</sup>; J Irazusta Cordoba<sup>1</sup>; E Lopez De Sa<sup>1</sup>; M Moreno Yanguela<sup>1</sup>; JL Lopez Sendon<sup>1</sup><sup>1</sup>University Hospital La Paz, Cardiology, Madrid, Spain

inflammatory syndrome and a moderate elevation of the hepatic transaminases (with the predominance of the aspartate aminotransferase); the cardiac enzymes (creatin kinase and creatine phosphokinase-MB) were normal.

At this point, corroborating the clinical and paraclinical data, the differential diagnosis was made between an infection with a systemic implication, neoplasia or an autoimmune disease.

Colchicine (one milligram per day) and Ibuprofen (six hundred milligrams every eight hours) were administered. Under this treatment, during the second day of the admission the patient became febrile, so hemocultures were taken and Ciprofloxacin was added to the treatment.

The echocardiography was repeated, bringing important information: medium size pericardial fluid with adhesions between the visceral and parietal layer, septal bouncing and significant respiratory variations of mitral and tricuspid flow velocity with preservation of myocardial velocities (tissue Doppler). These findings were conclusive for effusive-constrictive pericarditis.

Because of the persistent fever, the history of pharyngeal angina, acute inflammatory syndrome and polyserositis the presence of an infectious disease was strongly suspected. The patient was transferred to the Infectious Disease Hospital, where a rare form of pharyngeal infection with *Yersinia enterocolitica* was found; after 3 weeks of antibiotics, Colchicine and Ibuprofen treatment the echocardiography was normal.

We consider this case of a rare form of infection with *Yersinia enterocolitica*, leading to polyserositis and a transient form of constrictive-effusive pericarditis. Particular, the cardiac symptoms led to the diagnosis and cure of the infection.

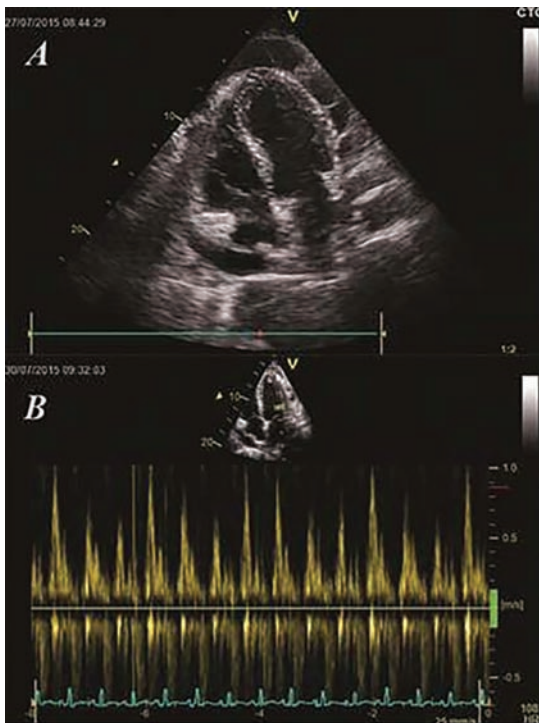


Fig 1A four chamber viewBmitral valve PW

## 1270

### Endomyocardial fibrosis secondary to hypereosinophilic syndrome

P Pablo Meras Colunga<sup>1</sup>; N Montoro<sup>1</sup>; J Irazusta<sup>1</sup>; V Rial<sup>1</sup>; E Refoyo<sup>1</sup>; S Valbuena<sup>1</sup>; G Guzman<sup>1</sup>; A Robles<sup>2</sup>; A Iniesta<sup>1</sup>; JL Lopez-Sendon<sup>1</sup>

<sup>1</sup>University Hospital La Paz, Cardiology, Madrid, Spain; <sup>2</sup>University Hospital La Paz, Internal Medicine, Madrid, Spain

We present the case of a 27-year-old man from Paraguay who was referred to our centre because of pain, paresthesias and ulcerated lesions in both lower limbs. An arteriogram showed diffuse arterial disease with areas of stenosis and occlusion as well as important collateral circulation. With the diagnosis of advanced lower extremity peripheral artery disease, medical treatment was started, but he finally required a left limb supracondylar amputation.

During the postoperative period, he suffered an acute pulmonary edema requiring intravenous diuretics and non invasive mechanical ventilation. An echocardiogram was performed, revealing severe left ventricular dysfunction with global hypokinesia and a diastolic restrictive pattern, secondary severe mitral regurgitation and mild right ventricular dysfunction.

Several complementary tests were performed, finding a constant elevation of eosinophiles and IgE levels. A cardiac resonance revealed circumferential subendocardial late gadolinium enhancement in both ventricles, suggesting endomyocardial fibrosis, without areas of edema in STIR sequences.

A wide differential diagnosis was attempted, dismissing most common etiologies. We ruled out infectious diseases, mainly parasitic infections, but also HIV, Lyme and Chagas disease, among others. We also considered celiac disease and other endocrinal diseases or nutritional deficits, Buerger disease, sarcoidosis, amyloidosis, hemochromatosis and acute myocarditis. Coronary artery disease was ruled out with an angio-CT.

Hypereosinophilic syndrome (HES) is a multisystemic disease as a result of maintained blood elevation of eosinophiles and IgE. Primary causes (hematologic disease) were dismissed by means of a bone marrow biopsy, as well as secondary causes (hypersensitivity, atopia, parasite infection, autoimmune disease, collagen disease, malignancy, eosinophilic pulmonary diseases, hyper-IgE syndrome, etc.). Finally, an idiopathic HES with cardiac and vascular – but also pulmonary and hematologic – involvement was diagnosed.

We initiated treatment with bisoprolol, enalapril, eplerenone and ivabradine. We also started corticosteroids and, later on, azathioprine, with analytical improvement but with no impact on left ventricular ejection fraction. A CRT-D was implanted for primary prevention of sudden cardiac death. The patient is currently in a stable situation with good functional class and no hospital readmissions.

Collaboration among different specialties is mandatory for the management of these patients with complex multisystemic diseases.

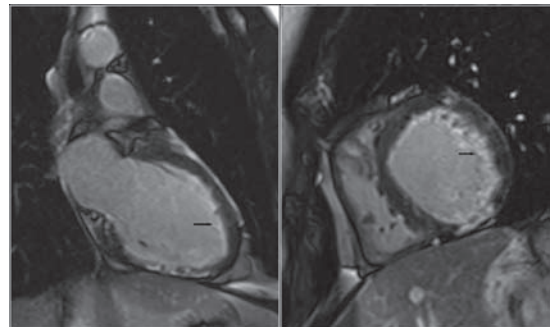


Image 1. CMR



## CLINICAL CASE 3: HEART (UNDER) ATTACK: CARDIAC INVOLVEMENT IN SYSTEMIC DISEASES

Monday 23 May 2016 11:00–12:30

Location: Agora

1293

### Hip to be square: cardiomyopathy of unknown origin

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**Background:** The pathogenesis of cardiomyopathies is very complex and variable, since genetic factors, post-translational alterations, endocrine abnormalities, microbial infections, and environmental factors can lead to the phenotype of dilated cardiomyopathy. Therefore, the work-up for the initial presentation of a patient with cardiomyopathy of unknown origin still remains a diagnostic challenge in clinical practice. We here describe a patient with signs of heart failure, neurological impairment and liver failure.

**Case presentation:** A 66-year old male was referred to our tertiary hospital with signs of heart failure (fatigue, dyspnea on exertion, orthopnea) and neurological impairment (loss of vision and hearing), as well as weight loss during the last months. Medical history included hypertension since 10 years and bilateral hip replacement with chronic left hip pain. Six months ago hypothyroidism was treated with levothyroxine and heart failure was diagnosed. Echocardiography at that time point showed a reduced left ventricular ejection fraction (LVEF = 38%), heart failure therapy was started. Initial laboratory findings at our institution showed reduced kidney function and elevated liver enzymes. Initial ECG was unremarkable, additional diagnostics including screening for vasculitis, amyloidosis, infectious or mitochondrial diseases were negative. Cardiac biopsy showed features of dilated cardiomyopathy including interstitial fibrosis with no evidence for an infiltrative or inflammatory process. The patient deteriorated rapidly and died despite maximal inotropic therapy. Autopsy revealed toxic cardiomyopathy by cobalt poisoning.

**Summary and Conclusion:** Cobalt intoxication was initially reported in the literature in the 1960s as beer-drinkers cardiomyopathy. Since then some cases have been described, mainly documenting cobalt toxicity from hip arthroplasties. In a patient presenting with heart failure, hypothyroidism, liver failure and a history of hip arthroplasty and ongoing hip pain, the work-up for DCM should include toxicological screening.

1294

### Hydroxychloroquine-induced cardiomyopathy in a patient with limited cutaneous systemic sclerosis

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**Introduction:** Hydroxychloroquine (HCQ) is a widely used medication in the management of many connective tissue diseases. Cardiac toxicity is a rare but serious complication related to the chronic use of HCQ. Possible manifestations are the development of cardiomyopathy or of conduction abnormalities. Herein, we present the case of a 58-year-old female with limited cutaneous systemic sclerosis who was admitted to our institution with HCQ-induced cardiotoxicity.

**Case presentation:** A 58-year-old woman with a 2-year history of limited cutaneous systemic sclerosis was referred to our institution for further work-up of progressive dyspnea (NYHA class 2–3) over a period of 2 months. Her cardiac history before admission includes a dual chamber pacemaker implantation (in 1993 due to complete AV-block). Her other medical history includes peripheral artery disease and cardiovascular risk factors such as arterial hypertension and hyperlipidemia. She was taking HCQ, sildenafil and a Iloprost. Physical examination revealed bilateral lower leg swelling. The electrocardiogram was normal. Initial investigations at the time of admission revealed an elevated NT-pro-BNP (17825ng/l). Transthoracic echocardiography revealed concentric LV hypertrophy (LV septal and posterior wall thickness measuring 1.9 cm and 1.4 cm, respectively) with a severely reduced systolic ejection fraction (EF) of 30% and an elevated filling pressure (E/A' 17)

with restrictive filling pattern (E/A 2.7). Right ventricular function was normal. In a right and left heart catheterization, significant coronary artery disease was excluded. Left ventricular end diastolic pressure (LVEDP) was elevated (LVEDP 30 mmHg). For further diagnostic work-up, endomyocardial biopsy was performed. The histopathologic examination excluded other cause such as amyloidosis, myocarditis or an acute vasculitic process. The examination showed Myocytes with numerous cytoplasmic vacuoles and low-grade diffuse interstitial fibrosis (Figure 1). Based on these findings, the diagnosis of HCQ-induced cardiomyopathy was confirmed. The drug was immediately discontinued and heart failure medication was initiated.

**Conclusion:** HCQ-induced cardiomyopathy is a rare but significant complication of HCQ-therapy and should be strongly suspected in patients developing conduction abnormalities or heart failure. To the best of our knowledge, this is one of the rare cases of HCQ-induced cardiomyopathy.

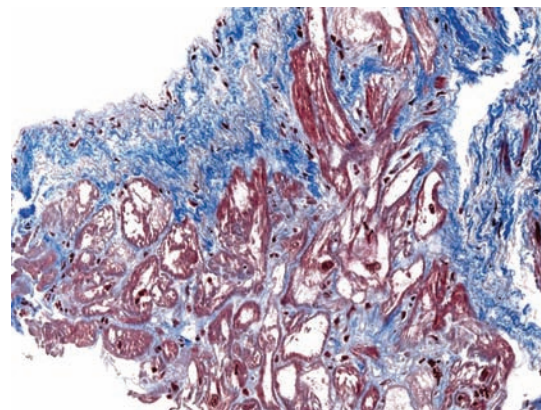


Figure 1

1295

### Createcine phosphokinase utility in diagnosing new onset heart failure

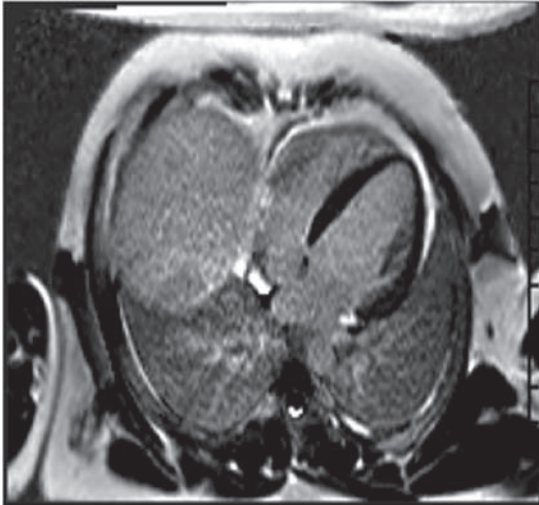
A Yehya<sup>1</sup>; RM Martin<sup>2</sup>; VP Polsani<sup>3</sup>; BS Stambler<sup>4</sup>  
<sup>1</sup>Piedmont Heart Institute, Advanced Heart Failure and Heart Transplant, Atlanta, United States of America; <sup>2</sup>Piedmont Heart Institute, Marcus Heart Valve Center, Atlanta, United States of America; <sup>3</sup>Piedmont Heart Institute, Cardiac Imaging, Atlanta, United States of America; <sup>4</sup>Piedmont Heart Institute, Cardiac Electrophysiology, Atlanta, United States of America

**Introduction:** creatine kinase is one the diagnostic laboratory testing that should be performed in all patients with cardiomyopathy according to the European Society of Cardiology (ESC) but not in the American College of Cardiology (ACC) and the Heart Failure Society of America (HFSA) guidelines.

**Case report:** a 21 year previously healthy, asymptomatic college student male referred to our clinic after his primary care physician auscultated irregular heart sounds. The patient denied palpitations, limitation of activities, dizziness, syncope or presyncope. His ECG demonstrated sinus rhythm with premature atrial contractions (PAC). To evaluate his PAC, a Holter monitor and a transthoracic echocardiogram (TTE) were ordered. His Holter monitor revealed moderate PAC burden (10.5% in 24 hours) and the TTE revealed global hypokinesis of the left ventricle (LV), with an estimated ejection fraction (EF) 35-40%. A CPK was ordered and was notably elevated at 6180 mcg/L (normal 24-204). Goal directed medical

therapy (GDMT) was initiated and a cardiac MRI was ordered after 3 months of GDMT demonstrating mild global hypokinesis with LVEF 48%. (Fig 1-4) Our patient was referred to a rheumatologist to rule out primary connective tissue disorder. Muscular dystrophy was suspected and genetic testing was performed revealing a hemizygous, in-frame deletion in the Duchenne muscular dystrophy gene. The clinical picture is most consistent with Becker's muscular dystrophy associated cardiomyopathy.

**Conclusion and Implication:** CPK testing was instrumental in establishing the etiology of the newly diagnosed cardiomyopathy in our patient. It was also important for defining his clinical management and overall prognosis. This underscores the importance of having CPK as part of the routine testing in our cardiomyopathy patients and calls for ACC and HFSA to include it in our initial diagnostic laboratory panel as the ESC does.



## 1296

### Hyponatremia- possible factor in biventricular pacing abnormalities

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**Introduction and case report description:** Hyperkalemia is an established cause of biventricular device malfunction, but data in the literature about hyponatremia is scarce. Reporting unusual causes is worthwhile for an appropriate management. We report the case of a 59-year-old patient implanted with a CRT cardioverter defibrillator (DDD, lower rate of 50beats/minute) two weeks before, with congestive heart failure symptomatology and generalized muscle weakness. The electrocardiogram (ECG) revealed sinus rhythm with a heart rate of 70bpm with only intermittent pacing spikes followed by biventricular capture. The patient had metabolic acidosis, with normal potassium and calcium levels but a significantly low serum sodium concentration (116mEq/l).

**Description of the problem, procedures, techniques:** QRS complexes, both paced and non- paced, were larger compared to his previous ones and a new first degree atrioventricular block was detected. The interrogation confirmed intermittent loss of atrial sensing leading to loss of biventricular pacing even at the highest sensitivity on the atrial lead. Atrial capture was absent even at the highest pacing voltage and impulse duration. The atrial lead impedance and radiological position and the ventricular pacing and sensing thresholds were normal. The problems improved after initiation of sodium replacement therapy and metabolic acidosis correction, but completely resolved only after reaching a sodium level of 127mEq/l. The paced QRS complex width returned to normal, atrial sensing was constant, the atrial pacing threshold improved and also the patient status improved significantly.

**Questions, problems or possible differential diagnosis:** The cause of CRT failure was unclear and initially we suspected an atrial lead problem- displacement, local inflammation or lead injury. Metabolic acidosis has also been described to induce pacing problems in certain conditions.

**Answers and discussion:** The normal impedance and radiological aspect made atrial lead problems unlikely but could not exclude local inflammation. The close temporal association between sodium correction and reversal of the pacing and conduction problems suggests that hyponatremia, added to metabolic acidosis, played an important role. A small amount of preclinical and clinical data suggests that hyponatremia can produce conduction disturbances and also pacing malfunction by altering fast sodium currents. It is highly unlikely that metabolic

acidosis alone was the cause of malfunction, as all reports describe it along with high extracellular potassium levels, which was not the case in our patient.

**Conclusions and implications for clinical practice:** Hyponatremia is likely to play an important role in cardiac device malfunction. The physician should be aware of this possible issue in order to avoid a delay in diagnosis, unnecessary medication and/or interventions, and potentially fatal hemodynamic deterioration.

## 1297

### Enterocutaneous fistula as a complication of left ventricular assist device after heart transplant

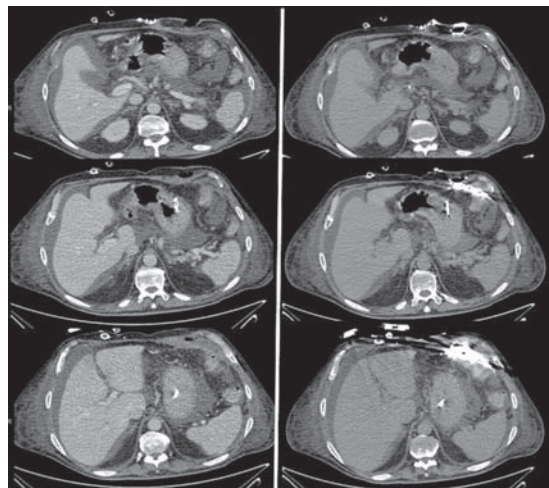
J Jesus Velasquez Rodriguez<sup>1</sup>; E Zatarain-Nicolas<sup>1</sup>; I Sousa-Casasnovas<sup>1</sup>; A Villa-Arranz<sup>1</sup>; J Fernandez-Yanez<sup>1</sup>; M Juarez-Fernandez<sup>1</sup>; G Cuerpo-Caballero<sup>2</sup>; JM Barrios-Gutierrez<sup>3</sup>; A Gonzalez-Pinto<sup>2</sup>; F Fernandez-Aviles<sup>1</sup>

<sup>1</sup>University Hospital Gregorio Maranon, Cardiology, Madrid, Spain; <sup>2</sup>University Hospital Gregorio Maranon, Cardiac Surgery, Madrid, Spain; <sup>3</sup>University Hospital Gregorio Maranon, Anaesthesiology, Madrid, Spain

**Introduction:** Left ventricular assist devices (LVAD) have changed end-stage heart failure prognosis. Most devices require abdominal wall transgression and create a potential for abdominal complications.

**Case report:** A 58-year-old male underwent uncomplicated implantation of a paracorporeal pulsatile-LVAD (PP-LVAD) for an end-stage ischemic cardiomyopathy as a bridge to heart transplantation (HT). He had several episodes of gastrointestinal bleeding during support. After a severe rectorrhagia an abdominal computed tomography (CT) showed active bleeding at the ascending colon, but colonoscopy and angiography could not localized the bleeding point for treatment. The inner cannula was directly in contact with splenic angle of colon but no signs of complication were observed. One month later, patient received a HT after 104 days of support. The inner cannula was difficult to remove due to intense fibrosis. It was done after graft implantation, in order to avoid lack of time because the graft arrival. The treatment after HT was basiliximab (one single dose at the first day), steroids, micophenolate mofetil from the beginning and tacrolimus was started the 14th day. The 11th day after surgery, fecaloid secretion started to drain through the wound of the inner cannula; CT confirmed the existence of an enterocutaneous fistula from the splenic flexure of the colon that was neither connected to the peritoneal cavity nor to thoracic cavity after injection of iodide contrast (picture). The CT also evidence the presence of a supradiaphragmatic retrosternal collection. Surgical drainage of the thoracic collection was decided and surgical exploration did not find connection with abdominal cavity. The microbiologic culture of the thoracic samples and wound samples were positive for *Enterococcus faecium*. The enterocutaneous fistula was decided to be treated by medical approach first, because there was no drainage of intestinal content to peritoneal cavity and the patient was without infection signs. Soon after the patient had respiratory deterioration with pulmonary distress and repeated atelectasis, oliguric renal failure and progression to septic shock. The patient had a poor outcome with severe sepsis refractory to proper antibiotic treatment and there were no chance to abdominal surgery due to instable situation so unfortunately he died.

**Clinical implications:** Intestinal complications related to LVAD during support are already described in literature. This is the first description of enterocutaneous fistula after HT due to removal of PP-LVAD support. The withdrawal of the cannula at the moment of HT can be complex because the intense fibrosis of the scar. Those patient may benefit from imaging diagnosis of the anatomic relationships of the cannula before HT. Early surgical approach may help to avoid future septic complications due to enterocutaneous fistula, even if there is no evidence of active infection at that moment.



1298

**An unusual treatment strategy and an infrequent comorbidity in chronic heart failure with reduced ejection fraction**

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<sup>2</sup>Medical Centre, Hungarian Defence Forces, Internal Medicine, Budapest,

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Budapest, Hungary; <sup>4</sup>Medical Centre, Hungarian Defence Forces, Radiology, Budapest, Hungary

**Background:** Chronic heart failure with reduced ejection fraction (HFrEF) is a complex clinical syndrome with significant morbidity and mortality. Patients with severe therapy-refractory heart failure often require prolonged hospitalization. Considerable attention is needed to handle all comorbidities and iatrogenic diseases.

**Case report:** We report the case of a 71-year-old cachectic man who was admitted to our department with refractory HFrEF (LVEF: 15%), in NYHA III-IV functional class. He had a history of COPD and a preceding continuous hospitalization for 5 months because of advanced HFrEF. At the time of admission he did receive neither ACEi nor beta blocker because of intolerance. But in the effect of the direct vasodilator regime (dihydralazine and nitrate) the patient later was able to tolerate an ACEi and a BB. We could even successfully titrate the doses of these drugs and it was possible to reach the optimal medical treatment of HFrEF. During hospitalization we took some blood cultures because of persistently elevated inflammatory markers (CRP: 54.4 mg/L, ESR: 100 mm/h, WBC: 9.5 G/L), which were positive for MRSA. CT

angiography (CTA) conducted as part of our investigation of significant weight loss, persistent atypical chest pain and MRSA bacteraemia revealed a pseudo-aneurysm (PA) of the descending thoracic aorta. After a negative result of a TOE a PET-CT scan was done for the detection of MRSA bacteraemia source as part of complex investigation. It visualized the PA as the only positive region. Based on the results of the afterwards performed control CTAs, PA size progression was confirmed. Because of the MRSA infected PA of descending thoracic aorta an aorta stent graft implantation was proposed by the interdisciplinary consultation (vascular surgeon, infectologist and cardiologists) after a six-week course of antibiotic (IV vancomycin). After the successful operation and a further six-week targeted treatment with antibiotics (IV vancomycin and gentamicin) the patient was discharged in clinically stable condition on optimal medical treatment of HFrEF and on triple combination of oral antibiotics (rifampicin, doxycycline, sulfamethoxazole/trimethoprim). Three months after the stent graft implantation follow-up tests verified normal conditions, and control CTA showed the graft in normal position without sign of inflammation. One year after the procedure the patient is still in stable condition both from the cardiology and infectology point of view (LVEF: 35%, NYHA I-II, CRP: 5.5 mg/L, WBC: 5.9 G/L, ESR: 20 mm/h).

**Conclusions:** The care of HFrEF patients is a complex problem and requires special attention. Comorbidities can be encountered frequently, which have great impact on hospitalizations and mortality. MRSA aortitis is a life-threatening disorder. Rapid and accurate diagnosis of the disease can be a challenge for the clinicians. Close collaboration between different medical professions is essential for proper treatment.



## RAPID FIRE 4 - DEVICES

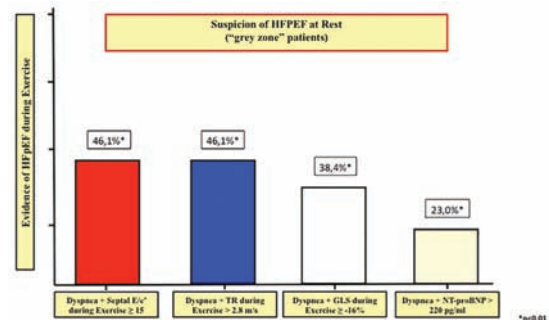
Monday 23 May 2016 14:15–15:45

Location: Agora

1344

**Non-invasive lung impedance-guided preemptive treatment in chronic heart failure patients: a randomized controlled trial (impedance-HF trial)**M Michael Shochat<sup>1</sup>; A Shotan<sup>1</sup>; I Kleiner<sup>2</sup>; I Dahan<sup>1</sup>; D Blondheim<sup>1</sup>; M Kazatsker<sup>1</sup>; A Asif<sup>1</sup>; J Weinstein<sup>2</sup>; S Meisel<sup>1</sup><sup>1</sup>Hillel Yaffe Medical Center, Heart Institute, Hadera, Israel; <sup>2</sup>Saroka Medical Center, Cardiology, Beer Sheva, Israel**Background:** Previous investigations have suggested that lung impedance (LI)-guided treatment reduces hospitalizations for heart failure (HF). A single-blind two-center trial was performed to evaluate this hypothesis.**Methods:** Study population included 256 patients with Chronic Heart Failure (CHF), Left Ventricle Ejection Fraction  $\leq 35\%$  in New York Heart Association class II-IV. Patients were randomized (1:1) to a control group treated by clinical assessment and a monitored group whose therapy was also assisted by LI. Noninvasive LI measurements were performed with a new high-sensitive device. The primary efficacy endpoint was HF hospitalizations. Secondary endpoints were all-cause hospitalizations and mortality. For statistical analyses were used Cox proportional-hazards, Poisson and negative binominal models.**Results:** The mean follow-up was  $48 \pm 32$  m (5221 visits, 511 patient-years follow-up, 10.6 visits/ patient-year) in the monitored group, and  $39 \pm 26$  m (4351 visits, 411 patient-years follow up, 10.6 visits/ patient-year) in the control group ( $p=0.01$ ). The groups were similar with respect to baseline characteristics. There were 67 vs. 158 HF hospitalizations during the first year (HR = 0.51, 95% CI 0.38-0.68,  $p < 0.0001$ , Number Needed to Treat [NNT] = 1.4) and 211 vs. 386 HF hospitalizations (HR = 0.63, 95% CI 0.53-0.75,  $p < 0.0001$ , NNT=1.9) during the entire follow-up among the monitored and control patients. All-cause mortality during the follow-up period included 42 patients in the monitored group and 59 patients in the control group (rate: 0.08 vs. 0.14 per patient-year follow-up, HR = 0.52, 95% CI: 0.35-0.78,  $p = 0.002$ , NNT=7.5). Cardiovascular (CV) death occurred in 26 and 47 patients, (rate 0.05 vs. 0.11, HR = 0.41, 95% CI: 0.25-0.67,  $p < 0.0001$ , NNT=6.1) in the monitored and control group, respectively. During the entire study period there were 13 deaths due to HF in the monitored and 31 HF deaths in the control groups (rate 0.03 vs. 0.08, HR = 0.30, 95% CI: 0.15-0.58,  $p = 0.0001$ , NNT=7.1). There was no significant difference in the incidence of non-CV deaths.**Conclusion:** The IMPEDANCE-HF is the first trial demonstrating that LI-guided pre-emptive therapy of worsening pulmonary congestion, prevents HF hospitalizations in CHF patients and reduces all- cause, CV and HF mortality in these patients.

1345

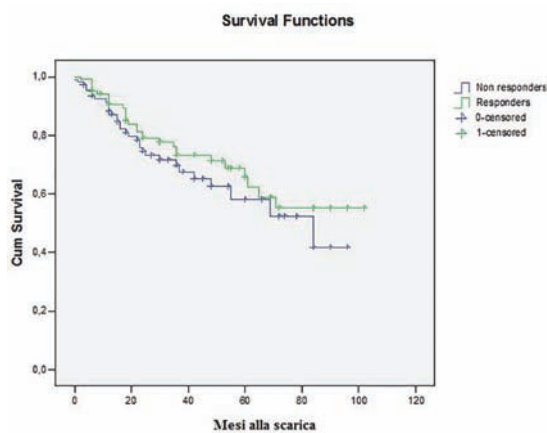
**Diagnostic relevance of diastolic stress-test echocardiography in patients with suspicion of heart failure with preserved ejection fraction**E Belyavskiy<sup>1</sup>; E Kraigher-Krainer<sup>1</sup>; DA Morris<sup>1</sup>; M Url-Michitsch<sup>2</sup>; Aravind K Radha Krishnan<sup>1</sup>; M Kropf<sup>1</sup>; R Kraft<sup>1</sup>; A Meinitzer<sup>3</sup>; A Schmidt<sup>2</sup>; B Pieske<sup>1</sup><sup>1</sup>Charite - Campus Virchow-Klinikum (CVK), Department of Internal Medicine and Cardiology, Berlin, Germany; <sup>2</sup>Medical University of Graz, Department of Cardiology, Graz, Austria; <sup>3</sup>Medical University of Graz, Clinical Institute of Medical and Chemical Laboratory Diagnostics, Graz, Austria**Aim:** The purpose of this study was to assess the diagnostic relevance of diastolic stress-test echocardiography (DST) in patients with suspicion of heart failure with preserved ejection fraction (HFPEF).**Methods:** Patients with suspicion of HFPEF (undetermined dyspnea NYHA class I-II, septal E/e' at rest  $9 - 14$ , and NT-proBNP at rest  $125 - 220$  pg/ml) and a control group constituted by asymptomatic patients with hypertensive heart disease (HHD) and healthy subjects were included. All patients were analyzed by conventional and 2D speckle-tracking echocardiography (STE) at rest and during exercise.**Results:** Fifty six subjects were included in the final analysis (13 with suspicion of HFPEF, 21 asymptomatic with HHD and 22 healthy subjects). Patients withsuspicion of HFPEF had significantly lower values of LV global longitudinal systolic strain (GLS), higher values of septal E/e', tricuspid regurgitation (TR) velocity and NT-proBNP during exercise than hypertensive and healthy subjects (GLS  $-18.7 \pm 4.2\%$  vs  $-21.6 \pm 3.8\%$  and  $-22.4 \pm 3.9\%$ ; E/e'  $14.0 \pm 3.1$  vs.  $8.8 \pm 1.7$  and  $8.1 \pm 1.4$ ; TR velocity  $2.52 \pm 0.67$  m/s vs.  $2.07 \pm 0.47$  m/s and  $2.01 \pm 0.21$  m/s; NT-proBNP  $125.6 \pm 92.4$  pg/ml vs.  $68.7 \pm 49.2$  pg/ml and  $73.5 \pm 38.1$  pg/ml). In line with these findings, 46.1 % of patients with suspicion of HFPEF had evidence of HFPEF during exercise, which was detected by DST (i.e. dyspnea and septal E/e' during exercise  $\geq 15$ ). Moreover, using a criteria of HFPEF as dyspnea + TR during exercise  $> 2.8$ m/s or dyspnea + GLS during exercise  $\geq -16\%$ , 46.1% and 38.4% of patients with suspicion of HFPEF had evidence of HFPEF during exercise, respectively.**Conclusion:** The findings of this study suggest that diastolic stress-test using both conventional and speckle-tracking echocardiography could be of great usefulness to diagnose HFPEF in patients in the diagnostic "grey zone".

1346

**Left ventricular dimension, but not reverse remodeling, predict the occurrence of malignant ventricular tachyarrhythmias in CRT patients.**A Alessandro Paoletti Perini<sup>1</sup>; I Ricceri<sup>1</sup>; P Pieragnoli<sup>1</sup>; G Ricciardi<sup>1</sup>; L Padeletti<sup>2</sup>  
<sup>1</sup>Careggi Hospital, Clinica Medica Department, Florence, Italy; <sup>2</sup>University of Florence, Florence, Italy**Introduction:** In chronic HF, CRT reduces hospitalizations and mortality, and improves LV performance by inducing left ventricular (LV) reverse remodeling. Burden of malignant ventricular arrhythmias (i.e. Ventricular Fibrillation (VF) and Ventricular Tachycardia (VT)) after CRT is reduced in responder patients.**Purpose:** aim of the present study is to evaluate the association between pre-implant LV dimensions, response to CRT and the long-term development of ventricular tachyarrhythmias requiring Implantable Cardioverter-Defibrillator (ICD) intervention, to assess whether initial LV size may help guide the implantation and programming of ICD associated with CRT.**Methods:** We enrolled 258 consecutive CRT-D patients implanted according to International Guidelines. An echocardiogram was performed at baseline and after 6 months. Occurrence of appropriate therapies (both shocks and ATPs) delivered by the device was assessed at each FU. According to previous literature, patients were regarded as responders if LV end systolic volume (LVESV) reduction was  $\geq 15\%$  at 6-month evaluation.**Results:** out of 258 CRT-D patients (76% males, mean age  $69 \pm 9$ ), 69 (27%) experienced at least 1 appropriate ICD therapy for VT/VF at a mean FU of  $37 \pm 24$  months (213 total events). At baseline, VT patients had greater LV dimensions than

non-VT ones (LV End Diastolic Diameter (LVEDD)  $70 \pm 8$  vs  $67 \pm 8$  mm,  $P = 0.009$ ; LV end systolic diameter (LVESD)  $59 \pm 8$  vs  $55 \pm 8$  mm,  $P = 0.001$ ); similarly, at 6 months, LV size was statistically related to appropriate ICD intervention (LVEDD  $68 \pm 8$  vs  $64 \pm 8$  mm,  $P < 0.001$ ; LVESD  $55 \pm 1$  vs  $51 \pm 9$  mm,  $P = 0.003$ ). A similar percentage of responders and non-responders, as traditionally defined, had at least 1 arrhythmic ventricular episode (48% vs 52%,  $P = 0.470$ ). In a multivariable Cox regression model comprehending age, gender, QRS duration, use of beta-blockers, etiology and baseline LV diameters, LVEDS (HR 1.034,  $p = 0.048$ ), ischemic etiology (HR 2.316,  $P = 0.003$ ) and female gender (HR 2.499,  $P = 0.021$ ) had independent association with ICD delivered-therapies. In a model comprehending age, gender, QRS duration, use of beta-blockers, etiology, responder status and 6 month LV diameters, both LVEDD (HR 1.054,  $P = 0.002$ ) and LVESD (HR 1.039,  $P = 0.013$ ), together with etiology and gender ( $P < 0.05$  for all), were associated to outcome, while responder status was not (HR 1.121,  $P = 0.682$ ).

**Conclusion:** In CRT-D patients, occurrence of appropriate ICD intervention show independent association to baseline and 6-month LV dimensions, rather than to the occurrence of LV reverse remodeling, traditionally defined as LVESV reduction  $\geq 15\%$  at 6-month FU.



Incidence of VF/VT

### 1347

#### Axial-flow left ventricular assist device pump speed increase is associated with increased peak exercise cardiac output and VO<sub>2</sub>, postponed anaerobic threshold and improved ventilatory efficiency

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**Background:** An increased cardiac output (CO) at peak exercise is associated with a larger oxygen consumption (VO<sub>2</sub>), provided that the arteriovenous difference of O<sub>2</sub> ( $\Delta(\text{Ca-Cv})\text{O}_2$ ) remains unchanged. At the anaerobic threshold, VO<sub>2</sub> depends on CO.

**Purpose:** To show that, in patients with chronic heart failure (HF) who underwent implantation of a continuous axial-flow left ventricular assist device (LVAD), a sharp increase in CO, achieved by changing the LVAD pump speed, is associated with an increase in VO<sub>2</sub> at the anaerobic threshold (AT) and at peak exercise.

**Methods:** Twenty patients with advanced HF who underwent LVAD implantation were enrolled; 15 patients successfully completed the measurements at peak exercise. Cardiopulmonary exercise tests were performed with simultaneous measurement of CO with the inert gas rebreathing technique at rest and at peak exercise, on two separate days, with the LVAD pump speed randomly set at 8000 rpm or 11000 rpm.

**Results:** A higher LVAD pump speed was associated with an increase in CO at rest (from  $3.4 \pm 0.9$  to  $3.8 \pm 1.0$  L/min,  $p = 0.04$ ) and at peak exercise (from  $5.3 \pm 1.3$  to  $5.9 \pm 1.4$  L/min,  $p < 0.01$ ). Similarly, VO<sub>2</sub> increased from  $788 \pm 169$  to  $841 \pm 152$  mL/min ( $p = 0.01$ ) at peak exercise and from  $568 \pm 116$  to  $619 \pm 124$  mL/min ( $p = 0.02$ ) at the anaerobic threshold. The arteriovenous difference of O<sub>2</sub> did not vary significantly, while ventilatory efficiency improved (VE/VCO<sub>2</sub> slope from  $39.9 \pm 5.4$  to  $34.9 \pm 8.3$ ,  $p < 0.01$ ) [Table 1].

**Conclusion:** In LVAD recipients, an increase in CO due to a higher LVAD pump speed is associated with a significant increase in peak VO<sub>2</sub>, anaerobic threshold and ventilatory efficiency.

Table 1

	Lower speed	Higher speed	P value
Peak VO <sub>2</sub> (mL/min)	788 ± 169	841 ± 152	0.01
Peak VO <sub>2</sub> (mL/kg/min)	10.0 ± 1.6	10.8 ± 2.0	0.01
Maximum ventilation (L/min)	39 ± 7	36 ± 10	NS
CO at rest (L/min)	5.3 ± 1.3	5.9 ± 1.4	< 0.01
$\Delta(\text{Ca-Cv})\text{O}_2$ at rest (mL/100 mL)	11.4 ± 4.5	9.9 ± 2.7	NS
$\Delta(\text{Ca-Cv})\text{O}_2$ at peak (mL/100 mL)	15. ± 3.9	15.1 ± 3.6	NS
Resting HR (bpm)	76 ± 9	72 ± 9	0.05
Peak HR (bpm)	101 ± 19	101 ± 19	NS
VE/VCO <sub>2</sub> slope	39.9 ± 5.4	34.9 ± 8.3	< 0.01
VO <sub>2</sub> AT (mL/min)	568 ± 116	619 ± 124	0.02
VO <sub>2</sub> AT (mL/kg/min)	7.3 ± 1.3	8.1 ± 1.6	0.01

### 1348

#### The heart mate risk score identifies patients with similar mortality risk across all INTERMACS classes in a large multicenter analysis: low INTERMACS class should not be a contraindication to LVAD

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**Background:** The Heart Mate Risk Score (HMRS) was recently proposed as a simple tool for risk stratification of LVAD recipients but has had conflicting estimates of its validity.

**Purpose:** To assess the performance of the Heart Mate Risk Score in a large multi-center cohort of patients, with a focus on its heterogeneity as a function of disease severity.

**Methods:** We performed a retrospective, longitudinal, comparative study using the INTERMACS database. We included all recipients of a primary continuous flow left ventricular assist device (CF-LVAD) with pre-implant data available to calculate the HMRS and excluded patients with CF-LVAD implant less than 90-day prior to database query or, CF-LVAD implant to replace previously placed VAD. Correlation with mortality was calculated with Cox models with an interaction by INTERMACS class (1 vs 2 vs 3+) Results - We identified 10,847 patients meeting inclusion criteria. 60.5% of patients were between the age of 50 and 69, 78.9 % were male, 14.1% were in INTERMACS class 1 and 37.3% were in INTERMACS class 2. HMRS showed a moderate discrimination with both short- (90 day, C-index 0.62) and long-term (5-year, C-index 0.59) mortality with no significant difference between axial and centrifugal devices. In fully-adjusted models, the Hazard for mortality comparing high HMRS and low HMRS categories was 2.92 ( $p < 0.001$ ) at 90 days and 1.85 at 5 years ( $p < 0.001$ ). Importantly, the HMRS had similar performance across INTERMACS classes and had better discrimination for mortality than INTERMACS classes (INTERMACS c-statistic = 0.58 at 90-day, 0.54 at 5-year). While INTERMACS class maintained a correlation with mortality after adjusting for HMRS level, calculation of a Net Reclassification Index (0.29 at 90 day,  $p < 0.05$ ) showed that addition of the HMRS to INTERMACS class appropriately reclassified mortality risk in up to 30% of patients. Patients with INTERMACS class 3+ and high HMRS had greater 90-day mortality risk than INTERMACS class 2 patients with low HMRS (9.6 vs 5.4%,  $p < 0.001$ ) and patients with mid-HMRS had similar 1-year and 2-year mortality risk independently of their INTERMACS category ( $p > 0.18$ ).

**Conclusion:** The HMRS is a valid tool to risk-stratify patients in all INTERMACS classes and may be more accurate than traditional INTERMACS classification. Risk stratification with the HMRS showed that patients within each INTERMACS class have a wide spectrum of mortality risk and low INTERMACS class should therefore not be considered per se a contraindication to mechanical support.

### 1349

#### The novel non-invasive ultrasound device for detection an early change in the brain in patients with heart failure.

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**Background:** Cognitive impairment has been described as a consequence of heart failure (HF). The exact mechanisms remain unclear probably it is due to embolic stroke or chronic cerebral hypoperfusion. It has been described that HF patients have more severe white matter hyperintensities (WMHs) when compared to healthy non-cardiac and cardiac controls. Acousticocerebrography (ACG) is a novel, non-invasive, transcranial ultrasound method that could potentially help to diagnose early stages of brain changes. ACG measure multispectral ultrasound signals that are propagated through the brain tissue, including: absorption coefficient, frequency dependent attenuation, speed of sound and tissue elasticity.

**Aim:** The aim was to compare the brains ACG signal with Magnetic Resonance (MRI) in patients in early stage of heart failure (EsHF) with WMHs.

**Methods:** From the group 352 Pts we selected 54 (age of  $66 \pm 6.7$ ) with EsHF treated with B-blocker 92,72%, ACE/ARBs 74,54%, Diuretics 43,63%. According to MRI data the patients (when WMHs was found) were assigned into four groups based on the number of WMHs: "L0"[0 to 4] WMHs, "L5"[5 to 9] WMHs, "L10"[10 to 29] WMHs and "L30"[ $>=30$ ] WMHs.

**Results:** It was proved that the ACG method could clearly differentiate a group of WMHs. (Fig. 1) For the patients with 0 to 4 WMHs (L0) and a group of patients with 30 and more WMHs (L30) this correlation is highly significant ( $p < 0.001$ ).

**Conclusions:** ACG is a new, effective method for detecting WML in patients with EsHF. The ACG measurement methodology may become increasingly useful to diagnose and to stratify patients with EsHF in order to individualize their treatment and maybe important to reduce their risk of cognitive impairment.

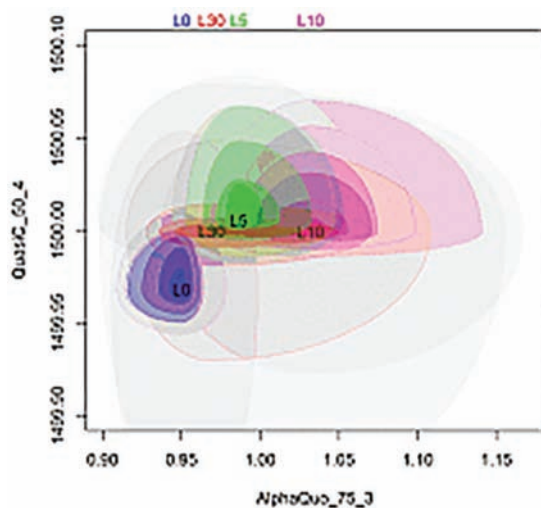


Fig.1

### 1350

#### Mortality in patients implanted with cardiac resynchronisation therapy with or without a defibrillator

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**Background:** The role of Cardiac Resynchronisation Therapy (CRT) in reducing morbidity and mortality in patients with heart failure is well established. However, incremental benefit of CRT-D (defibrillator) over CRT-P (pacemaker) remains uncertain.

**Purpose:** To evaluate whether in a standard UK District General Hospital population of heart failure patients implanted with CRT-P would have benefitted additionally from a defibrillator.

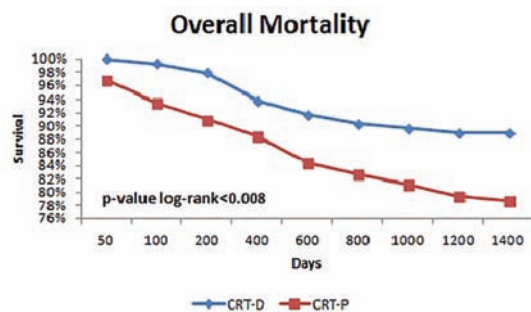
**Method:** This was a retrospective single-centre observational study comparing 267 patients implanted with either CRT-D or CRT-P devices between 2011 and 2015 at our institution. Data was collected from patient electronic records and follow-up visits. The median follow up duration was 2.2 (1.2-3.3) years.

**Results:** The patients implanted with CRT-P were older, had more advanced heart failure with more females (Table 1). The mortality was higher in the CRT-P group primarily due to non-cardiac causes 5.7% vs 15.6% ( $P < 0.001$ ) (Table 1). There were more documented ventricular arrhythmias in the CRT-D group and 12% received appropriate therapy, however in multivariate analysis Age $>75$  years was the only independent predictor of survival (OR 4.0 CI 1.7-9.5).

**Conclusions:** The higher mortality in patients implanted with CRT-P is mainly due to a higher age at implant and comorbidities. Therefore, on current selection criteria, CRT-P patients are unlikely to gain incremental benefit from the addition of a defibrillator.

Patient Characteristics			
	CRT-D	CRT-P	P-value
Number of Patients	145	122	
Mean Age yrs mean (SD)	70.6 (9.7)	79.2 (7.8)	$P < 0.0001$
> 75 yrs	39%	79%	$P < 0.0001$
Female	13%	24%	$P < 0.03$
NYHA III/IV	73%	85%	$P < 0.03$
Upgrade from chronic RV pacing	19.3%	27.9%	$P = 0.09$
VT/VF	19%	10%	$P < 0.03$
QRS ms mean (SD)	153 (20)	157 (25)	NS
Total Mortality	11%	21%	$P < 0.03$
Mortality: Cardiac	2.1%	5.7%	NS
Mortality: Non-cardiac	9%	15.6%	NS

SD- Standard Deviation, VT- Ventricular Tachycardia, VF- Ventricular Fibrillation, NS - Not Significant, RV -Right Ventricle.



### 1351

#### Myocardial scar on surface ECG: high eelvester score, but not QRS fragmentation, impairs response to cardiac resynchronization therapy.

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**Background:** Burden and transmural extension of myocardial scar impair response to Cardiac Resynchronization Therapy (CRT). Its presence may be assessed on surface ECG by either the Selvester Score (SSc) or the detection of QRS fragmentation (fQRS). True Left Bundle Branch Block (LBBB) has recently been identified as a pre-requisite for positive outcome after CRT, providing higher clinical benefit than LBBB as traditionally defined.

**Purpose:** To compare the prognostic significance of both scores in terms of left ventricular (LV) reverse remodeling (primary end-point) and major clinical events (secondary end-point), in the same cohort of CRT patients with true-LBBB on pre-implant surface ECG.

**Methods:** We retrospectively calculated the SSc and assessed the presence of fQRS on pre-implant ECGs of 178 consecutive patients with low left ventricular ejection fraction (LVEF  $\leq 35\%$ ), true-LBBB and NYHA class II-III despite optimal medical treatment, who underwent CRT-D implantation. Median value of SSc was chosen as cut-off for the analysis. Echocardiographic response to CRT (LV end-systolic volume reduction  $\geq 15\%$  or LVEF increase  $\geq 10\%$ ) was assessed six months after implantation. Clinical events comprehended cardiac mortality, hospitalizations due to heart failure (HF) and occurrence of ventricular arrhythmias requiring ICD intervention.

**Results:** Out of 178 consecutive patients with true LBBB, males were 120 (70%); mean age at implantation was  $70 \pm 10$  years; mean QRS duration was  $161 \pm 18$  ms; etiology was mostly not-ischemic (64%). Median SSc was 7; fQRS was present in 74 patients (41.6%). At 6 months, echocardiographic response occurred in 106 patients (59.5%). At multivariable analysis, SSc  $> 7$  was negatively associated with response (OR: 0.327; 95% C.I. 0.155-0.689;  $p = 0.003$ ), while fQRS showed no association (OR: 1.133; 95% C.I. 0.539-2.381;  $p = 0.742$ ). Response was independently associated also with female gender, absence of Diabetes Mellitus, Sinus Rhythm at implantation, and lower LVEF before CRT. Over a median follow-up of 24 (9-48) months,



28 deaths occurred (16%), of which 18 (10%) were diagnosed as cardiac deaths. Thirty-four patients (19%) were hospitalized for HF and 25 (14%) experienced at least one appropriate ICD intervention. At univariate Cox regression analysis no correlation was found between either SSc or fQRS and mortality, HF-hospitalizations, ventricular arrhythmias and a composite of these major adverse cardiac events (MACE).

**Conclusion:** SSc > 7 independently predicts non-response to CRT in true-LBBB HF patients undergoing CRT with defibrillation backup, and should be preferred to fQRS when looking for myocardial scar before implantation. However, neither SSc nor fQRS are associated with cardiac death, ventricular arrhythmias, HF-hospitalization or MACE.

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#### De novo aortic regurgitation after continuous flow left ventricular assist device implantation: a meta analysis

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**Background:** Continuous flow left ventricular assist devices (cf-LVAD) have become the standard of care for patients with advanced heart failure. De novo aortic regurgitation (AR) may occur after cf-LVAD implantation, and it harbors potential to adversely impact device performance and subsequently clinical outcomes.

**Purpose:** We aimed to determine the incidence of de-novo AR among cf-LVAD recipients, as well as to identify variables that are in correlation with its development. Odds ratios (OR) for dichotomous data and weighted mean differences (MD) with 95% confidence intervals (CI) for continuous data were calculated.

**Methods:** We performed a systematic search of PubMed and Cochrane Library for articles reporting on the incidence and predictors of de novo AR among patients with cf-LVAD. Significant AR was defined as more than mild in 5 studies, and as mild or greater in one.

**Results:** Six trials with a total of 468 patients were identified in the meta-analysis (Heartmate II 295 patients, HeartWare LVAD 130 patients, VentrAssist 2 patients, Jarvik 2000 3 patients, Evaheart 24 patients, Duraheart 14 patients). The combined incidence of de novo AR across the analyzed studies was 39%. Patients who developed de novo AR after cf-LVAD placement were older (MD 7.16 [95% CI 5.04, 9.29],  $P < 0.001$ ,  $I^2=39\%$ ), were less likely to be male (OR 0.49 [95% CI 0.29, 0.81],  $P=0.006$ ,  $I^2=0\%$ ) and had lower body surface area (BSA) (MD -0.13 [95% CI -0.18, -0.07],  $P < 0.001$ ,  $I^2=0\%$ ). Furthermore, they were more likely to have a persistently closed aortic valve (OR 5.82 [95% CI 3.69, 9.16],  $P < 0.001$ ,  $I^2=0\%$ ) and longer duration of support (208.06 [95% CI 116.68, 299.44],  $P < 0.001$ ,  $I^2=56\%$ ). Neither preoperative dimensions of the left ventricle (LV) nor LV ejection fraction had an impact on the development of de novo AR. Diabetes mellitus, hypertension or ischemic cardiomyopathy antedating cf-LVAD implantation had no effect on the subsequent development of de novo AR.

**Conclusions:** This meta-analysis illustrates that de novo AR occurs frequently after cf-LVAD implantation. Factors influencing its development and progression are older age, female gender, lower BSA, non-opening of the aortic valve and duration of cf-LVAD support.

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#### Effect of QRS narrowing after cardiac resynchronization therapy on functional mitral regurgitation

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**Purpose:** 1) To evaluate the predictors of FMR improvement after CRT, 2) To assess whether CRT-induced change in QRS duration ( $\Delta$ QRS) might have an impact on FMR response after CRT.

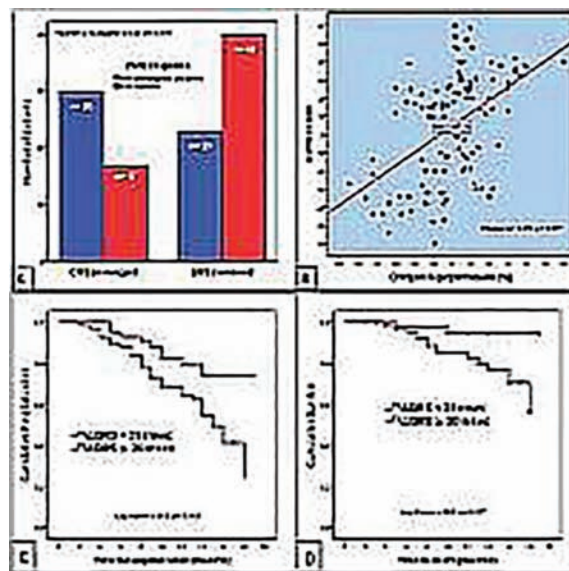
**Methods:** 110 CRT recipients were enrolled. CRT response ( $\geq 15$  reduction in LVESV) and FMR response (absolute reduction in FMR volume) were assessed with echocardiography before and 6-months after CRT. The study end-points included all-cause-death or hospitalization assessed in  $12 \pm 3$  months (range 1-18).

**Results:** A total of 71 (65%) patients responded to CRT at 6 months. FMR response was observed in 49 (69%) of the CRT responders and 8 (20%) of the CRT non-responders ( $p < 0.001$ ). The paced QRS durations were shorter ( $p = 0.012$ ) and the  $\Delta$ QRS values were higher ( $p = 0.003$ ) in FMR responders. There was a linear correlation between  $\Delta$ QRS and change in regurgitant volume ( $r = 0.49$ ,  $p < 0.001$ ). At multivariate analysis,  $\Delta$ QRS ( $p = 0.028$ ) independently predicted FMR response.

**Conclusion:** QRS narrowing after CRT independently predicts FMR response. A  $\Delta$ QRS  $\geq 20$  ms after CRT is associated with a favorable outcome in all clinical end-points.

#### Clinical outcome based on $\Delta$ QRS

	$\Delta$ QRS < 20 ms (n = 68)	$\Delta$ QRS $\geq$ 20 ms (n = 42)	p value
Improvement in NYHA class	30 (44%)	28 (66%)	0.027
Response to CRT	36 (53%)	35 (83%)	0.005
Reduction in FMR	22 (32%)	35 (83%)	< 0.001
Hospitalization	33 (49%)	9 (21%)	0.021
All-cause-death	14 (21%)	2 (5%)	0.022



QRS narrowing and FMR after CRT

1354

#### Cardiac resynchronization therapy combined with coronary artery bypass grafting in ischemic heart failure patients: long-term results of the RESCUE study

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**Aims:** Totally epicardial cardiac resynchronization therapy (CRT) is a novel treatment modality for patients with heart failure and systolic dyssynchrony undergoing coronary artery bypass grafting (CABG). In this study we have prospectively evaluated the long-term outcomes of totally epicardial CRT.

**Methods:** Between September 2007 and June 2009, one hundred seventy eight patients were randomly assigned to the CABG alone group (n = 87) and CABG with concomitant epicardial CRT implantation (n = 91). The primary endpoint of the study was all-cause mortality in the two groups between the day of surgery and August 13, 2013 (common closing date). The secondary outcomes included mode of death, adverse cardiac events and lead performance.

**Results:** The mean follow-up was  $55 \pm 10.7$  months. According to per-protocol analysis with treatment as a time-dependent variable to account for conversion from CABG to CABG+CRT, there were 24 deaths (35.8%) in the CABG group and 17 deaths (15.3%) in the CABG+CRT group. As compared to CABG alone, concomitant CRT was associated with reduced risk of both all-cause mortality (hazard ratio (HR) 0.43, 95% confidence interval (CI) 0.23 to 0.84,  $p = 0.012$ ) and cardiac death (HR 0.39, 95% CI 0.21 to 0.72,  $p = 0.002$ ). Eleven (12.6%) sudden deaths were observed in the CABG group in comparison to 4 (4.4%) in the CABG+CRT group ( $p = 0.048$ ). Hospital re-admission was required for 9 (9.9%) patients in CABG + CRT group and for 25 (28.7%) patients in CABG group (ER = 0.001). There were 4 (1.5%) epicardial lead failures.

**Conclusion:** The results of our study suggest that the procedure of coronary artery bypass grafting and totally epicardial CRT system implantation is safe and significantly improves the survival of patients with heart failure and dyssynchrony during long-term follow up.

1355

**Cardiac resynchronisation therapy in octogenarians**

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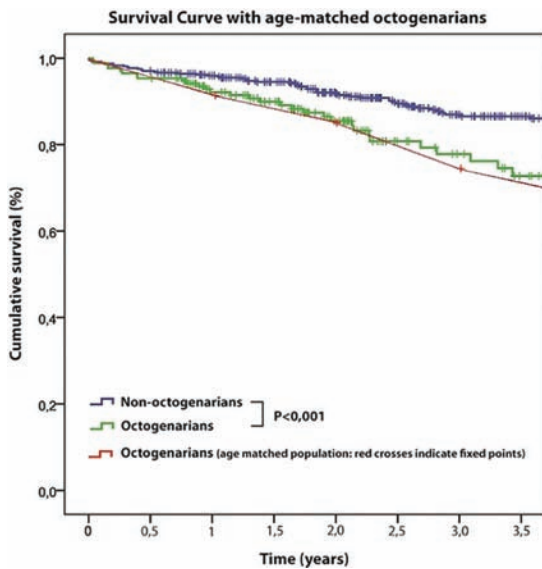
**Background:** Despite the high prevalence of chronic heart failure in octogenarians, these patients are systematically under-represented in clinical trials testing efficacy of cardiac resynchronization therapy (CRT).

**Purpose:** To evaluate clinical and echocardiographic response and long-term outcome after CRT in octogenarians.

**Methods:** A total of 687 consecutive CRT-recipients between October 2008 and July 2015 were retrospectively analyzed. Patients were dichotomous divided in octogenarians and non-octogenarians. Clinical improvement was analyzed as change in NYHA-class, echocardiographic response as change in ejection fraction (EF) and left ventricular end diastolic dimension (LVEDD) all at six month follow-up. For octogenarians annual death probability was calculated and compared with the general age-matched population using national actuarial life tables.

**Results:** A total of 166 octogenarians (83.3 ± 3.1 years) were compared with 459 non-octogenarians (68 ± 9.3 years). Both groups exhibited similar clinical response with equal change in NYHA-class (-0.88 ± 0.70 vs -0.89 ± 0.70; P = 0.88). Echocardiographic response was similar, with equal change in EF (12.6 ± 11.2% vs +12.9 ± 12.8%; P = 0.82) and LVEDD (-9.2 ± 12.5% vs -8.8 ± 16.9%; P = 0.82). Overall follow-up was 3.04 ± 1.89 years. Calculated annual mortality rate for octogenarians receiving CRT was 7.0% versus 7.5% for aged matched octogenarians in the general population (see figure 1; survival curve with age matched octogenarians plotted in red).

**Conclusion:** Despite advanced age, octogenarians retain the ability to mount clinical and echocardiographic response to CRT. Translating into an annual life-expectancy matching octogenarians in the general population.



Survival curve

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**The impact of persistent electrical dyssynchrony on predicting ventricular arrhythmias following cardiac resynchronization therapy**

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**Background:** Although response to cardiac resynchronization therapy (CRT) has been conventionally assessed with LV volume reduction, ventricular arrhythmias (VT/VF) are associated with poor outcome even in the “super-responders”.

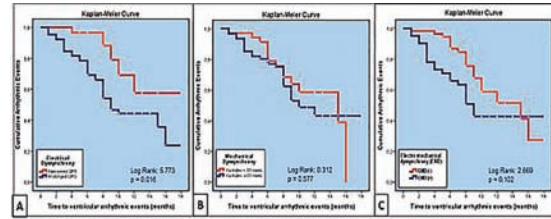
**Purpose:** To evaluate the predictors of VT/VF and the association of post-CRT persistent electrical and mechanical dyssynchrony with follow-up VT/VF.

**Methods:** Ninety-five patients receiving CRT were followed-up for 9 ± 3 months. A post-CRT prolonged QRS interval was defined as electrical dyssynchrony (ED). A Yu index ≥ 33 milliseconds was used to identify patients with persistent mechanical dyssynchrony (MD). Presence of both ED and MD was defined as electro-mechanical dyssynchrony (EMD). The first VT/VF episode defined as non-sustained VT on device interrogation and/or appropriate anti-tachycardia therapy for VT/VF were the end-points of the study.

**Results:** Forty-five patients who reached the study end-points had significantly

lower mean ΔQRS (baseline QRS – post-CRT QRS) intervals than those without VT/VF (-20.8 ± 28.9 ms vs. -6.6 ± 30.7 ms, p = 0.022). The baseline and post-CRT QRS intervals, and the Yu index values were not different in two groups. Patients with VT/VF were statistically more likely to have persistent ED (38% vs. 9%, p = 0.021). Kaplan-Meier curves showed that a negative ΔQRS was associated with a higher incidence of VT/VF during follow-up (p = 0.016). A multivariate Cox model revealed that QRS prolongation was an independent predictor of VT/VF after CRT (p = 0.029).

**Conclusions:** A negative ΔQRS, also called persistent ED is associated with VT/VF at follow-up. The narrowest possible QRS interval might be a reliable goal of both implantation and optimization of devices to reduce arrhythmic events after CRT.



Kaplan-Meier curves for prediction VT/VF

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**Multimodality Imaging in ICD Implantation Decision Making in Heart Failure Patients: Role of 123-Iodine Metaiodobenzylguanidine Imaging and Cardiac MRI**

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**Background:** According to guidelines, ICD therapy is recommended in prevention of sudden cardiac death (SCD) in heart failure (HF) patients (pts). Guidelines have several limitations because ICD indication is based mainly on left ventricular ejection fraction (EF). Recently, 123-iodine metaiodobenzylguanidine imaging (123-I MIBG), associated with cardiac magnetic resonance imaging (MRI), seems to identify, in pts candidate to ICD and independently from EF, pts at high risk of SCD (heart/mediastinum (H/M) ratio < 1.6 and a summed score (SS) > 26).

**Purpose:** Our aim is to assess the role of 123-I MIBG combined with cardiac MRI to predict ventricular arrhythmia (VA) causing ICD shock in HF pts

**Methods:** we enrolled 69 pts, consecutively admitted to our hospital with diagnosis of HF and EF ≤ 35%, who underwent 123-I MIBG imaging and cardiac MRI. SS > 26 was used as cut-off to identify high risk (group1) versus low risk (group 2) pts. Late gadolinium enhancement (LGE) was evaluated in the 2 groups. All pts of both groups underwent to ICD implantation. We assessed VA events and appropriate ICD therapy at 12 months follow-up.

**Results:** 21 pts were included in group 1 and 48 pts in group 2. All baseline characteristics were similar in 2 groups apart from the HF etiology. In group1, H/M ratio was 1.47 ± 0.24 and in group2 21.63 ± 0.27 (p = 0.015). The percentage of the pts with LGE was 70.9% in group 1 vs 39.1% in group2 (p = 0.023). At 12 months follow-up malignant VA events in group1 were 19.05% vs 4.17% in group2 (p < 0.037). Moreover VA events were statistically recorded greater in pts with both SS > 26 and LGE compared to pts with only SS > 26 (46.7% vs 19.6%, p = 0.046)

**Conclusion:** Our results seem to confirm that reduced 123-I MIBG uptake and presence of LGE are associated with the occurrence of life-threatening VA in HF pts independently from EF. The use of integrated imaging could be a useful tool in the future to increase the specificity of the selection of pts for ICD therapy.

Table 1

	Group 1 SS > 26 (n = 21)	Group 2 SS ≤ 26 (n = 48)	P value
H/M	1.47 ± 0.24	1.63 ± 0.27	0.015
Hypertension (%)	76.19	66.70	-
Diabetes (%)	23.81	16.67	-
Ischemic CM (%)	65.02	28.30	0.003
Idiopathic DCM (%)	34.98	68.90	0.003
EF %	26.05 ± 5.66	31.79 ± 10.30	0.005
ICD implantation	100%	100%	-
Malignant ventricular arrhythmia	4 (19.05%)	2 (4.17%)	0.037

1358

**Potential candidates to percutaneous left atrial decompression through interatrial shunt implantation among patients under evaluation for heart transplantation.**

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**Introduction:** Recently, a new approach for the treatment of advanced heart failure (HF) based on reducing left atrial pressure through a percutaneously implanted interatrial shunting device (IASD) has been demonstrated safe and effective. AIM: To evaluate the potential number of patients among those who underwent right heart catheterization (RHC) during evaluation for heart transplantation (HT) that met criteria for the use of and potential benefit from this new technology.

**Methods:** All patients sent to the HF clinic in our institution in the last 3 years who underwent RHC as part of the evaluation for HT were included. Clinical and hemodynamic parameters were gathered for all patients. Hemodynamic inclusion criteria for the subset of patients who may benefit from IASD within the first-in-man study included: Wedge pressure  $\geq 15$  and  $\leq 18$  mmHg, right atrial pressure (RAP)  $\geq 4$  and  $\leq 11$  mmHg, and systolic pulmonary artery pressure  $< 70$  mmHg.

**Results:** A total of 107 patients (84.1% males,  $56.8 \pm 10.9$  years of age) were included in this study. Of them, 74 patients (69.2%) were medically treated; 25 patients (23.4%) received HT; and 8 patients (7.4%) underwent an IASD implantation. Main reasons to avoid HT were adequate functional status (61.7%) and presence of comorbidities (36.4%). RHC mean parameters included RAP of  $10.7 \pm 7.7$  mmHg, systolic pulmonary artery pressure of  $47.3 \pm 16.6$  mmHg, wedge pressure of  $22.3 \pm 9.3$  mmHg, cardiac index of  $2.2 \pm 0.62$  L/min/m<sup>2</sup>, and pulmonary vascular resistance of  $2.8 \pm 1.8$  WU. Patients who underwent HT presented comparable RHC parameters to the other 2 groups, but worse NYHA class (III-IV in 100% vs. 82.7%,  $p = 0.034$ ). Up to 24 patients (22.4% of the study population) presented criteria for IASD implantation. Of them, 7 underwent HT (29.2%), 8 underwent IASD implantation (33.3%), and 9 (37.5%) were medically treated. At a mean follow-up of 1.5 years, 22 patients had died (16.3%) but none of them among patients who had undergone IASD implantation.

**Conclusions:** Patients evaluated for HT through RHC were finally medically treated in 3 out of 4 cases. One third of this subset of patients may benefit from percutaneous implantation of interatrial shunting devices according to RHC measurements. Indeed, initial experience with these devices was successfully performed in many of these cases.

1359

**Tri-ventricular pacing improves long-term survival and freedom from ventricular arrhythmias in advanced heart failure: results from a propensity-matched comparison.**

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<sup>1</sup>Barts Health NHS Trust, London, United Kingdom

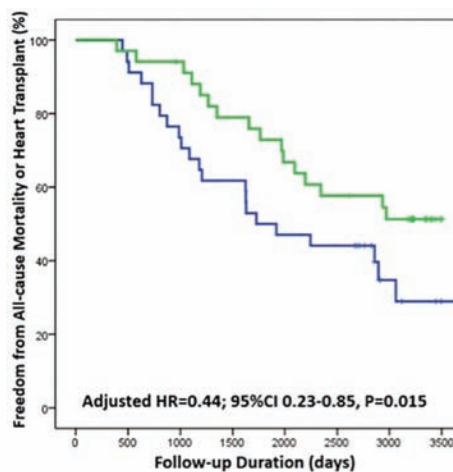
**Background:** Bi-Ventricular pacing (Bi-V) is an important adjunctive treatment in advanced heart failure, but almost one third of patients are non-responders. Adding a third ventricular lead (Tri-Ventricular pacing –Tri-V) has shown to be feasible and provide favourable acute results when assessed by echocardiographic, haemodynamic and clinical endpoints. However, long-term impact of this approach on survival and hard outcomes is unknown.

**Purpose:** We aimed to assess the long-term effects of Tri-V pacing and its impact on long-term survival.

**Methods:** Single-centre propensity score-matched cohort study comparing 34 advanced heart failure patients implanted with Tri-V devices with 34 controls treated with Bi-V comparing clinical outcomes (complications, survival and incidence of appropriate or inappropriate therapies) over a 10-year time interval.

**Results:** During a median of 2,478 days (IQR = 1,183-3,214) Tri-V patients presented with a comparable incidence of complications: lead dislodgement (Tri-V 0.86 vs. Bi-V 1.10 per 100 patient-years;  $P = 0.742$ ), device-related infection (Tri-V 1.83 vs. Bi-V 1.76 per 100 patient-years;  $P = 0.996$ ) and refractory phrenic nerve capture (Tri-V 0.48 vs. Bi-V 1.84 per 100 patient-years;  $P = 0.341$ ). However, Tri-V presented with a trend for shorter battery longevity (time to Box change: Tri-V  $1,758 \pm 360$  vs. Bi-V  $1,993 \pm 408$  days;  $P = 0.072$ ). Ventricular arrhythmia episodes requiring implantable cardioverter-defibrillator intervention occurred more frequently in the Bi-V group (Tri-V 6.55 vs. Bi-V 16.88 per 100 patient-years; adjusted HR = 0.31, 95%CI 0.14-0.66,  $P = 0.002$ ). Lower all-cause mortality and heart transplant was observed in the Tri-V group (Tri-V 6.99 vs. Bi-V 11.92 per 100 patient-years; adjusted HR = 0.44; 95%CI 0.23-0.85,  $P = 0.015$ ).

**Conclusion:** Tri-V displayed a similar safety profile when compared with Bi-V and was associated with potential benefits regarding long-term survival and ventricular arrhythmia burden. Further randomized controlled studies are required to confirm these promising results.



N at Risk	0	500	1000	1500	2000	2500	3000	3500
Bi-V	34	32	25	21	16	15	6	2
Tri-V	34	33	31	26	22	19	16	0



## MODERATED POSTER SESSION 5 – POPULATION STUDIES

Monday 23 May 2016 15:45–16:30

Location: Poster Area

1360

### Adhere to clinical guidelines concerning implantable cardioverter defibrillator deactivation?

Supported by Public Health Agency NI (Research & Development) and ESC/HFA Nurse Training Fellowship Grant 2014

LM Hill<sup>1</sup>; LM Hill<sup>2</sup>; SJ Mcilfratrick<sup>1</sup>; SJ Mcilfratrick<sup>3</sup>; BJ Taylor<sup>1</sup>; T Jaarsma<sup>4</sup>; A Stromberg<sup>4</sup>; D Fitzsimons<sup>1</sup>; D Fitzsimons<sup>2</sup>; D Fitzsimons<sup>3</sup>

<sup>1</sup>University of Ulster, Jordanstown, United Kingdom; <sup>2</sup>Belfast Health and Social Care Trust, Belfast, United Kingdom; <sup>3</sup>All Ireland Institute of Hospice and Palliative Care, Belfast, Ireland; <sup>4</sup>Linköping University, Linköping, Sweden

**Background:** An increasing number of heart failure patients receive an implantable cardioverter defibrillator (ICD) to prevent premature cardiac mortality. There is growing evidence that many patients receive multiple futile shocks from their device when nearing end-of-life. Recent studies indicate ICD deactivation is infrequently discussed with expert clinical guidelines not being implemented in practice.

**Purpose:** To examine the attitudes of healthcare professionals' through-out Europe regarding the discussion and deactivation of an ICD at end-of-life.

**Methods:** The factorial survey combines the strengths of experiment (random manipulation of variables) and survey design (improved recruitment), making it an ideal methodology to explore and measure the impact of implicit factors on decision-making. Data from a systematic literature review, retrospective case note review and ten case studies were refined to determine nine factors or Independent Variables (IV). The factorial survey consisted of a short demographic questionnaire followed by six unique clinical vignettes which embedded the IVs. The anonymised survey was distributed electronically through a secure IT platform to healthcare professionals in Europe involved in the management of patients with an ICD. Statistical analysis included multiple regression and ANOVA.

**Results:** A total of 1,518 vignettes were completed by 253 professionals (cardiologists, specialist nurses and cardiac physiologists). Preliminary results showed the majority of professionals agreed the cardiologist should initiate the discussion, although specialist nurses felt equipped to undertake this responsibility. Professionals in post for more than six years were found to be more confident in initiating the discussion ( $p=0.001$ ). There was diversity of opinion on when a discussion about deactivation should take place with an overall reluctance by professionals to discuss prior to device implantation. Consensus was found among professionals, and in line with guidelines, that deactivation should be discussed when death was imminent. Clinical indicators of severe heart failure ( $p < 0.0005$ ), presence of malignancy ( $p < 0.0005$ ) and a patient receiving multiple ICD shocks ( $p = 0.004$ ) were associated with an increased likelihood of a discussion. In terms of the decision to deactivate an ICD, professionals believed patients should be involved with many wishing for inclusion of next of kin.

**Conclusions:** Professionals are missing opportunities to inform patients and enable shared decision-making regarding their ICD. Innovative strategies across Europe require to be developed that aim to improve professionals' adherence to expert guidelines and ultimately benefit patient care.

1361

### Impact of ICD/CRT-D implantation on healthcare resources utilization: an Italian cohort study

F Achilli<sup>1</sup>; F Madotto<sup>2</sup>; LG Mantovani<sup>2</sup>; M Landolina<sup>3</sup>; M Lunati<sup>4</sup>; A Curnis<sup>5</sup>; M Marzeggall<sup>6</sup>; A Proclemer<sup>7</sup>; C Fornari<sup>2</sup>; G Cesana<sup>2</sup>

<sup>1</sup>San Gerardo de' Tintori Hospital, Cardiovascular Department, Monza, Italy; <sup>2</sup>University of Milano-Bicocca, Research Centre on Public Health (CESP), Monza, Italy; <sup>3</sup>Major Hospital, Cardiology Department, Crema, Italy; <sup>4</sup>Niguarda-Cà Granda Hospital, Cardiology Department, Milano, Italy; <sup>5</sup>Civili Hospital, Cardiology Department, Brescia, Italy; <sup>6</sup>"Maddalena Grassi" Foundation, Milano, Italy; <sup>7</sup>University Hospital Santa Maria della Misericordia, Udine, Italy

**Introduction:** Given the high burden of cardiovascular diseases, is crucial from a payer perspective to understand outcomes and costs of medical device use in clinical practice. We assessed clinical outcomes and the related healthcare resources utilization in patients (pts) implanted with ICD or CRT-D devices in an Italian Region.

**Methods:** Merged Lombardy Healthcare Administrative Databases (LHAD) information and clinical data recorded in the National ICD/CRT-D Registry (IRCAB) were used to identify pts implanted from 2000 to 2010 by means of indirect patient identifiers. Using this approach, 85.8% of LHAD pts have been linked with IRCAB files. Hospitalizations identified by ICD-9 codes, outpatient visits and drug consumption occurring within 3 years before and 8 years after device implantation were assessed.

**Results:** From 2003 to 2010, 12,525 pts (81.6% males, mean age 65.4+/-11.9 years) underwent a first device implantation (35.4% with single-chamber ICD, 29.4% with dual-chamber and 35.2% with CRT-D); 11,189 pts (89.4%) had dilated cardiomyopathy (44.2% ischemic, 45.1% idiopathic) and 49.0% had LVEF less than 30%. The number of first implantations increased over time being less than 135 implants in 2000 and more than 1850 implants/year from 2007 onwards; primary prevention indication increased from 12.8% in 2000 to 60% from 2007 onwards. Implant rate in 2005-2010 was 232.5/mln of person-years, whereas replacement rate was 10/100 pts-years. Pts were implanted after a median of 2 days [IQR: 1-7] from hospital admission (length of stay 6 days [IQR: 3-12]) in primary prevention and after 6 days [IQR: 2-11] (length of stay 10 days [IQR: 5-16]) in secondary prevention ( $p < 0.05$ ). The mean annual cardiovascular (CV) hospitalization rate/100 patients decreased from 95.7 (CI 95%: 93.5-97.9) in the year before implant to 47.5 (CI 95%: 45.7-49.3,  $p < 0.05$ ) in the 2nd year after the implant in ICD pts and from 107.0 (CI 95%: 103.9-110.2) to 52.2 (CI 95%: 49.6-54.9,  $p < 0.05$ ) in CRT-D pts. The total annual/pt costs for CV hospitalizations, outpatients visits and drugs significantly decreased from 5,441 € (CI 95%: 5,308€ - 5,613€) in the year before the implant to 2,525 € (CI 95%: 2,423€ - 2,621€) in the 2nd year after the implant.

**Conclusions:** ICD/CRT-D implantation appears to be effective not only in improving outcomes, but also in reducing CV costs both in ICD and CRT-D pts.

1362

### Cost utility of real-time pulmonary artery pressure monitoring using an implantable wireless pressure sensor from the perspective of the united kingdom national health service

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**Introduction:** Heart failure treatment guided by physicians with access to real-time pressure measurement from a wireless implantable pulmonary artery pressure (PAP) sensor has previously been shown to reduce hospital admissions for heart failure in the CHAMPION trial of 550 US heart failure patients. Cost effectiveness has also been previously demonstrated from the US health system perspective with an incremental cost effectiveness ratio (ICER) of \$30,167/QALY. PurposeThe system is CE marked but not yet reimbursed in Europe. Although demonstrably effective, uncertainty remains regarding the value of the system in European health systems where healthcare costs are significantly lower than in the US. We present a cost effectiveness analysis using treatment effects from the CHAMPION RCT to model the potential benefit to UK patients and value to the National Health Service.

**Methods:** A Markov cohort model consisting of two health states (stable heart failure and dead) was developed to estimate the cost effectiveness of PAP pressure guided treatment of heart failure using the CardioMEMS (St Jude Medical Inc) implantable pressure sensor compared to usual care strategies. Cost effectiveness was measured as the incremental cost per QALY gained. The time horizon was 10 years and no effect on mortality was modelled after 5 years. Mortality and hospitalisation rates

for usual care were taken from the literature, costs were calculated based on UK reference costs, quality of life values were modelled from the Champion trial and costs and QALYs were discounted at a rate of 3.5% a year. Distributions were assigned to model input variables in order to enable probabilistic sensitivity analysis to be performed to estimate uncertainty. Results in the base case analysis PAP guided heart failure therapy increased cost of treatment by £12,289 from £6,599 to £18,887 over the 10 year time horizon. Quality adjusted life years (QALY) per patient for usual care were 2.89 and 3.56 for PAP guided patients - an incremental increase in effectiveness of 0.67 QALYs. The resultant incremental cost effectiveness ratio is £18,291 per QALY gained. Varying the hazard ratio for mortality across the 95% confidence interval resulted in an ICER between £10,475/QALY and £59,276/QALY. The model was less sensitive to changes across the CI for the hazard ratio reduction in risk of heart failure hospitalisation where the ICER ranged from £17,293/QALY to £20,540/QALY. Assuming a willingness to pay threshold of £20,000 the system is cost effective in 81% of simulations.

**Conclusion:** The analysis indicates that integrating wireless pulmonary artery pressure monitoring into the management of UK heart failure patients is likely to be a cost effective addition to the heart failure treatment pathway for appropriate patients.

1363

**A cost analysis of HFPEF Vs HFREF in the first year following index hospitalization and enrollment in a disease management programme.**

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<sup>1</sup>Heart Failure Unit, St. Vincents University Hospital, Dublin, Ireland

**Background:** The index admission with heart failure (HF) is a milestone in the progression of the disease, often resulting in higher intensity medical care and ensuing readmissions. Whilst there is evidence to support enrolling patients in a heart failure disease management program (HF-DMP), there is a scarcity of literature differentiating costs based on ejection fraction.

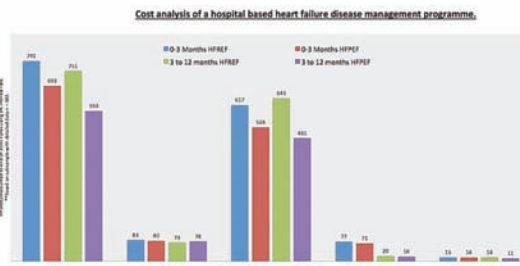
**Purpose:** To investigate the financial landscape of the first year following index hospitalization with HF and enrollment in an intensive 3-month hospital based HF-DMP, comparing HFREF with HFPEF.

**Methods:** 1292, consenting, consecutive patients admitted with a primary diagnosis of HF were enrolled in a hospital based, HF-DMP and categorized as HFPEF (EF ≥ 45%) and HFREF (EF < 45%). In addition to primary care and medication costs, DMP costs were evaluated using an assessment of scheduled and unscheduled DMP clinic visits, telephonic contact and medication changes over 3 months in addition to admissions to hospital over 1 year. Direct costs were included using a combination of casemix and microcosting techniques from the provider perspective.

**Results:** The total average cost per patient was higher in HFREF €13,011 (12011, 14078) than HFPEF, €12,206 (11009,13518) although confidence intervals overlapped. The cost of running a DMP was approximately 11% of the total annual cost of HF, with the majority of the expenditure allocated to hospitalizations, mainly the index admission and subsequent readmissions. Within the DMP, HFREF patients average cost was significantly greater than HFPEF patients, costing €8.78 a day versus €7.70 during a 90 day intensive DMP and €2.74 versus €2.16 a day for the remaining 9 months. The majority of the cost was associated to scheduled and titration visits. Table 1, Figure 1.

**Conclusion:** The majority of the financial outlay in the first year following index admission of HF is associated with hospitalization. The cost associated with the clinical workload in a HF-DMP is significantly higher amongst patients with HFREF than HFPEF.

Average (95% CI) cost per-patient Euros	HFREF (n = 879)	HFPEF (n = 413)
Index Admission (LOS based)	7660 (7047,8354)	6302 (5673,7004)
Readmissions	4287 (3574,5042)	5396 (4390,6494)
DMP Clinical Workload (0-3m)	791 (764,819)	693 (660,728)
DMP Clinical Workload (3-12m)	751 (701,802)	593 (533,655)
Medications	596 (579,613)	527 (505,550)
GP visits	594 (582,608)	569 (551,587)
All Costs	13011 (12011,14078)	12206 (11009,13518)



1364

**National trends and predictors of readmissions after HF hospitalization in Slovenia**

D Daniel Omersa<sup>1</sup>; J Farkas<sup>1</sup>; I Erzen<sup>1</sup>; M Lainscak<sup>2</sup>

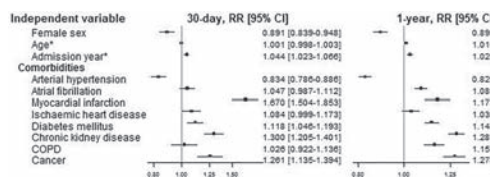
<sup>1</sup>National Institute of Public Health, Ljubljana, Slovenia; <sup>2</sup>General Hospital Celje, Department of Cardiology, Celje, Slovenia

**Introduction:** In addition to high mortality, patients with HF are frequently hospitalized and have high readmission rates. There are few studies with nationwide data regarding readmissions after HF hospitalizations, especially for central and east European countries. Thus our aim was to evaluate trends and predictors for HF readmission after HF hospitalization.

**Methods:** We recorded all HF hospitalizations from the Slovenian national hospital discharge registry between 2004 and 2012 where HF was coded in any diagnose fields. First HF hospitalization was defined as the first HF hospitalization of an individual after 4 years of observational period and 30-, 60-, 90-day and 1-year HF readmission as well as age, sex, year of admission and comorbidities were recorded. Annual readmission proportions were calculated and trends were assessed using ANOVA. Predictors for readmissions were evaluated using multiple log binomial regression analyses.

**Results:** A total of 156,900 HF hospitalizations in 79,865 patients were recorded (median age 77 yr., 54.3% women). Between 2008 and 2012 there were 43,636 (47.8%) first HF hospitalizations. In 11.7%, 17.2%, 20.9% and 37.5% of those first HF hospitalizations, 30-, 60-, 90-day and 1-year HF readmission followed, respectively. Between 2008 and 2011 increasing trends in annual HF readmission proportions were seen for all readmission endpoints (P < 0.05 for all). Male sex, myocardial infarction, cancer and chronic kidney disease were the most important independent predictors for all readmission endpoints (P < 0.001 for all, Figure). As predictors for HF readmission, myocardial infarction turned out to be less important predictor for 1-year HF readmission whereas chronic obstructive pulmonary disease (COPD) became significant only for 1-year HF readmission.

**Conclusion:** This retrospective observational study demonstrated increased trends in HF readmissions after HF hospitalization that were associated with specific comorbidities.



Predictors of HF readmission. \*per 1 yr.

1365

**Global variations in heart failure outcomes: INTER-CHF**

Novartis

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<sup>1</sup>McMaster University, Hamilton Health Sciences, Hamilton, Canada

**Background:** Heart failure (HF) is a global health problem. Most HF data comes from North America and Europe, with scant information from the rest of the world.

**Methods:** INTER-CHF is a prospective, longitudinal cohort study of 5823 participants conducted in 108 centers from 16 countries in Africa, Asia, the Middle East and South America. Patients with a clinical diagnosis of HF were prospectively enrolled over 17 months. Demographic features, risk factors, investigations and therapies were recorded at enrolment, and patients were followed for one year to determine mortality and HF hospitalization. Differences in mortality between regions were examined after adjustment for 12 key clinical variables (Model 1) and additionally for medication use (Model 2) and for socioeconomic variables (Model 3), using Cox proportional hazards analysis.

Unadjusted outcomes at one-year							
Variable	China n = 991	India n = 858	SE Asia n = 811	Middle East n = 1000	Africa n = 1294	South America n = 869	P-VALUE
Death at 1 Year (%)	7.1	19.9	13.9	8.9	26.4	8.4	<.0001
HF hospitalization at 1 Year (%)	27.5	16.3	17.6	25.1	24.3	16.1	<.0001
Death or HF hospitalization at 1 Year (%)	31	26.7	24.9	28.8	39	20.4	<.0001

HF=heart failure; SE=Southeast

**Results:** Among 5823 HF patients recruited, there were 858 deaths (14.7%) at one year. The unadjusted one-year mortality/HF hospitalization or mortality rates ranged from 26.4%/39% in Africa to 8.4%/20% in South America ( $p < 0.001$ , Table). Adjusting for clinical variables (Model 1) and comparing to patients in South America as the reference, patients from Africa and India [hazard ratio (HR)=3.3 [confidence interval (CI)=2.3-4.8 for both] had the highest mortality, with intermediate risk [HR=2.5 (CI=1.7-3.8) for patients in Southeast Asia and no excess risk for patients in China [HR = 0.75 (CI = 0.5-1.2)] or the Middle East [HR=1.2 (CI = 0.8-1.8)]. After additionally adjusting for medication use, followed by socioeconomic variables, the significantly higher mortality rates in Africa and India remained [HR=3.3 (CI=2.2-4.8) and HR=3.2 (CI=2.1-4.7), respectively].

**Conclusions:** Heart failure patients in Africa and India have markedly higher one-year mortality rates compared to patients from South America, China and the Middle East, even after adjustment for key clinical variables, medication use, and socioeconomic variables. Understanding the reasons for excess mortality in HF patients from these regions is crucial to improving patient care.

### 1366

#### Interpretability of the European Heart Failure Self-care Behaviour scale score

KP Wagenaar<sup>1</sup>; BDL Broekhuizen<sup>1</sup>; FH Rutten<sup>1</sup>; A Stromberg<sup>2</sup>; AW Hoes<sup>1</sup>; T Jaarsma<sup>2</sup>

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**Background:** The European Heart Failure Self-care behaviour scale (EHFScBs) is a validated patient-reported outcome questionnaire to measure self-care behaviour of heart failure (HF) patients. It is primarily used in research. It is, however, unknown how its score should be interpreted.

**Purpose:** To enhance better use, we aimed to assess the interpretability of the EHFScB scale.

**Methods:** We used cross-sectional data with 12 months follow up of 1,023 HF patients from the COACH study, a randomized trial on effects of support with a disease management program in HF patients (mean age 71 (SD 11) years, 63% male). At baseline demographic characteristics were measured. At baseline, and after 12 months all participants filled out questionnaires on self-care (EHFScB), HF related quality of life (Minnesota Living with Heart Failure Questionnaire (MLHFQ)), while the HF nurse or cardiologist assessed New York Heart Association functional classification (NYHA). In addition, during follow-up hospitalizations and mortality were registered. Interpretability refers to the meaning of score results and changes within. We operationalised interpretability by evaluating distributions of EHFScB scale scores across relevant subgroups by eyeballing, and by defining a threshold. The scale has a standardized score from 0-100, with a higher score meaning better self-care. The distribution of scores across the scale was explored in subgroups of a) severity of HF, b) duration of HF, c) LVEF, d) age, e) gender, f) depressive symptoms, g) knowledge on, and h) education in HF. A threshold of  $\geq 70$  was defined as adequate self-care, and  $< 70$  as inadequate self-care. The risk on hospitalisations and mortality using the threshold was tested with a Chi2 test.

**Results:** The distribution of the EHFScBs scores showed a similar pattern in the relevant subgroups with a mean between 57.8 (SD 18.0) and 70.0 (SD 23.6). The 559 HF patients with inadequate self-care (score  $< 70$ ) had significantly more all-cause hospitalizations than the 464 patients with adequate self-care (score  $\geq 70$ ).

**Conclusion:** Scores on the EHFScBs were equally distributed in relevant HF subgroups. A single threshold of '70' seems to discriminate between adequate and inadequate self-care.

### 1367

#### The caregiver burden inventory in evaluating the burden of heart failure patients' caregivers: a multicenter study

A Andrea Greco<sup>1</sup>; M Sala<sup>1</sup>; L Pancani<sup>1</sup>; D Baretta<sup>1</sup>; M D'addario<sup>1</sup>; A Petruzzo<sup>2</sup>; R Alvaro<sup>2</sup>; P Steca<sup>1</sup>; E Vellone<sup>2</sup>

<sup>1</sup>University of Milan-Bicocca, Department of psychology, Milan, Italy; <sup>2</sup>University of Rome Tor Vergata, Rome, Italy

**Background:** The importance of caregiver (CG) in the management of many diseases has been well documented, especially for chronic illnesses, as heart failure (HF). For this reason, the maintenance of an acceptable healthy condition and the avoidance of CGs' burden have been underlined as topic issues. Many studies have highlighted that CGs' burden negatively impacts on the quality of life of patients. Many instruments have been validated to measure CGs' burden in different illness contexts but very few have been validated in HF patients' CGs. Purpose. The aim of this study was dual: 1) to provide a psychometric validation of the Caregiver Burden Inventory - CBI in a cohort of HF patients' CGs; 2) to identify determinants of CG burden, considering socio-demographic, clinical, and psychological variables, measured both for patients and their CGs.

**Methods:** This was a cross-sectional study on Italian HF patients and their CGs, enrolled from different outpatient centers in 28 Italian provinces. CG was defined as the unpaid person, inside or outside the family, who provides the most informal care, as well as designated by the patients. CG strain, quality of life, perceived social support, and contributions to self-care, and patient comorbidities, cognitive function, contributions to self-care, activities of daily living, physical and emotional quality of life, as well as sociodemographic characteristics, duration, severity, and type of HF were measured. Confirmatory factor analyses (CFA) were used to evaluate the structural models of CBI dimensionality and multiple regression analyses were conducted to investigate determinants of CG burden.

**Results:** In total, 505 HF patients (44.6% female, mean age 75.6  $\pm$  10.7 years) and their CGs (52.2% female, mean age 56.9  $\pm$  14.8 years) were enrolled. CFA showed the items clustered into the original five factors proposed by Novak and Guest (1989): time-dependence, developmental, physical, social and emotional burden. This five-factor model fitted good ( $\chi^2(242)=513.287$ ,  $p < .001$ ; CFI=.95; RMSEA=.047; SRMR=.067), better than other different models, and the dimensions showed high internal consistency (Cronbach's alphas were .908, .917, .875, .893, and .925 respectively). Regression analyses revealed that CG quality of life, CG perceived social support, CG contributions to self-care, and patients disability in activities of daily living, as well as disease severity were the major predictors of CBI dimensions.

**Conclusions:** CBI proved to be a valid and reliable multidimensional instrument for evaluating the impact of burden of HF patients' CGs. This tool and the identified determinants of CG burden can be considered to tailor interventions aimed at improving CG outcomes. Finally, this study also suggest that the comparison of burden of CGs of patients with different disease is possible using this questionnaire.



# CLINICAL CASE CORNER 5: WHEN THE HEART IS BURNING: CASES OF INFLAMMATORY CARDIAC INVOLVEMENT PART II

Monday 23 May 2016 15:45–16:30

Location: Poster Area

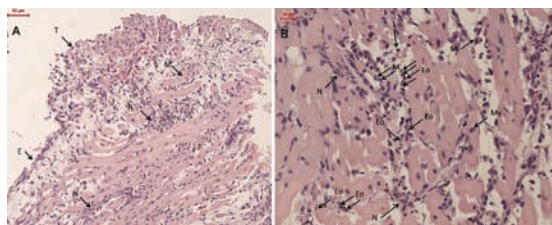
1368

## Acute tetraplegia in idiopathic necrotizing eosinophilic myocarditis

E Edda Bahlmann<sup>1</sup>; HS Van Der Schalk<sup>1</sup>; AG Ghanem<sup>1</sup>; ID Dotz<sup>1</sup>; DL Lassner<sup>2</sup>; UG Gross<sup>2</sup>; HS Schultheiss<sup>2</sup>; DK Kivelitz<sup>1</sup>; CT Terborg<sup>1</sup>; KK Kuck<sup>1</sup>

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We report a 59-year old man admitted after a motorcycle accident with a left-sided fracture of the tibial head Morre V, treated surgically. Four weeks later laboratory testing revealed increasing inflammatory markers and shortly later he presented confusion, fever, paresis of the right arm, angina and elevated troponin. Coronary angiography ruled out artery stenosis. Clinical signs of right- and soon after left-sided hemiplegia and aphasia followed. Cranial MRI revealed an extensive neurocranial infarction combined with small subcortical hemorrhage. Transesophageal echocardiography confirmed left ventricular (LV) hypertrophy with preserved ejection fraction but was negative for intracardial thrombi, endocarditis, foramen ovale or aortic atherosclerosis. Besides pneumonic infiltrations and congestion, thoracic CT scans revealed new onset and rapid progression of LV wall thickness and subendocardial ischemia. Soon after the patient was resuscitated due to ventricular fibrillation. In cardiac MRI late enhancement particularly in the inner layers probably consistent with myocarditis and apical appositional thrombus formation was found. LV endomyocardial biopsy samples confirmed the diagnosis of a severe active necrotizing eosinophilic myocarditis with endocardial thrombus apposition (figure). Intubation and tracheotomy became necessary because of persistent tetraplegia with dysphagia. Immunosuppressive therapy with prednisolone was immediately initiated and Azathioprine was added and resulted in fast recovery of serum hyper eosinophilia. In addition therapeutic anticoagulation was initiated. The patient was discharged to a neurorehabilitation centre. Discussion: Acute necrotizing eosinophilic myocarditis is a very rare, unclear and potentially fatal condition with variable clinical presentations. Association with parasitic infections, drugs, hypersensitivity reaction, hyper eosinophilic syndrome and paraneoplastic occurrence is reported. This case report is the first reporting a patient with acute necrotizing eosinophilic myocarditis complicated by tetraplegia. Our patient did not present with typically described heart failure symptoms due to cardiac dysfunction. Arrhythmias as in our patient is reported in some cases. The diagnosis is based on endomyocardial biopsy with apparent eosinophilic and lymphocytic infiltration with cell necrosis. Cardiac recovery after immunosuppression is described in patients with impaired left ventricular function. Clinical recognition in this scarce and untreated fatal condition is important to avoid most frequent diagnosis in post-mortem examinations. Figure. Endomyocardial biopsy specimen shows: A endothelium of the endocardium (E), thrombus (T) after necrosis of endothelium, necrosis (N) of myocytes (My) and dense infiltration of inflammatory cells, especially eosinophils; B dense infiltration of inflammatory cells, especially eosinophils (Eo) and macrophages (M) affecting myocytes (My) and necrosis (N).



Figure

1369

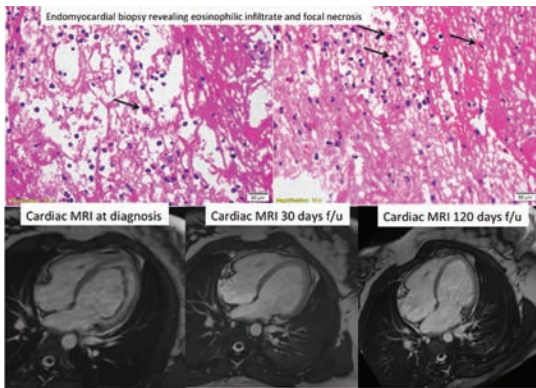
## Acute necrotizing eosinophilic myocarditis possibly triggered by anti-migraine drug as an uncommon cause of acute heart failure

G Bem<sup>1</sup>; F Hehn<sup>1</sup>; A Maulaz<sup>2</sup>; P Schvartzman<sup>3</sup>; C Astigarraga<sup>4</sup>; J Stiff<sup>5</sup>; BA Duso<sup>5</sup>; M Kronfeld<sup>1</sup>; L Luis Beck Da Silva<sup>1</sup>

<sup>1</sup>Federal University of Rio Grande do Sul - Hospital Clinicas of Porto Alegre, Porto Alegre, Brazil; <sup>2</sup>Hospital Moinhos de Vento, Neurology, Porto Alegre, Brazil;

<sup>3</sup>Hospital Moinhos de Vento, Radiology, Porto Alegre, Brazil; <sup>4</sup>Hospital Moinhos de Vento, Hematology, Porto Alegre, Brazil; <sup>5</sup>Hospital Moinhos de Vento, Gastroenterology, Porto Alegre, Brazil

A 29 years-old previously healthy women walked in to ER with a 14-day history of significant epigastric pain, which had become more intense and associated with retrosternal pain. An upper gastric endoscopy was normal 5 days prior to admission. She did not smoke and had no history of illicit-drug abuse. She was on no regular medication but had repeatedly been taking a combination of Isometheptene 30 mg, Dipyrone 300 mg and caffeine 30 mg (up to six pills a day) for recurrent migraines. Her first ECG, performed while patient was in pain, showed 1 mm ST segment depression in the anterior wall. Troponin was high in 13.0 ng/ml (normal < 0.16 ng/ml) and a first echocardiography had normal left ventricular function. On the first day, white cell count presented eosinophilia up to 19%. Stool exam negative for parasites. A cardiac MRI was suggestive for Myocarditis due to edema and midwall fibrosis on the lateral wall, basal, mid and apical segments of the septal wall and apical segment of the anterior wall. Borderline left ventricular global contractility. Viral markers and tests for autoimmunity were negative or inconclusive. Serum troponin plateau from day 3 to 4, when she was transferred to ICU due to signs of heart failure (HF), BNP >1200 pg/ml, orthopnea, dizziness and chest pain. Treatment for HF was initiated. On day 5, an empirical treatment with prednisone 60 mg/day PO was started, which brought relief of symptoms of HF and of chest pain. On day 7, patient reported a more intense than usual headache. Head MRI revealed multiple lesions involving the white matter of both hemispheres, with pitting and linear enhancement, associated with micro bleeding spots. The association with the additional clinical data and acute myocarditis suggested the possibility of systemic vasculitis with involvement of the central nervous system. A lumbar puncture revealed mild increase in liquor protein. A presumptive diagnosis was Central Nervous System (CNS) vasculitis but we could not exclude the possibility of being a reaction to the vasoconstrictor effects of patient's anti-migraine medication: Isometheptene. On day 8, it was performed an endomyocardial biopsy. Diagnosis of Acute Necrotizing Eosinophilic Myocarditis. (picture). Pulse therapy was started with Methylprednisolone 1g daily, IV, for 5 days. The patient has improved overall clinical status by day 1 of pulse therapy and tolerated well all the infusions. After therapy, troponin levels were reduced to normal (< 0.16 ng/ml), BNP reduced from 1200 to 400 pg/ml and echocardiography showed normal LV function. MRI control performed immediately after pulse therapy showed significant reduction in myocardial edema, preserved LV function and few apical foci of fibrosis. Patient was discharged in good general condition, without clinical manifestations of heart failure and with normal left ventricular function. Four months Cardiac MRI showed preserved LV function and minimal apical foci of fibrosis.



Endomyocardial biopsy and MRI follow-up

### 1370

#### Acute rheumatic valvulitis post-streptococcal glomerulonephritis

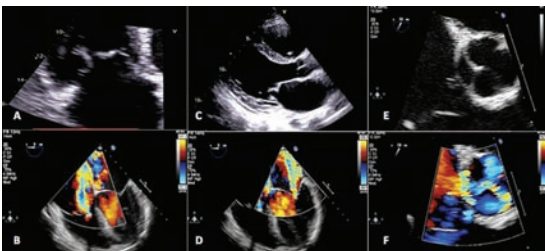
H A Hafisyatul Aiza Zainal Abidin<sup>1</sup>; MK Mohd Arshad<sup>1</sup>; JR Ismail<sup>1</sup>; ZO Ibrahim<sup>1</sup>; CW Lim<sup>1</sup>; E Abdul Rahman<sup>1</sup>; N Chua<sup>1</sup>; RN Khir<sup>1</sup>; S Kasim<sup>1</sup>

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**Introduction:** Acute rheumatic fever is still prevalent in developing countries. Cardiac involvement during the acute phase will lead to chronic sequelae of rheumatic heart disease. We report an unusual case of acute rheumatic fever post-streptococcal glomerulonephritis. Case report: A 14 year-old boy was admitted with a six weeks history of fever, vomiting and worsening shortness of breath. He was diagnosed with post-streptococcal glomerulonephritis a week prior to the onset of symptoms. On presentation, he was in left sided heart failure requiring intubation. Auscultation revealed a loud pansystolic murmur. White cell count was markedly raised as well C-reactive protein level. Echocardiography showed severe regurgitation of the mitral, aortic, tricuspid and pulmonary valves with rheumatic appearance (Figure 1). Left ventricular systolic function was depressed with ejection fraction of 45%. He was started with empirical intravenous benzylpenicillin and high dose hydrocortisone. He responded temporarily to therapy but rapidly deteriorated over a two week period. Description of the problem: This is a case of acute heart failure secondary to acute rheumatic valvulitis refractory to medical therapy. Mortality rate is high if not treated. Urgent surgical intervention during active rheumatic process is questionable. Questions and differential diagnosis: The diagnostic dilemma exists as there was a suspicious vegetation of the tricuspid valve. This raised a concern of concomitant infective endocarditis of the tricuspid valve. Is there a different outcome of valve replacement in patient with infective endocarditis as compared to acute rheumatic carditis?

**Answers and discussion:** Acute rheumatic fever is diagnosed with Jones criteria; evidence of antecedent streptococcal infection (required criteria), carditis (one major criteria) and fever and raised inflammatory markers (two minor criteria). Echocardiography examination is essential to diagnose cardiac involvement in the acute phase particularly rheumatic valvulitis. Features seen on transesophageal echocardiography strongly point the diagnosis towards rheumatic pathogenesis. This patient has severe heart failure due to hemodynamic derangements produced by severe regurgitation. Emergency valve replacement could potentially be life saving in this case.

**Conclusion and implication to clinical practice:** The decision for surgical intervention should be based on the severity of the haemodynamic disturbance rather than the active or inactive state of the rheumatic activity. Successful case has been reported although evidence is scarce.



Rheumatic valvulitis

### 1371

#### A case of idiopathic aortitis with clinical presentation consisting in acute decompensated heart failure: diagnosis, treatment, follow-up and pathophysiological considerations

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**Case description:** A 61 year old woman came to our attention with an acute decompensated cardiac insufficiency (ADHF). The findings of the physical examination were a III-IV holodiastolic murmur loudest at the left upper sternal border plus a clinical picture of dyspnea from minimal efforts, rales in the mid-basal lung fields, jugular distention, painful hepatomegaly and peripheral edema. Diagnostic and therapeutic techniques There was a fusiform aneurysm with a diameter of 62 mm involving the ascending aorta, identified by chest computed tomography. Moreover, an echocardiogram showed moderate aortic regurgitation and a dilated aortic root with substantially intact aortic valve, in the presence of preserved left ventricular ejection fraction (EF). Mainly based on these findings, the patient underwent surgical valve-sparing aortic root replacement. Her aortic histopathology revealed medial necrosis with an inflammatory infiltrate consisting of lymphocytes, plasma cells, macrophages and neutrophils. Rheumatologic and infectious laboratory tests were unremarkable, including antinuclear antibodies, anti-neutrophil cytoplasmic antibodies, rheumatoid factor, rapid plasma reagin, fluorescent treponemal antibodies and complement levels. She had no bacterial growth in blood, urine, and stool cultures. Diagnosis Given the pathologic findings in her aorta and lack of an identifiable secondary cause, the patient was diagnosed with idiopathic aortitis (IA). She was observed prospectively with periodic imaging and vascular examinations. At her three-month follow-up, she remained asymptomatic. Discussion In the case of our patient, her IA led to aneurysmal development and subsequent aortic root dilation. Over time, the dilation caused incompetence of the aortic valves, leading to worsening aortic regurgitation and high left ventricular filling pressures, leading to decompensation. The aortic valve itself was not compromised by the aortitis and surgical repair of the dilated root led to cure of the aortic regurgitation and, by association, of the heart failure. Pathophysiology There is some debate between scholars as to whether IA is a distinct entity or merely an early manifestation of systemic rheumatologic disease. Furthermore, management of IA is widely debated, because the decision to adopt a therapy with glucocorticoids or immunosuppressant agents would have a sound rationale only if an immunological origin has been proven. For this reason, in patients with suspected aortitis the European Society of Cardiology recommends periodic imaging and vascular examinations, as well as trending inflammatory biomarkers. Closing remarks a) Patients with suspected aortitis should undergo rheumatologic and immunologic assessments before making the diagnosis of idiopathic aortitis b) The modality of clinical presentation of our case was unusual, because it consisted of an ADHF clinical picture c) Glucocorticoid therapy in patients with IA remains controversial.

### 1372

#### Recurrent infection-myocarditis: is there an immunological memory leading to acute cardiac dysfunction, even after complete resolution in previous episodes?

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**Introduction:** Acute myocarditis is an inflammatory disease of the myocardium that manifests in an otherwise healthy person. Various triggers can be accountable, including infectious and noninfectious diseases. Recurrence of myocarditis is infrequent, and in respect to infection-associated myocarditis the rate of recurrence is unknown and described sporadically in a few case reports.

**Case report:** We present a case of recurrent myocarditis associated with different primary sites of infection and involvement of various pathogens. A 35 year-old healthy male presented to the emergency department (ED) with chest pain, three days after he was diagnosed with Group A streptococcus (GAS) pharyngitis. Past history included two prior episodes of infection-associated myocarditis, with similar clinical presentation. Left ventricular function was normal in Echo studies in both previous episodes, and the patient made a complete recovery. Patient presented with 1 mm ST segment elevation in lateral leads (I, aVL, V6), (figure 1). Troponin T was elevated at 66 ng/l (normal <14). A second troponin was markedly elevated, at 526 ng/l. C-Reactive protein at 121 mg% (normal <0.5). During first day of admission, he had a drop of BP to 85/60 mmHg. Echo demonstrated mild to moderate global LV systolic hypokinesia, and a borderline hypokinetic right ventricle. Under treatment with acetylsalicylic, amoxicillin, ramipril and bisoprolol symptoms have improved. A consecutive echo performed five days later showed recovery of cardiac function, with LV ejection fraction of 60%. He was released with complete resolution of his chest pain. ECG returned to baseline with normalization of troponin and CRP.



**Discussion:** Our patient was admitted three times with similar clinical presentation. His cardiac echo was normal in two first episodes, whereas on his last admission, he presented with evidence of cardiac dysfunction accompanied by hypotension. In this latest episode, CRP level was markedly elevated, compared with levels seen in the previous episodes. In patients with chronic myocarditis it has been demonstrated that the appearance of antimyosin autoantibodies correlate with development of systolic and diastolic LV dysfunction, and the question is whether recurrent episodes of myocarditis can lead to the expression of similar autoantibodies or other immune factors which are not expressed during remission, but can lead to intensification of response in subsequent exposures, resulting in more extensive myocardial damage. Study in that area is needed to evaluate whether immunological memory plays a role in magnification of cardiac damage during subsequent episodes of acute myocarditis. This knowledge may promote therapeutic approaches and help in identifying patients that might benefit from prophylactic immunosuppressive therapy



## 1373

### Severe dilated cardiomyopathy in myasthenia gravis requiring cardiac transplantation

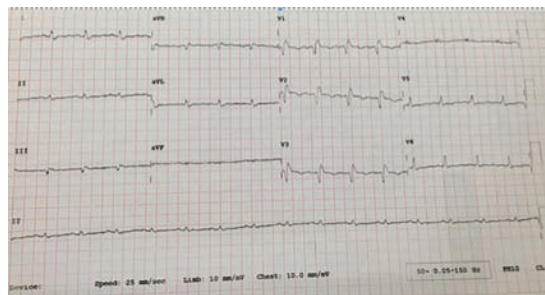
P M Haydock<sup>1</sup>; P J Cowburn<sup>1</sup>; A S Flett<sup>1</sup>

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Myasthenia Gravis (MG) is a rare autoimmune disorder of neuromuscular transmission, characterized by weakness and early fatigability. Cardiac involvement is rare, but case reports have described an association with Giant Cell Myocarditis (GCM), and Takotsubo Cardiomyopathy. We describe a case of dilated cardiomyopathy in a 17 year old male with MG and a thymoma, ultimately requiring cardiac transplantation and concurrent thymectomy.

The patient initially presented to the neurology service, following the onset of weakness over 1 year. There was no significant past medical or family history. He had features of early fatigability and markedly elevated serum acetylcholine receptor antibody levels. A CT scan demonstrated a thymoma in the anterior mediastinum. Pyridostigmine treatment was commenced to good effect and a plan was made for surgical resection. However, he re-presented with worsening fatigue, felt to be relapsing MG. He was thus admitted for intravenous immunoglobulin (IVIg) therapy. Examination revealed no neurological signs but his vital capacity was significantly reduced. Following the administration of IVIg the patient deteriorated and was found to be in acute heart failure. Echocardiography confirmed severe bi-ventricular dilatation and systolic dysfunction. His ECG is shown. The patient was transferred to the CCU for ongoing treatment. Cardiac MRI demonstrated a severely dilated left ventricle (LV) with an ejection fraction of 16%. The right ventricle (RV) was similarly dilated, and contained thrombus. Late gadolinium enhancement revealed extensive scar throughout both ventricles. Active infection was excluded and treatment with pulsed methylprednisolone for probable GCM was administered. Formal confirmation via endomyocardial biopsy was considered too risky in the context of RV thrombus and anticoagulation. The patient was subsequently assessed for cardiac transplantation but judged to be stable and discharged for ongoing review. One month later he had deteriorated and was placed on the active transplant waiting list. Given the high risk of intercurrent sudden death, a transvenous ICD was implanted. The implant proved challenging due to poor parameters despite multiple attempted lead positions - likely the result of the extensive scarring of the RV. Over six weeks the patient further deteriorated and was readmitted and listed acutely for transplantation. This was performed without the need for interim mechanical support and his thymoma was resected at the same time. Pathology from the explanted heart did not demonstrate any features of GCM and the findings were in keeping with idiopathic dilated cardiomyopathy (DCM).

This case is, to our knowledge, unique in describing a transplant, with concurrent thymectomy, for DCM in Myasthenia Gravis. It also demonstrates the importance of the awareness of potential heart failure where the clinical condition of Myasthenic patients deteriorates.



## 1374

### Multiple pseudotumorous crystalline deposits in small intestine, mesentery and lungs in terminal heart failure patient without gouty arthritis

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Sechenov First Moscow State Medical University, Moscow, Russian Federation;

<sup>3</sup>City Clinical Hospital No 64, Moscow, Russian Federation

**Introduction:** Atypical clinical manifestation of gout can vary from unusual disease progression to tophaceous deposits in atypical parts of the body, which can mimic other disease processes. We report a rare case of a patient with tophaceous gout affecting small intestine, mesentery and lungs.

**Case report:** A 52-year-old man with a past history of two myocardial infarction, arterial hypertension and anemia was admitted for terminal chronic heart failure. One year before patient was hospitalized for severe iron deficiency anemia and colonoscopy revealed tuberosus mass lesion with diameter of 3 sm in ileocecal valve region. Cytologic samples was suggestive of gastrointestinal stromal tumor. On current admission physical examination revealed abdominal mass. Laboratory test indicated hemoglobin of 43 g/l. On the 6th hour of hospitalization, despite the use of inotropic treatment, it was impossible to maintain hemodynamic stability, and the patient died. On postmortem examination multiple soft round-shaped outpouchings along the wall of the small intestine with focal luminal narrowing with approx 70% stenosis were found. Multiple deposits of mesentery coalesced into tumor-like mass (17x12 sm). Multiple round-shaped soft deposits were also observed in all lobes of both lungs. One year before result of chest computed tomography was considered normal. Histologically, the lesional tissue of lung (fig. 1A) and intestine (fig. 1B) exhibited granuloma formation and numerous giant cells. Possible differential diagnosis: Based on the clinical findings and histopathology, the differential diagnoses considered were tumor, tophaceous gout, tuberculosis. Answers and discussion: Histopathologic investigations revealed pink-colored urate crystals surrounded by granulomatous inflammation with foreign-body giant cells. Polarizing light microscopy of grey-brown ointment-like content of deposits in lungs, intestine and mesentery viewed negatively birefringent, needle-shaped monosodium urate crystals. Tuberculosis is characterized by the presence of epithelioid granuloma with Langhans giant cells, which were not observed. No other findings suggestive of gouty arthritis or tumor were obtained from the patient's pathological examination. Severe anemia was related to chronic hemorrhage from multiple intestine lesions.

**Conclusion:** We demonstrate a rare, if not unique, case of tophi presenting as a mesentery mass, multiple intestinal and especially pulmonary deposits in terminal heart failure patient without gouty arthritis.

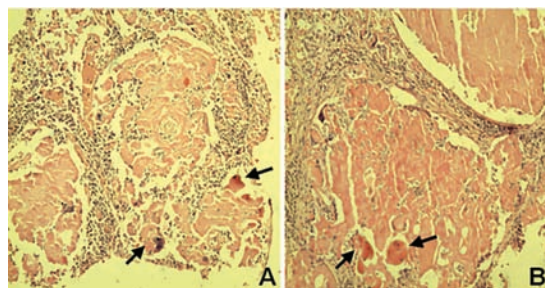


Figure 1. Granulomatous inflammation of



## RAPID FIRE 5 – COMORBIDITIES

Monday 23 May 2016 16:30–18:00

Location: Agora

1410

### Adaptive servo-ventilation in heart failure: results of a randomized, controlled clinical trial

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N Punjabi<sup>5</sup>; K Anstrom<sup>3</sup>; A Amy Blase<sup>4</sup>; J Lindenfeld<sup>6</sup>; O Oldenburg<sup>7</sup>

<sup>1</sup>Inova Heart and Vascular Institute, Falls Church, United States of America;

<sup>2</sup>Thomas Jefferson University Hospital, Philadelphia, United States of America;

<sup>3</sup>Duke Clinical Research Institute, Durham, United States of America; <sup>4</sup>ResMed,

San Diego, United States of America; <sup>5</sup>Johns Hopkins University of Baltimore,

Baltimore, United States of America; <sup>6</sup>Vanderbilt University, Nashville, United

States of America; <sup>7</sup>Heart and Diabetes Center NRW, Bad Oeynhausen, Germany

**Background:** Sleep disordered breathing is common in heart failure (HF) patients and is associated with worse outcomes in this patient population. The Cardiovascular Improvements with Minute Ventilation-targeted Adaptive Servo-Ventilation (MV-ASV) Therapy in Heart Failure (CAT-HF) trial was designed to examine whether MV-ASV improved outcomes in hospitalized HF patients. During the course of CAT-HF, new results from the Treatment of Predominant Central Sleep Apnea by Adaptive Servo Ventilation in Patients with Heart Failure (SERVE-HF) study indicated ASV therapy may be harmful in patients with left ventricular ejection fractions  $\leq 45\%$  and predominant central sleep apnea, a subgroup of patients enrolled in CAT-HF; as a result, enrollment in CAT-HF was discontinued.

**Purpose:** The CAT-HF Study was designed to evaluate the safety and efficacy of MV-ASV in addition to optimized medical therapy versus optimized medical therapy alone at 6 months, initiated in patients after a hospitalization for ADHF.

**Methods:** CAT-HF was a prospective, randomized, controlled, multicenter clinical trial (NCT: 01953874) in HF patients with either reduced or preserved ejection fraction and an Apnea-Hypopnea Index (AHI)  $\geq 15$  events per hour (obstructive or central) randomized to usual care or active treatment in a 1:1 ratio. 215 patients were intended to be randomized following a hospitalization for acute decompensated HF. The primary endpoint is a global rank composite of death, cardiovascular hospitalizations, and six minute walk distance at 6 months. Secondary endpoints include changes in functional parameters, biomarkers, quality of life, and sleep parameters. Results are expected to be completed by January 22, 2016.

**Results:** At the time of discontinuation, 126 patients were randomized. Mean age was 62 years, 26% were women, and 41% were African-American. At baseline, 81% had left ventricular ejection fraction  $\leq 45\%$ , the mean six minute walk distance was 206 meters, and the mean AHI was 35 events/hour.

**Conclusions:** The CAT-HF study was designed to assess the efficacy and safety of MV-ASV treatment in patients with obstructive or central sleep apnea after a hospitalization for acute decompensated HF. The results of this study will provide information regarding treatment in HF patients, and inform future clinical trials.

1411

### Clinical significance of tricuspid regurgitation severity in heart failure

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W Darawsha<sup>1</sup>; D Mutlak<sup>1</sup>

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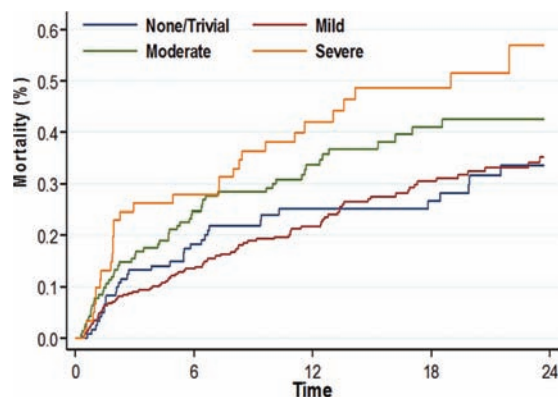
**Background:** Hemodynamically significant tricuspid regurgitation (TR) is common in patients with heart failure (HF) and has been reported to portend poor prognosis. However, it is still unknown whether TR is a surrogate marker of advanced myocardial and valvular heart disease or a mediator of disease progression.

**Methods:** We studied 623 patients admitted for HF. TR severity was assessed by echocardiography according to ESC guidelines. Congestion was assessed with a 10-point scale. The study endpoint was all-cause mortality with a median follow-up of 2 years.

**Results:** Higher TR grade was associated with several clinically significant cardiac abnormalities including LVEF  $< 45\%$ , moderate or severe mitral regurgitation, RV dysfunction and pulmonary artery systolic pressure (PASP) $>50$  mm Hg (All

$P < 0.001$ ). The median PASP was 35, 49, 58 and 60 mm Hg in patients with none/trivial, mild, moderate and severe TR, respectively ( $P < 0.001$ ). There was a graded increase in the number of signs of congestion with increasing TR severity ( $P < 0.001$ ). In addition, higher TR grade was associated with higher BNP, worse renal function and abnormal liver function tests. Kaplan-Meier analysis showed a graded increased probability of mortality during follow-up with increasing TR severity (Figure). However, in a multivariable Cox model adjusting for clinical and echocardiographic parameters, TR was not associated with increased mortality risk. Compared with patients with none/trivial TR, the adjusted hazard ratio for mortality was 0.88 (95% CI 0.53-1.47), 1.12 (95% CI 0.64-1.96) and 1.61 (95% CI 0.86-3.00) in patients with mild, moderate and severe TR, respectively.

**Conclusion:** In patients with HF, the association between TR and mortality can be explained by associated co-morbidities.



1412

### A simple score to discriminate pulmonary hypertension due to HFpEF

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**Background:** Right heart catheterization (RHC) is the gold standard technique to discriminate post capillary pulmonary hypertension due to heart failure with preserved ejection fraction (PH-HFPEF) from precapillary pulmonary hypertension (precapillary PH). Whether clinical exam and cardiac echocardiography could predict the catheterization results is still unknown.

**Purpose:** this study aims to identify clinical and echographic parameters that best discriminate PH-HFPEF from precapillary PH.

**Methods:** clinical exam and echocardiography were analyzed and compared to results from RHC in 158 patients referred to the french PH referral center for PH evaluation. RHC identified 78 PH-HFPEF patients that were compared to 78 precapillary PH patients (group 1 and 4 of PH classification).

**Results:** After the logistic regression analysis, a predictive model of PH-HFPEF was built using the following predictor characteristics: presence of diabetes mellitus (2 points), presence of atrial fibrillation (3 points), left atrial area (from 0 to 4 points), right ventricular diastolic area (from 0 to 2 points) and left ventricular mass index

(from 0 to 4 points). The score was internally validated using the bootstrap technique and showed good predictive characteristics: the C-index of Harrel was 0.94 and the calibration slope was 1.01 (0.75–1.30). With a score > 9, the sensitivity to diagnose PH-HFPEF was 100%. A score < 3 would predict 100% of precapillary PH.

**Conclusion:** By combining simple clinical and echographic parameters, as diabetes mellitus, atrial fibrillation, left atrial area, left ventricular mass index, right ventricular diastolic area, a score could predict accurately PH-HFPEF from precapillary PH.

#### 1413

##### Diabetes is associated with long-term adverse clinical outcomes in a multinational cohort of ambulatory patients with chronic heart failure. Results from the ESC-HFA Long-Term Heart Failure Registry.

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Coruna, CHUAC, Unidad de Insuficiencia Cardiaca Avanzada y Trasplante Cardiaco, La Coruna, Spain; <sup>8</sup>ANMCO Research Center, Florence, Italy; <sup>9</sup>Maria Cecilia Hospital, GVM Care & Research – ES Health Science Foundation, Cotignola, Italy

**Background:** Diabetes mellitus (DM) is associated with an increased risk of cardiovascular disease (CVD) and death. As the prevalence of DM has achieved pandemic proportions worldwide and chronic heart failure (CHF) is becoming increasingly common with ageing population, it is timely to evaluate the impact of DM on long-term adverse outcomes among patients with CHF.

**Purpose:** Currently, there is continuing debate on this topic, and therefore it warrants in-depth investigation.

**Methods:** We prospectively evaluated the impact of DM status and glycaemic control (as provided by haemoglobin A1c, HbA1c) on the risk of 1-year all-cause death, CVD death and hospitalization for HF in a multinational cohort of 9,428 ambulatory patients with CHF enrolled in the ESC-Heart Failure Long-Term Registry.

**Results:** Patients with known or newly diagnosed DM represented a considerable proportion of the study cohort (36.5%, n = 3,440). Compared with patients without DM, those with DM showed higher cumulative rates of 1-year all-cause death (9.4% vs. 7.2%; adjusted-HR [95% CI] 1.31 [1.10–1.56], p < 0.005), 1-year CVD death (4.8% vs. 3.8%; adjusted-HR 1.28 [1.00–1.63], p < 0.05) and 1-year HF hospitalization (13.8% vs. 9.3%; adjusted-HR 1.43 [1.23–1.65], p < 0.001). These adverse outcomes occurred independently of age, sex, body mass index, smoking, hypertension, estimated glomerular filtration rate, LV-ejection fraction, HF etiology, statin use, prior stroke or chronic obstructive pulmonary disease. Among the patients with CHF and DM, suboptimal glycaemic control was significantly associated with increased 1-year CVD death (adjusted-HR: 3.44 [1.06–11.15]), but not with 1-year all-cause death or hospitalizations for HF.

**Conclusions:** These results indicate that the presence of DM is associated with an increased risk of long-term adverse outcomes, independently of multiple clinical risk factors, among ambulatory patients with CHF. Since suboptimal glycaemic control is also closely associated with increased CVD mortality among patients with CHF and DM, a more effective and personalized treatment of diabetes should be considered in this high-risk patient population.

#### 1414

##### In anaemic heart failure patients abnormal erythropoietin is related to disease severity and renal impairment, but neither inflammation nor iron deficiency

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**Introduction:** Significant proportion of anaemic heart failure (HF) patients present with abnormal endogenous erythropoietin (EPO) levels and underlying pathomechanism are not fully explained. We investigated the adequacy of endogenous EPO levels in HF patients with anaemia and evaluated whether abnormal EPO levels are associated with iron deficiency (ID).

**Methods:** Study population comprised of 1821 chronic HF patients from Poland, Spain and the Netherlands. EPO was available in 1026 subjects, of whom 435

(mean age: 74 ± 10 years; men: 60%; New York Heart Association class I/II/III/IV: 9/30/50/11%; HFrEF: 49%) had anaemia (haemoglobin < 12.0 g/dL for women and < 13.0 g/dL for men). The adequacy of endogenous EPO levels was evaluated using the observed/predicted (O/P) ratio. Predicted level of EPO was calculated with the following formula:  $\log_{10}(\text{EPO}) = 4.640 - [0.274 \times \text{haemoglobin concentration}]$ . Patients with EPO levels higher than expected for a given haemoglobin (Hb) concentration (O/P ratio > 1.087) were considered EPO resistant, whereas EPO levels lower than expected (EPO O/P ratio < 0.916) indicated EPO deficiency. ID was defined as serum ferritin < 100 µg/L or serum ferritin 100–299 µg/L with transferrin saturation < 20%.

**Results:** EPO deficiency was found in 250 (57%) patients, 95 (22%) subjects were EPO resistant, and remaining 90 patients had adequate EPO levels (as expected for a given Hb level; O/P ratio: 0.916–1.087). Mean Hb in these 3 groups of patients was 10.7 ± 1.1, 12.0 ± 0.8, and 11.4 ± 1.0 g/dL, respectively (p < 0.001 for ANOVA). In the multivariable linear regression model, higher EPO O/P ratio was independently associated with advanced HF symptoms (higher NYHA class), higher plasma NT-proBNP, reduced LVEF, and concomitant ID, whereas lower EPO O/P ratio correlated with worse renal function (reduced eGFR calculated using a MDRD equation) (all p < 0.05). Patients identified as EPO resistant compared to subjects with adequate EPO levels had more severe HF symptoms (NYHA class III–IV: 75 vs. 59%, p = 0.02), higher plasma NT-proBNP (median 3670 vs. 2223 pg/ml, p = 0.03) and lower LVEF (37 ± 17 vs. 43 ± 16%, p = 0.008), whereas eGFR, serum C-reactive protein (CRP) and the prevalence of ID were similar in these 2 groups. Conversely, patients with EPO deficiency had worse renal function (median eGFR 68 vs. 84 ml/min/1.73 m<sup>2</sup>, p = 0.007) than subjects with adequate EPO levels, but these 2 groups did not differ regarding NYHA class, LVEF, NT-proBNP, CRP or the prevalence of ID.

**Conclusions:** More than half of HF patients with anaemia develop relative EPO deficiency, which is primarily due to renal impairment. Being the feature of advanced HF, EPO resistance is less prevalent pathology. ID does not contribute significantly to abnormal endogenous EPO levels.

#### 1415

##### Right ventricular dyssynchrony and exercise capacity in idiopathic pulmonary arterial hypertension

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**Background:** In idiopathic pulmonary arterial hypertension (IPAH), characterized by a severe functional limitation due to right heart failure, indices of resting right ventricle (RV) systolic function are not always able to explain the impairment of exercise capacity.

**Purpose:** Aim of our study was to evaluate if RV dyssynchrony at rest is related to effort tolerance measured by cardiopulmonary exercise test (CPET) and can explain reduced exercise capacity in patients with preserved RV systolic function.

**Methods:** One-hundred and five consecutive stable IPAH patients (majority NYHA class III, severe PH) underwent echocardiographic study and symptom limited CPET. RV dyssynchrony was evaluated by 2D speckle-tracking echocardiography calculating the standard deviation of the times to peak-systolic strain for the 4 mid-basal RV segments (RV-SD4). Patients were grouped by the median value of RV fractional area change (RVFAC, 38%) and compared for RV echocardiographic and CPET parameters.

**Results:** Patients with a RVFAC > 38% presented better morphological and functional echocardiographic parameters and CPET values than the other group. Analyzing the relationship between RVFAC and peak VO<sub>2</sub>, we found that a significant portion of patient with preserved RVFAC (> 38%) presented low peak VO<sub>2</sub>. Plotting RV-SD4 and peak VO<sub>2</sub>, is evident that most of the patients with preserved RVFAC and low peak VO<sub>2</sub> show significant RV dyssynchrony. Evaluating the VO<sub>2</sub> peak determinants by logistic analysis, model 1, considering only hemodynamic variables, showed cardiac index, right atrial (RA) pressure and pulmonary compliance as the independent predictors, with low predictivity (r<sup>2</sup> 0.31; p < 0.01). In model 2, considering only echocardiographic variables, and excluding RV dyssynchrony, RVFAC and RA area resulted as independent predictors, with low predictivity comparable to model 1 (r<sup>2</sup> 0.35; p = < 0.01). Adding dyssynchrony analysis to model 2, RV dyssynchrony significantly improved the power of the predictive model, emerging together with RVFAC and RA area as independent predictor of VO<sub>2</sub> peak (r<sup>2</sup> 0.48; model 3 vs model 1, p < 0.001; model 3 vs model 2, p < 0.001).

**Conclusions:** Our data show that RV dyssynchrony at rest is an independent predictor of peak VO<sub>2</sub> and may explain reduced exercise capacity in patients with preserved RV systolic function.

#### 1416

##### Ventricular recovery after bilateral lung transplantation for pulmonary arterial hypertension: a cardiac magnetic resonance study

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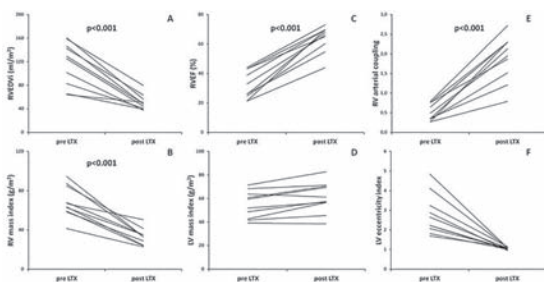
**Background:** Pulmonary arterial hypertension (PAH) is a serious and often fatal disease and many end-stage PAH patients require lung transplantation (LTX). Timing and type of LTX (i.e. lung versus heart-lung transplantation) is subject of intense debate yet reliable data regarding the effects of LTX on ventricular recovery are scarce. Given the shortage of organs for transplantation, more study on this topic is urgently needed.

**Purpose:** To investigate the effects of bilateral LTX on ventricular function in patients with severe PAH using cardiac magnetic resonance (CMR) imaging.

**Methods:** We studied patients with PAH who underwent bilateral LTX between 2000 and 2015 at our institution and in whom CMR was available both pre- and post-LTX. Right ventricular (RV) and left ventricular (LV) volumes, function and mass were measured and RV-arterial coupling, LV-eccentricity index and RV / LV ratio were calculated.

**Results:** We investigated 10 patients with PAH; their mean age was  $41 \pm 15$  years and pulmonary vascular resistance was 1020 dynes-sec-cm<sup>-5</sup>. After LTX, RV ejection fraction increased from 32 to 64% ( $p < 0.001$ ), RV volume decreased from 118 to 51 ml/m<sup>2</sup> ( $p < 0.001$ ), RV mass decreased from 69 to 33 g/m<sup>2</sup> ( $p < 0.001$ ) and RV-arterial coupling increased from 0.5 to 1.9 ( $p < 0.001$ ). In addition, LV mass significantly increased after LTX, from 55 to 61 g/m<sup>2</sup> ( $p = 0.005$ ). LTX resulted in a normalization of LV eccentricity index ( $p < 0.001$ ) and of RV / LV volume ( $p < 0.001$ ) and mass ratio ( $p < 0.001$ ) in all patients.

**Conclusion:** RV function and morphology markedly improved and also left-sided parameters returned toward normal after bilateral LTX for severe PAH. These results may potentially affect the discussion regarding lung versus heart-lung transplantation in these patients.



Ventricular recovery after LTX

#### 1417

##### Mid-regional pro-atrial natriuretic peptide predicts unfavorable clinical course in heart failure patients undergoing cardiac resynchronization therapy

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**Aims:** Cardiac resynchronization therapy (CRT) may improve outcome of patients with chronic heart failure (HF), but despite accurate selection, at least one third of patients receiving CRT remain non-responders. Aim of the study was to assess the properties of NT-proBNP, MR-proANP and MR-proADM to predict CRT response.

**Methods and Results:** A total of 137 chronic HF patients undergoing CRT device implantation were prospectively included. Blood was collected at the time of CRT implantation and after 6 months. CRT-response at 6 months and major adverse cardiovascular event (MACE) during 2 years were assessed. Baseline levels of MR-proANP and MR-proADM were lower in CRT responders compared to CRT non-responders (202 vs. 318 pmol/L,  $p = 0.009$ , and 843 vs. 1112 pmol/L,  $p = 0.02$ , respectively). A similar trend was observed also for NT-proBNP (1019 vs. 2227 pg/mL,  $p = 0.06$ ). At 6 months, CRT responders showed a decrease in MR-proANP levels, compared to an increase in CRT non-responders ( $-32$  vs.  $+7$  pmol/L,  $p = 0.02$ ). High baseline MR-proANP levels were associated with reduced likelihood of CRT-response (OR 0.41, 95% CI 0.24-0.71,  $p = 0.002$ ). Furthermore, levels of NT-proBNP, MR-proANP and MR-proADM were associated with increased risk of 2-year MACE (all  $p < 0.001$ ). Patients with MR-proANP levels  $< 250$  pmol/L, compared to patients with higher levels, had higher CRT response (74% vs. 46%,  $p = 0.003$ ) and lower MACE (10% vs. 39%,  $p < 0.001$ ).

**Conclusions:** Peripheral levels of MR-proANP show strong properties to predict adverse clinical course in HF patients receiving CRT.

#### 1418

##### Blood urea nitrogen to creatinine ratio in the general population and patients with acute heart failure

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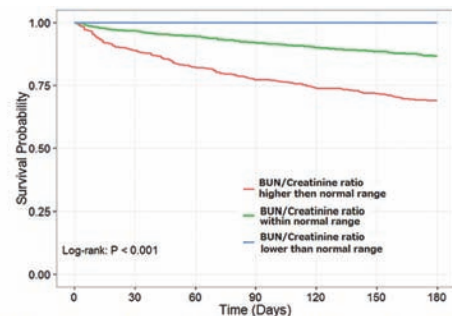
**Background:** The BUN/Creatinine ratio has been proposed as clinically relevant in acute heart failure, but data on the normal range/value of the ratio are lacking.

**Purpose:** Aim of this study is to define the normal range of BUN/Creatinine ratio and to investigate the clinical significance of BUN/Creatinine ratio in acute heart failure patients.

**Methods:** In 8692 subjects of the Prevention of Renal and Vascular End-stage Disease (PREVEND) cohort, we assessed the normal values of the BUN/Creatinine ratio. Based on these normal values, we derived a higher and lower than normal range of BUN/Creatinine ratio, exceeding 95% prediction intervals. We applied this normal range of BUN/Creatinine ratio to 2033 acute heart failure patients (PROTECT cohort).

**Results:** In the PROTECT cohort, 482 (24.6%) and 28 (1.4%) patients were classified into higher and lower than normal range groups, respectively. Patients with higher than normal range of BUN/Creatinine showed significantly worse survival (Log-rank:  $P < 0.001$ ). In Cox regression analysis, higher than normal range of BUN/Creatinine ratio group was an independent predictor for all-cause death through 180 days (HR: 1.86, 95% CI: 1.30-2.67,  $P < 0.001$ ) and death or cardiovascular or renal rehospitalization through 60 days (HR: 1.38, 95% CI: 1.03-1.83,  $P = 0.029$ ) even after adjustment for other prognostic factors including both creatinine and BUN.

**Conclusions:** BUN/Creatinine ratio is an age- and sex-related biomarker. BUN/Creatinine ratio is higher in acute HF patients compared with the general population, and a higher than normal range of BUN/Creatinine ratio is associated with worse prognosis independently from both creatinine and BUN.



BUN/Creatinine ratio	0	30	60	90	120	150	180
higher than normal range	462	427	394	370	355	344	277
within normal range	1446	1394	1363	1326	1298	1273	1062
lower than normal range	28	28	28	27	27	27	20

#### 1419

##### Right ventricular dysfunction as an independent predictor of longer hospital stay in patients with acute decompensated heart failure

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**Background:** Hospital length of stay (LOS) is a key determinant of heart failure hospitalization costs. Longer LOS is associated with lower performance on quality of care measures and higher rates of subsequent readmission and mortality. Right ventricular (RV) dysfunction predicted poor outcomes in patients with stable chronic HF, however, its prognostic value in the setting of acute decompensated heart failure (ADHF) patients has not been sufficiently clarified.

**Purpose:** To investigate the prognostic value of RV dysfunction in predicting longer LOS in ADHF patients. Methods. A prospective cohort study was conducted in our hospital to all patients admitted with ADHF and had data on baseline RV functions



assessed by tricuspid annular plane systolic excursion (TAPSE). Detailed clinical, laboratory and echocardiographic data were collected on admission. Clinical comorbidities including malnutrition, concomitant pneumonia and worsening renal function (WRF) were monitored during hospitalization. The primary outcome was hospital LOS. Cox regression analysis were used to identify independent predictors for longer LOS.

**Results:** Two hundred and fifty-nine patients presenting to the emergency department with the diagnosis of ADHF were included in this cohort study. On time-to-event analysis, diastolic blood pressure (HR 1.011, 95% CI 1.004-1.018,  $p=0.002$ ), hemoglobin levels (HR 1.102, 95% CI 1.045-1.162,  $p<0.001$ ), RV dysfunction (measured by TAPSE) (HR 0.659, 95% CI 0.506-0.857  $p=0.002$ ), WRF (HR 2.015, 95% CI 1.520-2.670,  $p<0.001$ ) and malnutrition (HR 5.965, 95% CI 4.402-8.082,  $p<0.001$ ) were associated with longer LOS. In a multivariate Cox regression model, RV dysfunction (HR 0.515, 95% CI 0.303-0.874,  $p<0.02$ ), WRF (HR 2.989, 95% CI 2.160-4.135,  $p<0.001$ ) and malnutrition (HR 8.211, 95% CI 5.883-11.459,  $p<0.001$ ) were the sole independent predictors of longer length of hospital stay.

**Conclusions:** Right ventricular dysfunction is an important predictor of longer length of hospital stay. Routine assessment of the right ventricle should be considered in the evaluation of patients with ADHF.

**1420**

**Multimorbidity and outcomes in patients with heart failure and reduced ejection fraction**

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**Objective:** Heart failure (HF) patients often have multiple chronic conditions (MCCs). In the current study, we examined incremental impact of MCCs in patients with HF and reduced ejection fraction (HFrEF).

**Methods:** Of the 2707 patients with advanced HF and EF < 35% in the Beta-Blocker Evaluation of Survival Trial (BEST), 59% had coronary artery disease (CAD), 37% had chronic kidney disease (CKD), 36% had diabetes mellitus (DM) and 24% had atrial fibrillation (AF), and 17.4%, 33.0%, 29.8%, 16.2% and 3.6% had none, 1, 2, 3, or all of these conditions. Using multivariable-adjusted Cox regression models, we examined association of having 1 to 4 morbidities with outcomes during an average of 2 years of follow-up, compared with no morbidity.

**Results:** Patients had a mean age of 60 years, 22% were women and 23% African American. Association of MCCs with all-cause hospital admission and all-cause mortality are displayed in Table. Similar associations were observed for HF hospitalizations. These associations appeared more pronounced among those < 65 years than among those ≥ 65 years.

**Conclusion:** In patients with advanced HFrEF, there appears to be a graded association between number of morbidities and outcomes, which appear to be more pronounced among younger patients.

**1421**

**Obstructive sleep apnea increases the risk of heart failure: a population-based follow-up study.**

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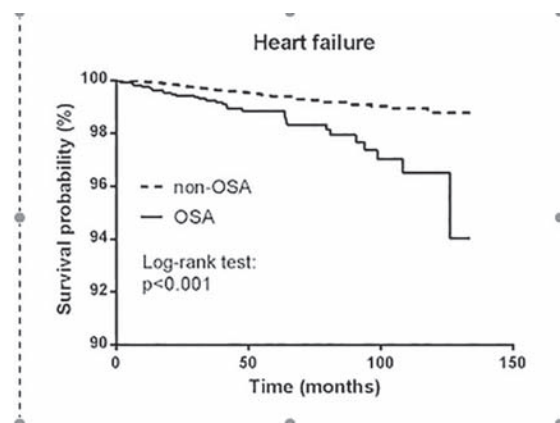
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**Background:** Obstructive sleep apnea (OSA) is related to heart failure (HF) is not clear. We aim to clarify the relationship between OSA and incidence of HF.

**Methods:** The population-based cohort study consisted of patients with newly diagnosed OSA between 2000 and 2009. The comparison cohort was matched for age, sex, diabetes mellitus and hypertension. All subjects previously been diagnosed with acute or chronic kidney disease were excluded. The primary end point was newly diagnosed with HF during the study period.

**Results:** We identified 6,866 subjects with OSA followed up for a median of 4.4 years. The median follow-up year from OSA to HF is 3.2 years with 2.5 months earlier than non-OSA cohort. Hazard Ratios (HR) for risk of HF with OSA versus non-OSA were 2.4 (95% CI, 2.07–3.44;  $p=0.045$ ) and 2.3 (95% CI, 2.0–2.6;  $p=0.019$ ) among those without hypertension or diabetes.

**Conclusion:** Our data provides the first prospective evidence that obstructive sleep apnea is significantly related to the occurrence of HF even without hypertension and diabetes.



**1422**

**Right ventriculoarterial coupling assessed by two-dimensional strain: a new parameter of right ventricular function independently associated with prognosis in chronic heart failure patients**

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Outcomes by number of morbidities

Outcome	Number of morbidity	Unadjusted events % (n/N)	Hazard ratios (95% confidence intervals)
Unadjusted	Age-sex-race-adjusted	Multivariable-adjusted*	
All-cause hospital admission	0	54% (255/472)	1 (Reference) 1 (Reference) 1 (Reference)
1	58% (515/892)	1.10 (0.94-1.27)	1.10 (0.94-1.29) 1.06 (0.90-1.24)
2	58% (515/808)	1.50 (1.29-1.74)	1.51 (1.28-1.78) 1.36 (1.14-1.61)
3	73% (318/438)	1.85 (1.57-2.19)	1.85 (1.54-2.22) 1.53 (1.25-1.86)
4	80% (78/97)	2.49 (1.93-3.22)	2.51 (1.92-3.28) 1.74 (1.31-2.30)
All-cause mortality	0	20% (94/472)	1 (Reference) 1 (Reference) 1 (Reference)
1	26% (231/892)	1.34 (1.06-1.71)	1.23 (0.96-1.57) 1.18 (0.92-1.52)
2	33% (266/808)	1.86 (1.47-2.38)	1.64 (1.28-2.11) 1.41 (1.08-1.83)
3	48% (210/438)	3.05 (2.39-3.89)	2.60 (1.99-3.39) 2.00 (1.51-2.66)
4	60% (58/97)	4.29 (3.09-5.96)	3.65 (2.58-5.16) 2.24 (1.55-3.24)

\*Adjusted for age, sex, race, smoking, duration of HF, history of hypertension, hyperlipidemia, peripheral arterial disease, randomization to beta-blocker bucindolol, the use of ACEI or ARB, digitalis, diuretics, vasodilators, anticoagulants, NYHA class, cardiothoracic ration, pulmonary edema, heart rate, systolic and diastolic blood pressure, left and right ventricular ejection fraction, serum potassium and hemoglobin

Variable	Univariate analysis			Multivariate analysis†		
	HR (95%CI)	p	C-index	HR (95%CI)	p	C-index
TAPSE	0.89 (0.84-0.94)	< 0.001	0.65	1.01 (0.94-1.09)	0.731	0.85
RV-fwLS	1.11 (1.07-1.16)	< 0.001	0.71	1.06(1.01-1.11)	0.011	0.86
TAPSE/PAP (mm/mm Hg)	0.02 (0.01-0.07)	< 0.001	0.73	0.75 (0.15-3.6)	0.725	0.85
RV-fwLS/PAP* (%/mm Hg)	0.04 (0.01-0.09)	< 0.001	0.76	0.26 (0.08-.85)	0.025	0.86

\*Ratio calculated on the basis of absolute values of right ventricular strain measures. †Multivariate models separately included right ventricular systolic function parameters due to collinearity.

The aim of this study was to evaluate right ventricular (RV) ventriculararterial coupling by 2-dimensional (2-D) strain and estimated right ventricular systolic pressure in order to assess their role in predicting mortality in chronic heart failure (CHF).

**Methods:** We enrolled 315 outpatients (77% males, 64 ± 13 years, NYHA class 2.2 ± 0.7, left ventricular ejection fraction, LVEF 33 ± 9%) with CHF (ESC criteria), in stable clinical conditions (>1 month) and in conventional therapy. All patients underwent a clinical evaluation, a routine chemistry and an echocardiogram. A right focused four-chamber view was analyzed by 2-D speckle tracking to evaluate the longitudinal strain of RV free wall (RV-fwLS). Moreover, the tricuspid annular plane systolic excursion (TAPSE), by mono-dimensional echo, and estimated right ventricular systolic pressure(PAPs) were measured. Ventriculararterial coupling was evaluated as the ration between the parameters of RV systolic function and PAPs.

**Results:** During a mean follow-up of 36 ± 26 months, 69 patients died. As shown in the table, at Cox univariate regression analysis TAPSE and RV-fwLS as well as their relative parameters of ventriculararterial coupling, i.e. TAPSE/PAP and RV-fwLS/PAP, were all associated to mortality. However, only RV-fwLS/PAP showed the greatest accuracy assessed by C-index value. Finally, RV-fwLS/PAP but not TAPSE/PAP remained significantly associated to events when separately included in multivariate Cox models with age, LVEF, logNTproBNP, glomerular filtration rate, NYHA class, mean arterial pressure. Figure shows Kaplan Meier curves according to RV-fwLS/PAP quartiles.

**Conclusions:** Our results suggest the possible usefulness of 2-D strain derived measures in order to evaluate right ventriculararterial coupling and to stratify patients' prognosis in CHF. RV systolic shortening assessed by 2-d strain combined to PAPs seems to allow a more accurate estimation of the length/force relationship than TAPSE/PAP.

estimation, which have already shown their prognostic value in heart failure. However, their calculation requires of multiple measurements that can limit its utility in daily practice.

**Purpose:** the aim of this study was to establish more simple parameters that permit a precise assessment of pulmonary artery pressure through cardiac MRI and to evaluate their prognostic value in HF.

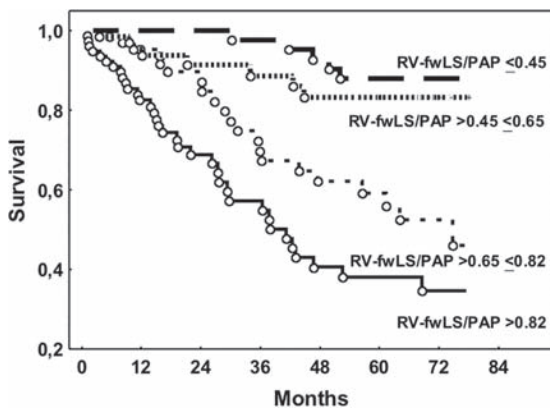
**Methods:** we prospectively included 151 patients (mean age 64.6 +/− 12.7 years, 71% male) admitted for acute HF with left ventricular dysfunction (LVD) (ejection fraction <40%). We measured the mean velocity at the pulmonary artery (mvPA) with cardiac MRI and divided our sample in two groups according to the optimal cutoff value for event prediction calculated by ROC curve (mvPA = 10cm/s). We considered readmission for HF and total mortality as primary events in the follow up and performed a survival analysis with a Kaplan-Meier survival curve.

**Results:** 67 patients had mvPA value <10cm/s. There were no differences in baseline characteristics between the two groups. During a mean follow up period of 13 months there were 66 events in the total sample; 47 of them in the group with lower mvPA (Log Rank 18.82, p < 0.0001); Figure 1. We identified mvPA and atrial fibrillation as independent predictors in Cox multivariable analysis (CI 95%, p < 0.008), Table 1. Right ventricular dysfunction was not an independent prognostic predictor in multivariable analysis.

**Conclusion:** mvPA below 10cm/s by cardiac MRI indicates a worse prognosis in patients with HF and LVD, independently of right ventricular function. Therefore this parameter could act as an early prognostic indicator in these patients.

Multivariable analysis		
Variable	HR (IC 95%)	p value
Late gadolinium enhancement	0.88 (0.47-1.66)	p = 0.7
Ischaemic cardiomyopathy	0.83(0.46-1.50)	p = 0.55
Severe left ventricular dysfunction < 30%	1.12 (0.63-2.02)	p = 0.31
Right ventricular dysfunction < 50%	1.15 (0.63-2.11)	p = 0.57
Atrial fibrillation	1.55 (1.12-1.77)	p = 0.041
mvAP	1.77 (1.22-2.35)	p = 0.001

mvAP: mean velocity at the pulmonary artery



Figure

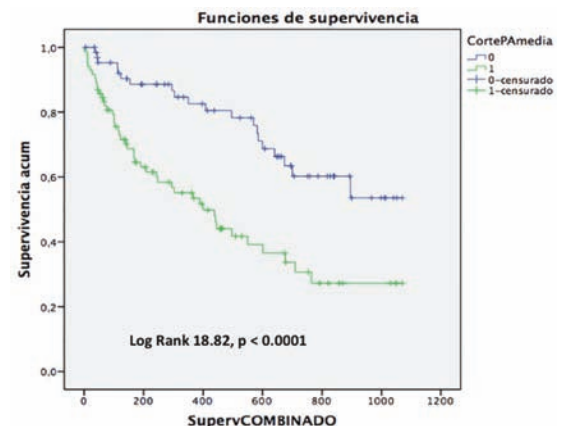
1423

**Mean velocity of the pulmonary artery estimated by cardiac MRI as a prognostic indicator in heart failure with reduced ejection fraction**

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**Introduction:** Pulmonary hypertension (PH) implies a worse prognosis in chronic heart failure (HF) specially when right ventricular dysfunction overcomes. Although cardiac catheterization is the gold standard technique for the diagnosis of PH as it allows to directly measure the pressure at the pulmonary artery Cardiac MRI permits an accurate evaluation of pulmonary pressure through vascular peripheral resistance



Survival free from primary events.

1424

**Prognostic impact of iron deficiency in heart failure with preserved and reduced ejection fraction**

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**Background:** Iron deficiency is associated with impaired exercise tolerance and symptom progression in patients with heart failure.

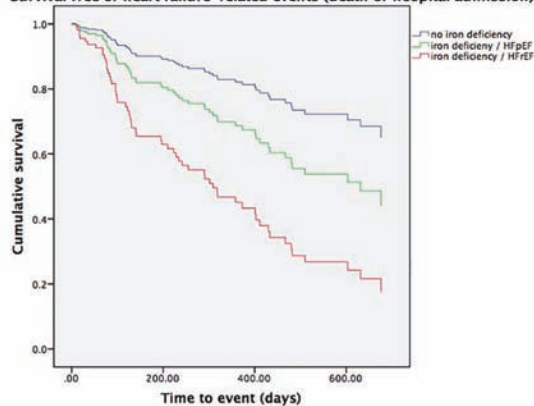
**Purpose:** To assess the prognostic impact of iron deficiency on heart failure-related events in outpatients with chronic, stable and optimally managed heart failure.

**Methods:** Consecutive patients referred for heart failure outpatient management at three centres were prospectively enrolled. Iron deficiency was defined as ferritin <100 mcg/L or ferritin 100-300 mcg/L and transferrin saturation <20%. Patients were followed for a minimum of six months for heart failure related events (i.e. death or hospitalization).

**Results:** A total of 469 patients (mean age 74 ± 11 years, 39% females, 47% with preserved left ventricular ejection fraction) were included; 119 (25%) experienced an event during a median follow up of 236 (interquartile range 85-411) days. In multivariate Cox model, iron deficiency emerged as a strong predictor of heart failure-related events (odds ratio /OR/ 2.062; 95% confidence interval /95%CI/ 1.234-3.445; p=0.006), even after adjustment for age, gender, NYHA class, ischemic etiology, natriuretic peptides, kidney function, and anemia. A significant trend for iron deficiency to predict heart failure-related events was retained in both, patients with reduced and (alas to a lesser extent) with preserved ejection fraction: OR 2.366 (95% CI 1.247-4.488, p=0.008) and OR 1.880 (95% CI 0.917-3.861, p=0.085), respectively (figure).

**Conclusions:** Iron deficiency is a predictor of adverse events in outpatients with both, heart failure with reduced and with preserved ejection fraction.

Survival free of heart failure-related events (death or hospital admission)



Iron deficiency and survival in HF

1425

**Early systolic anterior motion of interventricular septum due to increased right ventricular dyssynchrony predicts accurately impaired right ventricular ejection fraction**

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**Background:** Besides right ventricular (RV) ejection fraction (EF) <35%, RV dyssynchrony was described as an independent parameter of clinical outcome in pulmonary hypertension (PH) patients.

**Purpose:** This study examines a relation between RV dyssynchrony, RV EF and interventricular septum (IVS) motion patterns.

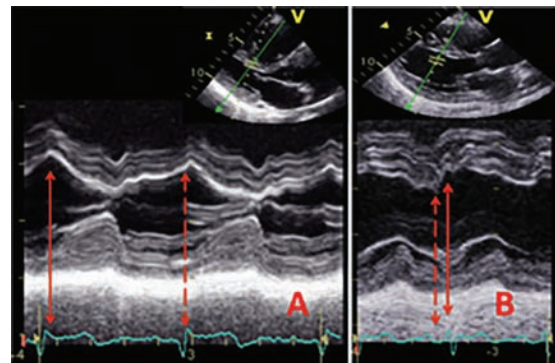
**Methods:** 24 men (63 ± 12 years), 68 women (66 ± 14 years) with pre-capillary PH were retrospectively studied. RV dyssynchrony was quantified as a standard deviation of time to peak systolic strain of basal and mid segments of RV free wall and IVS. Septal kinetics were assessed by M-mode. RVEF was quantified from 3D echo data sets. Post-systolic shortening (PSS) was quantified as a relation between max time to peak systolic strain of abovementioned RV segments to pulmonary valve closure time.

**Results:** PH patients with increased RV dyssynchrony (Table 1) showed early systolic anterior motion (ESAM) of IVS (Fig. A) that occurred within/after QRS complex and its peak was after the R-wave. It appeared in all patients with (positive) PSS in contrast to patients with end diastolic anterior motion (EDAM) (Fig. B). ESAM pattern showed 89% sensitivity and 96% specificity in detecting RV EF <35% (AUC 0,98; p<0,001), being more accurate than TAPSE <17 mm (67% sensitivity, 73% specificity; AUC 0,69; p=0,021). Although RV dyssynchrony correlated well with mPAP, RV free wall strain and RV EF (r=0,55, r=0,7, r=-0,85, all p<0,01), in the multi-variable analysis only the latter was an independent predictor (β=-0,63, p<0,01).

**Conclusions:** Increased RV dyssynchrony and, thus, PSS strongly correlated with the early systolic anterior motion of IVS. This M-mode sign could be applied as a stratification tool to detect the impaired RV ejection fraction.

	Pat. with EDAM of IVS (n = 57)	Pat. with ESAM of IVS (n = 35)	
RV dyssynchrony (ms)	16 ± 10	83 ± 23	p < 0,001
mPAP (mmHg)	36 ± 10	53 ± 16	p < 0,001
RV EF (%)	45 ± 7	27 ± 5	p < 0,001
RV free wall strain (%)	-26 ± 6	-14 ± 6	p < 0,001
PSS (%)	-9 ± 7	17 ± 11	p < 0,001
TAPSE (mm)	20 ± 4	16 ± 5	p < 0,001
Age (years)	67 ± 12	64 ± 15	p = 0,32

Characteristics of patients with different septal motion patterns



Interventricular septum motion patterns



## POSTER SESSION 3

Monday 23 May 2016

Location: Poster Area

### ACUTE HEART FAILURE

#### P1426

##### Repeated echocardiography in patients with inferior myocardial infarction and acute heart failure

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**Background:** Acute mitral regurgitation (AMR) is a frequent reason of acute heart failure (AHF) in patients with acute inferior myocardial infarction (AMI) and usually underdiagnosed.

**Purpose:** To examine the frequency of AMR as a reason of AHF in patients with first inferior ST elevation AMI.

**Methods:** In the study 62 patients with first acute inferior ST elevation myocardial infarction and signs of AHF on admission were included, 40 patients with moderate and 22 with severe AHF. Echocardiography was done every day in the first 3 days.

**Results:** AMR was diagnosed in 30 patients (48.4%). The reasons of AMR were papillary muscles dysfunction in 21 (16.1%) patients and papillary muscle rupture in 9 (14.5%) patients. The left ventricle ejection fraction was more than 40% in all patients with AMR. In the first day AMR was diagnosed in 15 patients, 11 and 4 patients in the second and third days consequently.

**Conclusion:** The reason of AHF in patients with first inferior ST elevation AMI was AMR in about half of the patients usually diagnosed in the first 3 days.

#### P1427

##### Performance of dynamic change of cardiac output in the diagnosis of acute heart failure (AHF) in patients with acute dyspnea. Comparison between patients with reduced and preserved left ventricular

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<sup>1</sup> fattouma bourguiba hospital, emergency department, monastir, Tunisia

**Aim of study:** To evaluate the diagnostic performance of cardiac output (CO) change with dynamic and pharmacological maneuvers in the diagnosis of AHF in patients with acute dyspnea, and to study the difference between those with reduced and preserved LVEF.

**Materials and Methods:** A prospective study conducted in the emergency department (ED) of our hospital including patients over 18 years admitted for acute dyspnea. We measure CO using thoracic bioimpedance: at baseline supine position (SP), during leg rising (LR), in sitting position (S), during Valsalva maneuver (VM) and after administration of sublingual nitroglycerin (NTG test). Heart failure (HF) is defined on the basis of clinical examination, serum levels of pro-BNP and echocardiographic findings. Patients were divided into three groups: control group including patients without HF (HF-), group with reduced LVEF (<50%) and group with preserved LVEF (≥50%).

**Results:** 291 patients were included in this study with an average age of 64 years and a sex-ratio (M / F) 0.62. In patients with HF and LVEF <50%, only NTG test is associated with a significant different change of CO compared to control group (respectively -23% versus -36%, p < 0.01) figure 1. In patients with HF and LVEF ≥50%, only VM is associated with a significant different change of CO compared to control group (respectively -21% versus -31%, p < 0.01) figure 2.

**Conclusion:** In patients presenting to the ED for acute dyspnea, HF can be detected by CO change with NTG test in patients with reduced LVEF and VM in patients with preserved LVEF.

Figure 1: Cardiac output change with dynamic maneuvers in patients with reduced LVEF

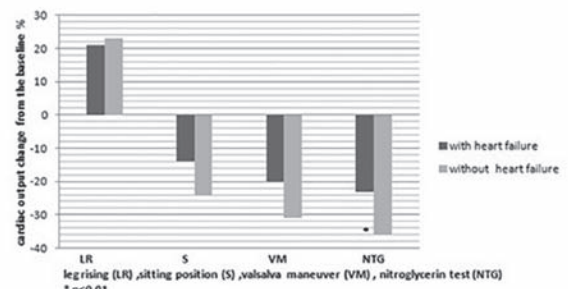
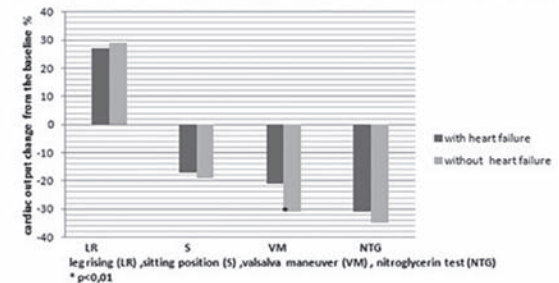


Figure 2: Cardiac output change with dynamic maneuvers in patients with preserved LVEF



#### P1428

##### Value of diagnostic investigations in the emergency room in patients suspected of having heart failure

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**Background/Introduction:** Diagnosis of heart failure (HF) cannot be solely based on signs or symptoms due to its low specificity or insensitivity. Therefore, the 2012 ESC HF Guidelines recommends that HF diagnosis be supported with diagnostic investigations in these patients. In the acute setting, the optimal exclusion cut-point for NT-proBNP is set at 300 pg/mL.

**Purpose:** To analyse the sensitivity (S), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) of diagnostic investigations in a contemporary cohort of patients with suspected HF.

**Methods:** Retrospective analysis of all patients admitted into the emergency department (ED) between January 1st - December 31st 2014 who had an NTproBNP determination for suspected HF. Diagnosis of HF was done according to the 2012 ESC HF Guidelines.

**Results:** A total of 820 patients were analysed. Mean age was 77.9 years, 52% were women. Comorbidities were frequent: 41% of patients had diabetes mellitus, 82% hypertension. Chronic kidney disease, chronic pulmonary disease, ischemic

heart disease or valve disease had a prevalence of around 25% each. Nine percent of patients had dementia and 14% had had a stroke. All patients had a chest X-ray and ECG done in the ED. HF was diagnosed in 64% of patients. Although NTproBNP was higher in patients with HF (median 4620 [p25-p75: 2085-9535] pg/mL vs 1307 [401-4070] in non-HF patients), 91% of the whole cohort had NTproBNP levels  $\geq$ 300 pg/mL (98% in HF vs 79% in non-HF patients,  $P < 0.001$ ). Value of diagnostic investigations are shown in Table 1.

**Conclusions:** The presence of pulmonary oedema and pleural effusion on chest X-ray had a high specificity for the diagnosis of acute HF. An abnormal ECG did not help to establish the diagnosis of HF. In a contemporary cohort of unselected elderly patients with comorbidities, an NTproBNP value of 300 pg/mL has little diagnostic value.

Table 1

	Frequency in the whole cohort, n (%)	S	Sp	PPV	NPV
Abnormal ECG	681 (85)	82%	14%	34%	58%
Cardiomegaly on chest X-ray	415 (51)	61%	67%	77%	49%
Pulmonary oedema on chest X-ray	108 (13)	18%	95%	86%	39%
Pleural effusion on chest X-ray	235 (29)	34%	80%	75%	41%
NTproBNP $\geq$ 300 pg/mL	749 (91)	88%	21%	69%	46%

**P1429**

**Heart failure diagnosis in the emergency department: are classical signs and symptoms useful?**

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<sup>1</sup>Hospital del Mar, Municipal Institute for Medical Research (IMIM), Barcelona, Spain; <sup>2</sup>Hospital del Mar, Department of Cardiology, Barcelona, Spain; <sup>3</sup>Autonomous University of Barcelona, Barcelona, Spain; <sup>4</sup>Hospital del Mar, Department of Cardiology, Municipal Institute for Medical Research (IMIM), Barcelona, Spain

**Background/Introduction:** Diagnosis of heart failure (HF) is challenging because most of its signs and symptoms lack specificity or are insensitive. The diagnostic value of classical HF signs and symptoms has seldom been evaluated in contemporary cohorts that include old or comorbid patients.

**Purpose:** To analyse the sensitivity (S), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) of classical HF signs and symptoms in a contemporary cohort.

**Methods:** Retrospective analysis of all patients admitted into the emergency department (ED) who had an NTproBNP determination for suspected HF from January 1st to December 31st 2014. Diagnosis of HF was done according to the 2012 ESC HF Guidelines.

**Results:** A total of 820 patients were analysed. Mean age was 77.9 years, 52% were women. Comorbidities were frequent: 41% of patients had diabetes mellitus, 82% hypertension. Chronic kidney disease, chronic pulmonary disease, ischemic heart disease or valve disease had a prevalence of around 25% each. Nine percent of patients had dementia and 14% had had a stroke. HF was diagnosed in 64% of patients. Diagnostic value of key signs and symptoms are described in Table 1. Presence or absence of hepatomegaly and third heart sound (gallop rhythm) were seldom documented on medical charts.

**Conclusions:** Only 2/3 of patients with suspected HF in the ED are diagnosed with HF. Breathlessness was the main complaint but specificity was low. The presence of paroxysmal nocturnal dyspnoea had the highest specificity.

Table 1

Signs/symptoms	Frequency in the whole cohort, n (%)	S	Sp	PPV	NPV
Breathlessness	720 (88)	96%	26%	70%	78%
Orthopnoea	330 (40)	52%	81%	83%	49%
Paroxysmal nocturnal dyspnoea	191 (23)	32%	92%	87%	43%
Ankle swelling	451 (55)	64%	61%	75%	49%
Elevated jugular venous pressure	246/622 (39)	51%	83%	85%	45%
Hepatojugular reflux	220/776 (28)	38%	88%	85%	44%
Cardiac murmur	196 (24)	27%	81%	71%	38%
Pulmonary crepitation	541 (66)	80%	59%	77%	62%
Tachycardia (> 120 beats per minute)	80 (10)	9%	89%	60%	36%

**P1430**

**Clinical characteristics of acute decompensated heart failure patients hospitalized in the intensive care unit of internal medicine departement**

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<sup>1</sup>UMF Carol Davila, Emergency Clinical Hospital Sf. Ioan, Internal Medicine Clinic, Bucharest, Romania; <sup>2</sup>UMF Carol Davila, Emergency Clinical Hospital Floreasca, Internal Medicine Clinic, Bucharest, Romania; <sup>3</sup>Emergency Clinical Hospital Sf. Ioan, Internal Medicine Department, Bucharest, Romania

**Introduction:** A large number of patients are hospitalized for acute decompensated heart failure in the internal medicine department of emergency hospital.

**Purpose:** to evaluate the prevalence and in-hospital characteristics of acute decompensated heart failure in patients consecutively admitted in the intensive care unit of Internal Medicine Clinic, from a university emergency hospital.

**Methods:** A retrospective study was conducted on 98 patients admitted for acute decompensated heart failure, from January 2013 to December 2014. Hemoglobin, BUN, serum creatinine, eGFR, uric acid, glycaemia, sodium and potassium levels, and acide-base balance were monitored. Transthoracic echocardiography was performed.

**Results:** 53% of patients were male and 47% were female. Mean age was 76.7+/-12.56 for males and 82.8+/-8.27 for females. Acute respiratory failure with dyspnea was the reason for admission in all patients. Hypertension was present in 66% of patients, diabetes mellitus in 30.61% and COPD in 19.38% of patients. Arterial acide-base balance was evaluated in 82.65% patients in the first day of admission. 41.83% of patients had acidosis. Respiratory acidosis associated to heart failure was prevalent, despite chronic kidney disease who was present in 55.10% of patients. LVEF <45% was measured in 73.46% of cases. 17.34% of patients had hyponatremia on admission. Uric acid was increased in 24.48% of patients. 26.53% of patients with acute decompensated heart failure had at least one infection in the first day of admission. The most prevalent bacteria were Klebsiella spp (34.61%).

**Conclusions:** Acute respiratory failure with acidosis was the principal reason for admission in acute decompensated heart failure.

**P1431**

**Critical analysis of a plasma NT-proBNP led acute heart failure service at our institution over 1 year**

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**Background:** Recent guidelines have suggested that patients presenting acutely with symptoms and signs of symptomatic heart failure should have NT-proBNP testing to exclude heart failure and help rationalise echo usage. We therefore evaluated such a system in a large tertiary centre cardiac unit. All patients presenting with possible heart failure underwent NT-proBNP testing. Those with values above 400ng/l automatically received an echocardiogram with a dedicated heart failure sonographer and a heart failure consultant review.

**Methods:** All consecutive patients who had plasma NTpro-BNP requested between 10/09/2014 and 09/09/2015 were included. Hospital databases and records were used to identify diagnoses, length of stay and inpatient mortality. Outpatient mortality was confirmed using Summary Care Records (range 4-16 months). Data was collected as part of our Institution's approved Clinical Audit.

**Results:** In total, 2144 patients had plasma NTpro-BNP testing because of the clinical suspicion of heart failure. 1791 patients (85%) had a NT-proBNP over 400ng/litre. 156 patients were discharged before the heart failure team could see the patients. These patients had a mortality rate of 9.6%. The average time for the heart failure team to review for heart failure patients was 1.01 days (SD 0.51). 1153 (70%) patients were reviewed within two days by the heart failure team and 1456 (89%) within three days. 737 patients had echocardiography to facilitate the heart failure review; the study was not repeated if it had been performed within 6 months. 34 patients were sent home with arrangements made for echocardiography within two weeks - of these, 6 patients had heart failure. In total, 605 patients had heart failure; 398 patients had Left Ventricular Systolic Dysfunction (LVSD) (65.7%), 138 patients had Heart failure with preserved Ejection Fraction (HFpEF) (22.8%), and 69 patients had Right Heart Failure (RHF) (11.4%). This represents an increase compared to results from 2013/2014. Patients with LVSD had a mortality rate of 25.8%, compared to 12.5% in HFpEF, 22.1% in RHF and 24% in patients without heart failure. Readmissions with heart failure was common; 79 patients presented twice, 20 patients presented three times, 5 patients presented 4 times, 2 patients presented 5 times during the year and 1 patient presented 6 times. However, the mortality for patients who readmitted was increased (LVSD 35.4%, HFpEF 27.6%, RHF 35.7%).

**Conclusions:** Our data suggests a NT-proBNP led acute heart failure service with a dedicated heart failure physiologist does diagnose patients with heart failure in a timely fashion. In our unselected cohort of over 2000 consecutive inpatients with

suspected heart failure over a year, only 31% of those with a raised NTproBNP level ended up with a clinical diagnosis of heart failure. Of these patients 67% had LV systolic dysfunction. This raises questions as to whether peptide testing as an acute screen is not specific enough.

#### P1432

##### High risk clinical profiles in severe forms of acute heart failure syndrome

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**Introduction:** Acute heart failure (AHF) is a syndrome with still high in-hospital and early post-discharge mortality. A lot of clinical and paraclinical parameters with prognostic value come from national and international registries. Just a few data related to clinical forms.

**Purpose:** identifying high risk clinical profiles for in-hospital mortality (IHM) in patients with severe clinical forms of AHF syndrome.

**Methods:** 228 patients with two severe forms of AHF syndrome: Chronic Decompensated Acute Heart Failure NYHA IV class (CDAHf NYHA IV class) and non-Acute Coronary Syndrome Pulmonary Edema (nonACS APE), admitted in an Emergency Hospital – Cardiology between 01.01-31.12.2013; divided and analyzed by etiology and clinical form. Biologic, clinic and echocardiographic parameters with prognostic value were established for each form; risk profiles were defined.

**Results:** 136 patients CDAHf NYHA IV class, 92 patients nonACS APE. Males, CDAHf vs non ACS APE 55.88% vs 45.65%, similar mean age (73years). Significant statistical differences ( $p < 0.001$ ) for cardiovascular risk factors incidence, higher for nonACS APE (hypertension - 89.13% vs 69.12%, dyslipidemia -76.09% vs 39.71%, type II diabetes mellitus 45.65% vs 32.35%) and for some comorbidities ( $p < 0.05$ ), higher in CDAHf NYHA IV class for atrial fibrillation (33.82% vs 19.56%) and history of HF (100% vs 80.43%). IHM was 17.54%, statistically significant associated with non ACS APE at admission (non ACS APE vs CDAHf, 9.64% vs 7.89%, RR=1.14,  $p = 0.005$ ). Regardless of etiology, for CDAHf NYHA IV class, the following parameters proved to have independent prognostic value for IHM: urea  $> 67$ mg/dl ( $p < 0.001$ ), sodium  $< 130$ mEq/l ( $p = 0.007$ ), systolic blood pressure at presentation  $< 100$ mmHg ( $p = 0.004$ ), right atrio-ventricular gradient  $> 41$ mmHg ( $p = 0.005$ ) and E/E'  $> 20$  ( $p = 0.006$ ), and for nonACS APE: sodium  $< 130$  mEq/l ( $p = 0.002$ ), EDT  $< 196$ ms ( $p = 0.03$ ), diastolic left ventricular diameter (DLVD)  $> 54$ mm ( $p = 0.15$ ).

**Conclusions:** There are enough clinical and paraclinical data to help us to define a high risk clinical profile in severe clinical forms of AHF syndrome. Our analysis highlighted a high risk for IHM for nonACS APE as clinical form ( $p = 0.005$ , RR=1.14), for CDAHf NYHA IV class with hypotension at admission, hyponatremia ( $< 130$ mEq/l) and high blood urea ( $> 67$ mg/dl) and echo with high filling pressure and pulmonary hypertension and for non ACS APE associated with hyponatremia ( $< 130$  mEq/l), high filling pressure (EDT  $< 196$ ms) and dilated left ventricle (DLVD  $> 54$ mm). Larger groups of patients are needed for risk score development, taking into account all of these parameters.

#### P1433

##### Relationship between clinical and hemodynamic presentation of heart failure deterioration and left ventricular ejection fraction - preliminary report

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<sup>1</sup>Institute of Military Medicine, Department of Cardiology and Internal Diseases, Warsaw, Poland

**Background:** Treatment of patients with heart failure (HF) deterioration is one of the most challenging problems in acute cardiovascular care. However, cardiovascular risk of the ones with mildly impaired and preserved left ventricular ejection fraction (LVEF) might be underestimated. The use of simple, noninvasive methods of hemodynamic assessment such as impedance cardiography (ICG), can support the hemodynamic assessment and adequate treatment strategy of those high risk patients.

**Aim:** We aimed to evaluate the clinical and hemodynamic status of patients with HF deterioration with respect to LVEF.

**Methods:** The study was performed in a group of 45 patients (37 men; mean age 73.1 years, mean LVEF 37.6%) hospitalized in the cardiology department because of HF deterioration (NYHA class 4;  $n = 17$ ). Clinical evaluation at admission included: NYHA class, NT-proBNP concentration and hemodynamic assessment of i.e. systolic and diastolic blood pressure (SBP, DBP), cardiac index (CI), systemic vascular resistance index (SVRI) and thoracic fluid content index (TFCI), measured by ICG. The analysis focused on comparison between patients with severe left ventricular systolic dysfunction (LVEF  $\leq 35\%$ ; mean LVEF 27.6%;  $n = 22$ ) and mild or no left ventricular systolic dysfunction (LVEF  $> 35\%$ ; mean LVEF 47.1%;  $n = 23$ ).

**Results:** The main differences between subgroup with LVEF  $\leq 35\%$  and LVEF  $> 35\%$  were: percentage of males (96% vs 70%;  $p = 0.023$ ) and age (80.0 vs 69.0 years;  $p = 0.004$ ). The prevalence of resting dyspnea (NYHA 4) was almost equal

(41% vs 35%;  $p = 0.671$ ). The only statistically significant hemodynamic distinctions were: lower SBP (128.5 vs 142.8 mmHg;  $p = 0.030$ ) and CI (2.77 vs. 3.34 l/kg/m<sup>2</sup>;  $p = 0.008$ ). The trend to higher TFCI (19.6 vs. 17.5 l/kOhm;  $p = 0.138$ ) and NT-proBNP concentration (5710 vs 4486 pg/mL;  $p = 0.151$ ) was also observed, but there was no significant difference in SVRI (2372 vs 2239 dyn\*s<sup>2</sup>/cm<sup>5</sup>;  $p = 0.589$ ).

**Conclusions:** The severity of clinical state and hemodynamic alterations in patients with HF deterioration are not related to great extent to LVEF. The early use of ICG in HF deterioration provides complex hemodynamic monitoring and seems to be justified.

#### P1434

##### The correlation between pressure gradient on tricuspid valve regurgitation and cardiac function in patient with left ventricular systolic dysfunction

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**Background and Purpose:** It is known that assessment of pulmonary artery pressure (PAP) can be a monitoring tool for managing heart failure (HF). However, the correlations between change of pressure gradient (PG) on tricuspid valve regurgitation (TR) as an indirect monitoring tool of PAP and functional change of left ventricular (LV) systolic function in patients with systolic dysfunction are not well known

**Methods:** From our echocardiographic laboratory database, we searched for and reviewed total 99 patients (59 males, 40 females; mean age  $68 \pm 13$  years) who had LV systolic dysfunction under 50% of ejection fraction (EF) on initial transthoracic echocardiography (TTE) and underwent follow up TTE consecutively two times. TTE data included evaluation of systolic function, pressure gradient of TR. Patients were subdivided into two groups and compared with percent changing of LVEF between 3rd and 1st TTE (Group 1 showed improvement over 30% of PG between 2nd and 1st TR ( $n = 50$ ) and the Group 2 showed under 30% improvement or aggravated PG of TR ( $n = 49$ )). And, the linear regression was applied to determine the relationships between percent change of PG of TR (between 2nd and 1st) and percent change of EF of LV (between 3rd and 1st).

**Results:** The initial mean EF of LV was  $31.9 \pm 10.6\%$  and 2nd and 3rd follow up mean EF showed significant improvement of EF ( $45.5 \pm 12.2$  and  $52.4 \pm 12.2\%$ ,  $p < 0.001$ ). The initial mean PG of TR was  $35.6 \pm 14.6$  mmHg and 2nd and 3rd follow up mean PG of TR showed significant improvement ( $24.8 \pm 12.2$  and  $26.4 \pm 12.2$  mmHg,  $P < 0.001$ ). The percent change of LVEF between 3rd and 1st TTE was significantly higher on Group 1 ( $43.8 \pm 17.7\%$  vs.  $31.8 \pm 19.9\%$ ,  $p = 0.003$ ). There was a negative correlation between percent change of PG (2nd and 1st TTE) and change of LVEF (3rd and 1st TTE) ( $r = -0.313$ ,  $p = 0.008$ )

**Conclusions:** When patients presented acute heart failure with LV systolic dysfunction, the improvement of PG of TR on follow up TTE could be an important marker of final improvement of LV systolic function.

#### P1435

##### Medium term prognosis of Egyptian patients hospitalised with acute decompensated heart failure

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**Background:** Heart failure represents a serious heart muscle disease that is associated with a bad outcome. Predictions the Middle East will be witnessing a growing epidemic in the next decade.

**Purpose:** To study different biochemical, electrophysiological, clinical and pharmaceutical parameters that affect heart failure prognosis in patients hospitalized with any form of decompensated heart failure.

**Methods:** We analyzed available inpatient data collected from Apr to Oct 2013 by heart failure unit in National Heart Institute in Egypt. The unit is the first heart failure unit nation wide with the largest number of admissions. Our study included 100 consecutive patients who were admitted with different forms and etiologies of decompensated heart failure. We assessed clinical, laboratory, electrocardiographic and echocardiographic indices with follow up 6 months for clinical status, re-hospitalization, death and major cardiovascular events.

**Results:** The mean age of our patients was ( $51.3 \pm 14.9$ ) years which is less than the mean age of heart failure patients in developed countries. Male patients were 66 and females were 34. We also found that heart failure secondary to ischemic heart disease represent the major cause of admission (54%) and the valvular heart disease was not uncommon (11%). Other etiologies were DCM (15%), HFpEF (8%), PPCM (6%), congenital heart disease (2%), chemotherapy induced cardiomyopathy, restrictive cardiomyopathy and tachyarrhythmia induced heart failure. 42% of our patients had a history of previous hospitalization due to heart failure. 86% were currently on heart failure treatment measures, of which (25.5%) were non compliant to medical treatment, (12%) of patients were not on treatment and (2%) were



first diagnosed as heart failure patients. On discharge, (75%) of discharged patients were on ACE-I or ARBs, (54%) were on BB, (91%) were on spironolactone and (65%) were on digoxin. Mortality was 9 and 18 during hospitalization and follow up period respectively giving a total mortality of 27. It was found that, patients who died in-hospital had significantly higher liver enzymes ALT ( $366 \pm 839$  vs.  $29.4 \pm 22.5$  U/L,  $p < 0.001$ ), and AST ( $276.7 \pm 637$  vs.  $29.4 \pm 22.5$  U/L,  $p < 0.001$ ) and significantly higher CK-MB. Cumulative re-hospitalization rate was 37 (40.6%) and (27%) of them were re-hospitalized more than once. Regarding 6 month mortality and rehospitalization : it was higher in the elderly patients, diabetics, and AF, those who were hypotensive, hyponatremic on admission and those who showed rising creatinine levels during hospitalization. Less mortality was noticed in patients receiving digoxin and BB.

**Conclusion:** Heart failure patients in Egypt have a different clinical profile, a lower mean age and worse prognosis compared with patients in western countries. Valvular heart disease is still responsible of significant proportion of heart failure. We probably need to improve our prescription increasing BB and decreasing digoxin.

#### P1436

##### Clinical outcomes of patients with decompensated heart failure

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**Introduction:** Heart failure is major source of morbidity and mortality in Latin America; however, demographic data, etiology, clinical presentation and prognosis have not been systematically analyzed in recent cohorts.

**Methods:** We analyzed a cohort of 409 patients admitted for decompensated heart failure in a tertiary hospital dedicated to cardiology from August 2013 through December 2015; demographic data, etiology (including Chagas' disease), clinical presentation and prognosis were reviewed.

**Results:** Mean age was  $55.3 \pm 15$  years and 254 (62.1%) patients were male; left ventricle ejection fraction was  $30 \pm 12\%$ ; 102 (24.9%) patients had ischemic heart disease, 97 (23.7%) Chagas' cardiomyopathy, 74 (18.1%) idiopathic dilated cardiomyopathy and 48 (11.7%) hypertensive disease. At admission BNP level was  $1486 \pm 1297$  pg/dL and creatinine  $1.96 \pm 1.2$  mg/dL. During hospital admission 45 (11%) patients were submitted to heart transplant and 128 (31.3%) died. 85 (20.7%) patients received an intraaortic balloon pump (IABP) and 54 died (63.5% mortality); patients with Chagas disease that received IABP had lower mortality as compared to other etiologies (51% vs 71%,  $P = 0.06$ )

**Conclusion:** Patients with decompensated heart failure have a high mortality rate. The use of IABP is of limited use in these circumstances.

#### P1437

##### The value of a simplified lung ultrasound protocol at hospital discharge in patients with acute heart failure

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Optimal timing of hospital discharge in patient with acute heart failure (AHF) is an important factor of preventing rehospitalizations. Our aim was to evaluate the value of a simplified lung ultrasound (LUS) protocol in assessing pre-discharge status of patients with AHF, correlating the LUS findings with the values of NT-proBNP.

**Methods:** 24 patients (18 men, 6 women, mean age 68,2 years) hospitalized with acute heart failure underwent LUS examination in the afternoon of the day before hospital discharge. In the next morning the NT-proBNP value was also determined. We applied a simplified LUS protocol using on the right three basal (anterior, lateral and posterior) and on the left two basal (lateral and posterior) examination areas. The LUS score was represented by the sum of B lines. The correlation between LUS findings and NT-proBNP values was analyzed using Fisher's exact test (significant  $p < 0,05$ ).

**Results:** 6 patients had  $< 15$  B lines, 16 patients had  $> 15$  B lines and 2 patients had pleural effusion on LUS, while 16 patients had the value of NT-proBNP  $> 1000$  pg/ml at discharge. The results of LUS correlated significantly ( $p = 0,0022$ ) with the NT-proBNP values – only one patient not having increased NT-proBNP in the group with  $> 15$  B lines.

**Conclusions:** Despite a relatively good clinical status, the majority of patients had high NT-proBNP values at the time of hospital discharge. LUS proved to be a useful tool in identifying patients with subclinical congestion reflected by the high NT-proBNP levels. These patients may need a prolongation of hospitalization and/or a more careful follow-up to prevent early readmission.

#### P1438

##### Correlation between low body mass index and clinical safety outcome measures of patients with congestive heart failure: perspective of a single-centre, prospective pilot study

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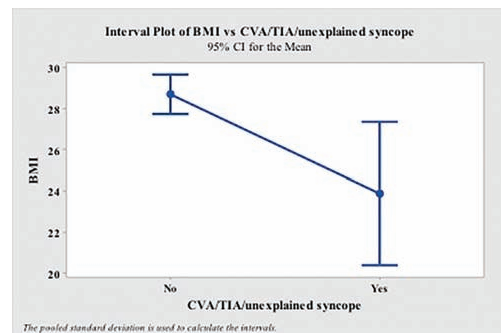
**Background/Introduction:** The correlation between low body mass index (BMI) and congestive heart failure (obesity paradox) has been described in the literature; however, the association between BMI and clinical outcome measures is not well characterized.

**Purpose:** This study aimed to describe the correlation among BMI and myocardial infarction (MI)/cerebrovascular accident (CVA)/mortality composite outcome, combined infection/bleeding and combined CVA/transient ischaemic attacks (TIA)/unexplained syncope outcome measures of patients with heart failure with reduced ejection fraction (HFrEF).

**Methods:** Retrospective analysis of prospectively collected data of a single centre heart failure registry in Saudi Arabia.

**Results:** Of 167 patients with HFrEF, 41 (25%) had BMI of  $\leq 24$  kg/m<sup>2</sup>. The low BMI group had higher composite MI/CVA/mortality (19% vs 3%;  $P = 0.014$ ) and composite infection/bleeding (12% vs 19%;  $P = 0.016$ ) rates compared with those with BMI of  $> 24$  kg/m<sup>2</sup>. Moreover, the study revealed that lower the BMI, higher the CVA/TIA/unexplained syncope (23.9, 5.5 vs 28.7, 6.2;  $P = 0.01$ ), higher the composite MI/CVA/mortality (26.4, 5.6 vs 29, 6.3;  $P = 0.014$ ) and lower the combined infection/bleeding (27.7, 5.8 vs 31.3, 7.3;  $P = 0.01$ ) rates.

**Conclusion:** Patients with HFrEF having BMI of  $\leq 24$  kg/m<sup>2</sup> had a higher incidence of MI/CVA/mortality, higher combined CVA/TIA/unexplained syncope incidence and lower combined incidence of bleeding/infection compared with those having BMI of  $> 24$  kg/m<sup>2</sup>.



CVA/TIA/syncope and BMI correlation

#### P1439

##### Gender and racial differences in surgical outcomes among adult patients with acute heart failure

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**Background:** Approximately three million U.S. adult females, age 20 and older, are living with heart failure (HF). While both males and females are affected by this cardiac syndrome, females are more likely than males to develop it, be discharged from the hospital for HF and to die from it compared to males. Black females have the highest prevalence of HF compared to White females and Black males. However, little is known about racial and gender differences in 30-day perioperative outcomes in patients with new or acute/worsening HF.

**Purpose:** To describe gender and racial differences in 30-day surgical morbidity and mortality outcomes among adult patients with new or acute/worsening HF.

**Methods:** A secondary analysis of 2012-2013 National Surgical Quality Improvement Program (NSQIP) data was conducted to compare 30-day morbidity (e.g., infection, myocardial infarction) and mortality of adults patients with new or acute/worsening HF undergoing surgical procedures (e.g., cardiac, orthopaedics, vascular).

**Results:** A total of 9548 NSQIP patients had HF of which 6827 (72%) were White and 1470 (15%) were Black; 5155 (54%) were male and 4393 (46%) were female. Males were more likely to be of White race, have diabetes mellitus, smoke, undergo vascular surgery, and be functionally independent. Females tended to be older and more likely to undergo general or orthopaedic surgery.

By multivariate analysis, females were more like to have a postoperative urinary tract infection (OR=2.012, 95% CI=1.497-2.704,  $p<.001$ ) and bleed excessively (OR=1.130, 95% CI=1.004-1.271,  $p=.043$ ), while males were more likely to suffer a cardiac arrest (OR=1.524, 95% CI=1.190-1.951,  $p=.001$ ) or myocardial infarction (OR=1.373, 95% CI=1.012-1.864,  $p=.042$ ). 30-day mortality rates did not differ by gender (670 males (13%) vs 558 females (13%),  $p=.690$ ), but did by race. Blacks were less likely to die compared to Whites (OR=0.691, 95% CI=0.552-0.866,  $p=.001$ ), but were more likely to develop renal failure (OR=1.567, 95% CI=1.107-2.218,  $p=.011$ ) and to require admission within 30 days (OR=1.175, 95% CI=1.007-1.372,  $p=.041$ ).

**Conclusions:** Gender and racial differences in 30-day surgical outcomes were noted for adults with acute HF. Further study is needed to identify the factors that lead to these differences.

#### P1440

##### In-hospital mortality in patients hospitalized for acute heart failure: comparison between actual and predicted

Novartis Farma provided a grant for statistical analysis

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**Introduction:** Clinical models predicting in-hospital mortality risk in patients hospitalized for acute heart failure (AHF) have been developed. Acute Decompensated Heart Failure National Registry (ADHERE) risk tree provides clinicians with a practical bedside tool using systolic blood pressure, creatinine and blood urea nitrogen obtained at hospital admission. Nonetheless, can not estimate accurately mortality in certain real-world populations.

**Purpose:** This study aims to compare in-hospital mortality risk predicted by ADHERE risk tree and the actual mortality in patients hospitalized for AHF.

**Methods:** Retrospective observational study that enrolled all patients hospitalized for AHF and discharged from an internal medicine department in 2012. Clinical records were queried for data collection from the 429 enrolled patients. Ten patients were excluded for lack of data to estimate ADHERE risk group. Chi-square test or Fisher's Exact test were performed to compare in-hospital mortality risk predicted by ADHERE risk tree and the actual mortality in patients hospitalized for AHF.

**Results:** Thirty four patients (7.9%) died during AHF hospitalization. Comparing this study population with the validation cohort of ADHERE risk tree, the first had higher mortality in Low Risk, Intermediate Risk 2 and Intermediate Risk 1 groups (4.5% vs 2.3%,  $p=0.017$ ; 12.5% vs 5.6%,  $p=0.024$  and 40.0 vs 13.2%,  $p=0.003$ , respectively).

**Conclusions:** Patients hospitalized for AHF in our department experienced higher global in-hospital mortality than patients enrolled in ADHERE validation cohort, reported as 4%. Nevertheless, our mortality rate is similar to recent observational surveys. When analysing groups of risk given by ADHERE risk tree, certain patients are more prone to die, presenting in-hospital mortality rate which is the double in Low Risk and Intermediate Risk 2 and fourfold in Intermediate Risk 1, comparing with ADHERE validation cohort stratification groups. These results improve our knowledge and should influence patient management since the very first hours at emergency room. Although a simple tool for managing these patients, ADHERE risk tree is not readily applicable and needs to be validated to specific populations and clinical scenarios.

#### P1441

##### The evolution of endothelial dysfunction, serum uric acid and NTproBNP in decompensated chronic heart failure

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**Background:** The complex hemodynamic and neurohumoral hyperactivation mechanism implied by heart failure pathophysiology has led to revolutionary treatments in the past 15-20 years. Furthermore, new pathophysiological models, such as endothelial dysfunction or oxidative stress, are being pursued, aiming for new risk and prognostic markers.

**Purpose:** Analyzing the relationship between endothelial dysfunction and serum uric acid (SUA) and NTproBNP for patients suffering from acute de novo and decompensated chronic heart failure. Method The study was based on data from 50 patients with an average age of  $70.84 \pm 8.72$  years suffering from decompensated chronic heart failure caused by ischemic cardiomyopathy. The most common causes for decompensation were ischemia aggravation and medication or sodium diet non-compliance. The cardiac function has been evaluated echocardiographically. The flow mediated vasodilatation method was used to evaluate endothelial function, values below 10% indicating cases of endothelial dysfunction. Also, the

dynamics of SUA and NTproBNP has been studied. Hyperuricemia, defined by values above 7 mg/dL in males and above 6 mg/dL in females, was found in 54% of the subjects. A decrease in the averages was observed during hospitalization both for SUA -  $7.22 \pm 2.77$  mg/dL at admission vs.  $5.94 \pm 1.86$  mg/dL at discharge - and NTproBNP -  $4935 \pm 4861$  µg/dL at admission vs.  $2660.62 \pm 3442$  µg/dL at discharge. Results A significant improvement in the endothelial function was observed during hospitalization, vasodilatation levels rising from an average of  $9.56\% \pm 6.25\%$  at admission to an average of  $17.80\% \pm 8.57\%$  at discharge ( $p < 0.0001$ ). While 29 of the subjects (58%) presented endothelial dysfunction at admission, the dysfunction was only present at discharge in 8 of the cases (16%) ( $p = 0.01$ ). Significant correlations have been found both between the vasodilatation and SUA evolution ( $r = 0.32$ ,  $p = 0.025$ ) and between the vasodilatation and NTproBNP evolution ( $r = 0.349$ ,  $p = 0.015$ ).

**Conclusions:** Interdependency between the endothelial function and the evolution and prognostic biological parameters seems to be present. The results suggest a connection between the endothelial dysfunction and acute and decompensated chronic heart failure pathophysiology. These parameters could lead to new risk and prognostic indicators.

#### P1442

##### Proportion of patients eligible for ivabradine at discharge after an acute decompensated heart failure hospitalisation

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**Introduction:** Heart rate (HR) is a modifiable risk factor of death and early hospitalizations in patients (pts) with systolic heart failure (HF). However recommended treatment optimization with the aim to achieve target HR ( $<70$  beat per minute -bpm-), is still unsatisfactory after acute HF hospitalization.

**Purpose:** To investigate the proportion of patients eligible for ivabradine treatment after an acute decompensated HF (ADHF) hospitalization and at the first outpatient appointment.

**Methods:** We evaluated retrospectively 309 consecutive pts discharged from 3 Italian hospitals with a HF dedicated team, between January 2012 and the end of September 2015, with a left ventricular ejection fraction (LVEF)  $\leq 40\%$ . Pts eligible for ivabradine were defined based on LVEF  $\leq 35\%$ , sinus HR  $\geq 70$  bpm, NYHA class II-IV.

**Results:** At discharge 71 pts (23.0%) were eligible for ivabradine. Among them 10 pts were discharge with ivabradine, 2 pts were already on this drug, and 59 pts (19.1%) although eligible did not receive ivabradine. Characteristics of 59 pts not on ivabradine at discharge were: age  $65 \pm 14$  years, female 32%, ischemic etiology 35.6%, median LVEF 28% (interquartile range -IQR: 25-30%), 40.7% were de novo cases, NYHA class III-IV 32.2%, with a mean systolic blood pressure of  $109 \pm 18$  mmHg, median HR 75 bpm (IQR): 72-84 bpm, a previous episode of atrial fibrillation (AF) in 32.2%, on beta-blockers 86.4% (median carvedilol dosage 15.6 mg/day; median bisoprolol dosage 2.5 mg/day), on amiodarone 37.3%, on digoxin 3.4%. At first outpatient appointment (after a median time of 3 months, IQR: 2-6 months) only 28 (9.1%) pts were still eligible for ivabradine. During the time between discharge and the first appointment we reported 2 deaths, 6 HF rehospitalizations, and 6 pts were lost at follow up. At the first appointment in 5 pts ivabradine was started, thus 24 (7.8%) pts were still without proper HR control without ivabradine prescription. The characteristics of this population not on ivabradine was  $68 \pm 14$  years, female 42%, ischemic etiology 37.5%, median LVEF 30% (interquartile range -IQR: 25-32%), NYHA class III-IV 20.8%, with a mean systolic blood pressure of  $120 \pm 24$  mmHg, median HR 78 bpm (IQR): 75-83 bpm, a previous episode of AF in 29.2%, on beta-blockers 79.2% (median carvedilol dosage 12.5 mg/day; median bisoprolol dosage 2.5 mg/day), on amiodarone 33.3%, on digoxin 8.3%. Conclusion(s): Even in HF specialized centers, 19.1% of pts discharged after an ADHF event were not on ivabradine although suitable for this treatment. At first outpatient appointment the proportion of pts still eligible for ivabradine was 7.6%. It must be noted that up to 32% of pts not on ivabradine at discharge had a previous episode of AF, and titration of beta-blockers could also be pursued. The attractive hypothesis that a more rapid achievement of HR target could reduce early events after ADHF needs perspective validation.

#### P1443

##### Diastolic dysfunction has differential impact on clinical outcomes of diabetic versus non-diabetic patients hospitalized with acute heart failure: a population based study

This research was supported by grants from the National Institutes of Health: PO1 HL 76611, R01 HL 84155

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**Background:** The association between diastolic dysfunction (DD) severity and clinical outcomes in patients hospitalized for acute heart failure (AHF) with and without

diabetes remains undefined. Our objective is to compare the clinical characteristics, echocardiographic characteristics, and clinical outcomes of those with and without diabetes hospitalized with AHF based on severity of DD.

**Methods:** Retrospective analysis of 428 adults residing in a County hospitalized from 2005 to 2008 for primary diagnosis of AHF and who had sufficient Doppler echocardiographic data to classify diastolic grade according to the American Society of Echocardiography (ASE) classification. Those with indeterminate diastolic grade were excluded. Demographic, clinical, laboratory, and echocardiographic data were collected. AHF was identified from ICD-9 codes. Mean follow up was  $6.5 \pm 3.2$  years.

**Results:** Of 428 subjects who had characterization of diastolic grade during hospitalization, 186 (43.5%) had diabetes mellitus (DM) and 242 (56.5%) did not have diabetes. Among those with both AHF and DM, 81.2% had moderate or severe DD (grade 2 or greater), whereas among those with AHF but not DM, 68.6% had moderate or severe DD. In subjects with both AHF and DM, those with moderate or severe DD had higher HbA1c levels ( $6.9 \pm 1.4$ ,  $p = 0.036$ ) compared to those with normal diastolic function ( $6.0 \pm 1.2$ ) or with mild DD ( $6.2 \pm 0.9$ ). Ejection fraction was similar among all diastolic grades (average 45.8%,  $p = 0.49$ ). Among those with AHF and DM, the severity of DD was associated with increased risk of cardiac and heart failure rehospitalization ( $p < 0.05$ ). However, among those with AHF but without DM, there was no association with diastolic grade and cardiac or heart failure rehospitalization.

**Conclusions:** Among those hospitalized for AHF, those with DM had a greater prevalence of moderate or severe DD compared to those without DM. Those with the most severe diastolic grade in the DM group were more likely to have higher HbA1c levels. Among those with both AHF and DM, there was an association between diastolic grade severity and cardiac and heart failure rehospitalization. This association is not seen among those without DM.

#### P1444 Non-recovery of renal function in acute heart failure is an independent predictor of long-term mortality

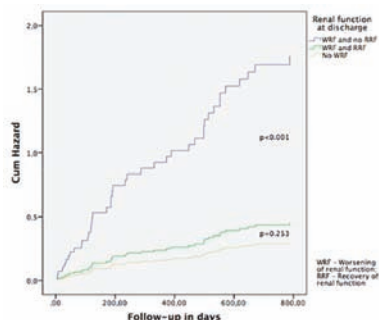
J Joao Carmo<sup>1</sup>; P Freitas<sup>1</sup>; MJ Baldo<sup>2</sup>; R Morais<sup>2</sup>; P Vicente<sup>2</sup>; A Leitao<sup>2</sup>; F Marques<sup>2</sup>; I Araujo<sup>2</sup>; L Campos<sup>2</sup>; C Fonseca<sup>2</sup>  
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**Background:** Renal dysfunction is one of the strongest risk marker in acute heart failure (AHF). Although admission serum creatinine (SCr) and worsening of SCr during hospitalization have been reported as risk predictors, significance of recovery of renal function at discharge is uncertain.

**Methods:** One hundred and thirty-five consecutive patients were admitted to our Heart Failure Unit with AHF. SCr was obtained on admission, during hospitalization and at discharge. Worsening of renal function (WRF) was defined as an increase of SCr  $> 0.3$  mg/dL during hospitalization when compared to admission SCr. The recovery of renal function was defined as a decrease of SCr  $> 0.3$  mg/dL at discharge, when compared to peak SCr. All cause mortality during long-term follow-up was assessed as clinical endpoint.

**Results:** The population had a mean age of  $75 \pm 12$  years, 53% were female and 54% presented at class IV NYHA. In patients with WRF during hospitalization ( $n = 46$ ), total mortality during mean follow-up of 20 months was 55.6% versus 28.9% in patients without WRF (log rank 0.001). Cox proportional hazard models identified non-recovery of renal function at discharge (hazard ratio HR 5.94, CI 95% 2.64 to 13.38,  $p < 0.001$ ), age (HR 1.04, 1.00 to 1.07,  $p = 0.048$ ), chronic obstructive pulmonary disease (HR 2.03, 1.03 to 3.98,  $p = 0.040$ ), use of a renin angiotensin system inhibitor (HR 0.27, 0.13 to 0.57,  $p = 0.001$ ), urea (HR 1.01, 1.00 to 1.02,  $p = 0.001$ ) and albumin (HR 0.41, 0.19 to 0.87,  $p = 0.019$ ) as independent predictors of long-term mortality. There was no significant difference in mortality between patients with WRF and recovery of renal function ( $n = 28$ ) and those without WRF ( $n = 89$ ) (HR 1.53, 0.74 to 3.16,  $p = 0.253$ ).

**Conclusion:** In patients with AHF, non-recovery of renal function is the strongest independent predictor of all-cause mortality at long-term follow-up.



#### P1445

##### Short term prognostic factors in patients hospitalized with acute heart failure

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**Background:** The perpetually growing burden of cardiovascular disease is one of the most important socioeconomic aspects of modern medicine. Hospitalization for heart failure symptoms is on the rise, because of an increase in incidence and the difficulties of managing such patients, both on the short and long term. There is a need to properly define the factors that impact the prognosis of patients, so as to implement new strategies of better care which might improve survival and quality of life.

**Purpose:** The purpose of our descriptive study was to analyze the records of the patients admitted for acute heart failure (AHF) in our cardiology unit, with a focus on certain parameters which influence treatment options and the decision to discharge.

**Material and methods:** From the total number of admissions in our secondary cardiology unit in 2014, almost 30% were for decompensated heart failure. The total number of patients was 189, a fifth of whom had multiple readmissions. Less than 4% of admissions were for acute pulmonary edema; the vast majority of patients had acutizations of chronic heart failure (NYHA class IV). The median age of the group was 76, with an even distribution on sexes. More than half of the patients had heart failure with preserved ejection fraction.

**Results:** The main underlying etiology was ischemic heart disease, with half of the patients also having valvular disease (mitral or aortic). For 20% of the subjects, the underlying pathology was hypertensive cardiopathy, while two thirds of the group had atrial fibrillation. More than half of the cases associated pulmonary hypertension.

Looking at relevant comorbidities, we found the prevalence of type II diabetes to be 36%. Half of the patients had chronic kidney disease, with 20% of them being stage 4. Important subgroups of patients were the 10% with persistent hypotension and also the cases which associated significant electrolyte disturbances.

The median hospitalization length was 8 days. We found no significant correlation between neither the NT-proBNP value, nor the degree of systemic congestion and the duration of admission. The only clear predictors of a longer hospital stay were hypotension and hyponatremia. By the end of the study period, 5% of the total number of patients had died in our clinic.

**Conclusions:** Hospitalization and discharge were mostly decided by the severity of dyspnea. Better ambulatory management is needed, as most patients admitted failure to adhere to medication and diet. The most important factors which influenced management during hospitalization were hyponatremia and hypotension.

#### P1446

##### Comparison of the effects between urapidil and nitroglycerin in patients with heart failure with preserved ejection fraction

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**Background:** Nowadays, heart failure (HF) is a common clinical syndrome with high morbidity and mortality. HF with preserved ejection fraction (HFPEF) presently accounts for approximately 40% of HF diagnoses, with a rising incidence, mortality and morbidity is rising.

**Objective:** The aim of this study was to evaluate whether an alpha1-adrenergic blocker (a1-blocker), urapidil, provides additional therapeutic benefits compared to nitroglycerin (NG) in treatment of different classification of HFPEF.

**Methods:** All patients enrolled met the following criteria: satisfied the standard diagnostic criteria for hypertension and acute HFPEF (Killip  $\geq$  II grade; NYHA  $\geq$  II grade). 102 patients suffered from acute HFPEF patients were assigned into two groups according to cardiac function: ejection fraction (EF)  $\geq 50\%$ ; N-terminal pro-B-type natriuretic peptide (NT-proBNP) were 450 ng/L, 900 ng/L, 1800 ng/L according to the age  $< 50$  years, 50-70 years,  $> 70$  years, respectively. That were Killip group ( $n = 51$ ; age,  $69.760 \pm 11.870$  years; EF,  $59.643 \pm 6.291\%$ ; NT-proBNP,  $3895.882 \pm 3419.372$  ng/L) and NYHA group ( $n = 51$ ; age,  $69.650 \pm 12.270$  years; EF,  $62.777 \pm 7.810\%$ ; NT-proBNP,  $4744.882 \pm 3577.651$  ng/L). Each group randomized to receive different treatment with urapidil or NG, respectively. Doses of urapidil and NG were administered to patients based on the standard protocols used for regular administration regimes for acute HF patients. Patient's blood pressure (BP) was constantly monitored during administration to provide constant information that might warrant adjustment of the dose rate and delivery time. Urapidil was administered at a rate of 50 or 100 mg/min for



an initial 6 hours and then adjusted to 300 mg/min for the remaining administration time. Accordingly, NG was administered at a rate of 10 mg/min for the initial 6 hours and then adjusted to a maximum rate of 20 mg/min for the remaining administration time. All patients were monitored for systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR) and received test for N-terminal pro-B-type natriuretic peptide (NT-proBNP) at different time points (0 hours, 48 hours and 7 days) after treatment.

**Results:** SBP ( $F=133.386, p<0.05$ ), DBP ( $F=71.583, p<0.05$ ), HR ( $F=35.796, p<0.05$ ) and NT-proBNP ( $F=75.754, p<0.05$ ) decreased significantly in each group. Without regard to Killip and NYHA, patients receiving urapidil showed significantly lower SBP at 48 hours ( $F=5.031, p<0.05$ ) and 7 days ( $F=5.811, p<0.05$ ), and significantly reduced levels of NT-proBNP at 48 hours ( $F=4.199, p<0.05$ ) and 7 days ( $F=4.094, p<0.05$ ) were observed than them of counterparts treated with NG. DBP of patients with urapidil in Killip group more decreased from baseline at 48 hours ( $p<0.05$ ) and 7 days ( $p<0.05$ ) compared to them in NYHA group.

**Conclusions:** Urapidil demonstrated better efficiency than NG on lowering SBP and NT-proBNP of patients suffered with HFPEF. More attention, it also could effectively reduce DBP of these cases classified by Killip.

#### P1447

##### Place of care is the main determining factor for outcome in acute heart failure patients

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**Introduction:** Acute heart failure is associated with high in-patient mortality. UK national heart failure audit has shown poorer outcome in patients who didn't have cardiology specialist input.

**Purpose:** Aim of the study is to determine the factors that predict poorer outcome in patients admitted with acute heart failure.

**Method:** Retrospective analysis of data on 250 patients who were discharged with the primary diagnosis of heart failure from year 2014-2015.

**Results:** There's no significant mortality rate difference in patients received cardiology specialist input, however mortality rate is significantly lower if it's divided according to the place of care. (Cardiology ward: 12.5% versus other medical wards: 25%,  $P$  value = 0.006)

Demographic data, co-morbidities, investigations and medications are shown in the table below.

Incidence of LV systolic dysfunction and ischemic heart disease is higher in cardiology ward patients.

**Conclusions:** There's significant lower mortality rate in heart failure patients treated in cardiology ward despite the presence of more significant co-morbidities.

These findings are likely to be attributed to better investigations and optimisation of medical treatment.

Cardiology versus other wards' patients

	Cardiology ward n = 158	Other medical wards n = 92	P value
Inpatient mortality	12.5%	25%	0.006
Age	78 years	82 years	
Hypertension	69%	70%	0.5
Diabetes	42%	45%	0.3
Ischemic heart disease	56%	45%	0.04
Asthma or COPD	30%	40%	0.08
Haemoglobin level	12	11.5	
Creatinine level	135	126	
ECG	97%	88%	0.0002
Atrial fibrillation	47%	60%	0.02
Echo or equivalent	92%	68%	0.0001
LV systolic dysfunction	47%	18%	0.0001
Triple therapy	24%	24%	0.4
ACE inhibitors/ACE blockers	70%	67%	0.3
Beta blockers	77%	67%	0.04
Spironolactone/Eplerenone	46%	37%	0.09
Medically stable on oral therapy	76%	55%	0.03

#### P1448

##### Ivabradine administration in cardiogenic shock is associated with cardiac stroke work index improvement

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**Background:** Cardiogenic shock (CS) is the most severe form of acute heart failure associated with poor prognosis. Among compensatory mechanisms to overcome cardiac output reduction, tachycardia is the first activated. However, tachycardia is accompanied by oxygen consumption increase that may further impair cardiac contractility.

**Purpose:** the aim of this observational, single-center study was to assess if administration of 5 mg ivabradine bid to patients with CS, receiving inotropes and vasopressor, was associated with improvement of echocardiographic hemodynamic parameters

**Methods:** Of 18 patients admitted for CS (M 42%,  $67 \pm 11.9$  years, LVEF  $29 \pm 6\%$ ), 9 patients were treated with ivabradine on top of optimal therapy while the others represented the control group. Patients were evaluated at baseline, after 24 h, 48 h, 72 h and 120 h with clinical and echocardiographic assessments.

**Results:** Baseline characteristics of groups were similar. There were no significant differences in HR and systolic blood pressure variations nor in cardiac index or stroke volume index over time between groups. However, ivabradine group presented a significant higher increase in stroke work index (from baseline 17.8 to 55 at 120 h) when compared to control group (from baseline 22.3 to 29 g/m/m<sup>2</sup>) ( $p=.034$ ).

**Conclusions:** Ivabradine use in patients with cardiogenic shock was associated with a significant increase in stroke work index that is an expression of cardiac mechanical work and contractility.

#### P1449

##### Management of heart failure after non-ST elevation MI; use of mineralocorticoid receptor antagonists and implications for devices.

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**Background:** The presence of heart failure following a non-ST elevation myocardial infarction (non-STEMI) is associated with a worse prognosis. Current UK and European Guidelines recognise the importance of identifying these higher risk patients and offering them disease modifying therapies including drugs and devices.

**Purpose:** We wanted to find out if these guidelines were being followed in a busy Heart Attack Centre in the South West of England; in particular, whether a mineralocorticoid receptor antagonist (MRA) was being prescribed to those with impaired LV function and either diabetes or signs of heart failure.

**Methods:** We performed a retrospective audit of consecutive patients identified as having non-STEMI on the MINAP database from April 2014 to March 2015. We assessed: 1. How many received an echocardiogram during their index admission; 2. Compliance with NICE recommended post MI medications on discharge; 3. Implications for device implantation rates according to NICE and ESC guidelines.

**Results:** 176 patients (mean age 70 years, 64% male) were recorded on the MINAP database with non-STEMI in the study period. 71% (125/176) had an echocardiogram during the index admission. 42% (53/125) had good left ventricular (LV) function and 30% (38/125) had moderately or severely impaired LV function (EF < 40%). Of those with impaired LV function post non-STEMI, 82% (31/38) either had diabetes or signs of pulmonary oedema; 6 of these had a documented contra-indication to a MRA. 56% (14/25) were prescribed a MRA in accordance with the NICE guidelines compared to > 95% compliance with guidelines recommending ACEi/BB/statin/antiplatelet agents. Mean length of stay for those with impaired LV function was 7.9 days. 71% (27/38) of the impaired LV function patients were followed up by our cardiology team with 11 referred back to their local hospital for follow up. 41% (11/27) had a repeat echo after at least one month to reassess LV function and assess requirement for implantable devices.

**Conclusions:** Nearly a third of patients had significantly impaired LV function following non-STEMI. Whilst most post-MI drugs were prescribed > 95% in compliance with the NICE guidelines, MRAs (spironolactone and eplerenone) were only prescribed in around half of suitable cases. The reasons for this could include poor documentation of contra-indication to MRA or lack of awareness of the guidelines. Follow-up reassessment of LV function after at least a month to detect functional recovery or indication for device therapy was also poor. Opportunities to prevent sudden death or worsening heart failure by implanting ICD or CRT devices could therefore have been missed. Management of non-STEMI patients complicated by heart failure might benefit from a closer link between the acute coronary syndrome and the heart failure teams to improve outcomes and reduce length of stay for patients.

## P1450

**The prognostic value of Nt pro BNP and echocardiographic markers in patients with intermediary high risk pulmonary embolism**

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**Purpose:** Intermediary risk pulmonary embolism (PE) represents a severe medical condition. The thrombolytic treatment for this condition is a debated subject, as there are few studies that prove the positive effect on hemodynamic stability. The ESC guidelines 2014 on the management of PE recommend the thrombolytic therapy on patients with intermediary – high risk PE. Method We selected 65 patients with intermediary risk PE, defined by both biochemical (Nt pro BNP) and echocardiographic markers (myocardial contraction velocity by TDI (MCV), tricuspid annulus peak systolic excursion (TAPSE), right ventricle diastolic diameter (RVD)) of right ventricle pressure overload. We divided the patients in two groups, a study group – 28 patients-, receiving thrombolytic therapy – 10mg t-PA bolus followed by 90 mg t-PA in 2 hours- and a control group -37 patients- which received only unfractionated heparine. The patients from study group did not have any contraindications for thrombolysis, were younger than 75 y.o., did not have severe renal failure (creatinine clearance > 30ml/min) and did not have anemic syndrome. The patients were assessed regarding the biochemical and echocardiographical signs of RV pressure overload on admission and on 48 hours after therapy and the results were compared between the two groups. Results All the echocardiographic markers had a statistically significant better improvement in the study group compared to control group. TAPSE increased with 56.49% in the study group compared to 31.44% in the control group (p 0.01), MCV increased with 23.12% in the study group compared to 14.2% in the control group (p 0.03) and RVD decreased with 21.59% in the study group compared to 11.21% in the control group (p 0.02). Meanwhile Nt pro BNP decreased with 71.59% in the study group compared to 52.07% in the control group (p 0.005). Referring to the correlation to the mortality rate Nt pro BNP was the only marker significantly statistical correlated with mortality, a cut-off value of 2423pg/ml being associated with increased mortality rate (p 0.015) with a 95% confidence interval. Regarding bleeding risk the bleeding rate in the study group was 10.23 % while in the control group it was 5.4% but there was only one case of major bleeding in the study group.

**Conclusions:** The positive effect of thrombolytic therapy on the prognosis of patients with intermediary-high risk PE is proven by the effect of thrombolysis on the echocardiographic and biochemical markers of RV dysfunction.

## P1451

**Characterisation of serelaxin pharmacokinetics using a population pharmacokinetics approach**

The study was sponsored by Novartis Pharma AG, Basel, Switzerland  
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**Purpose:** Serelaxin, a recombinant human relaxin-2, is in development for treatment of acute heart failure (AHF). This model-based covariate analysis aimed to investigate the impact of covariates (patient demographics, markers of kidney and liver function, inter-trial variability) on serelaxin pharmacokinetics (PK).

**Methods:** Pooled data from 8 randomised, single-dose serelaxin infusion trials: CRLX030A1201, CRLX030A2201, CRLX030A2202, CRLX030A2101, CRLX030A2102, CRLX030A2103, CRLX030X2201 and RLX.CHF.003 were used for developing the PK model. The model consisted of a 3-compartment disposition with linear elimination calibrated by a non-linear mixed effect approach using Monolix version 4.3.2 (Lixoft Inc.). Covariates on different model parameters such as clearance and volume of distribution were selected and ranked based on their predictive power using correlation-adjusted (marginal) correlation (CAR) scores. A backward elimination step was performed to obtain the best model with the least number of covariates and maximum explanatory power according to the Bayesian information criterion.

**Results:** The analysis included data from 416 subjects. Population estimates of clearance (central: CL; inter-compartmental: Q2, Q3) and volume of distribution (central: Vc; peripheral: Vp2, Vp3) for a typical Caucasian subject without HF were as shown in the table below. Based on the covariate analysis, eGFR and BMI were selected to explain the variability in CL and serelaxin concentration at steady state (Css). Correlation of eGFR with clearance implied that 15–20% of serelaxin clearance might be through renal clearance. The total volume of distribution (Vc+Vp2+Vp3) was markedly larger in the subjects with AHF (567 mL/kg) and chronic HF (461 mL/kg), compared with the population estimate (350 mL/kg) in those without HF. These differences may be due to abnormal fluid retention conditions commonly observed in patients with HF.

**Conclusion:** This population approach with a 3-compartment disposition model adequately characterises the serelaxin PK. Correlations were observed between

some of the covariates and serelaxin PK. The impact on serelaxin PK was moderate and thus considered to have no clinical relevance.

	CL (mL/h/kg)	Q <sub>2</sub> (mL/h/kg)	Q <sub>3</sub> (mL/h/kg)	V <sub>c</sub> (mL/kg)	V <sub>p2</sub> (mL/kg)	V <sub>p3</sub> (mL/kg)
Population estimate (± SD)	89.9 (± 1.5)	126.4 (± 6.8)	8.0 (± 0.4)	73.3 (± 4.5)	176.5 (± 7.8)	100.3 (± 3.2)
Coefficient of variation (%)	31.0	33.0	37.0	70.0	27.0	22.0

## P1452

**Impact of furosemide dosages on in-hospital and post-discharge outcomes in acute heart failure diabetic patients: a DAD-HF II sub-study**

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**Background:** The role of the addition of low-dose dopamine on top of low- or high-dose furosemide infusion in patients with acute decompensated heart failure (ADHF) has been assessed in the DAD-HF II trial and was found not to be associated with any beneficial effects in relation to renal parameters as well as survival end-points. Its role, however, in ADHF patients with diabetes, which portends increased incidence of worsening renal function with the use of diuretics during hospitalization, has never been evaluated.

**Purpose:** To assess the effect of these combinations in the subgroup of DAD-HF II patients with a history of diabetes mellitus.

**Methods and Results:** 161 ADHF patients (mean age, 78.1 years; 46% female; ejection fraction 30.9%) were randomized to 8-hour continuous infusions of: a) high-dose furosemide [HDF, n=50, diabetics n=24 (48%), 20 mg/h], b) low-dose furosemide and low-dose dopamine [LDFD, n=56, diabetics n=23 (41%), 5 mg/h and 5 µg kg<sup>-1</sup> min<sup>-1</sup> respectively], or c) low-dose furosemide [LDF, n=55, diabetics n=31 (56%) 5 mg/h]. The main outcomes were 60-day and one-year all-cause mortality (ACM) and hospitalization for HF (HHF). Dyspnea relief (Borg index), serum creatinine and length of stay (LOS) were also assessed.

The urinary output at 2, 4, 6, 8, and 24h was not significantly different in diabetics vs. non-diabetics in the three groups. No differences in the Borg index or LOS were noted. Baseline creatinine did not differ between the study groups in both diabetics and non-diabetics. However, peak creatinine was significantly higher in diabetic patients of the HDF group compared to LDF group (2.12 vs. 1.48 mg/dL, P=0.017). Neither the ACM at day 60 or at one year nor the HHF at day 60 or one year differed between HDF, LDFD, and LDF diabetic-subgroups groups, respectively.

**Conclusions:** In ADHF diabetic patients, treatment with HDF is associated with increased risk of worsening renal function as compared with lower doses of furosemide, regardless concomitant dopamine administration. This finding, however, is not associated with a worse short- and long-term prognosis.

## P1453

**Effect of baseline characteristics on mortality in the SURVIVE trial comparing levosimendan and dobutamine in acute heart failure: sub-analysis of the Finnish patients**

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**Background:** In the SURVIVE study [Mebazaa A. JAMA. 2007;297:1883-91], in 1327 acute heart failure patients from 9 countries, there was no statistically significant difference between levosimendan and dobutamine in the 180-day all-cause mortality. Country-specific differences in outcome were, however, present. In the Finnish sub-population, mortality was significantly lower in levosimendan treated patients.

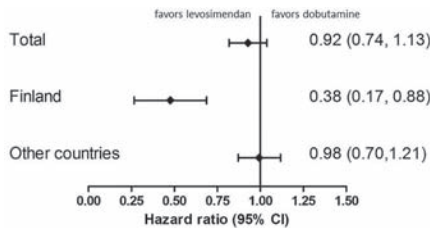
**Purpose:** We aim to understand the reasons for this disparity.

**Methods:** The risk factors for all-cause mortality were identified in the whole study population using multivariable Cox proportional hazards regression analysis. Those factors were evaluated in the Finnish 95 patients.

**Results:** The treatment by country interaction for mortality in Finland vs. other countries was significant, p=0.029 (see Figure). Levosimendan treated patients had a lower mortality compared to dobutamine; 8/47 (17%) vs. 19/48 (40%), Hazard ratio [95% CI] 0.38 [0.17, 0.88], p=0.023. Baseline variables predicting survival in the whole SURVIVE population included age, systolic blood pressure, heart rate,

myocardial infarction during admission, levels of NT-pro-BNP, glucose, creatinine, and alanine transferase, use of ACE inhibitors and  $\beta$ -blockers, oliguria, time from hospital admission to randomization, history of cardiac arrest, and left ventricular ejection fraction. Finnish patients were more frequently treated with  $\beta$ -blockers (88% vs. 52%,  $p < 0.0001$ ), their study drug treatment was started earlier (mean  $\pm$  SD  $41 \pm 40$  h vs.  $81 \pm 154$  h;  $p < 0.0001$ ), and acute myocardial infarction was more common at admission (39% vs. 16%,  $p < 0.0001$ ).

**Conclusions:** The significantly lower mortality in the Finnish patients treated with levosimendan was possibly due to different baseline characteristics, such as higher use of beta-blockers, higher frequency of myocardial infarction at admission, and to shorter delay between randomization and start of treatment.



180-day mortality in SURVIVE trial

**P1454**

**Acute hemodynamic effects of caval counterpulsation balloon in heart failure patients**

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**Background:** Up to the present, preload reduction in congestive heart failure (CHF) patients is performed with high potency diuretics. Last year, we reported in TCT/ACC U.S.A 2015 the hemodynamic changes of the first 6 CHF cases in humans, using Percutaneous Transluminal Caval flow Restriction (PTRC) procedure achieved with caval counterpulsation balloon (CCPB). This innovative method reduced preload in CHF. In this study we are reporting the results of the 6 consecutive patients with CHF, treated with intermittent preload reduction of caval flow with CCPB, guided by the respiratory phases.

**Methods:** 6 patients with CHF who met our protocol criteria, were evaluated. 4 were ischemic, and 2 non ischemic. The mean age was  $58 \pm 9$ . 4 male mean age  $55 \pm 6$  years, and 2 female mean age  $63 \pm 4$ . We performed baseline Doppler echocardiography, coronary angiography and right heart catheterization. Subsequently caval flow restriction was started, through the right femoral vein, catheter balloon was introduced in the femoral vein and echo guided, placed just before hepatic vein drainage. The balloon was inflated according to previous calculations, to cover Inferior Vena Cava (IVC) remaining area completing 100% (total occlusion), and 70% during expiration (sub-occlusion), assuming 30% inspiratory collapse, resulting intermittent flow. The balloon was kept inflated for 30 minutes, right catheterization and echocardiography were repeated during inflated balloon. The balloon was removed and deflated.

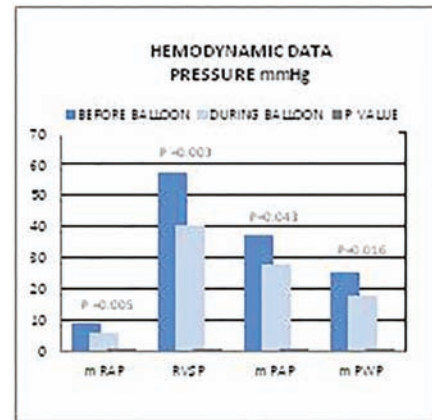
**Results:** Table 1. Hemodynamic Variables

**Conclusion:** We are reporting our hemodynamic and echocardiography experience in 6 patients with CHF treated with intermittent reduction of preload with CCPB. Hemodynamic and echocardiographic changes obtained in these patients, including preservation of cardiac output suggest, that this innovative approach can play a role in the treatment of CHF patients.

Table 1. Hemodynamic Variables

HEMODYNAMIC VARIABLES	BEFORE BALLOON	DURING BALLOON	% OF CHANGE	P VALUE	
1	Mean RAP mmHg	9.00	5.67	-37%	0.005
2	,s RVP mmHg	57.17	40.33	-30%	0.003
3	Mean PAP mmHg	37.50	28.00	-26%	0.043
4	Mean PWP (mmHg)	25.50	17.50	-32%	0.016
5	CARDIAC OUTPUT l/min	4.09	4.50	10%	0.157

Table 1  
Statistical significance was defined as  $P < 0.05$



Graphic 1 Hemodynamic Data.

**P1455**

**Prognostic utility of lung ultrasound pocket device in acute heart failure.**

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**Background and purpose:** Heart failure (HF) increases the risk of death during myocardial infarction (AMI) and the risk increases with severe symptoms of HF; It is necessary to develop rapid HF diagnosis techniques to improve management and minimized morbimortality. The aim of this study is to evaluate the short term prognostic significance of lung ultrasound performed at bedside with a pocket device (PD) in patients with heart failure in the acute myocardial infarction context.

**Methods:** 109 patients with AMI and HF symptoms, admitted to our coronary care unit and studied at bedside with PD were included. The interstitial lung water was determined by counting the B-lines according to BLUE and FALLS protocol. The management of patients was made according to European clinical practice guidelines. The primary endpoint was a composite of all-cause death or HF hospitalisation at 3 months from discharge.

**Results:** 76 of 109 patients included were men, the mean age was  $70 \pm 15$  years. The primary endpoint was observed in 22 patients (20,7%). Patients with events were older ( $79 \pm 6$  vs  $67 \pm 4$  years,  $p < 0.001$ ) and had more risk factors (hypertension 72% vs 49% and diabetes 74% vs 32%). No other significant differences in the clinical characteristics of the patients were found. The mean B-lines count was 10,5 (5-39) Patients who presented the primary endpoint had more B-lines (32 [12-40]) compared to those patients without events (13 [7-20],  $p < 0.001$ ). In the univariate analysis B-lines  $> 30$  was associated with the occurrence of the primary endpoint at 3 months (odds ratio : 1.5 [1.1-2.1],  $p = 0.002$ ). This relationship remained despite the inclusion of cardiac systolic function, NT-proBNP, age, hypertension and diabetes in the multivariate analysis (OR 1.7 [1.2-2.6],  $p = 0.009$ )

**Conclusion:** Lung ultrasonography assessed with a PD may represent a useful diagnostic tool in AHF, and may help with prognostic including prediction of mortality of the patients. These suggestions should be validated in large studies.

**CHRONIC HEART FAILURE**

**P1456**

**Hyperbaric oxygen therapy and correction of platelet aggregation in patients with chronic heart failure**

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**Objective:** To determine the influence of hyperbaric Oxygen Therapy on the aggregation of platelets in patients with chronic heart failure (CHF). Materials and

**Methods:** The study involved 50 patients with ischemic etiology of CHF, the average age of  $55.4 \pm 8.58$ let taking (57%) and receiving (43%) at a dose of 75mg cardiomagnil in the treatment of CHF. Before and after 5 sessions HBO mode 1.2 ATA 40minut exposure for 5 days, the platelet aggregation on a laser analyzer.

**Results:** The use of HBO accompanied by changes in the functional activity of platelets in 17% of patients receiving and not receiving 20% Cardiomagnil. This normalization of increased or decreased platelet aggregation was detected in 18% of patients taking Cardiomagnil and only 8% had never accept Cardiomagnil. At the same time maintained the increased platelet aggregation in 6% of patients on the background Cardiomagnil and 23% - not taking Cardiomagnil.



**Conclusion:** The use of HBO in the treatment of heart failure has a more pronounced effect on platelet aggregation, taking Cardiomagnil.

#### P1457

##### **Influence of revascularization methods in acute myocardial infarction on the level of brain natriuretic peptide and development of congestive heart failure in patients with post-MI**

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One of the highly topical problems of practical cardiology is the development of congestive heart failure (CHF) in patients with myocardial infarction (MI). It is important to measure the concentration of Brain Natriuretic Peptide (BNP) to confirm heart failure. BNP secretion increases in accordance with the intensity of post-infarction heart changes. The aim of the study was to investigate the impact of revascularization methods in acute myocardial infarction on the level of BNP and the development of congestive heart failure in patients with post-MI.

**Methods:** 101 patients with acute MI with ST-segment elevation were enrolled in the study. Their clinical symptoms of congestive heart failure were evaluated during discharge and over 1 year; echocardiography was assessed, as well as the level of BNP was determined. Mean age was  $56 \pm 9.99$  years; with 81.9% of men. All the patients depending on revascularization method in acute MI were divided into 3 groups: Group 1 (n=28; 27.7%) consisted of patients who underwent thrombolytic therapy (TLT), Group 2 (n=42; 41.6%) of patients with percutaneous coronary intervention (PCI), and Group 3 included patients without myocardial revascularization (n=31; 30.7%).

**Results:** Analysis of the results revealed that 74.7% of patients had BNP level exceeding the threshold.  $BNP \geq 125$  pg/ml was found in 76.2% of patients in Group 1, in Group 2 - in 69% of cases, in Group 3 in 85% of patients. The average concentration of BNP was significantly lower in patients who underwent PCI ( $150 \pm 90$ , 1 pg/ml), compared with an average level of  $BNP 270 \pm 117$ , 6 pg/ml in patients of Group 3 ( $3-2 = 0.000$ ). In addition, there is a clear tendency towards accuracy by comparing the average BNP level of Groups 1 and 2 ( $2-1 = 0.072$ ) with the lowest value in patients with a history of PCI. Analysis of BNP concentration in patients with  $EF > 50\%$  revealed that values of  $BNP \geq 125$  pg/ml were observed in 19.07% of patients in Group 1, in Group 2 in 21.45%, and in Group 3 in 20% of patients, which allowed us to confirm a likely probability of congestive heart failure with preserved EF in those patients. However, in 9.53% of patients in Group 1, in 21.45% - in Group 2 and 15% of patients in Group 3 with an index  $EF > 50\%$  BNP concentration was  $< 125$  pg/ml.

**Conclusions:** A lower BNP level was registered after a year of observation in patients with PCI in acute myocardial infarction.  $EF > 50\%$  in patients with congestive heart failure is higher in patients with revascularization. The absence of reperfusion contributes to a more severe course of post-MI heart failure.

#### P1458

##### **Infiltrative cardiomyopathy: a novel aetiology**

N/A

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A 52-year-old Afro-Caribbean male presented with a 6-month history of dyspnoea, decreasing exercise tolerance and paroxysmal nocturnal dyspnoea. Clinically he was in pulmonary oedema. He had a history of Rosai-Dorfman disease (RDD) and chronic hepatitis B. There was no previous cardiac history.

Transthoracic echocardiography (TTE) demonstrated biventricular hypertrophy with suggestion of a right atrial mass. Cardiovascular magnetic resonance (cMR) imaging revealed thickening of all four cardiac chambers. No right atrial mass was seen, however the right atrial wall was grossly thickened. There was normal gadolinium kinetics and no late enhancement.

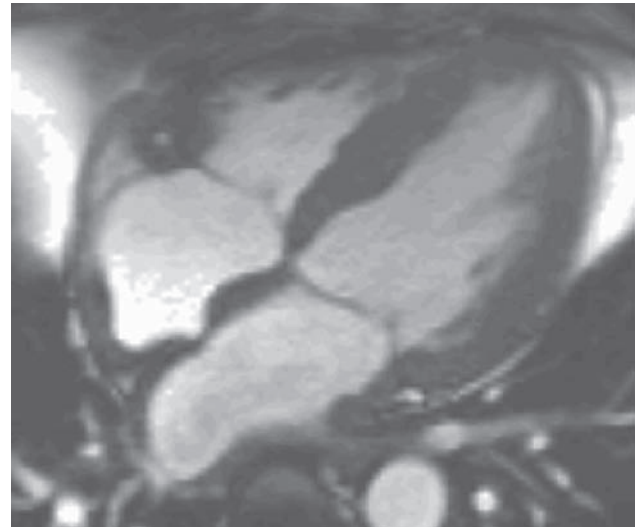
At this point the cardiac diagnosis was unclear. The cMR features were not consistent with a diagnosis of amyloidosis, sarcoidosis or hypereosinophilic syndrome.

The patient proceeded to an endomyocardial biopsy. Histological assessment demonstrated a lymphocytic and histiocytic infiltration with emperipolesis and positive S100 staining. These findings are characteristic of RDD. A diagnosis of cardiac RDD was therefore made.

The patient received cisplatin, etoposide and dexamethasone as medical therapy for RDD. Serial cMR demonstrated improvement in myocardial infiltration and a reduction in cardiac mass but progressive infiltration of the aortic valve and initially moderate, then severe aortic regurgitation. An intended aortic valve replacement has not been possible due to ongoing gastrointestinal and respiratory complications of immunosuppression.

Originally described in 1969, RDD is a rare, non-clonal proliferative disorder of histiocytes of unknown aetiology which typically causes bilateral painless cervical lymphadenopathy. Extra-nodal involvement most commonly involves the skin, nasal cavity, paranasal sinuses, orbit, upper respiratory tract and bone. Cardiac involvement is rare, occurring in  $< 1\%$  of cases.

To our knowledge, this case is unique as it is the first description of RDD involving all four cardiac chambers.



cMR: Infiltration of all four chambers

#### P1459

##### **Depression in patients with heart failure**

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**Background:** Re-hospitalisation represent a high burden in heart failure (HF). Fatigue is one of the most common complaint in patients with HF and depression is a frequent psychological symptom in these patients.

**Aim:** We assessed the relation between fatigue and depression and their impact on HF hospitalization rates in 1216 patients with HF admitted at a tertiary hospital. Patients were diagnosed based on ICD-9 codes and prescription of antidepressants: no symptom, fatigue, depression, and fatigue and depression.

**Results:** The hospitalisation rates were higher in women with depression and fatigue (OR 3.2, 95% CI 2.1-4.3). No difference was found between patients reporting fatigue and those reporting fatigue and depression in the re-hospitalisation rates.

**Conclusion:** Depression is a frequent occurrence in women with HF and when coupled with fatigue is associated with an increased risk or re-hospitalisation.

#### P1460

##### **Oscillatory breathing and respiratory muscles strength during exercise in congestive heart failure patients**

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**Background/Introduction:** Congestive Heart failure (CHF) patients often have breathing abnormalities due to increase of pulmonary stiffness. Oscillatory breathing (OB) is observed in part of these patients but we do not know if this is associated to respiratory muscles fatigue.

**Purpose:** Aim of this study was to evaluate effort of respiratory muscles in CHF patients. We selected patients with CHF in stable conditions. Inclusion criteria were  $LVEF < 40\%$  and presence of OB at cardiopulmonary exercise test (CPET).

**Methods:** We analyzed 45 CHF patients (41 males, 4 females, age  $68.4 \pm 10.6$  years) who presented OB at CPET and we measured, with a dedicated device, Maximal Expiratory Pressure (MEP) and maximal inspiratory Pressure (MIP) at rest (before CPET) and immediately after exercise. We calculated normal values of MIP and MEP by Black & Hyatt formula.

**Results:** MIP at rest was  $87 \pm 31\%$  of predicted, while right after effort  $83 \pm 25\%$ . MEP was at rest  $65 \pm 18\%$  of predicted and right after effort  $63 \pm 19\%$ . We observed a slight reduction after physical exercise, not statistically significant. This suggests that muscles do not get more tired after effort. Study population was then subdivided in 2 groups according to persistence of OB (group B, 18 patients) or its disappearance during effort (group A, 27 patients). In group A, MIP at rest was  $94 \pm 30\%$  of predicted, while after effort  $89 \pm 26\%$ . MEP was  $69 \pm 17\%$  at rest and  $67 \pm 18\%$  after effort. In group B MIP at rest was  $74 \pm 30\%$  of predicted

while after effort  $70 \pm 17\%$ . MEP was  $58 \pm 17\%$  at rest and  $57 \pm 20$  after effort. The difference between absolute values within the two groups (A vs B) resulted statistically significant: for MIP at rest  $p = 0.003$ , while after effort  $0.002$ , for MEP at rest  $p = 0.01$  while after effort  $0.02$ . Functional evaluation showed that the study population reached 43% of work predicted measured in watt, Group A 49% and group B 33% ( $p = 0.001$ ). Also, statistically significant difference between the two groups has been observed in  $VO_2$  peak values: in group A  $14.67 \pm 3.44$  ml/kg/min vs.  $10.96 \pm 2.73$  ml/kg/min in group B ( $p < 0.001$ ). In terms of  $VE/VC_{O_2}$  slope we observed also a significant difference:  $31.90 \pm 6.01$  (A) vs.  $43.45 \pm 13.88$  (B) ( $p < 0.001$ ).

**Conclusion:** In CHF patients the respiratory muscles are compromised at rest probably because of major stiffness and imbibition of pulmonary tissue. Our data showed differences in CHF patients with persistent OB. In particular, these data suggest that those patients are more compromised and have a worse prognosis. In fact significant differences have been found in terms of lower working capacity, lower  $VO_2$  peak, higher  $VE/VC_{O_2}$  slope, lower MIP and MEP and higher mortality.

#### P1461

##### Impaired gas diffusion in heart failure identifies patients with impaired right ventricle contractile reserve

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In heart failure (HF) patients, an altered gas diffusing capacity for carbon monoxide (DLCO) is a marker of lung capillary injury that bears relevant clinical and prognostic information. It is unknown whether an impaired right ventricular contractile reserve is linked to an impaired gas diffusion and may become synergic in causing exercise limitation and ventilation inefficiency.

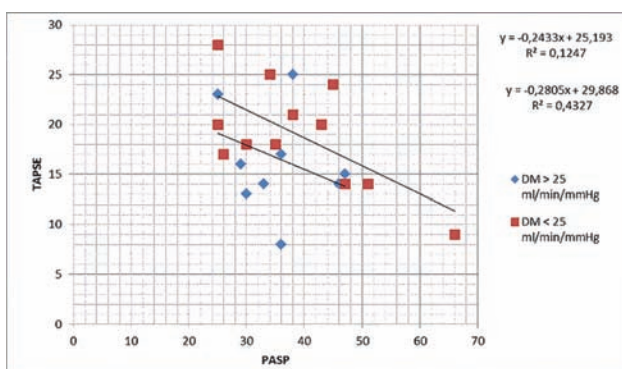
**Methods:** 23 HF patients (mean age  $64 \pm 10$ ; male 75%; NYHA II-III; mean left ventricular (LV) ejection fraction  $34 \pm 9\%$ ) underwent DLCO measurements with assessment of membrane component (DM) and capillary blood volume ( $V_c$ ) and maximal cardiopulmonary exercise testing (CPET, tilt-ergometer, personalized ramp protocol) combined with Echo-Doppler assessment of right ventricular function by assessing tricuspid annular peak systolic excursion (TAPSE) and pulmonary systolic pressure (PASP).

**Results:** Patients exhibited an abnormal gas diffusion (mean DLCO  $17.3 \pm 4.2$  ml/min/mmHg) with depressed alveolar-capillary membrane diffusing capacity (DM) component (mean  $24.3 \pm 8.5$  ml/min/mmHg) and elevated capillary volume (mean  $102.8 \pm 57.3$  ml) along with significant functional limitation (mean peak  $VO_2$   $12.8 \pm 3.8$  ml/kg/min) and ventilatory inefficiency (mean  $VE/VC_{O_2}$  slope:  $32.6 \pm 6.1$  and mean end-tidal of  $CO_2$  mean  $32.4 \pm 4.7$  mmHg).

Population was divided into two groups according to mean value of DM: patients with a DM  $< 25$  ml/min/mmHg ( $n = 10$ , group A) and patients with DM  $\geq 25$  ml/min/mmHg ( $n = 12$ , group B).

As shown in figure, group A exhibited an unfavorable TAPSE versus PASP relationship suggesting an impairment of RV contractile reserve. Group A presented with a lower peak  $VO_2$  (mean peak  $VO_2$   $11.8 \pm 3.7$  ml/kg/min) and a higher  $VE/VC_{O_2}$  slope (mean  $VE/VC_{O_2}$  slope:  $34.5 \pm 7.2$ ).

**Conclusions:** Our findings show a link between gas diffusion abnormalities and RV contractile reserve suggesting that interventions aimed at targeting the alveolar-capillary gas diffusion capacity and functional performance in HF population have to ideally combine a modulatory effect on right heart function.



#### P1462

##### Serum phosphorus level predicts worse outcome in patients with heart failure and vitamin D deficiency but not in patients with normal vitamin D status.

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**Background:** Recently there is growing interest in the calcium-phosphorus imbalance in heart failure patients. The aim of the study was to evaluate the impact of vitamin D insufficiency and its results on clinical prognosis in patients with systolic heart failure. **Material and**

**Methods:** 138 consecutive patients (aged  $49.7 \pm 11.3$  years, 24 women, 114 men) with left ventricular ejection fraction-LVEF  $\leq 45\%$  (mean  $28.1 \pm 8.4\%$ ) were included in the study. Patients were divided according to the 25-hydroxyvitamin D [25(OH)D] status into two groups: patients with low concentration of 25(OH)D ( $< 20$  ng/ml,  $n = 93$ , 67%) and control group ( $\geq 20$  ng/ml,  $n = 45$ , 33%). Patients were followed up for median 326.5 days (IQR 163-521). Any death or heart transplantation were considered as an end point ( $n = 11$ ).

**Results:** A higher level of parathormon (59 vs 48 pg/ml,  $p = 0.005$ ) and phosphorus ( $1.17$  vs  $1.1$  mmol/l,  $p = 0.003$ ) was observed in patients with concentration 25(OH)D  $< 20$  ng/ml compared to the control group. Cumulated event-free-survival was 85%. The 25(OH)D level showed no influence on survival. However, after exclusion of NT-pro-BNP from the analysis, serum phosphorus level was the strongest predictor of worse prognosis (HR 7.1/0.1 mmol/l),  $p = 0.02$ ) independently of renal function. The relationship was not seen in the control group.

**Conclusion:** Vitamin D deficiency is common among patients with systolic heart failure and it could impair the prognosis through calcium-phosphorus imbalance.

#### P1463

##### Degree of improvement in ejection fraction after coronary artery bypass grafting in patients with low preoperative left ventricular ejection fraction

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**Objective:** To determine if there is any degree of improvement in the left ventricular ejection fraction at one year after performance of coronary artery bypass grafting in patients with low preoperative ejection fraction.

**Methods:** A retrospective observational study was performed comparing the variability of ejection fraction in patients who had low preoperative ejection fraction (less than 45 percent) versus the left ventricular ejection fraction at one year after the surgery in all patients who underwent coronary artery bypass grafting in the period from 2010 to 2014 and we divide the variability at one year in 5 degrees of improvement: No improvement from 0 to 4%, mild improvement from 5 to 8%, moderate improvement from 9 to 12%, great improvement if it was higher than 12% and worsening if there was regression in the ejection fraction. From 479 coronary artery bypass grafting done, 43 were done in patients with low ejection fraction and the year follow up was available in a total of 34 patients.

**Results:** From the total of 34 patients selected for the study, 28 patients were men (82.4%) and had a mean age of  $62.42 \pm 3.59$  years. The mean preoperative ejection fraction was  $36.12 \pm 2.19\%$  been the lowest value 25%. In all patients was performed a complete revascularization. After one year of follow up the mean ejection fraction was  $45.56 \pm 3.05\%$ . The mean of the difference between preoperative ejection fraction and control ejection fraction was  $10.44 \pm 2.70\%$  that was statistically significant with a  $p < 0.0001$ . From the 34 patients 1 had no improvement (2.94%), 8 patients had mild improvement (23.53%), 9 patients had moderate improvement (38.24%) and 13 patients had great improvement (38.24%). Three patients had a reduce in their ejection fraction (8.82%) at one year follow up, and was only one death after one year.

**Conclusion:** Coronary artery bypass grafting is a safe procedure in patients with low left ventricular ejection fraction with very low mortality and a great improvement of ejection fraction after the surgery with the majority being in mild to great improvement over the preoperative ejection fraction.

#### P1464

##### Physical activity improved diastolic function in spinal cord-injured subjects

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**Purpose:** Subjects with spinal cord injury (SCI) have been reported to present impaired left ventricular (LV) diastolic function in comparison with able-bodied (AB) ones. The present study investigated the effect of regular physical activity on the cardiac structure and function of SCI subjects.

**Methods:** Fifty-eight SCI men (29 sedentary [SCI-S] and 29 athletes [SCI-A]) and 29 AB men were cross-sectionally evaluated by clinical, laboratory, hemodynamic, and

echocardiographic analysis. All enrolled subjects were normotensive, nondiabetic, nonsmoker, and normolipemic, and the studied groups presented similar age and body mass index.

**Results:** SCI-S presented similar LV structural and systolic parameters but higher E/Em (8.0 ± 0.5) and lower Em/Am (1.18 ± 0.09) ratios than SCI-A and AB (E/Em = 6.4 ± 0.3 and 5.9 ± 0.3, respectively; Em/Am = 1.57 ± 0.12 and 1.63 ± 0.08, respectively; all P < 0.05 compared with SCI-S). Analysis of SCI individuals according to injury level revealed that tetraplegic athletes had similar features compared with sedentary tetraplegic subjects, except for higher Em (10.9 ± 0.6 vs 8.6 ± 0.7 cm s, P < 0.05) and lower E/Em ratio (6.3 ± 0.4 vs 8.8 ± 0.8, P < 0.05), whereas paraplegic athletes had similar features compared with sedentary paraplegic individuals, except for higher LV end-diastolic diameter (49.4 ± 1.4 vs 45.0 ± 1.0 mm, P < 0.05) and Em/Am ratio (1.69 ± 0.20 vs 1.19 ± 0.08, P < 0.05) and lower LV relative wall thickness (0.330 ± 0.012 vs 0.369 ± 0.010, P < 0.05) and heart rate (67.1 ± 4.2 vs 81.9 ± 2.8 bpm, P < 0.05).

**Conclusion:** Regular physical activity is associated with improved LV diastolic function in SCI subjects and might exert distinct cardiac structural effects in tetraplegic and paraplegic subjects.

**P1465**

**Acutely decompensated chronic heart failure treatment in an elderly population**

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**Purpose:** To describe pharmacotherapy recommended on discharge in a population of elderly (80+ yrs) chronic heart failure (HF) patients admitted for an acute decompensation secondary to a hypertensive urgency in the clinical setting of an emergency hospital.

**Methods:** We included 270 consecutive patients admitted to the Internal Medicine Clinic from January through December 2015, separated in two groups – HF with reduced ejection fraction (HF-REF, 53 pts) and HF with preserved ejection fraction (HF-PEF, 217 pts) to compare the two groups in terms of cardiovascular medication recommended upon discharge.

**Results:** Beta-blockers were recommended more in patients with HF-REF (p < 0.01), but in only 2/3 of HF-REF hypertensive patients and in >50% of those with HF-PEF. Those with REF were recommended more diuretics (furosemide) than those with PEF (p < 0.01). Spironolactone was frequently recommended in both groups, however more in the hypertensive elderly HF-REF population (p < 0.01).

**Conclusions:** Elderly patients admitted for chronic HF acutely decompensated by a hypertensive urgency had in 80% of the cases HF-PEF, and most patients were admitted in NYHA class III. Use of both beta-blockers and spironolactone (recommended more in the CKD patients) was suboptimal, while loop diuretics were recommended on discharge in >50% of HF-REF patients.

	HF-REF NYHA III	HF-PEF NYHA IV	NYHA III	NYHA IV
No pts (total 270)	53 (19.62%)	217 (80.37%)		
Betablockers	40 (75.47%)	144 (66.35%)		
29	11	108	36	
Diuretics	44 (83.01%)	127 (47.03%)		
28	16	85	42	
Furosemide	33 (62.26%)	76 (35.02%)		
24	9	40	36	
ACEI	34 (64.15%)	159 (73.27%)		
22	12	84	75	
CCB	15 (28.30%)	82 (37.78%)		
10	5	44	38	
Spironolactone	28 (52.83%)	51 (23.50%)		
21	7	24	27	

**P1466**

**The combination drug valsartan/sacubitril (LCZ696) reduced pulse wave velocity and aortic systolic blood pressure in patients with stable heart failure with reduced ejection fraction**

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**Objective:** Dual neprilysin inhibition and angiotensin receptor blockade with LCZ696 has been shown therapeutic benefits in chronic heart failure (CHF) patients. The aim of the study was to assess LCZ696 effects on parameters of arterial stiffness in stable heart failure with reduced ejection fraction (HFrEF).

**Methods:** In the open-label follow-up to PARADIGM HF study 18 patients with stable HFrEF (16 male, 69 ± 9 years (M ± SD), arterial hypertension 83%, previous myocardial infarction 89%, diabetes mellitus 39%, dyslipidemia 56%, LVEF 32 ± 4%, serum creatinine 118 ± 21 μmol/l, eGFR 56 ± 13 ml/min/1.73m<sup>2</sup>, potassium 4.45 ± 0.35 mmol/l) were enrolled. Patients received a stable background treatment for at least a month (ACEI 94%, beta-blockers 100%, aldosterone receptor antagonists 83.3%, loop diuretics 72.2%). ACEI treatment was interrupted for 36 h and replaced with LCZ696 100 or 200 mg (11 patients) BID according to baseline brachial BP (mean dose 185.7 ± 36.3 mg BID). Applanation tonometry was performed baseline and after 6 month LCZ696 therapy. Wilcoxon test was considered significant if p < 0.05.

**Results:** Baseline brachial BP decreased from 137.1 ± 22.0/83.4 ± 11.8 to 120.5 ± 13.5/75.1 ± 9.3 mmHg (Δ -16.6 ± 14.2/-8.3 ± 10.3 mmHg, p < 0.05), heart rate did not change (78 ± 12 vs 75 ± 15 beats/min (Δ -2.7 ± 14.7 beats/min, p > 0.05)). Valsartan/sacubitril therapy was associated with significant decrease of carotid-femoral pulse wave velocity (11.5 ± 2.9 vs 10.2 ± 2.9 m/s, p < 0.05), central systolic (125 ± 16 vs 116 ± 15 mmHg, p = 0.005) and diastolic (78 ± 7 vs 74 ± 9 mmHg, p < 0.05) blood pressure. Central pulse pressure (45 ± 11 vs 41 ± 16 mmHg), augmentation pressure (16 ± 7.1 vs 13.8 ± 8.4 mmHg), augmentation index (29 ± 7 vs 28 ± 11%), time to reflected wave (128 ± 8 vs 132 ± 7 ms) did not change significantly (p > 0.05 for all comparisons).

**Conclusion:** In stable patients with heart failure with reduced ejection fraction 6 month valsartan/sacubitril therapy was associated with significant decrease of aortic systolic pressure and pulse wave velocity.

**P1467**

**Audit of a tertiary heart failure outpatient service to assess compliance with practice guidelines**

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**Background/Introduction:** The National Institute of Health and Care Excellence (NICE) updated guidelines for chronic heart failure (HF) in 2010; incorporating an electronic audit tool to measure outpatient care delivery. Previous local audit described high prescription rates of established therapies, monitoring and specialist follow-up; contrasting with a significant omission in inadequate access to cardiac rehabilitation.

**Purpose:** This re-audit assessed interim improvement.

**Methods:** Patients with HF (preserved and reduced ejection fraction) attending a tertiary cardiac centre in London between 01/01/2013 and 31/12/2014 were audited. The electronic format covered all HF clinics; capturing demographic data, aetiology of HF, prescribed medication, heart rhythm and rate, measures of clinical follow-up and compliance with rehabilitation.

**Results:** Five hundred and thirteen patients were included. Compared with 2011, there was an identical male preponderance (71%) and age profile (68 ± 14 years, (Mean ± SD)). Seventy-three percent lived outside of London. Predominant HF aetiologies included ischaemic heart disease (37% vs 40% in 2011), idiopathic dilated cardiomyopathy (26%, 20%) and primary valve disease (13%, 12%). Eighty-five percent (n = 434) had left ventricular systolic dysfunction (LVSD). For these patients, medication included 89% (77%, 2011) taking a beta-blocker, 91% (86%, 2011) an ACE-inhibitor or angiotensin receptor antagonist and 56% (44%, 2011) an aldosterone antagonist. Twenty-nine (6%) patients were prescribed Ivabradine. All patients (100%) received monitoring of mandatory indices (functional status, rhythm, biochemistry etc.) at least six-monthly.

Access to rehabilitation remained low. While 100% of patients were educated about the beneficial effects of exercise in HF, only 21 (4%) were enrolled in a supervised group exercise programme.

**Conclusion(s):** This audit demonstrated that a tertiary HF service has high rates of documentation, follow-up and compliance with guideline-based medical therapies. A notable omission was that access to rehabilitation remains poor. This may be influenced by the fact most patients reside outside London. Further lobbying with regional and national commissioners for HF based exercise services is imperative moving forward. Alternative strategies such as telehealth and multidisciplinary education for junior team members continue to be explored.



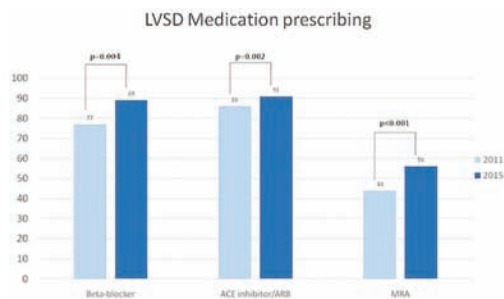


Figure 1 - LVSD medication rates

#### P1468

##### Metolazone therapy in heart failure patients

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**Background:** Metolazone (MTZ), a thiazide-like diuretic is used together with loop diuretics in the management of refractory congestive heart failure.

**Aim:** The aim of this study was to study the demographics of the heart failure population prescribed MTZ and to identify the event rates in this group.

**Method:** A retrospective analysis of data was taken of patients prescribed MTZ at Bradford Foundation Teaching Hospitals. The time period of prescription was from 1/1/14 to 31/12/14 and the 30 day and 1 year event rates in this group was studied.

**Results:** In the 12 month period, 50 patients were prescribed MTZ. 18 (36%) patients had Atrial Fibrillation, 18 (36%) had Chronic Kidney Disease, 20 (40%) had Diabetes, 15 (30%) had Hypertension, 23 (46%) had known ischaemic heart disease, 6 (12%) had an ICD/Bi-vent in-situ and 3 (6%) had a previous/current malignancy. The average number of concomitant factors was 2.5.

38 patients (76%) were Caucasian, 9 (18%) were South-Asian and 3 (6%) were Afro-Caribbean.

The mean age of patients receiving MTZ was 79.2 years (standard deviation - 14.25) ranging from 32-95.

23 patients (46%) had one or more readmission(s) within 12 months of which 13 patients (26%) were readmitted due to heart failure. 5 patients (10%) were readmitted within 30 days.

9 patients (18%) died within their first 30 days from admission and 26 patients (52%) who took MTZ died within 1 year. 14 patients (28%) died in hospital.

The average time to death was 102 days from the first dose of MTZ to the day of death.

**Conclusion:** 1. MTZ treatment is predominantly used in the elderly population in our local practice.

2. MTZ prescription is associated with a high readmission and mortality rate at 30 days and 1 year.

#### P1469

##### Are clinicians influenced by cognitive biases when investigating chronic heart failure?

This work was supported by the National Institute of Health Research Cardiovascular Biomedical Research Unit at the Bristol Heart Institute A K Angus K Nightingale<sup>1</sup>; Y Yanagisawa<sup>1</sup>; T Tallis<sup>2</sup>; D G Wilson<sup>1</sup>; Y Ismail<sup>1</sup>; A G Dastidar<sup>1</sup>; P Jeetley<sup>3</sup>; M Goonewardene<sup>4</sup>; B Whalley<sup>5</sup>

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**Background:** ESC guidelines for management of chronic heart failure (CHF) recommend non-invasive stress imaging to decide who should be investigated with coronary angiography and then undergo revascularization. We hypothesised that, like an addict who can't resist chocolate, cardiologists have cognitive biases that might influence their choice of investigations and treatment.

**Purpose:** First, we wanted to know whether these CHF guidelines were being followed. Secondly, we wanted to see if a cognitive bias (availability bias) might explain why clinicians request an angiogram without first performing a non-invasive stress imaging test in patients with CHF but no angina.

**Methods:** We performed a retrospective audit of 133 patients with CHF and no angina at a University Hospital in England who were listed for diagnostic coronary angiography. 97 were excluded as the angiogram was carried out during an admission with acute heart failure. 35 patients (21M, 14F), mean age 67 years old, were included. We carried out a survey of 35 cardiologists to assess attitudes and

behaviours towards investigations and treatments in CHF using 3 case scenarios. We also asked the 35 cardiologists and 50 GPs to choose a snack and then observed the impact of the availability of chocolate cake on their decision making.

**Results:** Non-invasive stress imaging was performed in only 23% (8/35) of CHF patients prior to angiography showing low compliance with the ESC guidelines. A further two had these tests after the angiogram. 60% (21/35) had normal coronary arteries or only mild atheroma. 9% (3/35) underwent coronary revascularization. Coronary angiography (CA) was viewed as much more readily available to cardiologists than non-invasive stress imaging such as stress echo (SE), myocardial perfusion scintigraphy (MPI) or stress perfusion cardiac MRI (weighted score of perceived availability CA 4.8 v SE 3.4 v MPI 3.9 v MRI 3.9). 88% (60/75) of clinicians said they would choose a healthy snack when writing a shopping list but only 37% (28/75) would still choose a healthy snack when offered chocolate cake as an additional option.

**Conclusions:** Coronary angiography is widely carried out in CHF patients without prior non-invasive stress imaging contrary to current ESC guidelines. One factor that could account for this is the greater perceived availability of coronary angiography compared to non-invasive stress imaging tests. Other cognitive factors that we did not investigate include financial pressures, prestige and the desire for action. In the same way that chocolate can change people's behaviour, we need to aware that the availability and status of coronary angiography can influence how clinicians investigate patients with CHF. Cognitive biases may account for some of the reasons why clinicians struggle to follow international clinical guidelines.

#### P1470

##### Effect on depression and anxiety on risk of death and hospitalisation in patients with congestive heart failure.

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**Background:** Many studies have shown an independent effect of depression on the prognosis of heart failure. Most Experts' communities recommend routine screening for depression in patients with cardiovascular disease and the subsequent directions of their psychiatrist for consultation for the appointment of therapy. Nevertheless so far there is no conclusive evidence of the effect of psychological methods and antidepressants treatment on the course of heart failure.

**Purpose:** of the study was to analyze effect of anxiety and depression on primary end point of the randomized clinical trial - mortality and hospitalization in patients with heart failure.

**Material and methods:** In 730 pts with CHF (NYHA III - IV) included in CHANCE (Congestive Heart failure: A multidisciplinary Non-pharmacological approach for Changing in re-hospitalization and prognosis), depression and anxiety was assessed by the Russian version of the Hospital Anxiety and Depression Scale (HADS). Using an integrated univariate and multivariate analysis we studied relationship between the depression and anxiety, as well as other clinical characteristics and non-pharmacologic multidisciplinary Disease Management Program (DMP), consisted of structured education and regular phone calls the mortality and hospitalization during 12 months follow-up.

**Results:** In univariate analyze have been found direct connection between HADS depression scale points with mortality OR 1.09 [95% CI: 1.02 - 1.16]. Presence of severe depression (HADS > 10) also significantly associated with higher mortality 1,24 (95% CI: 1,04 - 1,48). Neither depression nor anxiety demonstrates the connection with hospitalization in the univariate analysis. In multiple logistic regression we have include clinical variables typical for CHF pts, which have demonstrated the strong correlation with mortality in univariate analyze plus to depression and anxiety symptoms. Main independent predictors of prognosis (death and hospitalization of CHF) remain: NYHA FC - OR of 4.13 [95% CI: 2.54 - 6.72], history of myocardial infarction, OR 2.54 (95% CI: 1.50 - 4.28) and inclusion in active care group (DMP) - OR - 0.61 [95% CI: 0.37 - 0.99]. When included in a multiple logistic regression depression and anxiety have lost their connection with mortality.

**Conclusion:** In this study, depressive and anxiety disorders showed no independent effect on prognosis in patients with NYHA FC III-IV, while non-pharmacologic DMP significantly reduce risk of death plus hospitalizations

#### P1471

##### Drug therapy recommendations at discharge in patients with heart failure - do we follow ESC guidelines in Estonia

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**Background/Introduction:** ESC published the latest guidelines for management of heart failure (HF) in 2012, which recommends the use of beta-blockers (BB), angiotensin-converting-enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARB), mineralocorticoid receptor antagonists (MRA), loop-diuretics (D) and digoxin

in HF patients with reduced ejection fraction. These guidelines were endorsed by Estonian Society of Cardiology and translated as a pocket version to be used in everyday practice.

**Purpose:** To evaluate if drug recommendations at discharge for patients hospitalized with HF into biggest tertiary care centre in Estonia were in concordance with ESC guidelines.

**Methods:** All data were collected retrospectively from electronic discharge summaries by trained readers using pre-specified worksheet. Local guidelines of data protection were followed. We included all patients that were discharged from departments of cardiology with diagnosis of HF (codes I50.0-I50.9, ICD-10) from 01/10/2014 to 30/09/2015. Data about sex, age, length of stay in hospital, NYHA class and treatment recommendations at discharge for BB, ACEi or ARB, MRA, D and digoxin were collected. Data collection method did not allow differentiating between reduced and preserved ejection fraction HF patients. Data were analysed using MS-Excel 2013.

**Results:** There were 2182 patients (1251 men/931 women) discharged during the study period, mean age was 70 (19-99) years and mean length of stay 6.35 (0-40) days. For 98% of patients at least one drug was recommended at discharge. Patients with higher NYHA class were recommended more drug groups (Table1). Metoprolol, ramipril or telmisartan, torasemide and spironolactone were most commonly used BB, ACEi or ARB, D and MRA, respectively.

**Conclusion(s):** Due to the wide variability of grading NYHA class (i.e NYHA 0) and drug recommendations at discharge we recommend reassessing criteria for diagnosing and treating HF in our institution.

Table 1

	NYHA 0 (n=2)	NYHA I (n=139)	NYHA II (n=1128)	NYHA III (n=718)	NYHA IV (n=96)	NYHA N/A (n=99)	Total n=2182 (100%)
BB	1	106	1013	657	88	82	1947 (89%)
ACEi/ARB	0	88	889	558	53	73	1661 (76%)
MRA	0	4	167	250	58	31	510 (23%)
D	0	15	413	569	94	58	1149 (52%)
Digoxin	0	6	86	176	55	15	338 (15%)
All drug-groups	0	0	16	52	21	4	93 (4%)
No studied drugs	1	13	18	6	0	4	42 (1.9%)

NYHA classes reported and treatment recommendations according to NYHA class.

**P1472**

**Do we use beta-blockers in elderly patients with heart failure and reduced ejection fraction as we should?**

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**Background:** Several reports have demonstrated the benefits of using beta-blockers (BB) when treating elderly patients with heart failure and reduced ejection fraction (HF-REF).

**Purpose:** In this study we aim to address the use of BB in an elderly population of our area with HF-REF.

**Methods:** We studied patients aged ≥75 years with a left ventricular ejection fraction ≤35% referred to our echocardiography laboratory between January 2008 and December 2013.

The following information was recorded: mortality, cardiac events (defined as cardiac death or hospitalization due to heart failure) and medication use by the patient by the end of the follow up.

Our study also analysed those cases in which the heart failure treatment was not optimized according to the latest Guidelines in order to identify the reasons that could explain this situation.

The follow up consisted of a monitoring of the patient's electronic medical history, as well as a telephone interview when needed.

**Results:** 802 patients were included, 33,8% females. The median age of the group was 82 ± 4,9 years, and the median LVEF was 28 ± 6,5% at the moment of the inclusion.

The aetiology of the ventricular dysfunction was ischaemic in the 51,1% of the cases. With a median follow up of 32,7 ± 22,6 months, 496 (61,8%) cardiac events and 381 (47,5%) deaths took place.

71,7% of the patients were treated with BB. Multivariate survival analysis using the Cox regression model, showed that use of BB was associated with statistically significant lower total mortality rate (OR: 0,53; 0,39-0,71) and with less number of cardiac events (OR: 0,70; 0,54-0,90).

When analysing the reasons to avoid starting BB or to stop using them, the main cause we found was the presence of chronic lung disease (31,4%), followed by bradyarrhythmia (10,5%), asthenia (4,5%) and deterioration of HF. However, up to 30% of the patients that were not on BB did not present any formal contraindication for their use.

**Conclusion:** The use of BB in elderly patients with HF-REF was associated with a better prognosis. Nevertheless, we found a significant number of patients in which BB are not used as a therapeutic option even when there was no contraindications for their use. Awareness among professionals about the benefits of using BB in this kind of patients is needed in order to promote their use when possible.

**P1473**

**Gender specific clinical indicators of congestive heart failure in the middle east: Data from a single centre heart failure registry**

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**Background/Introduction:** Clinical outcome measures are the mainstay of cardiology trials. Congestive heart failure (CHF) measures have traditionally focused on average length of stay (LOS) and rehospitalisation and mortality rates.

**Purpose:** We aimed to identify the significant factors of gender variability of CHF patients with a reduced ejection fraction (HFrEF).

**Methods:** We performed gender comparison of statistically relevant variables using prospectively collected data of HFrEF patients hospitalised over a 12-month period.

**Results:** Of 174 consecutive patients, 135 (78%) were males and 39 (22%) were females. Compared to males, females had a statistically significant older age (64 vs. 58; P < 0.001), higher ejection fraction (EF) (28% vs. 23%; P = 0.023) and no history of active smoking (0% vs. 16%; P = 0.005) and less use of beta blockers (76% vs. 93%; P = 0.006), digitalis (2% vs. 12%; P = 0.009) and mineralocorticoid receptor antagonist drugs (35% vs. 55%; P = 0.025). After one year, both males and females had similar all-cause and heart failure hospitalisation and re-hospitalisation rates. Females showed no differences in in-house mortality, combined in-house mortality/30-day re-hospitalisation rates and composite myocardial infarction/stroke rates, compared to males. Males were more likely to require defibrillator device implantation (34% vs. 12%; P = 0.008)

**Conclusion:** Our findings showed that female HFrEF patients had similar LOS; in-house mortality, hospitalisation and rehospitalisation rates; less utilisation for implantable devices.

**Gender specific characteristics**

Baseline characteristics	Males (n = 135), mean, (SD)	Females (n = 39), mean, (SD)	P-value	95% CI for difference
Age	58 (13.5)	54 (9)	< 0.001	(-10.4, -3.03)
EF	23 (9.2)	28.2 (12.8)	0.02	(-9.61, -0.75)
Smoking	16%	0%	0.01	(0.09, 0.21)
Beta blockers upon discharge	93%	76%	0.01	(0.025, 0.30)
MRAs upon discharge	55%	35%	0.03	(0.024, 0.36)
Digitalis upon discharge	12%	2%	0.01	(0.02, 0.17)
Warfarin upon discharge	25%	10%	0.02	(0.02, 0.26)
CVA or TIA rate	21%	5%	< 0.001	(0.06, 0.26)
Annual Device implantation rate	34%	12%	0.01	(0.08, 0.35)

CVA, cerebrovascular accident; TIA, transient ischemic attack; MRAs, mineralocorticoid receptor antagonist drugs

## P1474

### Characteristics and co-morbidities of older UK heart failure patients treated with ivabradine: baseline data from the multi-centre live: life prospective cohort study

The Live Life study is funded by Servier Laboratories Ltd (UK).

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**Background:** The effects of ivabradine on cardiovascular mortality, hospitalisation and quality of life (QoL) in chronic heart failure (CHF) patients with left ventricular systolic dysfunction (LVSD) have been described (SHIFT mean age 60 ± 11yrs). Characteristics of older patients being initiated on ivabradine and its effects are limited.

**Purpose:** LIVE:LIFE is a UK Phase IV, multi-centre, open-label, prospective observational cohort study assessing QoL in patients aged ≥70 yrs over 6 months following clinically indicated initiation of ivabradine for CHF (NYHA II-IV, LVSD and sinus rhythm heart rate > 75 bpm). We describe the baseline characteristics of patients recruited.

**Methods:** Consenting patients in whom Ivabradine was initiated for clinical reasons were enrolled. Demographic, clinical, QoL (SF12, Minnesota Living with Heart Failure Questionnaire, MLWHFQ) & 6-minute walk test (6MWT) data were collected at baseline, 2 and 6 months.

**Results:** Between 17 December 2013 and 31 March 2015, 241 patients were recruited from 44 UK centres. 42% were female and 28% aged ≥80 yrs (mean 76 ± 6 yrs). Ischaemia was the commonest aetiology (63%) and 57% had been diagnosed for <2 yrs. Mean heart rate was 83 ± 10bpm, systolic blood pressure 124 ± 22mmHg, 52% were NYHA class III and 53% had severe LVSD. 54% received beta-blockers (39% intolerant) with a bisoprolol equivalent dose 4.0 ± 3.2 mg. Starting dose of ivabradine was 2.5mg bid in 56% of patients (44% 5mg bid). Baseline QoL: MLWHFQ total score 43 ± 24, physical 24 ± 12, emotional dimension 10 ± 8; SF-12 scores- Physical Component Summary: 35.73, Mental Component Summary: 45.15; 6MWT(n = 102) 253 ± 172m.

**Conclusions:** These contemporary observational data highlight the burden of complexity of comorbidities suffered by typical elderly patients initiated on ivabradine. Just over 50% patients are on beta-blockers, but use of ACEi/ARB is high. Polypharmacy is common and patients have impaired QoL and exercise capacity. Further data will help define the tolerability and impact of ivabradine on this real life population.

#### Comorbidities and medication

Comorbidity	N (%)	Medication	N (%)
Hypertension	144 (60)	Beta Blocker	131 (54)
MI, angina, CABG/PCI	125 (52)	ACEi / ARB	193 (80)
Asthma / COPD	105 (44)	Mineralocorticoid receptor antagonist	74 (31)
Smoking (current / ex)	166 (69)	Loop diuretic	193 (80)
Diabetes	80 (33)	Number of daily medications- mean(SD)	8.9 (3.3)
Stroke / TIA	40 (17)	Mobility issues	57 (23)
Cancer active/in remission	34 (14)		

## P1475

### Identifying barriers to a nurse-led heart failure team

British Heart Foundation

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**Background:** Heart failure (HF) is a chronic condition that has adverse effects for the sufferer in terms of mortality, morbidity and quality of life. A substantial body of evidence exists to support the treatment of HF in left ventricular systolic dysfunction (LVSD). Registry studies show that HF patients are more likely to be given such treatment if under the care of specialists i.e. cardiologists and HF specialist nurses.

**Purpose:** Our hospital has employed a predominantly nurse-led HF team since 2008. However, not all patients get referred to the team. This study set out to understand referral practices, to identify barriers and facilitate better access by all HF patients to specialist HF services.

**Methods:** The study used a mixed methods approach. Quantitative methods involved database interrogation, development, piloting and distribution of a HF referral questionnaire. All consultant physicians, cardiologists and their registrars, responsible for patients with a primary diagnosis of HF from 2012-2013

were identified and sent the questionnaire. Semi-structured interviews were conducted on a theoretical sample of the participants; qualitative analysis using grounded theory methods was undertaken to gain a better understanding of the results.

**Results:** The questionnaire identified answers from 13 physicians and 15 cardiologists (40% response). Analysis of the questionnaires revealed that 4 clinicians referred all HF patients to the specialist MDT. Cardiologists referred for education and follow up and did refer complex patients. Six physicians referred complex patients. Geriatricians felt that patients with frailty and multiple co-morbidities could not be managed by disease specific teams. Other reasons given for non-referral were: HF is easily managed without specialist input, HF nurses do not add anything to hospital management, confident in own management of HF; do not understand referral criteria, role or objectives of the team.

**Conclusion:** The study provided valuable information about the referral practices of clinicians responsible for the care of HF patients admitted to a large UK hospital. The main barrier to referrals to the inpatient HF team was lack of understanding of the roles, aims and objectives of the team, patient age and complexity.

## P1476

### Haemodynamic determinants of the biological variation of NT-proBNP in patients with stable chronic heart failure

This work was supported by non-restricted grant of Roche diagnostics International AG, Switzerland

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**Background:** Biological variation of amino-terminal probrain natriuretic peptide (NT-proBNP) in chronic heart failure (CHF) may affect blood levels and risk stratification. The sources of NT-proBNP variation are largely unknown.

**Methods and Results:** We performed NT-proBNP measurements, clinical and haemodynamic assessment in 50 patients with CHF who met criteria for clinical stability at 2 time intervals (1-week and 2-weeks). Haemodynamic variables were measured using inert gas rebreathing and impedance cardiography. Stability of heart rhythm was continuously monitored with external ECG event recorders throughout the complete study. Determinants of NT-proBNP-levels, and both absolute ( $\Delta$ NT-proBNPabs.) and relative changes ( $\Delta$ NT-proBNP%) were identified using univariable and stepwise multivariable linear regression analyses, respectively.

Clinical and haemodynamic variables did not change significantly between study visits. Independent predictors of NT-proBNP levels were diastolic blood pressure (DBP) ( $\beta=33.23$ , SE=8.55, P=0.0002) and estimated glomerular filtration rate ( $\beta=-21.19$ , SE=3.52, P<0.0001). While  $\Delta$ NT-proBNPabs. depended from change in left cardiac work index ( $\Delta$ LCWlabs.;  $\beta=154.09$ , SE=54.47, P=0.0077),  $\Delta$ NT-proBNP% was determined by relative changes of thoracic fluid content index ( $\Delta$ TFCI%;  $\beta=1.75$ , SE=0.62, P=0.008) and DBP ( $\Delta$ DBP%;  $\beta=1.41$ , SE=0.54, P=0.013). Overall, the forced common model including all hemodynamic and clinical variables determined 19% of absolute and 32% of relative variation of NT-proBNP.

**Conclusions:** Changes of LCWI, DBP, and TFCI are determinants of the biological variation of NT-proBNP. However, they account for only 20-30% of NT-proBNP variation

## P1477

### Use of common treatment regimens advocated by ESC guidelines for patients with chronic heart failure in Germany: a retrospective study of the Health Risk Institute healthcare claims database

This research was funded by Novartis Pharma AG, Basel, Switzerland

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**Background:** ESC guidelines provide recommendations for the treatment of patients with chronic heart failure (CHF) with reduced ejection fraction; similar medications may be given to those with preserved ejection fraction. Few data are available, however, regarding use of the recommended medications in German clinical practice. A retrospective study of anonymized healthcare claims data from the Health Risk Institute database was therefore conducted.

**Purpose:** The objectives were to investigate how patients with CHF are treated in Germany, and to describe patient characteristics and outcomes according to whether or not they received treatment regimens advocated by ESC CHF guidelines effective in 2011.

**Methods:** Data from patients with at least two recorded CHF-related diagnoses based on ICD-10 German Modification codes for CHF in a hospital or ambulatory setting in 2011 were analysed; about half of these patients were expected to have reduced ejection fraction. Use of guideline-compatible



treatment regimens was defined by the prescription of appropriate medication for the respective New York Heart Association (NYHA) classification, in two scenarios. Minimum requirements for the stricter regimen were: NYHA I, ACEI/ARB; NYHA II, ACEI/ARB +  $\beta$ -blocker + loop/thiazide diuretic; NYHA III–IV, ACEI/ARB +  $\beta$ -blocker + loop/thiazide diuretic + spironolactone/epplerenone. A second, less stringent regimen was defined as above except that it did not include spironolactone/epplerenone for NYHA III–IV.

**Results:** Of 123 925 patients identified, 25 863 (21%) had a specified NYHA classification. Only 45.1% (n = 11 669) of these individuals were treated according to the stricter regimen; 93.4% of patients with NYHA I and about half (55.7%) with NYHA II received such treatment. This fell to about one in five with NYHA III (20.6%) or NYHA IV (18.4%). The proportion of individuals treated in line with the stricter regimen declined with increasing age, falling from 53.4% of patients aged 55–59 years to 28.3% of those aged over 90 years, and was slightly higher in men (47.9%) than in women (42.2%). Similar proportions of patients were hospitalized whether treated according to the stricter regimen or not (62.7% and 65.3%, respectively). Mortality was lower among those treated according to the stricter regimen versus those who were not (6.7% vs. 16.2%). Compared with the stricter regimen, a greater proportion of patients received treatment with the less stringent regimen (45.1% vs 65.0%, respectively), especially those with NYHA III (66.5%) or NYHA IV (62.4%).

**Conclusions:** Use of treatment regimens advocated by ESC CHF guidelines may be further increased in German clinical practice, particularly when treating older patients and those with advanced disease.

#### P1478

##### Management of patients with chronic systolic heart failure at heart failure outpatient clinic improves survival after CRT and/or ICD implantation

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**Backgrounds:** Despite novel medical and device treatment of patients with chronic systolic heart failure (HFrEF), mortality still remains high.

**Aim:** The aim of the study was to investigate the effect of management at heart failure outpatient clinic on mortality among HFrEF patients after device (CRT and/or ICD) implantation.

**Patients and methods:** We followed 195 HFrEF patients (150 male, mean age: 65.3 ± 10.6 years, NYHA: 2.4 ± 0.8, EF: 27.1 ± 6.8%, ischaemic etiology: 57.4%) who received ICD (33.3%) CRT-P (14.9%) or CRT-D (51.8%) according to current guidelines, between 2010 and 2014. Every patient received optimal medical therapy and was followed at our electrophysiology clinic. The possibility of management at our heart failure outpatient clinic was offered for every patient, 116 of them accepted it. We compared the mortality of patients who participated at heart failure management and who did not, using Kaplan Meier method and log-rank test. The impact of heart failure management was evaluated with Cox regression.

**Results:** During follow-up period (mean: 41.7 ± 19.8 months) 72 patients died. Survival of patients who managed at heart failure outpatient clinic proved to be better significantly than who did not. (HR:0.493 CI:0.310–0.784 p=0.003) The survival benefit remained statistically significant (HR:0.409 CI:0.238–0.703 p=0.001), after adjustment with relevant baseline parameters (age, diabetes, ischaemic/non-ischaemic etiology, type of implanted device, LVEF, LVEDD, difference in ACEi and BB use and dosage).

**Conclusion:** Heart failure patients with CRT-P, CRT-D or ICD have survival benefit from management at heart failure outpatient clinic besides controlling their devices by electrophysiologists.

#### P1479

##### Chronic heart failure management with cardiac resynchronisation therapy - an evaluation of current practice in a tertiary centre

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**Introduction:** Heart failure causes significant morbidity and mortality, besides being an important economical burden on healthcare provision. When lifestyle advice and medical treatment is not enough, further management with cardiac resynchronisation therapy (CRT) may be indicated.

**Aim:** The aim of this study was to investigate the current management of Maltese heart failure patients who require CRT, in order to optimise service provision and ultimately long term patient care.

**Methods:** A retrospective cohort study was carried out. Data was collected from the clinical notes of 100 patients who had a CRT device system implanted in the local general hospital until 2012. Demographic data, together with indications for CRT, device used and technique of implantation, complications, patient symptomatology and re-admissions with heart failure after implantation, and mortality data was collected. Pearson Chi2 and 2-sample t-test analysis was performed together with survival assessment.

**Results:** Descriptive analysis showed that there were more frequent implantation of devices in patients who had moderate to severe heart failure symptoms, prolonged QRS duration >130ms and an EF < 35%, despite optimal medical therapy. This was consistent with current recommendations. Analysis with Pearson Chi2 testing did not show statistical significance when the patients who were readmitted to hospital were analysed also for mortality (p 0.266). 2-sample t-test analysis of variables recorded for readmissions with heart failure and mortality showed that out of all the comorbidities investigated, there was a correlation with impaired renal function (p < 0.001).

**Conclusion:** In most cases, current recommendations for CRT in Malta are being followed. The current pre-assessment clinic will undoubtedly re-enforce adequate patient selection for the device with extra care towards renal patients, and introduction of a specific follow-up device clinic is recommended to optimise the care of chronic heart failure patients.

Comorbidity	P-value Morbidity (Readmissions)	P-value Mortality
Diabetes mellitus	0.266	0.483
Ischaemic Heart Disease	0.192	0.203
Hypertension	0.416	0.096
Atrial Fibrillation	0.084	0.137
Renal Impairment	0.008	< 0.001
Cardiomyopathy	0.336	0.157
Alcoholic	0.942	0.627

#### P1480

##### View on in-hospital heart rate control in patients with heart failure with reduced ejection fraction in Russian Federation.

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**Purpose:** The aim of this study is to analyse the frequency of use of ivabradine and digoxin in patients with systolic HF in Russian hospital clinical practice (from the Russian hoSpital Heart Failure Registry (RUS-HFR)).

**Methods and Results:** The RUS-HFR is a prospective, multicentre, observational study conducted in 3 Cardiac centers (No.1-St.Petersburg, No.2-Samara, No.3-Orenburg). Inclusion criteria: HF NYHA I-IV, LVEF ≤ 40%, age 18–75 yrs. From Oct 2012 to Jan 2014, 524 patients were enrolled. Age 60.0 ± 9.6 yrs; 80.5% men; most patients with HF III NYHA. Mean LVEF was 28.8%. AF was present in 43.2/46.2/47.4% and eGFR < 60 mL/min/1.73 m<sup>2</sup> in 26.6/43.1/41.5% of the patients, respectively. The use of RAS blockers,  $\beta$ -AB, MRAs and diuretics at hospital discharge was comparable with European registers and did not differ between the centers. Only 4.6/0.8/0.7% and 6.6/1.5/3.7% patients were receiving ivabradine prior to admission and much more at discharge, respectively. Digoxin prior to admission was taken in 9.7/12.3/5.2% cases, including 1.9/2.3/0.17% of patients in sinus rhythm. 4.6/33.1/51.9% of patients were on digoxin at hospital discharge, including 0/13.1/17.0% of patients in sinus rhythm. Only in the center No.1 has been observed reduction in the frequency of digoxin use and the absence of this drug in patients in sinus rhythm at discharge. Check of digoxin blood levels in centers was not performed.

**Conclusion:** There was a problem of adequate rate control in patients with CHF, especially in the period of decompensation. The RUS-HFR showed that ivabradine for heart rate control in HF patients with reduced ejection fraction in Russia was not as widely used as recommended. The prescription of digoxin, mostly in atrial fibrillation, remained high and increased in some centers multiplies in times during the period from admission to discharge and decreased only in specialized heart failure center. There is a heterogeneous approach in the application of digoxin, especially in sinus rhythm, among the Russian cardiological centers.

#### P1481

##### Optimising heart failure management: peritoneal dialysis for selective advanced heart failure patients has shown reduction in hospital readmissions and decrease in annual health care cost.

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**Background/Introduction:** Heart failure (HF) is a complex chronic syndrome with significant morbidity and mortality. Success with HF is improving patient's quality

of life (QOL) by (a) controlling their symptoms and (b) avoiding hospitalizations. Healthcare practitioners are required to heighten their awareness to improve the quality care of advanced stage HF and close the gap between practice and clinical outcomes. Peritoneal dialysis (PD) has been proposed as a therapeutic alternative for patients with refractory HF and has resulted in effective HF management by reducing hospital readmissions and reducing annual healthcare costs.

**Purpose:** To determine if PD is a therapeutic option for patients with refractory HF by assessing for clinical outcomes such as hospitalizations and mortality. An examination of cost-benefit ratio of PD treatment versus traditional HF therapy will be analyzed to determine a reduction in annual health care costs while improving QOL for HF patients.

**Methods:** A retrospective chart review was conducted at a cardiac center on advanced HF clinic patients (NYHA class III/IV) not responding to conventional HF therapy. All patients had a minimum of two emergency room (ER) visits or hospitalization for HF within a year prior to PD therapy. A comparison of this patient population 18 months prior to PD and 18 months post PD was analyzed to determine if PD was an effective approach to improve HF management, reduce hospital readmissions, and annual healthcare costs.

**Results:** The advanced HF patients (n = 15) had NYHA Class 3-4 symptoms with renal dysfunction (average GFR 25mls/min). The average age was 74.5 years old with 53% having non-ischemic cardiomyopathy. Many patients had three co-morbidities (n = 12: 80%). The overall mortality according to the Kaplan-Meier survival curve revealed a life expectancy of 86%, 68% and 39% after 12, 18 and 24 months of PD therapy respectively. Prior to receiving PD, these 15 patients had 98 urgent cardiac clinic visits, 27 ER visits, 14 hospitalizations (Length of stay (LOS) = 278 days), 200 cardiac clinic telephone calls and 20 renal clinic visits. During PD therapy there were significant reductions in hospitalizations, ER visits, telephone and clinic visits. This resulted in 1 ER visit, 1 hospitalization (LOS = 14 days), 4 clinic telephone calls, 21 routine cardiac clinic visits and 48 routine PD renal clinic visits. There were no documented peritonitis cases. The economic analysis indicated a cost-benefit ratio of 2.32 revealing a financial savings to the health care system.

**Conclusions:** Despite a small sample size, these results demonstrated that PD may be an effective means of improving HF management by reducing readmission and hospital resources. QOL gains have not been considered in the analysis but should be considered as a part of a more complete economic analysis. Further research should also focus on improve identification for patients to benefit from palliative PD therapy.

#### P1482

##### MultiSENSE patient diary use versus HF decompensation

Boston Scientific

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**Background:** Standard management of heart failure (HF) involves teaching patients to adhere to medical therapy, monitor weights and symptoms to detect early HF, and then to take action once early HF is detected. In a clinical trial that included recording weight, medications and symptoms in a diary, we hypothesized that greater diary use would be associated with fewer worsening HF events (WHE).

**Methods:** The Multisensor Chronic Evaluations in Ambulatory Heart Failure (Multi-SENSE) study is a prospective, observational study where patients' CRT-D devices were converted to devices capable continuous ambulatory measurements of trans-thoracic impedances, heart sounds, body acceleration and respiration values in addition to existing CRT-D measurements. Patients were asked to complete a diary to record daily weights and medication changes and weekly self-assessment of symptoms. WHE were collected and were adjudicated by a panel of clinicians. Data from 500 patients were characterized by how frequently they completed diary responses as either never answered (Never), answered <50% of the time (<50), or answered ≥50% of the time (≥50) in each of weights, medications changes or symptoms. A WHE event rate (WHE rate) for each patient was the number of adjudicated WHE divided by the patient's duration in study. The WHE rates were compared among groups for weight, medication change, and symptom responses.

**Results:** For each characterization group, Table 1 shows number of patients (N Pts) and the average WHE rate (WHEavg) for weight, medication and symptom diary use. p values are Wilcoxon test for differences among the three groups. Note, only whether a patient responded is considered and not the actual response value.

**Conclusion:** Patients that consistently answered the weight (p = 0.02) and symptom (p = 0.0003) questions in the diary had fewer WHE than those that did not. However, consistently recording medications (p = 0.29) was not associated with fewer WHE. It may be that patients that actively pay attention to their weights and especially symptoms do not decompensate as frequently.

Table 1 WHE rate versus responses

Group	Weights		Medications		Symptoms	
	N Pts	WHEavg	N Pts	WHEavg	N Pts	WHEavg
Never	44	0.52	100	0.38	84	0.60
<50	146	0.34	170	0.26	170	0.21
≥50	310	0.22	230	0.25	246	0.22
P		0.023		0.290		0.0003

The patients are grouped by % responses (never, <50 and ≥ 50) for the three diary components. Average WHE rates are compared (p is Wilcoxon difference among groups).

#### P1483

##### How the elderly patients with chronic heart failure are treated in clinical practice? - the analysis of DATA-HELP registry.

Merck Serono.

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**Background:** Systolic heart failure (HF) represents a cardio-geriatric syndrome. Advanced age is a known risk factor for HF development and poor outcome in HF. Importantly, the implementation of the ESC guidelines in the elderly patients may be challenging in the everyday clinical practice.

**Purpose:** The aim of our study was to assess an implementation of the ESC guidelines regarding the management of systolic HF across different age groups.

**Methods:** We analyzed 5289 outpatients (mean age: 67 ± 11, 63% of men) from the DATA-HELP registry, that comprises a contemporary, representative group of patients with stable, systolic HF treated in Poland.

**Results:** There was the following age distribution in examined patients: <50 (5%), 50-64 (37%), 65-79 (43%), ≥80 years (14%). Management across age-groups is presented in the Table.

**Conclusions:** Elderly patients represent big population of patients with systolic HF. Disease-modifying evidence-based therapies are less frequently applied in target doses in the elderly, whereas symptomatic treatments usually is used more often than in other age groups.

Applied treatment in studied groups:

	WOMENMEN							
	<50	50-64	65-79	≥80	<50	50-64	65-79	≥80
Age group (years old)								
Number of patients, n (%)	64 (3)	586 (29)	930 (46)	396 (20)	224 (6)	1404 (41)	1403 (41)	382 (11)
Patients received a target dose of ACEI/ ARB (%)	26	38	30	21***	28	33	32	20***
Patients received a target dose of beta-adrenolitics (%)	13	15	9	8***	24	16	10	7***
Patients received target dose of MRA (%)	13	18	18	17	18	18	20	17
Loop diuretics- yes (%)	41	56	61	73***	61	58	67	70***
Digoxin- yes (%)	14	16	25	29***	21	18	20	22
CRT- yes (%)	3	4	1	1**	7	4	4	2*
ICD- yes (%)	6	5	4	3	18	10	9	5

\*P < 0.05 \*\*P < 0.01 \*\*\*P < 0.0001; ACEI- angiotensin-converting-enzyme inhibitor; ARB- angiotensin receptor blocker; MRA- mineralocorticoid receptor antagonist; CRT- cardiac resynchronization therapy; ICD- implantable cardiac defibrillator.

**P1484**

**Icelandic heart failure patients at time of economic crisis: patient reported outcomes**

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**Introduction:** Since 2008 the economic crisis has hit many European countries hard. There are indications that economic crises directly affect the health of the public. In general, patients with chronic diseases such as heart failure (HF) use a high proportion of healthcare and it might therefore be expected that they suffer most from economic hardship, potentially leading to decline in health status.

**Purpose:** To describe the characteristics, health status, social and economic status of patients who attend a HF outpatient clinic and assess if there is a relationship between health status and economic factors.

**Methods:** In this cross sectional study data was collected with mailed questionnaires and from electronic patient journals in 2014. Patient reported outcomes were measured with nine previously validated and structured instruments on self-care (European Heart Failure Self-care Scale-EHFScB), heart-failure related knowledge (Dutch Heart Failure Knowledge Scale-DHFKS), symptoms (Edmonton Symptom Assessment System-ESAS), anxiety and depression (Hospital Anxiety and Depression Scale-HAD-S), sense of security (Sense of Security in Care-SEC-P) and health related quality of life (The health related quality of life aspects-EQ5D and Kansas City Cardiomyopathy Questionnaire-KCCQ). In addition patients answered questions regarding, background, access, the use and cost of healthcare. Clinical data was extracted from electronic patient records.

**Results:** 124 participated, mean age was 73 (± 14.9) and 69% were males. Most were either in New York Heart Association functional class II (37%) or III (55%). Cost of healthcare had changed for 71% since 2008. Patients reported a mean prevalence of 4.8 (± 2.56) symptoms. Most common was tiredness (82%), shortness of breath (77%) and drowsiness (76%). The mean score of self-care on the EHFScB scale was 29.7 (± 7.9) and HF knowledge was high 11.6 (± 3.07). Patients rated their overall health on average 65 (± 22.8) with the EQ-5D visual analogue scale. The overall summary score and the clinical summary score of KCCQ was 61.3 (± 23.4) and 63.17 (± 23.8) respectively. No difference was found in patient-reported outcomes between those who had and had not experienced changes in their out-of-pocket costs since 2009.

**Conclusions:** Health status of Icelandic HF patients is similar to other European countries and patients managed their disease well during and after a time of economic crisis. The result give valuable information on directions to take in the development of outpatient services for heart failure patients.

**P1485**

**Ranolazine reduces symptoms and arrhythmia in patients with ischaemic left ventricular dysfunction**

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**Background:** Ranolazine decreases the frequency of arrhythmias during the acute phases of ischemic heart disease (IHD), but it remains unknown if it has similar effects in the chronic phase of the disease. We performed a prospective, randomized, cross-over pilot trial to test the hypothesis that chronic treatment with ranolazine can reduce the incidence of documented arrhythmias and the related symptoms of palpitation in stable patients with IHD and left ventricular dysfunction.

**Methods:** We randomized 105 patients with stable IHD, LV function <40% and symptoms of angina and palpitations already on therapy with beta-blockers and/or calcium antagonists to ranolazine (750 mg bid, n = 53) or placebo (n = 52) for 30 days (until T-1). After a wash-out period to avoid any carryover effect, cross-over was performed, and patients were switched to the other drug which was continued for 30 days (until T-2). All patients underwent symptom-limited exercise stress testing and 48-hour ECG Holter monitoring at T1 and T2. During the study period, patients were told to use a OmronN<sup>®</sup> portable ECG monitor HCG-801 device in case of symptoms of palpitations.

**Results:** Ranolazine reduced the number of anginal episodes more commonly than placebo (5 ± 8 episodes/30 days vs. 21 ± 24 episodes/30 day, p = 0.001) and increased exercise durations at 1 mm ST-segment depression (514 ± 211 s vs. 402 ± 287 s, p = 0.025) and at onset of angina (614 ± 199 s vs. 519 ± 151 s, p = 0.007) at stress testing. These effects were coupled by significant decreases with ranolazine as compared with placebo treatment periods in the occurrence of frequent (> 1,000 beats) supraventricular arrhythmias (33% vs 52%, p = 0.01) and complex ventricular arrhythmias (17% vs 30%, p = 0.045). Complete resolution of symptoms of palpitations was significantly more common with ranolazine than placebo (31/53 vs 16/52 patients, p = 0.008). Also, portable ECG recordings

showed that arrhythmias were less common during ranolazine vs. placebo, with significant decreases in number (7 ± 10 episodes/30 days vs. 23 ± 29 episodes/30 day, p = 0.001) and duration (10 ± 18 min/30 days vs. 19 ± 21 min/30 day, p = 0.021) of symptomatic arrhythmic episodes. No severe side effects were recorded during the trial period.

**Conclusion:** The antianginal and antiischemic properties of ranolazine are paralleled by significant decreases in the occurrence of both arrhythmias and the related symptoms of palpitations in stable patients with IHD and left ventricular dysfunction.

**P1486**

**Dosing of heart failure treatments in newly diagnosed unselected patients in sweden: compliance with european society of cardiology guidelines**

This research was funded by Novartis Pharma AG, Basel, Switzerland G Wikstrom<sup>1</sup>; K Boman<sup>2</sup>; M Olofsson<sup>2</sup>; K Lindmark<sup>3</sup>; R Lahoz<sup>4</sup>; S Corda<sup>4</sup>; V Wintzell<sup>5</sup>; R Linder<sup>6</sup>; A Gondos<sup>6</sup>; J Stalhammar<sup>7</sup>

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**Background:** A clear understanding of dosing patterns of heart failure (HF) treatments in newly diagnosed patients will allow healthcare professionals to evaluate the implementation of ESC guidelines (Eur Heart J 2012) in the real world.

**Purpose:** To compare treatment dosing patterns of patients newly diagnosed with HF (reduced ejection fraction, HF-rEF; left ventricular EF ≤ 50%) with ESC guidelines.

**Methods:** Patients in Sweden, were identified via primary and secondary care electronic medical records. Patients aged ≥ 18 years with a first HF diagnosis from 1 Jan 2010 to 31 Mar 2015 were included. A 9-year look-back period was applied per patient to exclude prevalent cases. Data from patients with confirmed HF-rEF were analysed. A patient's maintenance HF treatment was identified from the Swedish Prescribed Drug Register. Maintenance treatment was assumed to start within 90 days after treatment initiation. A prescribed maintenance treatment dose was defined as the median prescribed maintenance dose by patient and treatment and was estimated based on the assumption that the duration of each dispensation during maintenance was 90 days.

**Results:** Of 8777 records, 728 patients with HF-rEF were identified (33.1% women; mean [SD] age: 70.8 [14.9] years; mean [SD] body mass index: 26.7 [5.4] kg/m<sup>2</sup>; mean [SD] Charlson comorbidity index: 1.9 [2.3]). Of the treatments analysed (Table 1), only 1.4% of patients prescribed losartan but 96.8% of those prescribed spironolactone received the recommended dose.

**Conclusions:** The proportion of patients with HF-rEF achieving ESC-recommended doses for HF treatments varied greatly. Various factors may influence this, such as patient-specific factors, dosing regimen, individual treatment goals and structural reasons in the healthcare system. Evaluation of such factors is needed to ensure that patients receive appropriate doses.

	n(%) receiving ≥50%	n(%) receiving ≥100%
enalapril (n = 321)	214(66.7)	135(42.1)
ramipril (n = 102)	73(71.6)	45(44.1)
losartan (n = 142)	48(33.8)	2(1.4)
bisoprolol (n = 299)	180(60.2)	74(24.7)
carvedilol (n = 24)	17(70.8)	7(29.2)
metoprolol succinate (n = 281)	132(47.0)	33(11.7)
candesartan (n = 95)	55(57.9)	27(28.4)
eplerenone (n = 34)	32(94.1)	9(26.5)
spironolactone (n = 401)	397(99.0)	388(96.8)

**P1487**

**High-preciseness ECG in patients after heart transplantation**

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The purpose of research was assessment of parameters of high-precision ECG in patients after heart transplantation and a comparison with this values of control group.

**Material and methods:** The study included 40 healthy subjects (aged 44.2 ± 15.6) and 39 patients after orthotopic heart transplantation (aged 42.8 ± 11.9); follow-up



28,6 ± 9,43 months after allograft transplantation. Parameters of microvolt T-wave alternation (mTWA), heart rate turbulence (HRT), the intervals QT et JT dispersion and acceleration/deceleration (DC/AC) indexes of heart rate were analyzed. All patients were examined by echocardiography, Holter monitoring ECG and 7-min high-definition ECG (Intecard-7). ECG parameters of patients who had transplanted heart (TH) with no signs of rejection of allograft were compared with the control group (CG) of the healthy subjects.

**Results:** ECG data of TH pts showed an increase mTWA ( $p < 0,005$ ) and significant ( $p < 0,05$ ) decrease of indexes deceleration (DC 2.0 { 1,0; 4,5} {6,5 vs 10,2; 17,5} ms) and acceleration heart rate (AC {2,0 1,3; 6,5} {6,7 vs 10,2; 17,7 } ms) despite signs of reinnervation TH according to data of the heart rate variability (HRV). Thus, the HRV in the early period (1 to 3 months after TH) demonstrated a total denervation of transplanted heart: SDNN 44.5 ± 13.4ms, SDNNi 12.1 ± 6.55ms, rMSSD 18.6 ± 14.6ms, LF \ HF 0.16 ± 0.18; but after 28,6 ± 9,43 months follow-up HRV parameters (SDNN 64.5 ± 16.9 ms, SDNNi 32.6 ± 9.72 ms,  $p = 0,000$ ; rMSSD 27.8 ± 13.4 ms,  $p = 0,006$ ; LF \ HF 1.42 ± 0.52,  $p = 0,000$ ) were significantly improved showing signs of the emergence of physiological innervation still more dominance of sympathetic reinnervation above the parasympathetic autonomic regulation of rhythm. In the stepwise discriminant analysis were included all ECG parameters (TH and CG) with significant differences  $p < 0,05$ . As result of the analysis (data are demonstrated table below), significant differences in the comparison groups were revealed: test mTWA (% pathological mTWA:  $F = 6,3$ ;  $p = 0,015$  and the average values of mTWA:  $F = 22,9$ ;  $p = 0,00001$ ); JT dispersion (JTd:  $F = 6,4$ ;  $p = 0,014$ ).

**Conclusion:** The dominant sympathetic reinnervation characterized by sympathetic-vagal imbalance in TH pts also has evidence of myocardial electric instability is associated with markers of high-precision ECG: mTWA and JT dispersion.

#### Result of stepwise discriminant analysis

Parameters of high-precision ECG	Wilks' - Lambda	Partial - Lambda	F-remove (1,58)	p-level
Test of mTWA (mean parameter mTWA)	0,896319	0,717207	22,86923	0,000012
Test of mTWA (% percent of pathological mTWA)	0,712681	0,902013	6,30065	0,014881
Interval JT dispersion	0,713871	0,900509	6,40804	0,014093

#### P1488

##### Prevalence of cardiovascular risk factors in patients followed in a heart failure clinic

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**Background:** Heart failure (HF) is the end stage of several diseases. Its prevalence and incidence remain high, with high rates of morbidity and mortality. The importance of the cardiovascular risk factors (CVRF) in patients with heart failure is well established, and the monitoring of CVRF essential and part of the treatment, since its presence worsens the prognosis of these patients.

**Purpose:** To evaluate the prevalence of cardiovascular risk factors in patients followed in Heart Failure Clinic (HFC).

**Methods:** We included all patients in the HFC from a single center. Patients were admitted in the HFC with a previous diagnosis of HF for at least 6 months or prior hospitalization for acute HF. The CVRF assessed were: arterial hypertension (AHT), dyslipidemia, diabetes mellitus (DM), obesity, smoking and chronic kidney disease (CKD, defined as glomerular filtration rate  $\leq 60$  mL/min/1.73m<sup>2</sup>); the presence of cerebrovascular disease (CVD) and excessive alcohol consumption were also evaluated.

**Results:** Included 306 patients, 25.2% were female, with mean age of 60.99 years. 41.8% have ischemic etiology as the cause of HF. 33.7% have atrial fibrillation. 3.6% do not exhibit any of the evaluated CVRF. AHT is the most prevalent CVRF, being present in 61.1%, followed by dyslipidemia (52.3%), smoking (34.0%), DM (33.7%), CKD (33.3%), excessive alcohol consumption (33.0%), obesity (20.3%) and CVD (9.2%). 85.6% have at least two CVRF. 34.6% of patients simultaneously present the two most significant CVRF (AHT and dyslipidemia), and 78.9% have at least one of these CVRF.

**Conclusion:** The prevalence of CVRF is high in this population of patients followed in HFC, with AHT and dyslipidemia being the most prevalent.

#### P1489

##### Prognostic importance of atrial fibrillation in patients with heart failure

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**Background:** Heart failure (HF) keeps increasing prevalence and incidence, with high mortality rate. Atrial fibrillation (AF) is the most common cardiac arrhythmia in the general population, with an estimated prevalence between 1.5% to 2%, and a prevalence of about 30% in patients (pts) with HF.

**Purpose:** To evaluate the impact of permanent AF in the prognosis of pts with chronic HF and reduced ejection fraction.

**Methods:** Retrospective study where were included pts followed in a HF clinic (HFC) from a single center. The pts had reduced ejection fraction and were admitted in the HFC with a previous diagnosis of HF for at least 6 months or had prior hospitalization for acute HF. Pts with follow-up (FU) of less than 12 months were excluded. Pts were divided into 2 groups: with FA (G1) and without AF (G2). The groups were compared as to their clinical and echocardiographic characteristics and the occurrence of significant cardiac events - hospitalization for HF (hHF), hospitalization for acute coronary syndrome (hACS), cardiovascular mortality (CVM), non-cardiovascular mortality cause (nCVM). For statistical analysis we used the SPSS 22.0.

**Results:** Included 270 pts, mean age 61.2 ± 13.5 years. 74.1% were male. 41.9% had ischemic etiology and 64.4% severe depression of left ventricular systolic function. Average FU time was 35.9 ± 16 months. 91 (33.7%) integrated G1 and 179 (66.3%) G2. In univariate analysis, the pts in G1 were older ( $p < 0,001$ ) and had more chronic renal dysfunction (glomerular filtration rate  $\leq 60$  mL/min/1.73m<sup>2</sup>;  $p = 0,017$ ). In G2, there were more male pts ( $p = 0,026$ ) and a higher incidence of dyslipidemia ( $p = 0,04$ ). During the FU, the pts in G1 showed higher CVM ( $p < 0,001$ ) nCVM ( $p = 0,033$ ) and hHF ( $p < 0,001$ ); hACS showed no significant differences ( $p = 0,552$ ).

**Conclusion:** In this study in pts with HF, with the exception of ACS, the presence of AF was associated with a greater number of events.

#### P1490

##### Serum drug levels as a new diagnostic tool for non-adherence to therapy in chronic heart failure patients

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**Purpose:** The aim of the study is to assess the frequency of non-adherence to the recommended therapy in chronic heart failure patients and to evaluate its impact on the disease course

**Methods:** Stable chronic heart failure patients with established medication were enrolled to the study. They passed three study visits (enrollment (M1), month three (M3) and month nine (M9)) and two-year follow-up. Blood sampling was performed during study visits and serum levels of prescribed medications were used as an indicator of drug adherence. Serum drug levels were evaluated by liquid chromatography and mass spectrometry. The subjects were labeled as non-adherent when the serum level of at least one of the evaluated drugs was below the limit of quantification.

**Results:** Forty chronic heart failure patients (age 64.4 ± 11.4 years, 23men/17women, LV EF 30.6 ± 10.9%, NYHA class median 2) were prospectively enrolled. On the average 3.9 ± 1,1 (median 4) drugs per blood sample were measured.

All of the evaluated drugs were detected in the sera of 27patients (67.5%), the non-adherence was diagnosed in 13 patients (32.5%).

At the end of two-year follow-up next indicators were compared between adherent and non-adherent group: overall mortality (29.6%vs15.4%,  $p = 0,35$ ), heart failure mortality (22.2%vs15.4%,  $p = 0,63$ ), need for emergency visit/hospitalization due to worsening heart failure (1event 11.1%vs0%,  $p = 0,23$ ,  $\geq 2$  events 3.7%vs0%,  $p = 0,52$ ), gender (men 66.7%vs38.5%,  $p = 0,10$ ), NTpro-BNP (327.8 ± 482.2vs112.1 ± 128.7 pmol/l,  $p = 0,43$ ), LV EF (30.0 ± 10.9%vs31.9 ± 10.8%,  $p = 0,62$ ) and NYHA class (2.4 ± 0.6vs2.4 ± 0.6,  $p = 0,60$ ).

**Conclusions:** Our data suggest that the non-adherence to the recommended therapy may be present in significant part of chronic heart failure patients (32.5% in our study). We assume that the estimation of serum drug levels is an useful diagnostic tool in clinical evaluation in these patients. We did not found any difference between groups of adherent and non-adherent patients during two-year follow-up.

**Limitations:** The main limitation is the size of the study population

## P1491

**What diagnostic problems do we have among primary care of the heart disease patients.**

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**Background:** Slovakia with 5.5 millions of inhabitants belongs to the countries with the highest cardio-vascular mortality in Europe.

Aim of the study was to create the national registry of the heart failure patients from the primary care physicians, internal medicine and cardiologists of the 310 centers in the country.

**Patients and methods:** 7032 heart failure patients (3281 men-46.4% and 3751 women-53.3%) were followed up during one year (2014-2015). Demography ( $\pm$ SD): height:167.8 $\pm$ 8.8cm, weight:83.5 $\pm$ 15.7kg, waist: 98.3 $\pm$ 14.7cm, BMI:29.5 $\pm$ 5.4cm<sup>2</sup>, BPs:137.8 $\pm$ 17.0mmHg, BPD:81.5 $\pm$ 10.2mmHg in NYHA class II: 3819, III: 2260, I:696, IV:109pts. Ischaemic etiology was in 52.8%, hypertension 33.7%, cardiomyopathy 5.2, valvular disease in 4.2% of pts.

**Results:** Incremental trend between NYHA class and NT-proBNP levels ( $\pm$ SD ng/l) was seen: NYHA I:587.1 $\pm$ 1650.2, II:919.99 $\pm$ 1410.82, III:1658.71 $\pm$ 2250.16, IV:2729.84 $\pm$ 3309.73. ECG sinus rhythm was in 76.5% pts, non-sinus in 20%, pacemaker 4.2% and atrial fibrillation in 25.2%, AV blocks 5.8%, BBB in 21.4%, ischemia at rest in 64.2%. X-ray increased CTI was in 58.9% and lung congestion in 21.3% of the followed. Echocardiographic normal LVEF was in 23.5%, between 0.55-0.40 in 41.9%, 0.40 -0.30 in 19.4%,  $\leq$ 0.30 in 4.9% and correlated with the severity of the clinical status of pts. None of the followed pts had exercise test ever performed (even not 6min walking test). Despite heart failure diagnosis, 20% of them remained smokers and 13.4% took regular alcohol.

**Conclusion:** National registry creation of the heart failure patients may improve the follow-up, complex management and improvement of their prognosis.

## P1492

**The xanthine oxidase activity in patients with congestive heart failure**

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**Background:** Several data suggest the role of the xanthine oxidase metabolic pathway in the pathophysiology of congestive heart failure (CHF). Changes in xanthine metabolism in patients with concomitant chronic kidney disease (CKD) considered due to impaired renal excretion of uric acid and thus not associated with increased xanthine oxidase activity.

**Purpose:** The goal of our study was to determine the changes in the activity of xanthine oxidase in patients with congestive heart failure and concomitant chronic kidney disease.

**Methods:** 112 patients with congestive heart failure NYHA class II-III (51 men and 61 women; mean age 72.5 $\pm$ 8.6 years) were included in the study. 72 patients had concomitant CKD with glomerular filtration rate (GFR) <60 mL/min/1.73 m<sup>2</sup> (1st group) and 40 without concomitant CKD (2nd group).

Xanthine metabolism was studied by determining serum uric acid level and the xanthine oxidase activity. Xanthine oxidase activity was determined fluorometrically by using standard assay kit.

**Results:** Serum uric acid level was slightly increased in patients with CHF (7.47 $\pm$ 0.18 mg/dL) and 62.5% (70 of 112) patients had asymptomatic hyperuricemia (defined as serum uric acid level  $\geq$ 7.0 mg/dL). Mean xanthine oxidase activity was 6.46 $\pm$ 0.59 mU/mg in patients with CHF. Uric acid level and the xanthine oxidase activity were higher in patients with NYHA class III compare with NYHA class II (mean uric acid level 8.50 $\pm$ 0.39 mg/dL vs 6.88 $\pm$ 0.25mg/dL, respectively,  $p$  < 0.01; and mean xanthine oxidase activity 7.22 $\pm$ 1.20 mU/mg vs 5.96 $\pm$ 0.61 mU/mg, respectively,  $p$  > 0.05).

It was found insignificant increase of serum uric acid level in patients with concomitant CKD (in the 1st group 7.63 $\pm$ 0.27 mg/dL and the 2nd group 7.46 $\pm$ 0.39 mg/dL, respectively; =0.73). Xanthine oxidase activity was significantly higher in the 1st group as compared with the 2nd group (7.51 $\pm$ 0.77 vs 4.69 $\pm$ 0.77 mU/mg, respectively;  $p$  < 0.05). In a multiple regression model, significant relationship between the xanthine oxidase activity and decrease of GFR was found, independent of serum uric acid level, ejection fraction of left ventricular, NYHA class, age and sex ( $p$  < 0.05).

**Conclusions:** There is a strong relationship between the xanthine oxidase activity and decrease of GFR in patients with congestive heart failure and concomitant CKD. Some studies have shown that an elevation in the enzymatic activity of xanthine oxidase can lead to increases in oxidative stress, endothelial dysfunction, and reduced myocardial function in patients with congestive heart failure.

## P1493

**Impact of a treatment with L-arginine on clinical and hemodynamic parameters in CHF**

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**Objective:** To assess the effect of the combination of L-arginine with basic therapy (BT) on clinical and functional parameters of patients suffering from chronic heart failure (CHF) caused by dilated cardiomyopathy (DCM), and DCM with a primary lesion of right (DKMPpzh).

**Material and Methods:** The study included 52 patients. All studies were performed: physical examination on a scale SHOKS; biochemical blood tests; ECG; Echocardiography; Test 6-minute walk (TSHH) to measuring the length of distance traveled (DPD). All patients received BT and L-arginine (Tivortin, "Yuri Farm", Ukraine) as a 4.2% solution intravenously with 100 ml of 1 times per day (8-10dne) with subsequent transition to oral solution of 5- 10 ml 3 times a day for 4 weeks. Depending on the type of cardiomyopathy patients were divided into 2gruppy: 1g. - 22 patients with DKMPpzh; 2g. - 30 patients with dilated cardiomyopathy.

**Results:** The groups were comparable in age, but in 1g. dominated by females (77,3% vs 30%, respectively, in groups 1 and 2,  $p$  < 0,05). The heart rate in the analyzed groups did not differ significantly, but the numbers of blood pressure, both systolic and diastolic blood at baseline were higher in 1g. ( $p$  < 0,05). The therapy with L-arginine in combination with the BT changes in the heart rate has not been revealed, however, in both groups there was a slight increase in blood pressure and decrease heart failure functional class, with more pronounced in 1g. BT combination with L-arginine has also contributed to the improvement of the parameters of intracardiac hemodynamics in both groups of patients. In particular, 1g. observed a decrease in the size of the bulk of the right heart, with inotropic myocardial function was characterized by an increase in ejection fraction as the RV and LV. This, in turn, was followed by a decrease in the average level of pulmonary artery pressure (PASP) of 10.7% and a decrease in the number of individuals with the presence of tricuspid regurgitation. During 2g. combination therapy with L-arginine contributed to the increase in LVEF and the normalization of PASP values (all  $P$  < 0.05). It should be noted that the combined treatment with L-arginine in WT subjects us patients was not associated with any side effects and, therefore, did not require discontinuation.

**Conclusions:** CHF due to DCM with a primary lesion of the right ventricle, is more common among women and is characterized by relatively intact heart rate and blood pressure. Use of a 4-week course of L-arginine in the complex treatment of chronic heart failure, regardless of its topographical features, improves parameters of intracardiac hemodynamics and reduction of PASP.

## P1494

**FEW16 questionnaire as new instrument in patients with heart failure with preserved ejection fraction**

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**Introduction:** In heart failure, improvement of quality of life (QoL) is a major therapy goal. Physical well-being as important part of QoL has not yet been sufficiently covered by disease-specific instruments. A QoL questionnaire, FEW16 was developed for assessing the subjective physical wellbeing.

**Purpose:** The aim of this analysis was to validate the FEW16 questionnaire in heart failure patients with preserved ejection fraction (HFpEF) from the Exercise Training in Diastolic Heart Failure (Ex-DHF-P) trial.

**Methods:** Ex-DHF-P was a prospective, randomized, controlled study, with a goal to determine the effects of physical training on exercise capacity and QoL in patients with diastolic heart failure. 64 HFpEF patients (65 years, 56% female) were randomized to usual care with ( $n$  = 44) or without training ( $n$  = 20). At baseline and at 3 months, patients were clinically evaluated and QoL (SF36), physical wellbeing (FEW16) and depression (PHQ-D) were assessed.

**Results:** FEW16s' Cronbachs' Alpha coefficients were 0.85-0.93. The crossvalidity with SF36 and PHQ-D was highly significant but more so for psychological aspects. At baseline, the FEW16 score correlated with age, the subscale Resilience with age and 6 minute walking distance. At follow-up, the FEW16 total and Resilience scores had improved in the training group.

In contrast to the SF36, the FEW16 did not detect differences between the groups in Ex-DHF-P. The FEW16 showed good internal consistency and correlation with the SF36 and PHQ-D. Although it did not reflect significantly different changes between the two groups, its total score and Resilience improved after training.

**Conclusions:** We consider the FEW16 a questionnaire rather for psychological or general well-being than for physical well-being alone. To measure physical well-being, the SF36 Subscale vitality seemed to be more useful.

#### P1495

##### The ACE gene and ejection fraction in the uzbek patients having Q-MI

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**The aim:** Evaluation of the interrelationship between ACE gene with myocardial hypertrophy (MH) of the left ventricle (LV) and ejection fraction (EF) in the patients of Uzbek nationality having Q-wave myocardial infarction (Q-MI).

**Materials and methods:** there were analyzed data of 46 pts who were males with Q-MI. The mean age of pts was  $51,7 \pm 9$  y. All pts were performed analysis for presence of combination I and D of the ACE gene (I/I, I/D, D/D). Isolation of DNA genome was performed from the peripheral blood with use of kit DIALomDNAPrep 200 (Laboratory Isogen, Russia). PCR reaction was performed with use of the kit for genotyping on the polymorphic marker I/D of gene ACE on the amplifier GeneAmpPCRSYSTEM 9700 (Applied Biosystems, USA). In dependence on the results of analysis the pts were divided into 3 grps: gr I (n = 11), 23%, having combination of alleles I/I, gr II (n = 22) 47,8% with combination I/D, gr III (n = 13) 28,3% with combination D/D. On the 10-14 days of the AMI EchoCG were made in all pts.

**Results:** The comparative analysis of the data of the EchoCG showed that myocardium mass of the LV, wall thickness of the LV prevailed unreliably in the gr of pts with genotype D/D with the following values: MMLV  $292,2 \pm 103,6$  mg, IVS  $1,3 \pm 0,3$  cm. At the same time in gr I/I the thickness of IVS was reliably less and accounted  $1,0 \pm 0,3$  cm (p 1-3=0,02), and myocardial mass of LV was  $239,7 \pm 45,3$  g. In group I/D these parameters were as follows:  $253,4 \pm 103,6$  mg and  $1,04 \pm 0,3$  cm, respectively (p<0,05). The parameter of the ejection was also the least value in the gr with genotype D/D and accounted  $47,5 \pm 10,9\%$ , however in grs with genotype I/I and I/D, on the average, was  $51,5 \pm 10,25\%$  and  $48,9 \pm 11,24\%$  (p1-2 =0,4; p1-3=0,1) respectively. Conclusion. In the Uzbek population among the patient having Q-MI I/D the combination of the alleles of ACE gene occurred mostly frequent. In the carriers of D/D gene combination after AMI there was noted lower ejection fraction of the LV, high parameters of the MMLV, thickness of the IVS, PWLV in comparison with parameters of the pts with genotype I/I and I/D.

#### P1496

##### Influenza vaccination reduces relative risk of dementia in patients with heart failure

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**Background:** There is evidence that vaccination for influenza may decrease risk of acute cardiovascular event in patient with chronic heart failure (CHF). There is a higher prevalence rate of dementia in patients with CHF due to impaired circulatory status in brain. The purpose of this study was to test the hypothesis that influenza vaccination could reduce occurrence rate of dementia in patients with HF. **METHOD:** Using the Taiwan Longitudinal Health Insurance Database 2001 to 2012 (LHID2001-2012), this cohort study comprised patients (age > 60 years) with a recorded diagnosis of CHF (n = 20509) between January 1, 2001 and December 31, 2012. Each patient was followed-up using entry data until the end of 2012. Cox proportional hazard regressions were used to evaluate the dementia-free survival rates, after adjusting for known confounding factors.

**Results:** We found that patients with CHF receiving influenza vaccination had a lower risk in dementia development after adjusting for potential confounders [adjusted hazard ratio (HR) 0.65, 95% confidence interval (CI) 0.60-0.71, p < 0.001]. When stratified by patient's age, the adjusted HR for dementia was 0.56 (95% CI, 0.51-0.61, p < 0.001) for vaccinated patients with CHF aged over 70 years, but adjusted HR was 0.74 in the subgroup aged from 60 to 69 years. There was a lower adjusted HR (0.60, 95% CI 0.54-0.68) for dementia in male CHF patient receiving influenza vaccination compared with vaccinated female CHF patient (0.69, 95% CI 0.62-0.76). There was a significant reduction of dementia risk in elderly patient with CHF received more than three times influenza vaccination. (Adjusted HR 0.45, 95% CI 0.40-0.51, P < 0.001)

**Conclusions:** Our data showed that there was a lower rate of dementia development in elderly patient with CHF receiving influenza vaccination, particular in male, aged over 70 years, and receiving more than three times influenza vaccine injection.

#### P1497

##### Long-term results of percutaneous coronary interventions at coronary heart diseases pts with low ejection fraction

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**The purpose:** to study clinical efficiency of percutaneous coronary interventions and its influence on myocardial contractility at CHD pts with low ejection fraction (EF) of the left ventricle (LV) in the long-term period (24 month) without estimate viability of the myocardium.

**Materials and methods:** From January, 2013 year to December 2014 year PCI have been executed at 1266 pts with various forms of CHD. At pts CHD with low EF of the LV PCI have been executed at 11.9 % (138) pts. In the research conducted by us it has been included 65 (47.1 %) pts with low fraction of emission LV (less than 45 %) at which it was possible to study the long-term results. Pts of a male have made - 80.0 % (52), and female - 20.0 % (13). The age of pts fluctuated from 39 till 76 years, and has on the average made  $59,5 \pm 8,4$  years. From the standard risk factors most often met an arterial hypertension - at 87.7 %, (57) pts, hyperlipidemia - at 90.7 % (59); a diabetes mellitus at 40% (26) pts. The EF LV fluctuated from 27.3 % to 45 %, and has on the average made  $38,5 \pm 4,9\%$ . In 44.6 % (29) cases PCI have been executed at pts with acute myocardial infarction; in 40 % (26) cases at a stable angina II-IV FC, and in 15.4 % (10) cases at an unstable angina. Three-vascular lesion of a coronary channel took place in 47.7 % (31) cases, two-vascular in 29.2 % (19) and one-vascular lesion in 23.1 % (15) cases. At pts with multivascular lesion (n = 50) in 62 % (30) cases the incomplete functional is executed; in 20 % (11) cases full functional and in 18 % (9) cases full anatomic myocardial revascularization is executed. In total it has been implanted 115 stents (on the average 1.8 stents on one pt) from them of 80 % (92) drug eluting stents; 15.7 % (18) bare metal stents and 4.3 % (5) bioabsorbed vascular skeletons 'ABSORB'.

**Results:** In our research frequency of angiographic success at implantation stents at pts CHD with low EF LV has made 92.3 % (60), and clinical success at a hospital stage - 85.7 % (59). Frequency of development of complications has made 12.3 % (8) cases; from them dissection a coronary artery has developed in 62.5 % (5) cases; the 'no-reflow' phenomenon has developed in 25 % (2) cases and in 1 case the bleeding from a gastroenteric path took place. Frequency of development myocardial infarction type 4 and a lethal outcome equaled - 0. In the long-term period the EF LV fluctuated from 30 % to 61,5%, and has on the average made  $43,5 \pm 6,9$  % (=0.000). Increase the EF LV was observed at 60 % (39) pts, decrease at 15.4 % (10) pts and at 10.8 (7) pts ejection fraction of LV has not changed. The lethal outcome has developed at 8 (12.3%) pts, operation CABG is executed at 1(1.5%) the pt.

**Conclusion:** Thus, frequency of clinical success at a hospital stage of supervision has made 85.7% (59) cases. In the long-term period authentic increase of an average index of EF LV to  $43,5 \pm 6,9\%$  was marked at initial  $38,5 \pm 4,9$  % (=0.000).

#### P1498

##### Chronic heart failure and anxiety and depression disorders

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**Objective:** to define the presence and severity of anxiety and depression disorders and assess the impact on life quality in patients with chronic heart failure (CHF).

**Materials and methods:** A total of 130 individuals with CHF NYHA functional class (FC) II, III with previous Q-wave myocardial infarction (MI), mean-age  $60,66 \pm ,64$  y.o. Mean left ventricular ejection fraction was  $50,1 \pm 5,78\%$ . Signs of CHF FC II were seen in 58,5% subjects, FC III in 41,5% subjects. All patients had general physical examination. Medical treatment included beta-blocking agents, ACE-inhibitors or angiotensin receptor blockers, aspirin, statins, and diuretics. Assessment of the presence and severity of anxiety and depression disorders was made using Hospital Anxiety and Depression Scale (HADS), and life quality (LQ) was assessed Minnesota Questionnaire (MLHFQ).

**Results:** As per HADS, anxiety and depression disorders were shown in 46,9% subjects. Signs of isolated depression was defined in 22,3% cases, and anxiety was defined in 24,6% cases. The LQ values in patients with co-disorders were 1,5 times worse compared to patients with normal psychoemotional state. A correlation between LQ and depression severity (r=0,45, <0,001) was shown, as well as between LQ and anxiety severity (r=0,48, <0,001), as well as depression and anxiety (r=0,51, <0,001). It was obvious that 10,8% subjects suffered from depression and anxiety, and LQ in this group was 1.6 times worse compared to subjects without depression and anxiety. In group of subjects with CHF FC II, depression and anxiety disorders were defined in 30,3% subjects, and 9,2% subjects had both depression and anxiety, and signs of isolated depression and anxiety were defined in 4% and 26,3% cases, respectively. In CHF FC III, depression and anxiety was seen in 70,4 % subjects, and signs of isolated depression and anxiety were seen in 48,2% and 22,2% cases, respectively. This group showed a correlation between LQ and depression severity (r=0,48, <0,001), LQ and anxiety severity (r=0,57, <0,001). The



severity of anxiety and depression in patients with CHF FC III exceeds normal limits based on HADS values (1,4 and 1,7 times, respectively). 11,1% subjects showed signs of both anxiety and depression, and LQ in this group was worse compared to isolated anxiety and depression (<0,01). Conclusion. Thus, our study has defined the detection frequency of anxiety and depression in subjects with CHF to be 46,9%. Life quality in subjects with CHF is significantly impaired in the presence of anxiety and/or depression, and when the combination of anxiety and depression is present, this impairment is more prominent. Increased severity of HF FC is combined with the increased number of subjects with depression and anxiety disorders, and in CHF FC III depression prevails while in CHF FC II it is anxiety.

#### P1499

##### Features of clinical manifestations in obese patients with heart failure with preserved ejection fraction and obstructive sleep apnea

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**Purpose:** To assess clinical manifestations of obstructive sleep apnea (OSA) in patients with chronic heart failure (CHF) and preserved ejection fraction (EF).

**Methods:** The study included patients with clinical manifestations of CHF with preserved ejection fraction of left ventricle (EF>50%). Cause of CHF was stable ischaemic heart disease and essential hypertension. Disturbance of breathing during sleep assessed according to respiratory monitoring with the calculation of the index of apnea / hypopnea (IAH). Patients were underwent echocardiography investigations with estimation of left ventricular contractility, dimensions of heart chambers.

**Results:** We examined 60 patients (23 women and 37 men), mean age 67+9 years, BMI - 32,6+5,3 kg/m<sup>2</sup> with CHF with preserved ejection fraction of left ventricle. 42 (70 %) patients had CHF NYHA class II, 18 (30%) patients - CHF NYHA class III. OSA was revealed in 49 (81,7%) patients. The most frequent clinical manifestations of heart failure were dyspnoea (100%), peripheral edema of the lower extremities (55%). According to degrees of severity OSA the patients were distributed as follows: OSA mild degree (5 <IAH > 15) - 19 (38,8%), moderate OSA (15 <IAH > 30) 12 (24,5%) and severe OSA (IAH > 30) - 18 (36,7%) patients. The analysis of clinical manifestations showed that symptoms of CHF were directly dependent on the severity of OSA. There were no statistically significant differences in echocardiographic parameters between groups of patients with and without OSA, but in patients with OSA right ventricular sizes were slightly larger. It was found that the degree of functional classes of congestive heart failure depended on the severity of IAH. IAH <5% were observed only in patients with heart failure functional class 2 (11 patients (26,2%)); IAH 5-15 were revealed in 17 (41,1%) patients with CHF NYHA class II; IAH 15-30 were detected in 5 (27,8%) patients with CHF NYHA class III; clinical signs of right heart failure occurred in 9 (29%) patients with OSA mild and moderate degrees. IAH >30 was observed in 11 (61,1%) patients with CHF NYHA class III; peripheral edema and enlarged liver were found in 16 (89%) patients with severe OSA.

**Conclusions:** Our study demonstrated features of clinical manifestations in patients with heart failure with preserved ejection fraction of left ventricle and obstructive sleep apnea. The presence of severe OSA (IAH > 30) in patients with chronic heart failure are often accompanied with clinical signs of right heart failure (peripheral edema of the lower limbs, enlarged liver). The most prominent clinical manifestations (higher functional class) of CHF observed in patients with severe OSA. Thus, the presence of breathing disorders during sleep in patients with heart failure with preserved ejection fraction can be considered as a possible risk factor for the progression of chronic heart failure and determines the features of its clinical manifestations.

#### P1500

##### Heart failure in nonagenarian

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**Background:** Heart failure (HF) is a common disease with an increasing incidence due to the aging population. Older age groups are not clearly characterized.

**Purpose:** To characterize the nonagenarian HF patients and compare them with the younger age groups.

**Methods:** We retrospectively evaluated all hospitalizations for HF in the cardiology service of a single center over a period of six years. Only the first episode of each patient was included. The patients were divided in two groups according to the age: Group 1 (≥90 years) and group 2 (<90 years).

It was evaluated the days of hospitalization, history of acute myocardial infarction, cerebrovascular accident or atrial fibrillation (AF). It was also assessed the etiology of HF, the need of aminergic support, the value of BNP, ejection fraction (EF), complications during hospitalization and in-hospital mortality.

**Results:** During the reporting period, there were 1006 patients who met the inclusion criteria, 936 patients in Group 1 and 70 patients in Group 2. In group 1, a predominance of males (52.1%), 76.15 ± 9.65 years and mean duration of hospitalization 8.75 ± 6.51 days, most of them because of chronic decompensated HF (78.9 %). In older age, female predominance (67.1%) with a mean duration of hospitalization 7.30 ± 3.98 days and 75.7% of admissions due to chronic decompensated HF. BNP at admission was about 850 pg/ml in both groups. 73.2% of nonagenarian had EF≥50% (55.48 ± 15.56%) while in the other group only 51.8% (48.76 ± 16.29%) had preserved EF. The most common complication in both groups was the acute kidney injury (18.0% in group 1 and 24.3% in Group 2), and in-hospital mortality was 6.4% in group 1 and 12,9% in nonagenarian.

**Conclusion:** As expected, mortality was higher in nonagenarian patients, however, this study showed that the duration of hospitalization in these patients was lower than in the younger age groups and the complications during hospitalization were not significantly different in the two groups. It was found that nonagenarian have predominantly HF with preserved EF. This population continues to require better characterization with additional studies.

#### P1501

##### Females in the polish population of heart failure pilot survey: the clinical characteristics, pharmacotherapy and outcomes in the one-year follow-up.

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**Background:** In the Heart Failure Pilot Survey (The ESC-HF Pilot) clinical and epidemiological data of 5118 subjects was collected. Females have not always been fully represented in clinical trials. Gender-related differences in heart failure patients are still unclear. Aim of study: The aim of study was to describe female population included in the Polish Population of Heart Failure Pilot Survey: the clinical presentation, pharmacotherapy and clinical outcomes in the one-year follow-up.

**Methods:** The ESC-HF Pilot study was a prospective, multicentre, observational survey conducted in 136 cardiology centres in 12 European countries, including Poland in the years 2009-2011. In this research the following data were analysed: demographics, presence of cardiovascular risk factors, etiology of heart failure, biochemical, echocardiographic and electrocardiographic parameters, pharmacological treatment and outcomes in patients enrolled in Poland to the Heart Failure Pilot Survey (892 patients).

**Results:** The study population consist of 33.6% females. Female patients compared to male patients with HF characterized by: older age 70.8 ± 12.4 vs. 63.8 ± 13.1 (p<0.05), higher systolic blood pressure 136.3mmHg ± 30.8 vs. 130.6mmHg ± 23.2 (p<0.05), higher left ventricular ejection fraction 47.4% ± 13.2 vs. 39.0% ± 13.6 (p<0.05), higher NYHA functional class 2.9 vs. 2.7 (p<0.05), higher level of BNP 1826.9 pg/ml, vs. 1183.2 pg/ml (p<0.05), longer QTc 401.9ms ± 38.7 vs. 389.7ms ± 45.8 (p<0.05). Significantly more often in women than in men occurred hypertension (p<0.05), thyroid dysfunction (p<0.05) and depression (p<0.05). Females were longer hospitalized in ICCU 4.1days vs. 2.8 days (p<0.05). Females compared to males were more often treated by ARB and CCB, but less frequently by ACEI, BB and Eplerenone. There were no significant differences in the rate of deaths in the one-year follow-up between female patients and male patients (99 [11%] subjects died).

**Conclusions:** 1.The results of ESC-HF Pilot Survey from Polish Centers showed significant gender-related differences in clinical presentation and pharmacological treatment of heart failure. 2.The clinical outcomes were similar in female patients and male patients with heart failure in the one-year follow-up in spite of differences in clinical characteristics and pharmacotherapy.

#### P1502

##### Assessment of the dynamics of silent ischemia on the effects of heart rate reducing drugs in patients with ischemic heart disease and diabetes in an actual ambulatory practice.

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**Purpose:** To determine the dynamics of silent ischemia and the duration of its single episode in patients with ischemic heart disease (IHD) and diabetes mellitus (DM) on the effects of the prolonged use of drugs that lower heart rate in an ambulatory practice.

**Material and methods:** Dispensary group of patients, DM 713 people, including patients with CHD and DM. The dynamics of silent ischemia were analyzed according to Holter monitoring (HM) in the first 14 days and on the eighth visit post 184 days of therapy, where episodes of silent ischemia (ESI) were determined by the intensity of horizontal displacement of ST segment more than 2.0 mm in terms of time in minutes (min) and related physical activity (PA).

**Results:** Using "closed envelopes," or double blind method, two groups were created (Group I and Group II), each group consisting of 40 people. In Group I, were titrated beta-blockers (BAB) (metoprolol tartrate) until reaching the optimal dose. In Group I, in addition to standard therapy patients also received ivabradine with titration from 10 mg per day (58.3%) to 15 mg per day (41.7%) in the second and third visit in order to achieve a significant decrease in heart rate (HR) frequency. Groups were similar in gender, age, initial heart rate, blood pressure, IHD and DM duration. Provision of standard therapy in both groups had no significant differences in the frequency of BAB, ACE inhibitors, diuretics, calcium antagonists, and aspirin. All patients in the two groups took hypoglycemic pills. In Group I, 20.7% of patients and in Group II, 28% of the patients received statins. According to HM ECG, on the day 14, the number of ESI accompanied by physical activity in Group1 is 3.06 ± 2.0 and Group I 4.6 ± 2.7. These findings indicate that the number of occurred episodes in Group II is 1.6 times higher than in Group1 (p=0.06). After 184 days, there is a decrease in number of ESI in Group I (2.7 ± 3.0, p=0.64) and in Group II, (0.7 ± 0.77, p < 0.0001). Duration (D) of one (O) ESI with heightened physical activity in Group I is 3.0 ± 3.2 min, and in Group II, it is 3.5 ± 2.1 min (p=0.29). After 184 days DOESI in Group I is 1.95 ± 1.4 min, (p=0.14) and in DOESI in Group2 1.6 ± 1.9 min, (p=0.01). The results indicate a decrease in DOESI for both groups; specifically 54% in Group2 and 35% decrease in Group1.

**Conclusion:** Long term use of ivabradine and beta-blockers in patients with ischemic heart disease and diabetes leads to a significant reduction in the frequency and duration of episodes of silent ischemia in real ambulatory practice.

#### P1503

##### Does elevated right atrial pressure predict post heart transplant outcomes?

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**Purpose:** Orthotopic heart transplantation (OHT) is the definitive treatment for end stage heart failure. Patient selection is key in improving post OHT outcomes. Pre-operative right ventricular dysfunction is associated with worse outcomes after mechanical circulatory support but its effect on post OHT outcomes has been a matter of discussion in the literature. Right atrial (RA) pressure is commonly used as a surrogate for RV function. We compared post OHT outcomes in patients with and without preoperative elevated RA pressure.

**Methods:** An analysis of 135 patients who underwent isolated OHT at our institution from January 1993-October 2015 was performed. Groups were divided based on preoperative RA pressure. Baseline characteristics and post OHT outcomes (post OHT length of stay; 30 day, 1 year and 3 year survival and clinically significant rejection in the 1st year) were compared. Results :Pre OHT characteristics were similar between the 2 groups except for a difference in age and PVR. Post heart transplant survival was worse in the group with pre transplant RA pressure > 15mmHg. Conclusion :Pre-operative elevated RA pressure was associated with a worse short and intermediate term (1 and 3 year) survival after OHT. There was no difference in post transplant rejection in the first year. Possible factors for poor survival include underestimation of pulmonary hypertension or organ dysfunction. RA pressures are readily available and may allow for a more accurate prediction of post OHT outcomes.

#### P1504

##### Elevated heart rate is associated with cardiac denervation and neurohormonal activation in patients with heart failure: data from a randomised clinical trial comparing ivabradine versus pyridostigmine

The study was supported by Foundation for Research Support of the State of Rio de Janeiro (FAPERJ)

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**Background:** In the SHIFT Study, heart rate (HR) reduction with ivabradine was associated with improved survival and reduction in hospitalisations. Pyridostigmine is a cholinergic agonist that has been shown to enhance vagal tonus both in normal and HF patients.

**Purpose:** We sought to assess the relationship of baseline HR with clinical, neurohormonal and cardiac sympathetic activity in 16 patients included in a clinical trial comparing ivabradine versus pyridostigmine.

**Methods:** Patients with chronic heart failure (HF) who were in sinus rhythm with resting HR > 70 bpm despite optimal medical treatment were included in a randomized, double-blind study comparing ivabradine versus pyridostigmine. This report refers to baseline data from the 16 initial patients. Baseline HR (before randomisation to one of the drugs) was assessed and patients were classified into two groups, below or above mean HR. The two groups were compared regarding clinical characteristics, biomarkers, ejection fraction, functional capacity, and cardiac sympathetic activity as assessed by 123-iodine-metaiodobenzylguanidine (MIBG) myocardial scintigraphy.

**Results:** Mean HR was 83.5 ± 11.5 bpm (range 72 to 104). All patients were on carvedilol (daily dose was 50 mg in 14 patients and 25 mg in 2 patients). Seven (43.7%) patients were above mean HR. These patients had a trend for worse NYHA functional class (class III and IV 57.1% vs 11.1%, p=0.10), a lower 6-min walk distance (292.3 ± 93 vs 465.2 ± 97.1, p=0.0029), higher values of N-Terminal-proBNP (median 708.4 vs 76.1 pg/mL, p=0.035) and lower late heart/mediastine rate, indicating cardiac denervation (1.48 ± 0.12 vs 1.74 ± 0.09, p=0.006). No difference was observed regarding peripheral edema (0% vs 33%, p=0.21) nor total body water estimation as assessed by bioelectrical impedance vector analysis (BIVA) (hydration index 73.6 ± 0.05% vs 75.8 ± 3.75%, p=0.28).

**Conclusion:** Elevated baseline HR in patients with HF under optimal medical treatment was associated with worse functional capacity, neurohormonal activation and cardiac denervation but not with congestion.

#### P1505

##### Profile changes of heart transplant recipient in an Argentinean single centre

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**Introduction:** Advances in the treatment of advanced heart failure, considering mechanical circulatory support devices, have conditioned the survival rates and characteristics of patients (p) included in the heart transplant (HTx) waiting list. Objective To analyze the HTx recipients (R) characteristics in an Argentinean Centre.

**Material and Methods:** A retrospective analysis was performed on 465 HTx R. The population was divided into 2 groups by era: group 1 (G1), 181 p who underwent HTx between February/1993 and December/2003, and Group 2 (G2), 286 p, between January/2004 and December/2015. We analyzed the clinical and demographic variables at HTx. Continuous variables were expressed as mean and standard deviation or median and interquartile, and categorical variables as absolute values and percentages. Kaplan Meier survival analysis and Log Rank test were performed. Results We classified the different clinical status into p on mechanical circulatory and/or respiratory support 65 p (36%) vs. 128 p (45%) (p 0.04); on IV inotropes, 23 p (12%) vs. 86 p (30%) (p 0.001) and at home with oral medication while on the waiting list 94 p (52%) vs. 72 p (25%) (p 0.001). Overall in hospital mortality was G1, 22 p (13%) vs. G2, 35 p (12%) (p 0.4). Survival at 1.5 and 10 years in both groups was 79% vs. 80%; 63% vs. 68%; 47% vs. 65% (p 0.04) respectively (see Figure 1) Conclusion We found a higher risk profile in G2 due to older age, female gender, severe PH, Chagas disease and mechanical circulatory support requirement, though it did not present a significant impact on mortality.

Table 1

VARIABLES	G1	G 2	p
Age (years)	49 ± 13	50 ± 13	0.02
Age > 65 years	8% (15p)	9% (25p)	0.02
Gender (male)	82%	74%	0.02
Cardiomyopathy	24% (47 p)	32% (90 p)	0.04
Coronary Artery Disease	65% (117 p)	34% (99 p)	0.0001
Chagas Disease	2.8% (5 p)	9% (8(6 p)	0.006
Renal Failure (Cr > 1.5 mg/dl)	18% (34p)	20%58p	0.13
BMI > 30	5% (9p)	14% (41p)	0.04
BMI < 18	3% (6p)	2% (5p)	0.04
Pulmonar Hypertension (PH)(TPG > 12/ > 2.5 Woods)	35% (65 p)	57% (164 p)	0.001

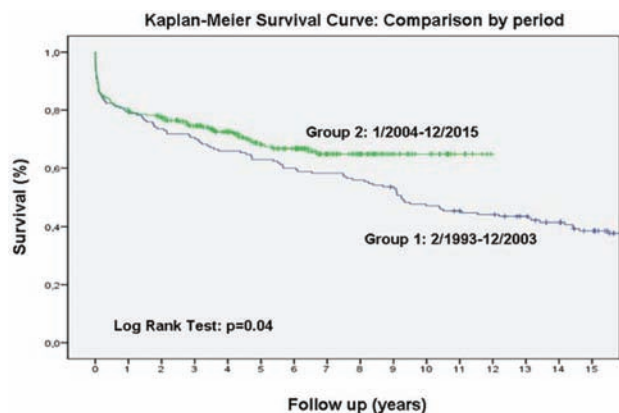


Figure 1 - Survival curve

**P1506**

**Heterogeneity of readmission rate and in-hospital mortality of patients with heart failure based on the volume of patients at each hospital: analysis of administrative data of a nationwide population**

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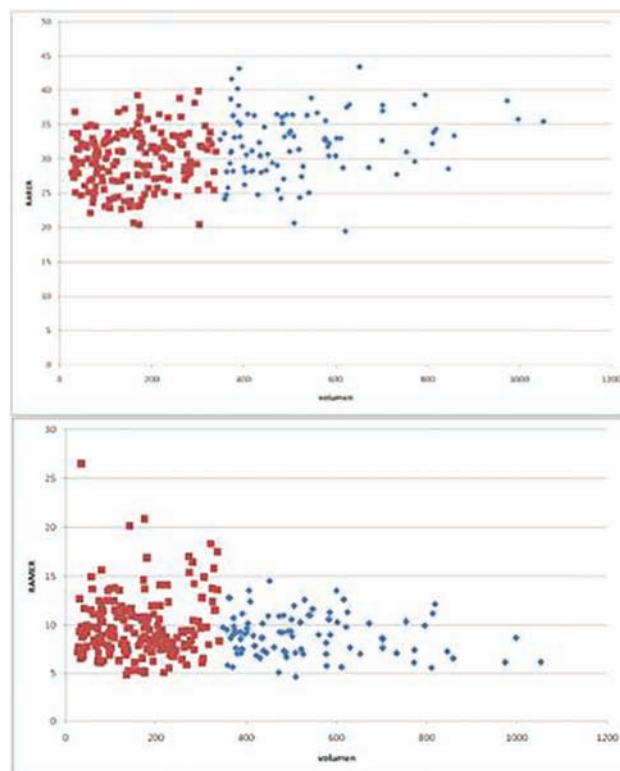
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**Introduction:** It is well known that heart failure (HF) is a disease with high morbidity and mortality. We present, for the first time, the influence of the volume of hospital patients in HF in-hospital mortality and readmission rate at 1 year in a whole country (Spain, 46.77 millions population).

**Methods:** All the discharges from Spanish hospitals corresponding to 2012-2013 with a primary diagnosis of HF, according to the ICD-9-CM classification, were analyzed. High-volume hospitals were considered those with HF hospitalizations  $\geq 340$  per year, and the low-volume  $<340$ . Crude and adjusted in-hospital mortality and rate of readmissions at 1 year were analyzed.

**Results:** 400,861 hospital admissions were recorded; 77,652 of them had HF as primary diagnosis. The mean age of the patients was  $79.2 \pm 9.9$  years, with 50% of patients 81 years or more. In-hospital mortality was statistically significantly lower in the high-volume centers compared to low-volume, both the crude rate (8.6% vs. 10.3% in the first hospitalization, and 13.9% vs. 15.8% at 1 year,  $p < 0.001$ ) and the adjusted rate (RAMER) (9% vs. 9.9%;  $p = 0.006$ ). Similarly, readmission rate was statistically significantly lower in the high-volume centers compared to low-volume at 1 year (31.2% vs. 28.1%;  $p < 0.001$ ), also adjusted rates (RARER) (32.2% vs. 30%;  $p < 0.001$ ), with no significant difference in readmissions at 1 month (10.1% vs. 9.5%;  $p = 0.1$ ). Figure 1 shows the scatter plots between hospital volume and both adjusted rates (RAMER and RARER).

**Conclusions:** According to our results, the volume of patients treated for HF in a hospital affects their prognosis. Thus, lower hospital volume of patients involves greater heterogeneity in in-hospital mortality and readmission rates in HF patients.



Scatter plots hospital volume

**P1507**

**Heart failure in nonagenarians. Clinical profile and prognostic factors of short-term mortality and readmission**

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**Introduction:** Lack of information exists about the clinical characteristics and prognosis of very old patients with heart failure (HF). Better knowledge of this population may help to design appropriate follow-up protocols and treatments.

**Purpose:** To describe clinical profile and prognosis of nonagenarians hospitalized by decompensated HF. **Methods.** Descriptive retrospective study that included nonagenarian patients admitted to a university hospital with HF as main diagnosis, during an eight-month period. Clinical, analytical and echocardiographic variables were included, as well as treatment. We analysed in-hospital mortality, 30-day mortality and readmissions.

**Results:** Of all HF admissions, 31% (76 patients) were nonagenarians, with a mean age of 93.4 years and frequent comorbidities: hypertension (92%), chronic kidney disease (45%) and atrial fibrillation (67%) but only 17% with diabetes mellitus. In-hospital mortality rate was 14.5% (11 patients) and 10 patients died later on the next month after discharge, meaning that cumulative mortality at 30 days was 27.6%. HF was the cause of death in 71% of the cases. Readmission rate was 21.5% in the first 30 days, 40% because of HF. Renal function parameters (urea, creatinine and glomerular filtration rate) correlated with in-hospital mortality and readmission. High NT-proBNP levels at discharge or lack of NT-proBNP variation during admission were both 30-day mortality and readmission predictors. There was a tendency to increase HF related drugs prescription at discharge.

**Conclusions:** Very old patients have high mortality rate in the first month after HF hospitalization, mainly related to HF. Renal function parameters and NT-proBNP levels are useful to identify high-risk patients for death or readmission at 30 days.



## ADVANCED HEART FAILURE

## P1508

**Dealings perception of gravity of complex patients in heart failure**L Baumworcel<sup>1</sup>; MW Montera<sup>1</sup>; ET Mesquita<sup>1</sup><sup>1</sup>Hospital Pro Cardiaco, Centro de Insuficiência Cardíaca, Rio de Janeiro, Brazil

Heart failure is the final pathway of the majority of heart disease. These patients progress for years with various comorbidities and often become frail patients. Upon reaching the stage as D of the disease when no longer have other forms of treatment to improve the quality of life we find a challenge to communication in connection with the patient and family. Understand this perception of care varies with each patient and family, and often these patients hospitalized and has not yet been discussed with family issues related to palliative care. Such that discuss end of life care in Latin culture can bring a negative perception of service quality if not done properly. Thinking in these respects, one heart failure clinic of a city Hospital created a discussion protocol with families in formal meetings in a reception room to the family. This meeting is invited to be present the patient family or the responsible and every physician involved in the case. The purpose of this meeting is to take all the doubts that the family can have with time and without any external interruption. After all the discussion, all the presents sign a book with the summary of the meeting pledging to return the assembled front of any new doubt or drastic change with the patient. The experience of this group with this protocol already covers 38 severe patients using artificial mechanical support or cardiogenic shock. There were no more complaints or negative perceptual signals from families independent of the treatment outcome of these critically ill patients. This result shows that the realizing formal meetings improve the family patient perception and the aggregate value of this treatment chain.

## P1509

**Lost of chance for enzymatic treatment of a family with Fabry disease and severe right heart failure.**N N Nora Nabila Ali Tatar-Chentir<sup>1</sup>; BT Boumediene<sup>1</sup>; HB Haddak<sup>1</sup><sup>1</sup>University Hospital Centre Mustapha, Algiers, Algeria

**Purpose:** Anderson-Fabry disease is a rare genetic lysosomal storage disease, inherited in an X-linked manner. The rarity of Fabry disease to many clinicians sometimes leads to misdiagnoses. Little is known from biventricular hypertrophy in this context. The aim of our study is to describe cardiac complications for the mother and three of her sons.

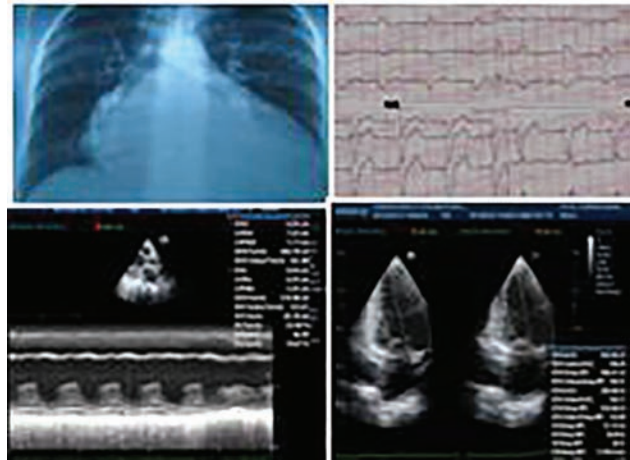
**Methods:** Medical histories, Clinical features, chest radiography, electrocardiograms (ECG) and echocardiography data of the mother and three of her sons were assessed.

**Results:** On the five brothers one of them presented a sudden death several years ago. Two brothers respectively 27 and 30 years old were hospitalized in our unit, for severe right heart failure with hepatomegaly leg edemas and abundance of ascites. In addition, one of the brothers had a history of syncope preceded by palpitations. Corneal opacities were reported in the two brothers. Major cardiomegaly in the two brothers with pleural effusion in one of them, persistent atrial fibrillation (AF) and repolarization abnormalities on ECG in the two brothers. In the same way, on echocardiography in the two brothers, we observed ectatic right atria with indexed volume around 300ml/m<sup>2</sup>, area around 100 cm<sup>2</sup>, dense spontaneous contrast grade IV of Fatkins, severe tricuspid regurgitation. Presence of atria septal aneurysm towards the left atrium. Presence of left and right ventricular hypertrophy with preserved left ventricular function and elevated left ventricular filling, severely depressed right systolic function and severe depression parameters of diastolic function.

The mother 56 years old and her fourth son, 24 years old, referred in our outpatient unit were in New York Heart Association class 3 with the same echocardiography findings.

A medical treatment including angiotensin converting enzyme inhibitors (ACE), loop diuretic, aldosterone antagonist and vitamine K antagonist therapy was prescribed without significant improvement in symptoms and echocardiographic parameters over 1 month.

**Conclusion:** Imaging of the myocardium has been explored as a non-invasive way of early screening and diagnosing patients. Correct diagnosis is of vital importance because the condition is potentially reversible with treatment by enzyme replacement therapy in the early stages of the disease that isn't the case of this family screened at the terminal stage with severe cardiac Fabry Disease.



Preterminal HF in Fabry Disease

## P1510

**Risk factors of early allograft vasculopathy in patients after heart transplantation**A K Alena Kurlianskaya<sup>1</sup>; T A Trofimova<sup>1</sup>; V I Stelmashok<sup>1</sup>; O L Polonetsky<sup>1</sup>; A Y Ostrovsky<sup>1</sup>; T L Denisevich<sup>1</sup>; Y P Ostrovsky<sup>1</sup><sup>1</sup>Research & Practical Centre "Cardiology", Minsk, Belarus

**Aim:** observe the risk factors of early cardiac allograft vasculopathy (CAV) in patients after heart transplantation.

**Methods:** 127 patients after heart transplantation were recruited. After 24 ± 3 post-transplant months, coronary angiography and intravascular ultrasonography were done. To determine risk factors of early CAV on the stage when the lesion of coronary arteries is not advanced and angiography lacks the sensitivity, another statistical method using "Classification of the entire coronary tree" (CCT) was performed.

**Results and conclusion:** According to CA no significant coronary artery luminal narrowing was detected. IVUS results revealed various severity of the coronary arteries impairment in 58 (75%) pts. The high probability of significant changes in the coronary tree (IVUS) has been detected in pts after HT, who initially had degree of histocompatibility in HLA system less than 62.5% and tacrolimus after 3 months ≥ 10,4 ng/ml. Mild lesions in the coronary tree in early period after HT were associated with: 1. hypertension, BMI ≥ 33,5 kg/m<sup>2</sup>, triglyceride ≥ 2,67 mmol/L after 6 months HT; 2. examination after 12 months showed low HDL < 1.06 mmol/L in combination with high LDL ≥ 2,22 mmol/L; tacrolimus ≥ 7,65 ng/ml in combination with increased CRP ≥ 4,47 mg/l. Risk factors identified by the analysis of "CCT" were divided into two groups: immunological (histocompatibility in HLA-system, myeloperoxidase) and non-immunological (metabolic syndrome signs), analyzed in subgroups of patients treated with different immunosuppressive agents. The subgroups with Everolimus (1) or without Everolimus (2) treatment were comparable in the relative percentage of pts with risk factors of early lesions in coronary arteries, according to "CCT" analysis. In 2 group percentage of pts with signs of metabolic syndrome was 41.7%, in 1 group - 58.8% (p = 0.218). Percentage of pts with immunological factors in 2 group 58.3%, in 1 group - 41.2% (p = 0.220). However, among 1 group pts immunosuppressive agent unlike 2 group, cases with progression of lesion in the coronary tree were not detected (follow-up IVUS data). In 2 group progression of CAV was indicated in 21.7% of pts with signs of metabolic syndrome, and in 10% of cases with immunological risk factors.

## P1511

**Is there a heart rate paradox in heart transplantation?**U Umut Kocabas<sup>1</sup>; E Kaya<sup>1</sup>; S Ertugay<sup>2</sup>; P Ozturk<sup>2</sup>; C Engin<sup>2</sup>; S Nalbantgil<sup>1</sup>; M Zoghi<sup>1</sup>; T Yagdi<sup>2</sup>; M Ozbaran<sup>2</sup><sup>1</sup>Ege University, Department of Cardiology, Izmir, Turkey; <sup>2</sup>Ege University, Department of Cardiovascular Surgery, Izmir, Turkey

**Introduction:** Elevated heart rate (HR) is associated with adverse cardiovascular outcomes in patients with heart failure. After heart transplantation (HTx), cardiac denervation has a variable effect on HR. However, impact of HR after HTx over prognosis is still unclear. In this study, we aimed to evaluate the prognostic impact of HR in HTx patients.

**Methods:** We studied 140 consecutive HTx patients' data retrospectively (78.6% male, mean age: 39 ± 14). Patients were divided into two groups according to first-month resting HR after HTx: group 1, HR ≤ 80 bpm (mean 76.2 ± 6.7) and group

2, HR>80 bpm (mean 103.9±12.9). Rejection and all-cause mortality rates were compared between groups.

**Results:** Thirty patients were included in group 1 and 110 patients in group 2. No significant differences were detected between groups when compared according to demographic data, risk factors, NYHA and etiology of heart failure. The most common reasons for morbidity and mortality after HTx such as right ventricular failure, infection, cerebrovascular accident, arrhythmia and rejection were similar between groups (Table). Long-term (>1 year) mortality rate was 50% in group 1 and 28.2% in group 2 (p=0.03).

**Conclusion:** Although HR did not affect the rate of rejection in heart transplant patients, all-cause long-term mortality tended to be higher among patients with lower HR.

Table: The comparison of group 1 and group 2.

	HR<80 bpm (n=90, 21.4%)	HR>80 bpm (n=110, 78.6%)	P value
<b>Demographic data and clinical parameters before HTx</b>			
Age (yrs)	36±15.6	40.9±14.2	0.12
Sex (male, %)	80	78.2	0.97
Etiology (Dilated CMP, %)	40	52.7	0.57
NYHA (Class III, %)	55	62	0.24
Atrial fibrillation (%)	15	19	0.12
LVEF (%)	24±10	22±8	0.14
<b>Complications after HTx</b>			
Right ventricular failure (%)	26.7	18.3	0.31
Infection (%)	53.3	48.6	0.68
Cerebrovascular accident (%)	6.7	4.6	0.64
Arrhythmia (%)	23.3	18.3	0.60
<b>Rejection and all-cause mortality rates</b>			
Rejection (%)	55.6	55.2	0.98
One-year mortality (%)	29.3	30	0.68
Long-term mortality (%)	50	28.2	0.03

Table

**P1512**

**Prognostic implication of biomarkers ST2, NT-proBNP, Galectin-3 during long-term observation in patients with advanced heart failure**

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**Aim:** To reveal predictors of adverse cardiac events in pts with different functional class (FC) of severity by NYHA after acute decompensated heart failure (HF).

**Methods:** The study involved pts with HF: I-II FC – 70 pts, III-IV FC – 68 pts. We performed biochemical blood analysis: NT-proBNP, ST2, Galectin-3, Cardiac troponin-I. The clinical course was evaluated on the start and within 6 months of observation. Adverse cardiac events - death, cardiac transplantation, emergency hospitalization with decompensation. By applying the statistical module "Classification Trees" we identified predictors of adverse cardiac events (ACE) in pts with CF of different FC.

**Results and conclusions:** Within 6 months 18.8 % of patients with HF developed ACE, precisely I-II FC – 11.4% of cases, III-IV FC – 26.5% of cases.

Classification Trees (CT) were built to minimize the errors of false classification. We used dimensional branching algorithm by the method of CART (Classification And Regression Trees). Importance (rank) of the selected predictors was scored (maximum rank - 100 points). As a result, there were received 3 statistically significant decision trees. The predictors revealed basing on the CT analysis were presented in table 1.

I-II FC of HF pts - the predictors of unfavorable course included of NT-proBNP (rank-78) considering end-diastolic volume of the left ventricle (EDV) (rank - 100).

III-IV FC of HF pts - 2 statistically significant CT. The first decision tree included the following predictors of unfavorable cause of the disease: concentration of ST-2 (rank - 87) and myocardial mass index of the left ventricle (MMI LV) (rank - 100).

The second CT for III-IV FC of HF showed the highest classification accuracy (100%) and was based on the sequential analysis of the following laboratory parameters: Galectin (rank-60), of NT-proBNP (rank-72) and atherogenic factor value (rank-100).

**The predictors of unfavorable course**

FC CHF	Predictors	favorable outcome*	unfavorable outcome*	Classification accuracy
I-II	NT-proBNP≥4683 pg/ml	100%	78.0%	96.4%
I-II	NT-proBNP<4683 pg/ml and EDV≥411 ml	100%	78.0%	96.4%
III-IV	ST-2≥53 pg/ml	96.5%	100%	97.3%
III-IV	ST-2<53 pg/ml and MMI LV≥262	96.5%	100%	97.3%
III-IV	Galectin≥16 ng/ml and NT-proBNP≥1587 pg/ml	100%	100%	100%
III-IV	Galectin<16.2 ng/ml and atherogenic factor≥5.5	100%	100%	100%

\*Discrimination accuracy

**P1513**

**Tissue doppler derived right ventricular isovolumic contraction velocity predicts prognosis in advanced heart failure patients with dilated cardiomyopathy**

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**Background:** Right ventricular (RV) function has gained attention recently as a prognostic predictor even in patients who have left-sided heart failure. In routine echocardiographic practice, RV longitudinal parameters such as tricuspid annular plane systolic excursion (TAPSE) and tissue Doppler derived systolic tricuspid annular motion velocity (S') are useful because those are easily obtained and have high reproducibility. Tissue Doppler derived tricuspid isovolumic peak contraction velocity (IVCv) is also easily obtained same as S', relatively afterload-independent longitudinal parameter, and has been reported as a prognostic predictor in patients with pulmonary hypertension. However, IVCv for predicting prognosis in advanced heart failure has been unclarified.

**Purpose:** To test the hypothesis that IVCv predicts prognosis in advanced heart failure patients with dilated cardiomyopathy.

**Methods:** We enrolled 60 dilated cardiomyopathy patients with left ventricular ejection fraction <35% who were admitted to our hospital for evaluation or treatment of heart failure. All patients underwent coronary angiography and myocardial biopsy. TAPSE, S' and IVCv were obtained for RV systolic parameters. Primary cardiac events were defined as left ventricular assist device implantation or cardiac death within one year after echocardiography.

**Results:** All patients were classified as New York Heart Association class III or IV. Thirty-four events occurred (4 deaths, 30 left ventricular assist devices). Univariate analysis showed that age, systolic blood pressure, plasma brain natriuretic peptide level, left atrial volume index, left ventricular end-systolic volume index, transmitral E/A ratio, E-wave deceleration time, tricuspid regurgitation velocity and IVCv were predictors of outcome, whereas TAPSE and S' were not. Multivariate stepwise analysis revealed that systolic blood pressure (p<0.01) and IVCv (p<0.05) were independent predictors of events. From the receiver-operating characteristics curve, cut-off value of IVCv to predict outcome was 6.5 cm/sec (area under the curve=0.70). Kaplan-Meier analysis showed that one-year event rate was significantly higher (log-rank, p<0.01) in patients with IVCv <6.5 cm/sec than in those with IVCv ≥ 6.5 cm/sec.

**Conclusion:** IVCv, an easy, noninvasive and reproducible parameter derived by tissue Doppler, is an independent predictor of one year events in advanced heart failure patients with dilated cardiomyopathy.

**P1514**

**Ventricular assist device in pediatric patients**

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**Introduction:** Berlin Heart EXCOR Pediatric ventricular assist device (VAD) is currently used as mechanical circulatory support device for adolescents, infants and small children with advanced heart failure.

**Purpose:** To report the preliminary experience of a third level centre of Pediatric Cardiology and Cardiac Surgery with VAD

**Methods:** Between April 2009 and January 2016, 10 children (6 male and 4 female) followed in our Department of Pediatric Cardiology underwent Berlin Heart EXCOR pediatric VAD implantation at the Cardiac Surgery Division of our Hospital. Two cycles of i.v. inotropic therapy were undertaken before implantation (dobutamine and levosimendan), and all the patients underwent imaging evaluation (including cardiac MRI in 3 patients) and cardiac catheterization.

**Results:** The median age at implant was 8,8 years (2 to 15 years), the mean weight was 36,6 Kg (10 Kg to 65 Kg), and the median support time was 127 days (5-459 days). The diagnosis was myocarditis in 6 patients, a case of idiopathic dilated cardiomyopathy, a case chemotherapy-induced cardiomyopathy and a single case of heart failure secondary to valve disease. Four patients received a BIVAD and 6 patients a LVAD. Three patients underwent cardiac Magnetic Resonance Imaging (MRI), showing diffuse subepicardial enhancement without signs of intracellular and interstitial edema, capillary leakage and hyperemia. Endomyocardial biopsy and viral genome PCR were performed in all patients at VAD implantation. Diffuse fibrotic replacement without signs of active inflammation were evidenced in all the patients, and only in one case a viral etiology (CMV) was revealed. Out of the 10 paediatric patients, 7 were bridged to heart transplantation, 2 died on support, and 1 is still waiting for heart transplantation. After heart transplant, an Extra Corporeal Membrane Oxygenation (ECMO) was needed in 3 patients, 3 patients had chest wound infection and one had hyperacute rejection and bleeding problems. Patients

receiving biventricular support had a more favorable clinical course compared with children implanted with left ventricular assist device.

**Conclusions:** In agreement with literature, our experience confirmed that Berlin Heart EXCOR pediatric VAD could provide satisfactory and safe circulatory support for children with end-stage heart diseases. Timing of device implantation and the careful choice between univentricular/biventricular support represent important prognostic factors in patients with end stage disease.

### P1515

#### Management of end-stage heart failure patients with or without ventricular assist device: an observational comparison of clinical and economic outcomes

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**Background:** Heart transplantation (HT) and ventricular assist devices (VAD) for the management of end-stage heart failure have not been thoroughly compared. We compare the outcomes and use of resources with these 2 strategies in 2 European countries.

**Methods:** We studied 83 patients (pts) managed by VAD in first intention in Germany (groupI) and 141 managed with HT in first intention, in France (groupII). The primary endpoint was 2-year survival. KM analyses were performed after the application of propensity score weights, to mitigate the effects of non-random group assignment. The secondary endpoints were resource utilisation and costs. Subgroup analyses were performed.

**Results:** GroupI was more hemodynamically compromised, and 28% underwent HT versus 55% in groupII ( $P < 0.001$ ) after a longer median wait ( $P < 0.001$ ), Table 1. The adjusted probability of survival (APS) was 49% in groupI versus 67% in groupII ( $P < 0.001$ ). The mean cumulated 2-year costs were € 281,361 ± 156,223 in groupI, and € 47,638 ± 35,061 in groupII ( $P < 0.0001$ ). Among HT patients, the APS in groupI versus groupII was 84% versus 73%, respectively (ns), though, in the subgroups treated with inotropes, was 84% in groupI versus 66% in groupII ( $P = 0.01$ ).

**Conclusions:** HT after VAD therapy yielded results similar to HT non-preceded by VAD, and better results in pts treated with inotropes at the inclusion time. The group I strategy was more expensive.

Table 1

	Group I (n= 83)	Group II (n = 141)
Age, y	52.9 ± 13.8	50.8 ± 13.4
Men	72 (87)	113 (80)
Body surface area, m <sup>2</sup>	2.0 ± 0.2	1.9 ± 0.2
Left ventricular ejection fraction, %	18 ± 9	23 ± 9
Mean systemic blood pressure, mmHg*	67 ± 14	79 ± 13
Heart rate, bpm	88 ± 23	85 ± 21
Ischemic heart disease*	43 (52)	54 (38)
Prior cardiac surgery	29 (35)	36 (26)
Inotrope*	81 (98)	68 (48)
Veno-arterial extracorporeal membrane oxygenation	18 (22)	42 (30)
Mechanical ventilation	30 (36)	48 (34)
Ultrafiltration*	25 (30)	22 (16)
INTERMACS profile at time of study enrolment* Profile 1 - 3	74 (89)	63 (45)

Values are means ± SD, or numbers (%) of observations INTERMACS = Interagency Registry for Mechanically Assisted Circulatory Support \* $P < 0.05$

### P1516

#### Optimizing outcomes after heart transplantation in patients with cardiac amyloidosis - a single center analysis of 43 patients in 2 eras

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**Introduction:** The prognosis of symptomatic cardiac amyloidosis - either of light chain (AL) or transthyretin (ATTR) type - is poor due to limited causative treatment options. Heart transplantation (HTX) might enable causative therapy and ultimately improve prognosis. However, previous reports suggested unfavorable survival after HTX in this population compared to HTX recipients with other indications as ischemic or dilative heart disease.

**Methods and results:** Forty-three patients with cardiac amyloidosis (AL n = 29; ATTR n = 14) underwent HTX at the University of Heidelberg Amyloidosis Centre between 2001 to 2015 and were analyzed retrospectively. In all patients with cardiac amyloidosis an exceptional high-urgency (HU) status was requested at Eurotransplant due to extremely poor prognosis. We analyzed the patients in two separate eras: 2001 to 2007 (era 1) and 2008 to 2015 (era 2). The time point separating these two eras was selected because it followed the initial publication of selection criteria for patients with AL amyloidosis undergoing HTX and autologous stem-cell transplantation (ASCT), and because it coincided with more restricted selection of patients as well as significant advances in chemotherapy of AL amyloidosis. Patients were subjected to continuous follow up after HTX in our outpatient clinic and a Kaplan-Meier survival analysis was performed. Both groups (era 1 and 2) were compared to all other patients, who received HTX because of other indications than amyloidosis and who were listed at Eurotransplant in HU status (n = 178). Patient characterization did not reveal significant differences in era 1 compared to era 2 except a lower number of organs affected by amyloidosis ( $1.8 \pm 0.2$  vs.  $1.3 \pm 0.1$ ;  $p < 0.05$ ) in era 2 (2008-2015), reflecting a more restrictive patient selection in this era. However, while patients in era 1 (2001 to 2007) showed impaired survival after HTX compared to the control HU group. Interestingly, in era 2 the survival of amyloidosis patients measured up to the survival of the other HU HTX patients and was significantly improved compared to era 1 amyloidosis HTX patients.

**Conclusions:** HTX in advanced cardiac amyloidosis - either of AL or ATTR type - is a promising approach to allow causative treatment and finally improve poor survival of cardiac amyloidosis patients. Our data demonstrates that HU HTX - for AL combined with subsequent stem cell therapy - offers a successful treatment option to improve the poor outcome of this population. Furthermore, the data demonstrates that outcome of patients improved in era 2 (2008-2015) compared to era 1 (2001-2007). This era effect appears to be related to patient selection restricted to patients with sole cardiac involvement. Our data demonstrates that HTX in advanced cardiac amyloidosis should be restricted to highly selected patients in specialized centres.

## ATRIAL FIBRILLATION

### P1517

#### Atrial fibrillation and heart failure - experience of one hospital center

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**Background:** Atrial fibrillation is a condition frequently associated to heart failure. It is responsible for acute decompensation of heart failure and for thromboembolic complications. Despite good guidelines, therapeutic decision is frequently difficult because of the hemorrhagic risk.

**Purpose:** We present the experience of one hospital center regarding patients with atrial fibrillation with/out heart failure.

**Methods:** We studied a group of patients with atrial fibrillation consecutively admitted to our hospital center during a 6-month period. The evaluation consisted in case history and clinical examination, lab tests and transthoracic echocardiography.

**Results:** The study group consisted in 217 patients, aged 74 ± 9 years, of whom 76% with permanent atrial fibrillation. The prevalence of major cardiovascular risk factors was as follows: arterial hypertension - 80%, dyslipidemia - 43%, obesity - 28%, diabetes mellitus - 34%, smoking - 22%. Thyroid disease was associated in 25% of cases. Heart failure was diagnosed in 86% of patients, with NYHA class III and IV in 75% of cases. Values of NT-proBNP were high irrespective of the presence or absence of heart failure. Higher levels were encountered in permanent versus paroxysmal atrial fibrillation ( $p < 0.01$ ). CHA2DS2-Vasc score had values equal or greater than 2 in 97% of patients, with 68% of patients having values between 4 and 6. Two thirds of patients had HAS-BLED score of at least 3. Anticoagulants were prescribed in 68% of patients (acenocumarol - 46%, NOAC - 22%). 24% of patients were given single antiplatelet therapy, 2% were given dual antiplatelet therapy, whereas no antithrombotic therapy was given in 6% of patients, half of them having CHA2DS2-Vasc scores 0 or 1. 10% of patients experienced hemorrhagic events, with no major hemorrhage encountered. There were no thromboembolic events during the index hospitalization. Echocardiographic evaluation showed preserved left ventricular ejection fraction in 53% of cases, mitral regurgitation in 60%, tricuspid regurgitation in 46% and aortic regurgitation in 24% of cases. All patients survived the index hospitalization. There was a net improvement of NYHA functional class from admission to discharge in patients with heart failure ( $p < 0.01$ ).



**Conclusions:** Heart failure complicates a great proportion of atrial fibrillation cases requiring hospitalization. NT-proBNP level may not be useful for the diagnosis of heart failure in the setting of atrial fibrillation. Anticoagulant therapy should be given to patients with high thromboembolic risk even in the presence of high hemorrhagic risk.

### P1518

#### Recurrent atrial fibrillation in patients with diastolic heart failure, effects of metoprolol and diltiazem on arterial stiffness

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**Objective:** Diastolic heart failure (DHF) is accompanied by increased arterial wall stiffness, as well as long-standing hypertension and atrial fibrillation (AF). From the epidemiological point of view these conditions are closely related. Beta-blockers have lower efficacy in strokes prevention comparing to renin-angiotensin-aldosterone system blockers and amlodipine due to their less reduction of central blood pressure and pulse pressure. There is no data regarding effects of diltiazem on arterial stiffness in DHF patients with AF.

**Aim:** the purpose of this study was to compare parameters of arterial stiffness in AF patients with DHF under metoprolol (M) and diltiazem (D) treatment.

**Methods:** The study included 55 patients (40% men) aged 66 (62; 73) years with mild-to-moderate AH, one year anamnesis of recurrent AF and DHF. Clinical characteristics of M group patients (n=31) and D group patients (n=24) were similar. All patients were performed applanation tonometry before and 3 months after treatment.

**Results:** All baseline hemodynamic parameters were similar in both groups. There was significant reduction of heart rate (HR) in both groups [by 15 bpm in M group,  $p < 0,001$  and by 11 bpm in D group,  $p < 0,001$ ] and SBP [by 18 mm Hg in M group,  $p < 0,005$  and by 15 mm Hg in D group,  $p=0,03$ ], but changes in cSBP were significant only in D group ( $p=0,03$ ). DBP and cDBP decreased significantly in M group by 4 mm Hg in both cases ( $p=0,03$ ). Prolongation of ED was observed in both groups, but changes reached significance only in M group (+35 ms,  $p < 0,001$ ). There were no difference in medians of Alx-HR75, but analysis of  $\Delta$ Alx-HR75 showed opposite changes [+11% in M group and -5% in D group,  $p=0,003$ ]. Both drugs showed PWVcf reduction [from 9,3 (7,5; 12,4) to 7,7 (6,5; 10) m/s in M group,  $p=0,03$ ] and [9,4 (7,1; 10,5) to 9,2 (7,8; 11) m/s in D group,  $p=0,02$ ]. However during follow-up period AF recurrence was similar in both groups: 18 (58%) in M group and 18 (75%) pts in D group ( $p=0,31$ ).

**Conclusion:** Both metoprolol and diltiazem significantly decreased HR, brachial and central BP. Three months follow-up resulted in a significant reduction in arterial stiffness, determined by PWVcf. Despite the favorable effect of diltiazem on the pulse wave contour by reducing Alx-HR75, no difference was observed in frequency of AF recurrence in metoprolol and diltiazem groups.

### P1519

#### Management of antithrombotic therapy in atrial fibrillation of patients with aortic stenosis undergoing transcatheter aortic valve implantation.

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**Background:** Many cardiac patients undergoing transcatheter aortic valve implantation (TAVI) required combined antithrombotic therapy consisting of an anticoagulant and inhibition of platelet function, due to atrial fibrillation. Currently the optimal combination of anticoagulants and anti-platelet therapy is unknown, but it is well established that the combination increased bleeding rates. The aim of this study was to analyze prevalence ischaemic and bleeding events in patients with atrial fibrillation undergoing TAVI in according to management of antithrombotic therapy

**Methods:** A total of 131 consecutive patients with aortic stenosis and atrial fibrillation undergoing TAVI were evaluated, between April 2008 and December 2014.

**Results:** The patients were characterized by had a HAS-BLED score  $2.35 \pm 0.5$ , CHADS2  $3.4 \pm 1.07$  and CHAD2-Vasc score  $5.13 \pm 1.3$ . Six patients (4.8%) were treated in monotherapy with an oral anticoagulant, 4 (3.2%) triple antithrombotic therapy, dual antiplatelet in 42 patients (33.9%) and 72 patients (58.1%) with oral anticoagulant and a thienopyridine. We found differences in mortality in according to antithrombotic therapy: 16.7% vs. 0% vs. 35.7% vs. 13.9%,  $p=0.023$ , respectively, [OR=0.628 (95% CI 0.417-0.946),  $p=0.026$ ]. There were no differences in events 0% vs. 0% vs. 19% vs. 6.9%,  $p=0.172$ , [OR=0.693 (95% CI 0.407-1.181),  $p=0.178$ ]. Of patients treated with oral anticoagulant, 17 received non VKA oral anti-coagulant (NOACs). In patients were treated with an oral anticoagulant, there were differences in events but not in mortality in according to AVK vs. NOACs 2.8% vs. 33.3%, OR=17.5 (95% CI 2.98-102),  $p=0.001$  and 11.1% vs. 20%, OR=2 (95% CI 0.463-8.639),  $p=0.346$ .

**Conclusions:** in this study seems to suggest that treatment with vitamin K antagonist and thienopyridine seems to be the safest therapy after TAVI.

### P1520

#### Heart failure and atrial fibrillation, a tricky par or not so

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**Introduction:** The presence of atrial fibrillation (AF) is common in patients admitted for heart failure (HF), and may even be its decompensation cause. The prognostic impact of HF in patients with AF is well defined, but the opposite relationship remains controversial.

**Purpose:** To evaluate the prognosis impact of AF presence in patients admitted for HF.

**Methods:** We evaluated all hospitalizations for HF in a cardiology unit, for a six years period. Only the first episode of each patient was included. Were divided them into 2 groups: AF group: patient with history of or AF at admission; SR group: patients without AF. In-hospital mortality (IHM) and one year follow-up was used as end-points. Further sub-analysis of in-hospital mortality according to ejection fraction (EF) and admission BNP was carried out.

**Results:** We evaluated 969 admissions, corresponding same number of patients, mean age 77.2 10.1 years, 51.0% male. The overall results and the sub-analysis are presented in table.

**Conclusion:** In this population we did not evidence any immediate nor follow-up prognosis impact of the AF diagnosis in patients admitted for HF. There was even a trend to lower mortality in patients with AF, but those had a theoretically less severe HF. This can translate a lower admission threshold for patients with AF and HF. Given this possible selection bias, it will be difficult to confirm or refute any relationship between FA and the prognosis of patients with HF.

#### Comparison between SR group and AF group

	SR Group	AF Group	
Males	51,1%	51,0%	p=n.s.
Mean age	76,9 y	77,7 y	p=n.s.
EF	47%	51%	p=0,01
BNP admission (pg/mL)	1008	704	p=0,00
IHM	7,6%	6,0%	p=n.s.
12 months readmission	37,1%	36,1%	p=n.s.
12 months mortality	12,3%	11,5%	p=n.s.
EF $\leq$ 35%	N = 112; IHM=4,5%	N = 92; IH=7,6%	p=n.s.
EF 36-54%	n = 141; IHM=4,3%	n = 138; IHM=1,4%	p=n.s.
EF > 55%	n = 156 IHM = 3,8%	n = 228; IHM=3,1%	p=n.s.
EF unknown	n = 37; IHM=45,9%	n = 55; IHM=27,3%	p=n.s.
BNP <400	N = 147; IHM=1,5%	n = 223; IHM=2,2%	p=n.s.
BNP 400-800	n = 108; IHM=6,5%	n = 138; IHM=4,3%	p=n.s.
BNP > 800	n = 180; IHM=10,6%	n = 131; IHM=13%	p=n.s.

### P1521

#### The worse prognosis in patients with new onset atrial fibrillation, acute coronary syndrome and mild left ventricle systolic dysfunction.

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**Background:** Patients with atrial fibrillation (AF) and acute coronary syndrome (ACS) constitute a high-risk population, especially in patients with systolic heart failure. However, the impact of new onset AF on patients with ACS and mild left ventricle (LV) systolic dysfunction remains unclear.

**Aim:** This study was conducted to estimate clinical significance, in-hospital and long-term mortality in patients with acute coronary syndrome, new onset AF and mild LV systolic dysfunction.

**Methods:** We conducted the cohort study, which included consecutive 237 patients with ACS and mild LV systolic dysfunction (EF 41-54%) diagnosed according to the ESC guidelines, hospitalized in the Department of Coronary Heart Disease and Heart Failure in Cracow between January 2008 and June 2010. The exclusion criteria were: valvular heart disease, pericarditis, permanent AF, active thyroid disease and cancer. We divided patients into two groups: 1st group – 36 pts with new onset AF during ACS (15 M, mean age  $73.7 \pm 9,1$ ) and 2nd group – 201 pts without new onset AF during ACS (141 M, mean age  $63,3 \pm 11,1$ ). After the follow-up of 43-73 months we

contacted with 29 (80,5%) pts from 1st group and 157 (78,1%) pts from the 2nd group.

**Results:** In contrary to the pts without AF, pts with new onset AF were characterized by: older age (73.7 vs. 63.3 yrs.,  $p < 0.001$ ), women prevalence (58.3 vs. 29.9 %;  $p < 0.001$ ) and higher heart rate at admission to the hospital (117 vs. 77/min.;  $p < 0.001$ ). During hospitalization in these pts more often were observed renal dysfunction (47 vs. 21 %;  $p < 0.001$ ), in angiography left main coronary disease (17.1 vs. 6.5 %,  $p < 0.001$ ) and in echocardiography LV diastolic dysfunction (93.5 vs. 70.7 %;  $p < 0.001$ ). What is more, in these patients were also significant higher rate of cardiac arrest during hospitalization (16.7 vs. 0.5 %;  $p < 0.001$ ) and in-hospital mortality rate (2.8 vs. 0.0 %;  $p = 0.017$ ). Follow up revealed higher reoccurrence of atrial fibrillation in the AF group (38 vs. 13%,  $p = 0.002$ ) and all-cause mortality rate (22.5 vs. 0.7 %,  $p = 0.007$ ). Stroke-related mortality rate was 3.7 vs. 0.6 % ( $p = 0.157$ ) and cardiovascular-disease related mortality was 3.7 vs. 3.2% ( $p = 0.893$ ).

**Conclusions:** Renal dysfunction, left main coronary disease and left ventricle diastolic dysfunction are comorbidities observed during hospitalization in patient with new onset AF, acute coronary syndrome and mild LV systolic dysfunction. This study revealed that in these patients were also higher in-hospital and long-term mortality.

### P1522

#### The impact of heart failure and left ventricular dysfunction in predicting stroke and thromboembolism in non valvular atrial fibrillation patients treated with direct oral anticoagulants

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**Background:** The CHA2DS2-VASc score does not always accurately assess the thromboembolic risk of the patient suffering from Non Valvular Atrial Fibrillation (NVAF) and, thus, it would be useful to have additional parameters to stratify it. The presence of Heart Failure (HF) has been proposed as a risk factor for stroke and is included in CHA2DS2-VASc score.

**Purpose:** Our objective was to assess the effect of HF and left ventricular dysfunction on the endpoint of stroke or systemic embolism in NVAF patients treated with direct oral anticoagulants.

**Methods:** In a hospital-based population of 169 patients with NVAF treated with DOACs (90 with dabigatran, 65 with apixaban and 14 with rivaroxaban at recommended dose), we evaluated the following variables: CHA2DS2-VASc, presence of HF clinically assessed, left ventricle end-diastolic diameter (LVEDD) and left ventricle ejection fraction (LVEF) both assessed by echocardiography and 1-year incidence of ischemic stroke, TIA or systemic embolism. For statistical analysis we used Spearman's correlation test and point-biserial correlation test.

**Results:** Among 169 patients, the mean age was  $74.2 \pm 9.9$  years and 96 were males. Mean CHA2DS2-VASc was  $3.8 \pm 1.7$ ; 48 patients (28.4 %) had heart failure. Echocardiographic parameters were: LVEDD  $50.9 \pm 7.3$  mm, LVEF  $47.9 \pm 10.3$  %. After 1 year of follow up, 3 patients (1.77 %) had ischemic stroke, TIA or systemic embolism. All 3 patients had HF. A significant correlation between CHA2DS2-VASc and LVEF ( $r = -0.215$ ;  $p < 0.01$ ) was observed; no statistically significant correlation between CHA2DS2-VASc and LVEDD was detected. No significant correlation was found between CHA2DS2-VASc and 1-year incidence of ischemic stroke, TIA or systemic embolism. However, significant correlations between presence of HF, LVEDD, LVEF and 1-year incidence of ischemic stroke, TIA or systemic embolism were observed (respectively  $\rho = 0.25$  and  $p < 0.01$ ,  $\rho = 0.22$  and  $p = 0.01$ ,  $\rho = -0.24$  and  $p < 0.01$ ).

**Conclusion:** The presence of heart failure and echocardiographic data such as left ventricle ejection fraction and left ventricle end diastolic diameter can be useful parameters, in addition to CHA2DS2-VASc score, in thromboembolic risk stratification for the management of therapy with DOACs in patients with NVAF, particularly in CHA2DS2-VASc 1 patients affected by isolated heart failure, in which the indication for anticoagulation is debated. Further studies, with larger number of patients, will be needed.

### P1523

#### SAME-TT2r2 score and quality of anticoagulation in a cohort of elderly heart failure patients with non valvular atrial fibrillation

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**Background/Objectives:** SAME-TT2R2 score (Sex female, Age<60, Medical History-more than 2 comorbidities, Treatment interacting, Tobacco use  $\times 2$  and Race non white  $\times 2$ ) has been proposed as a practical tool based on clinical and demographic criteria, to determine prospectively the patients with Non Valvular Atrial Fibrillation (AF) that will do well or not on Antivitamin K (AVK) treatment. The aim of this pilot study is to determine if this score is useful in our elderly patients with Heart Failure and Non Valvular Atrial Fibrillation

**Patients and methods:** We included prospectively outpatients seen from may 2014 to may 2015, in our Heart Failure Management Unit, with a diagnostic of Non Valvular Atrial Fibrillation (excluding those with prosthetic or significant valvulopathy). Data were recruited prospectively from laboratory and electronic records, and follow up was done in outpatient clinic and by telephone for a minimum of three months, and a maximum of 9. Charlson, CHADS2-VASc, HAS-BLED and SAME-TT2R2 scores were done at inclusion. Time in therapeutic range (TTR) was analysed by Rosendaal method.

**Results:** 60 consecutive patients were included. 55 completed minimum follow up, and 46 (76%) reached maximum follow-up. Mean follow up was 279 days, with a range of 112-334. 2 patients died in follow-up. In 5 cases data were not accessible, and one patient stopped anticoagulation because of major hemorrhage. In all patients antivitamin K used was acenocumarol. Mean age was 80<sup>9</sup> (57-90), and 38 (63%) were women. Mean Charlson Score was 2<sup>83</sup> (rank 1-5), mean CHADS2-VASc score was 5.48 (range 2-7), and mean HAS-BLED was 3.67 (range 2-6). 34 patients (61%) were below 65% of Time in Therapeutic Range (TTR) measured by Rosendaal method (rank 14-88%). Mean SAME-TT2R2 was 2.08, (rank 1 - 5). 42 patients (76%), had a SAME-TT2R2 over 2 points, and 13 (24%) patients had a SAME-TT2R2 score of 1 point. Patients with a SAME-TT2R2 score of 1 are slightly younger (78.5 vs 81<sup>6</sup> years,  $p = 0<sup>14</sup>$ ), with lower CHADS2-VASc and HAS-BLED scores (5 vs 5<sup>6</sup>, and 3<sup>2</sup> vs 3<sup>8</sup>,  $p = 0<sup>11</sup>$  and 0<sup>08</sup> respectively, ns), and 53% of them were on adequate TTR > 65%, with a mean time in Therapeutic range of 63,8% ; patients with a SAME-TT2R2 score over 2 points, were slightly older, had higher CHADS2-VASc and HAS-BLED scores and only 33% of them were > 65% of TTR ( $p = 0.18$ ), with a mean TTR of 60<sup>07</sup>%. 61,8% of women were <65% of TTR, in contrast with 38,2% of men ( $p = 0.08$ )

**Conclusions:** as described, it is difficult to achieve an adequate TTR > 65% in elderly patients with Non Valvular Atrial Fibrillation and Heart Failure, even in low SAME-TT2R2 scores, and it has to be carefully monitored. Two thirds of elderly patients with SAME-TT2R2 score over 1 point (which are usually older women and have higher CHADS2-VASc, and HAS BLED scores) will not reach a correct target of TTR > 65% on AVK, so we must consider the use of Direct Oral Anticoagulants specially in this patients.

### P1524

#### Comparing prognostic role of atrial fibrillation in predominantly HF elderly patients with HFrEF and HFpEF in community setting.

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**Background:** Information on comparative prognostic impact of atrial fibrillation (AF) in patients with HFpEF compared with HFrEF is still controversial.

**Objectives:** To compare prognostic contributor of AF according to CHADS2-VASc and comorbidity burden in EF-HF phenotypes (LVEF < 50% - HFrEF, LVEF  $\geq 50\%$  - HFpEF) in a community-based population.

**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:** The study population comprised 2314 HF patients (mean age  $78 \pm 8$ , 57% men). Of these: 941 (41 %) patients with LVEF < 50% were identified as HFrEF; 1373 (59%) patients as HFpEF. The high mean age, comorbidity rates (mean  $3.2 \pm 2.5$ ) and CHA2DS2-VASc ( $4.1 \pm 1.2$ ) were similar between EF-HF phenotypes. In overall population, there was a high prevalence of chronic AF (55%). At a follow-up of  $28 \pm 14$  months, 472 (20%) patients died. AF was associated with higher mortality rates (HR 1.7 [IC 1.2-1.9];  $p = 0.001$ ), HF hospitalization (HR 1.4 [IC 1.3-1.7];  $p < 0.001$ ) and all-cause hospitalization (HR 1.9 [IC 1.3-2.6];  $p < 0.001$ ), contributing to a higher hazard of mortality and morbidity in HFpEF vs HFrEF ( $p = 0.001$  for interaction test). After adjustment for all univariable predictors, including CHA2DS2-VASc and comorbidity burden, AF remained independently associated with high mortality and morbidity.

**Conclusion:** In real-world HF population, AF contributed significantly to worse outcome in overall population irrespective CHADS2-VASc and comorbidity with higher prognostic impact in patients with HFpEF compared to HFrEF. These observations suggest that in community-based HF population aggressive management of AF may have a great impact in patients with HFpEF.

### P1525

#### Restoration of sinus rhythm in patients with acute heart failure and atrial fibrillation

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**Background:** Atrial fibrillation (AF) is frequent in acute heart failure (AHF) and associated with poor outcome among patients with AHF. However, little is known about restoration of sinus rhythm in patients with AHF and AF.

**Methods:** From the Korean Acute Heart Failure (KorAHF) registry, a prospective multicenter cohort for consecutive patients who were admitted for AHF, those with AF during hospitalization and available electrocardiogram at discharge were extracted.

**Results:** Among 1,420 patients who had AF during AHF hospitalization, 368 (18.5%) patients were restored sinus rhythm at discharge. Sinus rhythm were spontaneously restored in 126 (34.2%) of 368 patients, 196 (53.3%) patients underwent the pharmacological conversion, and 46 (12.5%) underwent the electrical conversion. Among three groups, Electrical conversion group showed lower systolic blood pressure and higher heart rate than spontaneous and pharmacologic conversion group at admission. Otherwise, there was no significant difference by method for the restoration of sinus rhythm. Patients with sinus rhythm at discharge (SC group) were more likely to be newly developed AF during hospitalization than patients with AF at discharge (AF group) (72.5% vs. 35.2%,  $p < 0.001$ ). A history of heart failure was more common in AF group (46.4% vs. 31.8%,  $p < 0.001$ ). The etiology of AHF was different between two groups. Ischemic cardiomyopathy was more common in SC group than in AF group (41.8% vs. 19.8%,  $p < 0.001$ ). The proportion of HF with reduced ejection fraction (EF) versus preserved EF was not significantly different between two groups. The mean left atrial (LA) diameter was greater in AF group than in SC group ( $52.3 \pm 8.5$  vs.  $45.9 \pm 8.9$  mm,  $p < 0.001$ ). In multivariate logistic regression, sinus conversion during hospitalization was associated with new-onset AF (OR 2.41, 95% CI 1.63-3.57,  $p < 0.001$ ), ischemic etiology (OR 1.61, 95% CI 1.22-2.13,  $p = 0.001$ ), and LA diameter (OR 0.927, 95% CI 0.91-0.94,  $p < 0.001$ ). Area under the curve of LA diameter for predicting sinus rhythm restoration was 0.702 (95% CI 0.670-0.734,  $p < 0.001$ ) and baseline LA diameter 48.25mm showed optimal predictive value.

**Conclusion:** The restoration of sinus rhythm in patients with AHF and AF was associated with new-onset AF, ischemic cardiomyopathy and smaller LA size. Further investigation will be needed to establish the strategy of restoration of sinus rhythm in AF patients with AHF.

#### P1526

##### Presence of atrial fibrillation worsens prognosis in patients with myocardial infarction.

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**Background:** Atrial fibrillation (AF) is the most common sustained arrhythmia as is an independent risk factor for myocardial infarction (MI). Some studies associated AF to worse prognosis in patients with MI.

**Aim:** This study aims to understand the impact of AF in the prognosis of patients with MI.

**Methods:** Selected patients admitted with MI in a coronary unit from 2007 to 2014. Collected clinical, analytical, echocardiographic and angiographic data. The patients were divided in two groups according to the presence of AF. A one year follow up was performed. Statistical analysis in SPSS 20.

**Results:** In the sample ( $n = 1500$ ) 70,1% were males. The mean age was  $69,1 \pm 12,9$  years and higher in the AF group (67,6 vs 77,3 years,  $p < 0,001$ ). The patient with STEMI were 43,4% and the patient with NSTEMI were 56,6%. The AF was associated with lower systolic (141,4 vs 132,7mmHg,  $p < 0,001$ ) and diastolic (82,7 vs 76,7mmHg,  $p < 0,001$ ) pressure and higher Killip class at admission (1,33 vs 1,76,  $p < 0,001$ ) and maximum Killip class (1,62 vs 2,32,  $p < 0,001$ ).

Blood analysis showed increased levels of creatinine ( $1,27$  vs  $1,37$ mg/dL,  $p = 0,009$ ) and C-reactive protein ( $2,12$  vs  $3,46$ mg/dL,  $p < 0,001$ ) in patients with AF as well as lower haemoglobin ( $14,1$  vs  $13,4$ g/L,  $p < 0,001$ ). Although there was no difference in the troponin between the groups, the patients with AF had higher BNP levels ( $812,9$  vs  $401,9$ pg/mL,  $p < 0,001$ ). The ejection fraction was lower in patients with AF (54,95% vs 50,91%,  $p = 0,005$ ). There was no difference in angiographic parameters ( $p = 0,07$ ). AF led to longer hospitalization (7,06 vs 9,20 days,  $p < 0,001$ ) increase risk of complications (29,8% vs 39,2%,  $p = 0,008$ ), and increased mortality during hospitalization (6,7% vs 11,4%,  $p = 0,022$ ). AF worsen prognosis after discharge with higher cardiovascular event rate (27,8% vs 42,9%,  $p < 0,001$ ), stroke rate (0,9% vs 4,2%,  $p = 0,001$ ) and higher mortality (2,8% vs 11,8%,  $p < 0,001$ )

**Conclusions:** This study showed that previous AF significantly worsen prognosis in patients with STEMI, increasing the risk of heart failure, complications and death during hospitalization, as well as stroke, cardiovascular event or death during the follow up.

## ATRIAL FIBRILLATION

#### P1527

##### Pseudo-coronary scenario of inflammatory viral cardiomyopathy

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Cardiomyopathy is one of the most severe and complicated cardiovascular diseases which leads to development of acute and chronic heart failure. The progress in molecular biochemistry and genetics allows to significant enhancement of its diagnostics. New data has confirmed that cardiomyopathies represent a complex nosological structure. The establishment of diagnosis demands a close attention of clinicians and necessity to go beyond the usual diagnostics schemes.

The purpose of the article is to show a clinical case of pseudo-coronary scenario of inflammatory viral cardiomyopathy. We described the unexpected case of a 50-year-old woman, with medical history of ischemic heart disease, who was admitted to the intensive care unit complaining of chest pain, dyspnea and fatigue. Clinically, we saw signs of pulmonary edema, atrial fibrillation with left bundle branch block, impairment of left ventricular function with progressive increase of myocardial necrosis biomarkers. Clinical findings were evaluated as acute coronary syndrome. The patient underwent percutaneous coronary angiography which had showed absence of coronary atherosclerosis. Following verification of diagnosis was accomplished using routine, as well as modern imaging technologies, including cardiac magnetic resonance imaging, 2D-speckle tracking echocardiography, endomyocardial biopsy with immunohistochemical analysis. As a result, the diagnosis of inflammatory viral dilated cardiomyopathy was established.

Our clinical case example shows that in spite of the experience, in routine practice the diagnostics of cardiomyopathy is still a difficult and time-consuming task and its success depends on the specialists' coordinated work. Non-invasive heart imaging, such as echocardiography and magnetic resonance image retain their value in routine clinical practice. The implementation of endomyocardial biopsy significantly expands our ability to detect inflammatory cardiomyopathy, and immunohistochemical analysis allows us not only to identify and characterize the cells of the inflammatory infiltrate, but also to identify a number of infectious agents, particularly -viruses. In this clinical case example we want to attract attention to the fact that the establishment of diagnosis and therapy prescription of such complex group of diseases demands all our accumulated knowledge, available resources of diagnostics and treatment, as well as adjustment of patients to treatment compliance and the follow-up importance.

#### P1528

##### Increased mortality is associated with proof of perforin-positive cardiac cell infiltration and male gender in a large cohort of patients with inflammatory cardiomyopathy

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**Aims:** We analysed possible influence of perforin-dependent infiltration upon long-term mortality in patients with inflammatory cardiomyopathy (CMI).

**Background:** We previously demonstrated that left ventricular function deteriorates and progresses to substantial cardiac dysfunction in patients with perforin-positive myocardial cell infiltration.

**Methods and Results:** Between 2003 and 2013, 2389 consecutive patients with clinically suspected CMI who underwent endomyocardial biopsy (EMB) were enrolled. EMBs were performed at first admission after exclusion of ischemic of valvular heart disease, and CMI was confirmed in 1717 patients. Follow-up was up to 10.0 years (mean  $17.8 \pm 25.4$  months) and information on vital status was obtained from official resident data files. Multivariable statistical analysis was conducted for all CMI patients regarding significant predictors of all-cause mortality or need for heart transplantation (HTX). Multiple Cox regression analysis revealed perforin above the calculated the cut off point of  $2.9/\text{mm}^2$  as a strong predictor of impaired survival with hazard ratio (HR) of 1.881, 95% confidence interval (CI) 1.177-3.008,  $p = 0.008$ , independent of LV function and other myocardial inflammation markers (CD3, Mac-1, LFA-1, HLA-1, and ICAM-1). Unexpectedly, male sex emerged as another strong adverse predictor of survival in CMI (HR 1.863, CI 1.096-3.168,  $p = 0.022$ ). Whereas LVEF course is adversely affected by myocardial perforin, multivariate analysis indicates that LVEF explains only part of the observed overall mortality.

**Conclusion:** Perforin-positive cardiac cell infiltration and male gender are interacting adverse predictors of long term-mortality in CMI, independent of LV function and other myocardial inflammation markers. Furthermore, exact quantification of immune cells is necessary to assess the prognosis.



**P1529****Predictor of stress induced cardiomyopathy in critically ill pneumonia patients.**

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**Introduction:** Stress induced cardiomyopathy (SIC) is caused by stressful situation such as not only emotional but also serious medical illness. SIC sometimes occurs after pneumonia and it worsens the prognosis of pneumonia, but the predictor of SIC after pneumonia is unknown.

**Method and Result:** We selected consecutive 13 patients with SIC after pneumonia and age and sex matched 38 patients who received ICU care with pneumonia without SIC from 2013. Mean age was 72.3 ± 12.3 and 72.4 ± 14.2 years in each SIC and non-SIC group (p = 0.971). There were no significant between-group differences in the rates of male, diabetes, hypertension, stroke, and cancer. There was no significant difference in WBC count between 2 groups. Troponin T was significantly higher. (0.48 ± 0.47 vs. 0.05 ± 0.03 ng/ml, p = 0.011) Serum sodium level was higher in SIC (140.9 ± 6.8 vs. 135.7 ± 5.2 mmol/L, p < 0.01) but both were in normal ranges. Hemoglobin and Hematocrit level were significantly lower in SIC group (10.7 ± 1.2 vs. 11.8 ± 2.2 g/dl, 31.8 ± 3.8 vs. 35.0 ± 6.5% all p < 0.05).

**Conclusion:** In critically ill pneumonia patients anemia might be a risk factor or predictor for progression to SIC. Other cardiovascular risk factor and history of stroke or cancer did not affect the rate of SIC from pneumonia.

**P1530****Heart failure is the most frequent complication in a portuguese population of left ventricular non-compaction cardiomyopathy - a multicenter study**

Bial, Medinfa, MSD, Trigénis  
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**Introduction:** Left ventricular non-compaction cardiomyopathy (LVNC) has great morphologic variability, and its clinical features and prognosis are also variable. It is known that it 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 86 patients with LVNC, 57% males, with mean age 51 ± 19 years. Symptoms were present at diagnosis in 61,6% of patients, and dyspnea (37,2%) and palpitations (30,2%) were the most common symptoms. The most frequent initial clinical presentation was heart failure (30,2%), followed by arrhythmia (15,1%) and embolic events (8,1%). Only 2,3% had episodes of syncope prior to diagnosis. Diagnosis was established by echocardiogram in 80,2% of patients. The average LV ejection fraction was 48 ± 16%, with 25% of the patients having an ejection fraction < 35%. There were criteria for diastolic dysfunction in 49% of the patients, with grade I in 39,9%, grade II in 33,3% and grade III in 27,8%. The average LV end-diastolic diameter was 56mm, with 25% having a diameter > 60mm. Most patients were in sinus rhythm (89%). A history of atrial fibrillation was present on 11,9% of the patients, supraventricular tachycardia in 15,3% and non-sustained ventricular tachycardia in 22% of the cases. Family history of LVNC was identified in 8,1% of cases.

In the medium term (mean follow up of 3,4 years), patients with LVNC presented heart failure in 30%, arrhythmia in 14%, embolic events in 6% and death in 4,7% of cases.

**Conclusions:** In this Portuguese population of patients with LVNC, heart failure was present in about one third of the cases and was the most frequent clinical complication in the medium term follow up. The presence of systolic and diastolic dysfunction and LV dilation was frequent in these patients.

**P1531****Analysis of death dynamics in patients with peripartum cardiomyopathy**

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**Objective:** Analysis of the dynamics of deaths in patients with peripartum cardiomyopathy (PCM) with long-term of observation.

**Material and Methods:** We observed 50 patients suffering from PCM, aged from 20 to 41 years (mean age 28,2 ± 0,8 years). The study of the dynamics of the disease lasted from 3 to 175 months (mean 67,4 ± 5,4 months). Complex examination included an electrocardiogram, HMECG, echocardiogram, and 6-minute walking test definition of functional class (FC) of heart failure (HF) by NYHA. Repeated contact with patients or relatives held each year.

Results of the study. Depending on the outcome of the disease retrospectively, all patients were divided into 2 groups. The first group comprised 17 patients with PCM who died in the period from 3 to 131 months of observation (36,6 ± 7,2 months.). The second group consisted of 33 patients who survived during the 31 to 175 months (average 83,1 ± 5,7 months; p < 0.001) surveillance. The study of the dynamics of the disease found that in a group of survivors of the 12-month standard therapy of CHF were complete recovery of left ventricular function (LVEF increase of more than 55%) was noted in 19 (38%) cases. As noted above, the cumulative mortality at 67.4 ± 5.4 months was 34% (n = 17). This death in the first year follow-up was 8% (n = 4), (3 deaths due to progression of heart failure, one case developed pulmonary embolism). During the second year of follow another 3 patients died (in one case, death occurred suddenly, in 2 cases - the progression of heart failure). As a result, the cumulative mortality was 14% (n = 7). During the third year of follow marked another 4 deaths due to progression of heart failure (22%). On 4 and 5 years of observations recorded 2 cases of deaths and then another 2 cases from PCM, respectively, due to the growth of HF (30%). Subsequently, in 2 cases death was observed due to the SD (34%). It should be noted that the four (8%) of the patients survived for more than 10 years, 12 (24%) - from 7 to 9 years, 11 (22%) - from 5 to 6 and 8 (16%) - survived for more than 4 years.

**Conclusions:** Thus, analysis of the dynamics of mortality in patients with peripartum cardiomyopathy showed that the maximum adverse outcomes (30%) observed in the first 5 years of observation, with the leading cause of death (26%) had progressive heart failure. At the same time against the background of optimal drug therapy, patients' life prognosis with PCM favorable, and in 38% cases, accompanied by a complete recovery of left ventricular function.

**P1532****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 10 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 192 patients with TC. During the hospital stay (7.1 ± 6.2 days), cardiogenic shock occurred in 7.8% of patients. Other complications: heart failure (24%), atrial fibrillation (8.9%), acute pulmonary edema (4.2%), complete AV block (2.6%), ventricular tachycardia (VT) (2.1%), LV thrombus (1.6%), stroke / AIT (1.6%), and death (2.1%). In patients with TC, the factors associated with the occurrence of cardiogenic shock were the history of heart failure (14.3% vs 1.4%, p = 0.004), chronic renal failure (23.1% vs 6.4%, p = 0.033), the clinical presentation with dyspnea (53.8% vs 25.3%, p = 0.027), bifascicular block in ECG (6.7% vs 0.6%, p = 0.025), the in-hospital occurrence of complete AV block (13.3% vs 1.7%, p = 0.007). In the multivariate analysis, history of heart failure (p = 0.037), chronic renal failure (p = 0.006), the clinical presentation with dyspnea (p = 0.036), the in-hospital occurrence of complete AV block (p = 0.001) were identified as independent predictors of the occurrence of cardiogenic shock during hospitalization of patients with TC.

**Conclusion:** In this Portuguese multicenter study an history of heart failure, chronic renal failure, the clinical presentation with dyspnea and the in-hospital occurrence of complete AV block were identified as independent predictors of cardiogenic shock in patients with TC.

## P1533

**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 10 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 heart failure and then conducted a multivariate analysis to establish the independent predictors of heart failure in patients with TC.

**Results:** We included 192 patients with TC. During the hospital stay ( $7.1 \pm 6.2$  days), cardiogenic shock occurred in 7.8% of patients. Other complications: heart failure (24%), atrial fibrillation (8.9%), acute pulmonary edema (4.2%), complete AV block (2.6%), ventricular tachycardia (VT) (2.1%), LV thrombus (1.6%), Stroke / AIT (1.6%), and death (2.1%). In patients with TC, the factors associated with the development of heart failure were the history of heart failure (10.8% vs 0%,  $p < 0.001$ ), chronic renal failure (21.6% vs 3.4%,  $p < 0.001$ ), the clinical presentation with dyspnea (59.5% vs 16.5%,  $p < 0.001$ ), complete AV block (8.7% vs 0.7%,  $p = 0.003$ ) and worse LV ejection fraction ( $37.0 \pm 11\%$  vs  $45.7 \pm 9\%$ ,  $p < 0.001$ ). In the multivariate analysis, chronic renal failure ( $p = 0.012$ ), the clinical presentation with dyspnea ( $p = 0.002$ ), complete AV block ( $p = 0.028$ ) and worse LV ejection fraction ( $p = 0.003$ ) 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. Chronic renal failure, the clinical presentation with dyspnea, complete AV block and worse LV ejection fraction were identified as independent predictors of the heart failure during hospitalization of patients with TC.

## P1534

**Heart failure during hospitalization is associated with takotsubo cardiomyopathy recurrence at follow-up: a portuguese multicenter study**

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**Introduction:** 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.

**Aim:** 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 10 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 192 patients with TC with a mean follow up of  $45 \pm 32$  months. Recurrence of TC was diagnosed in 4.7% of cases. The following factors were associated with recurrence of TC: chronic renal failure (33.3% vs 6.8%,  $p = 0.018$ ), the presence of ST-segment depression in the initial ECG (22.2% vs 4.9%,  $p = 0.029$ ) and the occurrence of HF during hospitalization (54.4% vs 23.0%,  $p = 0.040$ ).

**Conclusion:** Chronic renal failure, ST-segment depression in the initial ECG and occurrence of HF during hospitalization were associated with recurrence of TC.

## P1535

**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.

**Purpose:** To identify predictors of heart failure in patients with LVNC.

**Methods:** A Portuguese multicenter study involving 10 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 86 patients with LVNC. Heart failure was present in 30.2% of patients. In patients with LVNC, the factors associated with the development of heart failure were older age ( $60 \pm 18$  vs  $48 \pm 18$  years,  $p = 0.004$ ), presence of symptoms on diagnosis (84.6% vs 31.7%,  $p < 0.001$ ), higher LV end-diastolic diameter ( $61 \pm 7$ mm vs  $53 \pm 8$ mm,  $p < 0.001$ ), lower LV ejection fraction ( $37 \pm 12\%$  vs  $54 \pm 16\%$ ,  $p < 0.001$ ), diastolic dysfunction (78.6% vs 34.5%,  $p = 0.007$ ), mitral valve regurgitation (53.8% vs 21.7%,  $p = 0.003$ ), late gadolinium enhancement in cardiac magnetic resonance (36.4% vs 11.9%,  $p = 0.021$ ), left bundle branch block (24.0% vs 3.3%,  $p = 0.003$ ) and bifascicular block (8% vs 0%,  $p = 0.027$ ).

Patients with LVNC and heart failure have higher frequency of ventricular tachycardia in 24h-Holter (43.8% vs 14%,  $p = 0.014$ ) and there was only one sudden death in the 3.4 years of follow up.

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 older age, the presence of symptoms on diagnosis, higher LV end-diastolic diameter, lower LV ejection fraction, diastolic dysfunction, mitral valve regurgitation, late gadolinium enhancement in cardiac magnetic resonance and left bundle branch block or bifascicular block in ECG. Patients with LVNC and heart failure had a higher frequency of ventricular tachycardia and sudden death in the follow-up.

## P1536

**Myotonic dystrophy - must we bother for the heart?**

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**Background:** Myotonic dystrophy is the most common hereditary neuro-muscular disorder. Cardiac involvement may also be present.

**Purpose:** The purpose was to look for the presence, type and frequency of cardiac involvement in patients with Myotonic dystrophy type 1.

**Patients and methods:** We evaluated 37 patients (22 women) at mean age  $38.4 \pm 13.4$  years. A clinical exam, ECG, Holter ECG and transthoracic chocardiology were performed.

**Results**

Rhythm and conduction disturbances were found in 59,5% of the patients. Most common findings were A-V block 1st degree in six patients (16,2%), wide QRS complex ( $> 100$  ms) in 18 patients (48,6%) – LBbB in 3 patients, RBbB in 5 and impaired intraventricular conduction in 10 patients. In one patient with A-V block 3rd degree permanent pace maker was implanted. Atrial fibrillation was registered in 2 patients. In four (10,8%) patients repolarization abnormalities were registered. The other findings were left ventricular systolic dysfunction in 3 patients (8,1%) and in 11 (29,7%) – diastolic dysfunction. Right ventricular abnormalities were not detected.

**Conclusion:** The most common findings were rhythm and conduction disturbances. Heart failure symptoms were not present despite the presence of myocardial dysfunction. Cardiologist must be aware of the cardiac manifestations of the disease in order to follow and treat the patients properly.

## P1537

**Genotype-phenotype correlation in cardiac mutated transthyretin amyloidosis (m-ATTR)**

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**Background:** Despite a remarkably similar echocardiographic (or MRI) presentation, the prevalence of some findings such as low peripheral ECG voltages or the extent of serum cardiac biomarker increase, as well as overall prognosis, are quite different when comparing light-chain (AL) vs. mutated transthyretin (m-ATTR) cardiac amyloidosis, overall survival being much worse in cardiac AL. However, since cardiac m-ATTR may be caused by at least 100 different TTR mutations, potential genotype-phenotype correlations should be taken into consideration in order to properly compare these two different aetiologies of cardiac amyloidosis.

**Objective and Methods:** Genotype-phenotype correlations were evaluated by comparing NT-proBNP release and systo-diastolic function in 173 cardiac AL and 102 cardiac m-ATTR patients at diagnosis. Patients with renal dysfunction (MDRD-estimated glomerular filtration rate < 60 mg/dl) were excluded. Survival was assessed over a median follow-up of 38.9 months (range, 19-75 months).

**Results:** Despite lower left ventricular mass index (LVMI, an index of the extent of cardiac amyloid deposition) [174(138-195) vs. 196(156-145) g/m<sup>2</sup>, median(IQ range),  $p < 0.001$ ], cardiac AL was characterised by a 6-fold higher serum NTproBNP level [5931(2330-11957) vs. 994(564-2328) pg/ml,  $p < 0.001$ ], associated with a more severe extent of diastolic dysfunction [(E/E' ratio: 10.1 (6.7-13.7) vs. 8.4 (6.0-11.2),  $p < 0.02$ ] and comparable systolic function and global longitudinal strain. When subdividing cardiac m-ATTR patients according to the different genotypes, serum NT-proBNP levels were remarkably different among the 23 observed TTR mutations. When compared with LVMI-matched cardiac AL patients, Ile68Leu and Val122Ile patients ( $n = 13$  and  $n = 6$ , respectively) had superimposable NTproBNP levels [4795(1821-8889) pg/ml,  $p = ns$  vs. AL] associated with a comparable extent of systolic and diastolic dysfunction. In contrast, NT-proBNP levels were remarkably lower in Val30Met and Glu89Gln ( $n = 28$  and  $n = 20$ ) patients ([718(446-1287) pg/ml,  $p < 0.01$  vs. AL]), who had higher midwall fractional shortening, longitudinal systolic shortening and global strain, associated with lower E/E' ratio, compatible with a much more preserved systolic and diastolic function. Prognosis was remarkably different, Val30Met and Glu89Gln patients having a much better survival than AL, Ile68Leu and Val122Ile patients ( $p < 0.01$ ).

**Conclusions:** In cardiac m-ATTR, the extent of NT-proBNP release is critically dependent on the TTR-related amyloid type, Ile68Leu and Val122Ile being remarkably more toxic than Val30Met and Glu89Gln mutations at comparable extent of amyloid deposition. Such a higher toxicity also translates into a worse prognosis, survival in Ile68Leu and Val122Ile mutations being comparable with cardiac AL amyloidosis.

### P1538

#### Influence of triggering events on the clinical course of takotsubo cardiomyopathy

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**Purpose:** Tako-tsubo cardiomyopathy (TTC) is frequently preceded by emotional or physical stress. In a large registry, this study evaluated the influence of triggering events on the manifestation and the clinical course of TTC.

**Methods:** From 37 heart centres, 324 pts (296f, 28m, age  $68 \pm 12$ ) were included in a registry according to the following criteria: 1) acute chest symptoms, 2) ischemic ECG changes, 3) reversible LV akinesia not corresponding to a single coronary artery territory, 4) absence of coronary artery stenoses >50%. All pts were asked if a stressful event preceded TTC onset.

**Results:** A trigger event was identified in 77%. Emotional stress was reported by 117 (36%) and physical stress by 104 pts (31%). A combination of both stress modalities felt to be equal was reported by 29 pts (9%). In 74 pts (23%) no trigger could be identified. The four groups were compared by analysis of variance.

Age was similar in all groups. Physical stress was more frequent in males (57% vs 30%,  $p = 0.005$ ) whereas emotional stress or no identifiable trigger were more prevalent in women. Pts with emotional stress as compared with physical, both or no stress more frequently complained about angina (94% vs 57% vs 59% vs 64%,  $p < 0.0001$ ) and less frequently about dyspnea (3% vs 24% vs 34% vs 15%,  $p < 0.0001$ ). There was a trend towards a longer prehospital delay with emotional than with physical stress ( $8.9 \pm 7.4$  vs  $6.9 \pm 7.3$  hours,  $p = 0.05$ ). Heart rate after symptom onset was lower with emotional than with physical stress ( $81 \pm 18$  vs  $93 \pm 26$ /min,  $p = 0.007$ ). The QTc interval was longer in emotional stress as compared to pts without a triggering event ( $513 \pm 61$  vs  $486 \pm 59$  ms,  $p = 0.03$ ). Other ECG parameters, cardiac markers, LV ejection fraction and complications in the clinical course were similar in all groups.

Since pulmonary disease often is the physical trigger for TTC, a pre-medication with betamimetics was more frequently seen in pts with physical stress (18%) or both stress modalities (31%) than in pts with emotional (2%) or no stress (0%),  $p < 0.0001$ . During the acute phase pts without a trigger more frequently required catecholamines (12% vs 0% vs 6% vs 5%,  $p = 0.009$ ) or intraaortic balloon pumping (4% vs 0%,  $p = 0.03$ ) than pts with stressful events.

**Conclusion:** Pts with emotional stress triggering TTC frequently complain about angina, have a longer prehospital delay and a lower heart rate. Due to pulmonary disease pts with physical or both stress forms more frequently have dyspnea and a pre-treatment with betamimetics which may play a pathophysiological role in TTC. Pts without a trigger have a more severe clinical course.

### P1539

#### Effects of hypoxic adaptation on the endothelial dysfunction in the ischemic cardiomyopathy patients

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**THE PURPOSE** of this research was to estimate the influence of normobaric intermittent hypoxia adaptation (NIHA) on the endothelium functional (EF) state in the ICMP patients.

**Materials and Methods:** We studied 50 ICMP patients ( $57.01 \pm 1.38$  years) with depressed left ventricle (LV) systolic function less than 35% and CHF class II-IV NYHA treated with the 10-days NIHA course against CHF drug management with no significant differences. EF state was assessed by endothelium-dependent flow-mediated vasodilation (FMD) as measured by using ultrasonography of the brachial artery with reactive hyperemia test. We also analysed the changes of the biochemical ETd markers levels, such as endothelin-1 (ET-1, pg/ml), tumor necrosis factor-alpha (TNF- $\alpha$ , ng/ml), homocysteine (HCY,  $\mu$ mol/l), brain natriuretic peptide (BNP, pg/ml).

**Results:** The initial CHF severity was determined by depressed LV contractile function against maladaptive LV remodeling, multiple myocardial perfusion defects and the presence of ETd with the high level of the biochemical ETd and CHF markers. We marked the reduction of endothelium-dependent vasodilatation. After the 10-days NIHA course we revealed significant changes in the EF state. The number of the patients with normal endothelium-dependent FMD increased from 28,57% to 60% ( $p < 0,05$ ) and the number of vasoconstrictor reactions decreased from 29% to 6%. We noted the increase in the endothelium-depend FMD from  $4,09 \pm 1,49$  to  $9,42 \pm 1,11$  ( $p < 0,05$ ). The concentration of ET-1 after NIHA decreased from  $2,04 \pm 0,23$  to  $1,03 \pm 0,14$  ( $p < 0,05$ ), TNF- $\alpha$  from  $19,59 \pm 2,67$  to  $10,43 \pm 3,28$  ( $p < 0,05$ ), HCY - from  $15,46 \pm 0,90$  to  $11,77 \pm 0,73$  ( $p < 0,05$ ). The EF state improvement reflected on the clinical CHF course. The BNP concentration decreased from  $612,20 \pm 136,19$  to  $399,79 \pm 139,16$  ( $p < 0,05$ ).

**Conclusion:** The use of NIHA helps to improve the EF state and provides a more favorable course of the main pathological process in the ICMP patients with CHF thus allowed to assume a more adequate protection from early cardiovascular events.

### P1540

#### Clinical outcome of peripartum cardiomyopathy-a study in a tertiary cardiac hospital

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**Background:** Peripartum cardiomyopathy is an idiopathic serious heart failure of last month of pregnancy or the first 5 months of puerperium in absence of any determinable heart disease. Echocardiographic criteria was added with the definition later which include left ventricular ejection fraction < 0.45 or M-mode fractional shortening <30% (or both) and end-diastolic dimension > 2.7cm/m<sup>2</sup>. The incidence is high in developing country than others. Patients deteriorate very rapid but there is also probability of spontaneous recovery. Risk factors include multiparity, advanced maternal age, multiple pregnancies, pre-eclampsia, chronic hypertension, smoking, alcoholism and malnutrition. Conventional heart failure therapies-diuretic, Selective Beta-blocker (BB), Angiotensin converting enzyme inhibitor (ACEI) or Angiotensin receptor blocker (ARB) and anticoagulant are the treatment of choice.

**Purpose:** To study the clinical profile, to analysis of pregnancy outcomes of the cardiomyopathy pregnant women, treatment protocol and follow up after treatment and prognosis.

**Methods:** 72 patients admitted with peripartum cardiomyopathy from July 2009 to June 2014 in a tertiary cardiac hospital of a developing country, were considered for this retrospective study by inclusion and exclusion criteria. They have treated with diuretic, BB, ACEI or ARB, vitamin B complex and anticoagulant who had thromboembolic manifestation. Patients were regularly followed up clinically and by electrocardiogram and colour doppler echocardiography.

**Results:** Primiparous are 28 (39%) of the total study population. 52 patients (72%) were clinically improved and 34 (48%) the left ventricular functional status returned to normal with the treatment. 12 cases (15%) developed persistent cardiomyopathy that is persistent left ventricular dysfunction beyond six months of presentation. 10 women (14%) presented with thromboembolic events and anticoagulant were prescribed for life long for secondary prevention. Maternal mortality was 8(13%). Among



all live births, 4 had intra uterine growth retardation and another 3 had died during the neonatal period.

**Conclusion:** The patients of peripartum cardiomyopathy were improved symptomatically and prognosis was good with the treatment of diuretic, selective BB, ACEI or ARB and vitamin B complex. Regular clinical follow up with echocardiography and monitoring of INR are advised if the patients on anticoagulant to reduce the morbidity and mortality. Further study is needed whether Vitamin B complex may has any role to improve the prognosis of peripartum cardiomyopathy.

**P1541**

**Peripartum cardiomyopathy: case series and follow up, a single center experience**

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**Background and aim:** Peripartum cardiomyopathy (PPCM) is a pregnancy related myocardial dysfunction characterized by the development of heart failure without underlying cause. It has been associated with considerable morbidity and mortality but full recovery is a possibility. Our aim is to study women admitted with PPCM to our hospital and follow their outcomes.

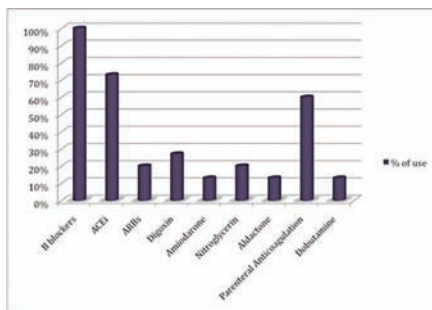
**Methods:** We prospectively collected demographic, clinical, echocardiographical and basic biochemical data for women admitted with PPCM for period of January 2010 till December 2015. PPCM was diagnosed if heart failure confined to time of last month of pregnancy and 5 months after delivery without defined cause. Follow up data for recovery of myocardium and future pregnancies were documented.

**Results:** We included 15 women with PPCM confirmed diagnosis. Mean age was 29 ± 6.6 year. 53% has pregnancy induced hypertension, 47% had pre-eclampsia and 53% were multigravida women. Breast-feeding was documented in 47% of women. Left ventricular ejection fraction was 28.7 ± 6.3 at time of diagnosis. There was no maternal mortality. B blockers and RAAS inhibitors are the main stay of treatment. 10 women showed complete recovery of their myocardial function, 3 of them had reconceived with no documented relapse of PPCM. 2 underwent dobutamine stress echo before re-conception.

**Conclusion:** PPCM is uncommon in our society. Recovery is anticipated with comprehensive anti-failure medications. Normal stress echocardiogram seems to be a favorable prognostic marker for future pregnancies.

Baseline data	Value
Age (mean ± SD)	29 ± 6.6
Hypertension diagnosed in pregnancy % (n)	53 (8)
Pre-eclampsia % (n)	47 (7)
Multi-gravida % (n)	53 (8)
Systolic blood pressure (mean ± SD)	140.4 ± 23.6
Diastolic blood pressure (mean ± SD)	91.8 ± 18.2
Heart rate (mean ± SD)	133.7 ± 19.4
QRS duration (mean ± SD)	77.1 ± 8.1
Left ventricular dimension in diastole (mean ± SD)	55.6 ± 5.8
Left ventricular dimension in systole (mean ± SD)	47.2 ± 7.9
Ejection fraction (mean ± SD)	28.7 ± 6.3
Hemoglobin (mean ± SD)	11.4 ± 1.9
Troponin (mean ± SD)	0.7 ± 2.1

Baseline data for 15 women with PPCM at diagnosis.



Medications used for treatment of PPCM

**P1542**

**Comparative analysis of left ventricular systolic function in females with peripartum cardiomyopathy and idiopathic cardiomyopathy.**

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<sup>1</sup>University of Lagos, Lagos, Nigeria; <sup>2</sup>Lagos University Teaching Hospital, Lagos, Nigeria

**Purpose:** Peripartum cardiomyopathy, PPCM, has been defined as an idiopathic cardiomyopathy presenting with heart failure secondary to left ventricular (LV) systolic dysfunction towards the end of pregnancy or in the months following delivery. It is a diagnosis of exclusion when no other cause of heart failure is found. The LV may not be dilated but the ejection fraction is nearly always reduced below 45%. Recent observations from the USA suggests that the genetic basis of PPCM and idiopathic dilated cardiomyopathy, DCM, may be similar and that recovery and outcome of subsequent pregnancies may not be as bad as earlier observed.

We therefore decided to compare the ventricular function and some ECG parameters of the PPCM in our cohort and females with idiopathic dilated cardiomyopathy.

**Methods:** PPCM and female patients with DCM who presented in acutely decompensated heart failure evaluated. Demographic, clinical parameters were obtained and ECG and echocardiographic evaluation was carried out.

**Results:** There were 31 patients with PPCM and 17 females with IDCM. The PPCM patients were younger, 31.71 ± 6.16 Vs 48.58 ± 18.49, p 0.002. There was no difference in the BMI and NYHA class, p, 0.94 and 0.74 respectively. The heart rate, SBP and DBP were also similar, p, 0.23, 0.59 and 0.99. The PPCM patients had significantly lower ejection fraction than the IDCM patients, 25.70 ± 10.44 Vs 37.12 ± 9.10%, p = 0.002. The LVDD was lower in the PPCM with a trend, 6.38 ± 0.76 Vs 5.87 ± 0.95cm, p = 0.07 but the systolic dimensions and wall thickness were similar in both groups.

**Conclusion:** We conclude that there may be more severe LV systolic dysfunction in patients with PPCM than IDCM despite being younger and this would portend a worse outcome.

**P1543**

**Dobutamine Stress echocardiography for predicting LV reverse-remodeling in idiopathic dilated cardiomyopathy**

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**Background:** The identification of contractile reserve during pharmacologic stress echocardiography may be helpful for predicting contractility recovery in idiopathic dilated cardiomyopathy (DCM). The purpose of the present study was to assess for prediction of reversible LV systolic function in patients with idiopathic DCM.

**Method** We prospectively included hospitalized patients with newly diagnosis of DCM from Mar. 2012 to May, 2014. We exclude patients with AF, LBBB, significant CAD, previous beta blocker treatment, high basal heart rate >100 bpm/min and uncontrolled hypertension. Thirty-three patients (were male, aged 54 ± 12 years) with DCM underwent baseline echocardiography and stress echocardiography. The dobutamine infusion was terminated at the maximal dose (40 γ·kg·min) or if the maximal heart rate was achieved. Changes of LVEF, E/e' and wall motion score index in response to dobutamine infusion (ΔLVEF-dobutamine) were measured. Cardiovascular magnetic resonance (CMR) was used to assess late gadolinium enhancement (LGE)- extent. LV reverse remodeling (RR) was defined as an increase of LV ejection-fraction ≥ 10 units combined with LV end-diastolic volume decrease ≥ 10% at follow-up echocardiography.

**Results:** Thirty-three patients (42 % male, aged 62 ± 14 years) with DCM were included. The majority of patients were in functional NYHA class II-III (76.3%). Baseline EF was 31 ± 5% by Teich method, 30 ± 3% by Simpson's method and 28 ± 10% by CMR. After dobutamine infusion, change of HR and EF was 26 ± 22 bpm/min and 5 ± 5%. In CMR, LGE was noted in 33 % of patients (6 of 18 patients). 18 patients were follow-up (mean 10 ± 4 months) and 3 patients were died. LV RR was 27.3 % of all patients (50% of 18 patients). In multivariate analysis of LVRR, change of LVEF (>5%, 0.042) and LGE by CMR (0.026) was significant predictor of LVRR.

**Conclusion:** Dobutamine Stress echocardiography and CMR was useful to predict LV reverse-remodeling in idiopathic dilated cardiomyopathy. Large number of study patient and further long-term data was needed.

**P1544**

**The evolution of the phenotype in a family with a missense mutation of the Lamin A/C (LMNA) gene with an initially isolated cardiac involvement: a 17 years observation.**

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**Introduction:** Lamins A and C are components of the nuclear envelope transcribed by the LMNA gene, encoded on chromosome 1q21.2–q21.3. The mutations of this gene may cause different phenotypic expressions. The long-term evolution of the phenotype in families with a prevalent cardiac involvement at the baseline evaluation is not yet completely defined.

**Purpose:** The aim of this observation is to describe the 17 years follow up of a family with a missense mutation in the exon 1 (c.178 C/G, p.Arg 60 Gly) of the LMNA gene, with a baseline isolated cardiac phenotype.

**Methods and results:** Full clinical and laboratory details are available from the 3rd generation (fig.1). Pts. III2, III3 and III6 showed an identical initial phenotype at the age of 37, 38 and 28, respectively, characterized by a dilated cardiomyopathy and A-V conduction defects. All of them underwent heart transplantation and pt. III2 died soon after from postoperative complications. Pt. III7 developed 3rd degree A-V block treated with a pacemaker, but did not show any systolic dysfunction and died from unknown cause at the age of 57. Several years after the first observation, pts. III3, III6 and III7 showed a progressive severe lipodystrophy with a dramatic subcutaneous fat reduction. Pts. III3 and III6 developed also a clinically relevant peripheral neuropathy at the age of 45 and 39, respectively. Pt. III3 died at the age of 50 from allograft vasculopathy and cachexia. Pts. IV2, IV4 and IV5, all with positive genotype, did not manifest any phenotypic expression at their first evaluation in the childhood. However, a reduction of subcutaneous fat was evident since they were twenties. Pts. IV4 and IV5 presented soon after a mild reduction of the EF. Second degree AV block Mobitz 2 was detected in pt. IV4, while the cardiac MRI of pt. IV5 at the age of 28 was consistent with several areas of intramyocardial delayed enhancement. Conclusion. This long-term observation shows an evolving complex phenotype in a family with heterozygous mutation for the LMNA gene and initially isolated cardiac expression. A strict evaluation of the individuals with a positive genotype allows to detect the age of onset, the characteristics and the evolution of the overlapping phenotypic expressions.

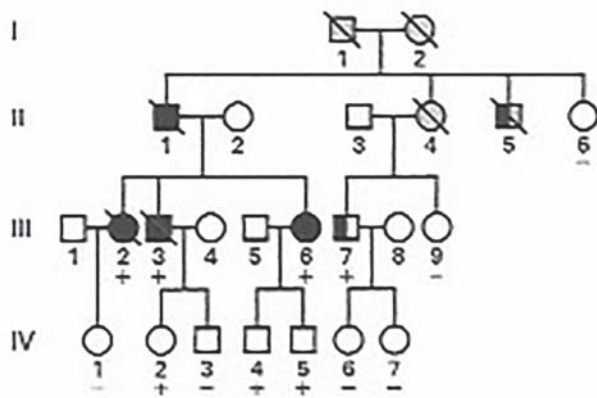


Figure 1

#### P1546

##### Surgical ventricular reconstruction in cases of ischemic dilative cardiomyopathy: outcome at 13 years in 61 patients

no funds

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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 of 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 all cases.

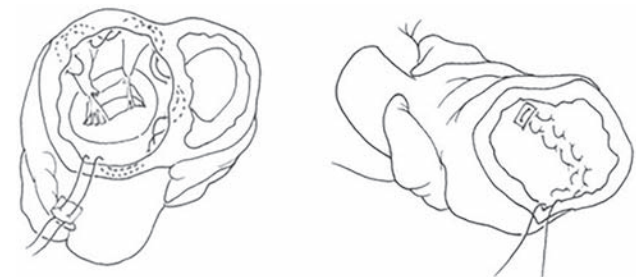
**Results:** Total early-in-hospital mortality was 3,4%, (0% in the last 31 cases). Reduction of LVED diameter, improvement of EF and NYHA class after surgery and at last follow-up were statistically significant ( $p < 0,05$ ). Residual mitral incompetence. at discharge was absent in 34 patients (59,6%), moderate in 2 (3,5%), mild in the remaining. 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 patients.

**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.

#### Change of Eslvv and Ejection Fraction

Echo Findings (n = 61)	Total	Surg 1 (n = 30)	Surg 2 (n = 31)	P value
ESLVV (ml)	- 49,7%			
Preintervention	173,2 ± 48,1	173,4 ± 57,2	173,1 ± 40,5	n.s
Discharge	86,0 ± 31,0	109,0 ± 72,9	72,9 ± 18,1	n.s
Follow-up	121,9 ± 63,1	131,9 ± 31,1	117,2 ± 74,0	n.s
EF (%)				
Preintervention	29,1 ± 9,5	29,1 ± 10,0	29,1 ± 9,2	n.s
Discharge	37,4 ± 8,1	36,8 ± 8,2	38,1 ± 8,1	n.s
Follow-up	35,1 ± 10,8	34,1 ± 7,0	35,7 ± 12,6	n.s

Reduction of left ventricular end-systolic volume was 50% or more in all cases, with no difference in the two groups of patients



modified surgical technique

#### P1546

##### Phenotype of dilated cardiomyopathy with Lamina gene single nucleotide polymorphisms

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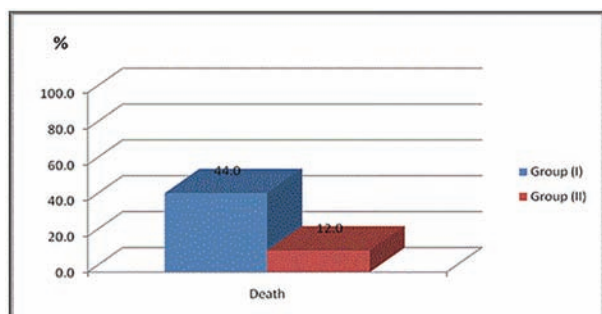
The objective of this study was to assess genotype-phenotype correlations in patient with dilated cardiomyopathy (DCM) due single nucleotide polymorphisms (SNPs) in lamina (LMNA) gene.

**Methods:** We examined 129 patients with DCM (18 family) who had a primary manifestation of conduction or arrhythmic disturbances before dilated phenotype (aged  $44,7 \pm 11,9$ ; 69% male, NYHA  $2,6 \pm 0,9$ ; LVEF  $25,9 \pm 9,92\%$ ). Exons (12) in the functional regions and the adjacent part of introns of the LMNA gene were amplified with polymerase chain reactions (PCR) and the PCR products were sequenced. Genetic testing, echocardiographic and electrocardiographic\24h-Holter ECG data including QTc dispersion, heart rate turbulence (HRT), microvolt T-wave alternans (mTWA), age, gender, NYHA, 6-MWT, serum BNP and CPK levels were analyzed.

**Results:** Disease-causing (according to Jpred3) missens-mutation in LMNA gene was found in 3 DCM patients: 190P, 520A, r528A. The largest three SNPs were identified numerically. The first is c.1908C>T (H566H, rs4641) which was located at exon 10 of LMNA gene. It was found in 25 (19,4%) DCM cases (TT and TC genotypes). According to NCBI, this SNP does not alter the primary sequence of the protein lamin as it determines synonymous codon for histidine at position 566. But positive correlation was revealed between rs4641 (C>T) SNP and non-sustained ventricular tachycardia (Spearman  $k = 0,57$ ;  $p = 0,009$ ), mTWA ( $k = 0,61$ ;  $p = 0,0007$ ). The second was c.1489-41C>T (rs553016) which located intron between 8 and 9 exons of LMNA gene. It was found in 18 (14%) DCM pts. The third was c.861C>T (A287A, rs538089) which was located at exon 5 of LMNA gene. It was found in 16 (12,4%) DCM cases. No association between last listed LMNA gene SNPs (rs553016, rs538089) and phenotype correlation was found in DCM patients. Such as T1908C selectively splicing transcripts decide lamin A/C relatively content, which may affect the relative content of mRNA and protein production, thus affecting the gene function. However the mechanism of T861C and T1489-41C in DCM is still unclear.

**Conclusions:** One-third of the DCM Belarus pts with primary manifestation of conduction or arrhythmic disturbances are carriers of the mutation\SNPs in LMNA gene. Thus, the SNPs of LMNA gene mentioned above are subject associated with DCM and require a detailed genetic analysis.

## P1547

**Does pulmonary hypertension impact clinical outcome or mortality in dilated cardiomyopathy patients?**M Mohammad El Tahlawi<sup>1</sup>; M Radwan<sup>2</sup>; M Abdelsamie<sup>1</sup>; M Wafaie<sup>1</sup><sup>1</sup>Zagazig University Hospitals, Cardiology, Zagazig, Egypt; <sup>2</sup>National Heart Institute, Cardiology, Cairo, Egypt**Background:** Elevated pulmonary arterial pressure has been established as a predictor of mortality and morbidity in patients with heart failure.**Aim:** This study aims to evaluate the impact of pulmonary hypertension (PHT) on the short term outcome of patients with DCM.**Patients and methods:** This study included all patients who were admitted to our center's CCU with DCM between January 2014 and July 2014. Patients were divided into 2 groups: Group I: Dilated cardiomyopathy with PHT (PHT group). Group II: Dilated cardiomyopathy without PHT (Non PHT group). All patients were subjected to clinical examination, resting 12 lead ECG done on admission, trans thoracic echocardiography, and laboratory analysis including liver function and serum creatinine. Follow up: All patients were followed up for 6 months as regard physical examination, ECG, labs investigation (liver function, serum creatinine) and echocardiography. End Point: mortality.**Results:** The study involved 50 patients with DCM; 25 patients with PHT and 25 without PHT. There was a significant difference between both group regarding mortality. The incidence of mortality in DCM with PHT group was (44%) vs 12% in Non PHT group ( $P < 0.05$ ). There was significant difference between both groups regarding clinical signs of heart failure especially basal crepitations and lower limb edema ( $P < 0.05$ ). This difference disappeared 6 months later. There was also significant difference between both groups regarding ejection fraction and fraction shortening at the beginning of admission and six months later ( $p < 0.05$ ). There was no significant difference between both groups regarding serum creatinine at the beginning of the admission. However, This difference became significant 6 months later ( $p < 0.05$ ) with more renal impairment occurred more in PHT group.**Conclusion** The presence of PHT is associated with worse clinical scenario and outcome in patients with DCM. The incidence of cardiac death in DCM patients increased with the presence of PHT. DCM patients with PHT need close and more frequent follow up.

**Figure (1) Percentage difference between group (I PHT) versus group (II Non PHT) in relation to mortality.  $P < 0.05$**

Figure 1

## P1548

**Comparative analysis of intracardiac hemodynamic parameters estimated by using echocardiography and rheocardiography in hypertrophic cardiomyopathy patients with heart failure with preserved ejection**V Y Vera Kaplunova<sup>1</sup>; GA Shakaryants<sup>1</sup>; MV Kozhevnikova<sup>1</sup>; Al Malakhov<sup>1</sup>; NV Khabarova<sup>1</sup>; EV Privalova<sup>1</sup>; YUN Belenkov<sup>1</sup><sup>1</sup>I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation**Purpose:** to assess the association between parameters of intracardiac hemodynamic measured by echocardiography (ECO) and rheocardiography (RCG) in hypertrophic cardiomyopathy (HCM) patients with heart failure with preserved ejection fraction (HF/pEF).**Methods:** 40 patients (21 men, 19 women) with HF/pEF included in the study. 47,5% (n = 19) of patients had a progressive course (PC) of the disease and 52,5% (n = 21) - stable course (SC). Diastolic function was estimated by ECO and RCG. RCG is the electrical impedance method which was performed on RheoCardioMonitor system. The frequency of the probe current is 100 kHz with an amplitude of 3 mA. We evaluated intracardiac hemodynamic parameters by ECO (ejection fraction (EF), E/A, end-diastolic volume (EDV), end-diastolic size (EDS), end-systolic size (ESS),

end-systolic volume (ESV), left atrium (LA), systolic output (SO)) and specific rheocardiography parameters (ejection fraction - 1 (EF1), cardiac output (CO), cardiac index (CI), ejection velocity (EV), system vascular resistance (SVR), end-diastolic pressure in left ventricle (EDP), end-diastolic volume (EDV)).

**Results:** The largest value of E/A was observed in patients with PC (E/A=1.044,  $p = 0.074$ ). There was no difference of ejection fraction (EF) levels measured by ECO  $60,52 \pm 6,25$  and RCG  $60,07 \pm 10,1$  ( $p < 0,074$ ). EF was correlated with EV ( $r = 0,3904$ ;  $p = 0,0128$ ). There were significant differences in EDP between SC ( $19,6 \pm 1,99$ ) and PC ( $12,06 \pm 3,08$ ) groups ( $p = 0,032$ ). The positive correlation were revealed in EDP and PSO ( $r = 0,4170$ ;  $p = 0,0074$ ). The negative correlation was identified between EDP and EDS ( $r = -0,40$ ;  $p = 0,0025$ ), EDP and SO ( $r = -0,52$ ;  $p = 0,0034$ ).**Conclusion:** 1. Intracardiac hemodynamic parameters estimated by using ECO and RCG in HCM patients with HF/pEF were comparable. 2. It was found that the increase of EDP measured by RCG correlate with decrease of EDS and SO measured by ECO. 3. The most severe diastolic dysfunction revealed in progressive course of HCM. 4. The increase of EDP is more common for patients with progressive course of HCM.

## P1549

**Clinical risk factors of new onset atrial fibrillation in patient with hypertrophic cardiomyopathy.**J-H Jung-Hyun Choi<sup>1</sup>; BW Kim<sup>1</sup>; JH Choi<sup>1</sup>; TJ Hong<sup>1</sup><sup>1</sup>Busan National University Hospital, Busan, Korea Republic of**Backgrounds:** Atrial fibrillation (AF) is common clinical manifestation of HCM patients. Prevalence of AF in HCM patients is known to approximately 20%. There are limited data available to predictive factor of AF in patient of HCM. The aim of this study is to investigate of clinical risk factor of AF in HCM patients.**Methods:** This study is retrospective observational study. We investigated the HCM patients who performed echocardiography and had sinus rhythm at presentation (n = 40) from 2011 to 2015 in a national university hospital. We divided into two groups according to newly developed AF during follow up period (AF group: n = 40) and maintained sinus rhythm (Sinus group: n = 360). AF was defined by electrocardiogram and Holter monitoring at index visit. We compared clinical characteristics and conventional echocardiographic parameter and atrial electromechanical delays. AEMD was defined as the time interval between the onset of ECG P wave and the initial (AEMDi) or peak a' wave (AEMDp) on the medial mitral annular tissue Doppler velocity curve (TDI) or PW Doppler at the mitral valve inflow level. Results Compared to sinus rhythm group, new onset AF group had more complained dyspnea. Compared to sinus group, new onset AF group has higher conventional echocardiographic parameter including RVSP ( $36,58 \pm 14,89$  vs  $31,00 \pm 7,99$ ,  $p = 0,001$ ), LAVI ( $59,01 \pm 24,09$  vs  $43,58 \pm 16,37$ ,  $p < 0,001$ ), Mitral E velocity ( $77,03 \pm 27,78$  vs  $61,74 \pm 17,56$ ,  $p < 0,001$ ) and AEMDi ( $72,07 \pm 15,90$  vs  $63,08 \pm 15,43$ ,  $p = 0,004$ ), AEMDp ( $152,41 \pm 27,59$  vs  $141,98 \pm 15,43$ ,  $p = 0,022$ ) by PW Doppler. After using multivariate logistic regression, we found that LAVI (OR=1.028 [1.006-1.051],  $p = 0,012$ ), AEMDi by PW Doppler (1.029 [1.000-1.059],  $p = 0,049$ ) are independent predictive factors of new onset AF in HCM patients. Conclusion This observational study shows AEMDi by PW Doppler may have an additional predictive value to LAVI of new onset AF in HCM patients

## P1550

**Effects of alcohol septal ablation on markers of inflammation and signal peptides in patients with obstructive hypertrophic cardiomyopathy**F Pelliccia<sup>1</sup>; C Cianfrocca<sup>2</sup>; L Gatta<sup>3</sup>; V Pasceri<sup>2</sup>; A Auriti<sup>2</sup>; C Pristipino<sup>2</sup>; G M C Giuseppe M C Rosano<sup>3</sup><sup>1</sup>Umberto I Polyclinic of Rome, Rome, Italy; <sup>2</sup>San Filippo Neri Hospital, Rome, Italy; <sup>3</sup>San Raffaele Pisana Hospital IRCCS, Rome, Italy**Introduction:** Alcohol septal ablation (ASA) has become a diffuse therapeutic approach in hypertrophic cardiomyopathy (HC) leading to reduced obstruction, relief of symptoms, and improvement in global LV function. It remains unknown, however, if ASA exerts favorable effects on markers of inflammation and signal peptides. Accordingly, we prospectively assessed whether changes in biochemical indexes occur after ASA in HC.**Methods:** We studied 10 patients (6 women,  $66 \pm 13$  years) with obstructive HC who underwent ASA. Before ASA and 6 months later, erythrocyte sedimentation rate (ESR), high-sensitivity C-reactive protein (hsCRP), nuclear factor-kappa B (NF-kB), interleukin (IL)-6, tumor necrosis factor-alpha (TNF-alpha), and the glycoprotein carbohydrate antigen 125 (CA125) were evaluated in all patients. Measurements were done according to standard techniques. NFkB was quantified by a sensitive multi-well colorimetric assay for active NF-kB.**Results:** ASA was successful in all patients, with NYHA functional class decreasing from  $3.5 \pm 1.1$  to  $1.6 \pm 1.0$  and LV outflow tract gradient reducing from  $101 \pm 45$  to  $18 \pm 12$  mm Hg. Procedural complications included only the need of permanent pace-maker in 3 patients. Over follow-up, no death occurred and obstruction recurred in 1 patient who underwent myectomy. Hematologic evaluation at 6-month follow-up did not show any significant change in ESR (from  $15 \pm 3$  to  $12 \pm 5$  mm/h,



$p < 0.05$ ), hsCRP (from  $3.2 \pm 2.1$  to  $2.9 \pm 2.0$  mg/l,  $p < 0.05$ ), and IL-6 from  $4.2 \pm 3.1$  to  $4.0 \pm 2.7$  pg/ml,  $p < 0.05$ ). Conversely, there was evidence of significant decreases in NF- $\kappa$ B (from  $10.5 \pm 6.5$  to  $4.1 \pm 3.9$  ng/ $\mu$ g cell protein,  $p < 0.05$ ), TNF (from  $3.5 \pm 2.9$  to  $1.1 \pm 1.9$  pg/ml,  $p < 0.05$ ), and CA125 (from  $13.4 \pm 9.8$  to  $7.9 \pm 8.9$  U/ml,  $p < 0.05$ ).

**Conclusions:** Signal peptides, but not markers of inflammation, decrease significantly after ASA in patients with obstructive HC. These findings suggest that symptomatic and functional improvement after the procedure can be ascribed, at least partly, to favourable changes that occur in some biochemical indexes.

#### P1551

##### Hypertrophic cardiomyopathy: an experience in southeastern Sweden

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**Background:** Hypertrophic cardiomyopathy (HCM) is the most common cause of sudden unexpected death in young athletes and the second most common inherited cardiovascular disease marked by genetic and phenotypic heterogeneity.

**Purpose:** The aim of this study is to identify the genetic and phenotypic aspects of the disease in southeastern Swedish population.

**Methods:** In this retrospective descriptive study 50 unrelated adult patients with the clinical diagnosis of HCM according to the diagnostic criteria of international guidelines followed between 2010 and 2015 at a County Hospital in the southeast region in Sweden were included, using a checklist of parameters. Next generation sequencing was used to analyze the 16 genes of the Cardiomyopathy Gene panel.

**Results:** The mean age of the patients at diagnosis was  $47 \pm 16.8$ . Most patients were male (64%). 64% had symptoms according to NYHA II class. 4% had as initial presentation sudden cardiac death. Arrhythmias, such as Atrial Fibrillation was identified at 32% of patients and ventricular Tachycardia at 34% during Holter monitoring. 38% had a family history of sudden cardiac death (SCD). At ECHO-graphic findings 14% had a maximal wall thickness-MLVWT > 30mm, 32% had Left Ventricular Outflow Tract Velocities- LVOT > 4m/s at rest, 16% had EF < 50%, 40% had systolic anterior motion-SAM. Regarding their treatment, 12% had undergone an alcohol septal ablation, 20% had a pacemaker and 24% had an Implantable Cardioverter Defibrillator (ICD). Of the 50 HCM patients 35, (70%) had undergone genetic testing. 2 denied to genetic testing. 23% had MYBPC3 genetic variants -1 of unknown significance VUS, 14% had MYH7 pathogenic genetic variants, and 34% had no detected pathogenic variants. 17% of patients are still waiting for the result. In one patient presented with sudden cardiac death (SCD) a disease-causing genetic variant in TNNT-2 gen was identified. Those with MYH7 genetic variants were younger and there were 2 individuals with pathogenic MYH7 variants and SCD. 34% of their first degree relatives were offered a genetic testing whereas 58% of their first degree relatives were regularly followed-up with ECHO, Holter, and exercise test according to guidelines. Conclusion This study represents one of the first comprehensive attempts to characterize the genotypes and phenotypes related to HCM in southeastern Sweden. Furthermore this project highlights that HCM patients and their family members can successfully be diagnosed, treated, risk stratified and provided with genetic testing and counselling at a County Hospital in Sweden.

## CO-MORBIDITIES

#### P1552

##### Carotid involvement in patients with non-ischemic heart failure

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**Background:** Carotid involvement represents an asymptomatic condition which can lead to life-threatening complications including stroke and cardiac ischemia, when the stenosis becomes significant. Heart failure patients have already an elevated morbidity and mortality risk, therefore carotid ultrasound screening can be a useful tool to detect and manage existing alterations.

**Purpose:** To identify carotid changes in patients with established non-ischemic heart failure.

**Methods:** We included in our study 30 patients (12 male, 18 female), mean age  $57.96$  years, previously diagnosed with non-ischemic heart failure and asymptomatic from carotid standpoint (no stroke or transient ischemic attack in the last 6 months), admitted to our Internal Medicine Department. We performed carotid ultrasound, measuring intima-media wall thickness and assessing the degree of stenosis. We considered incipient changes for intima-media thickness > 1 mm and significant stenosis for values > 60%.

**Results:** The majority of the patients (50%) had incipient changes, followed by non-significant stenosis (33,33%), no changes (10%) and significant stenosis

(6,66%). We could observe this pattern in the female (61,11%) and diastolic dysfunction (69,23%) subgroups. In our other subgroups we observed a different pattern, with the predominance of non-significant stenosis: men (41,66%), systolic dysfunction (44,44%) and combined systolic and diastolic dysfunction (50%).

**Conclusions:** Heart failure patients are likely to have some form of carotid involvement. We often focus on the coronary changes in these patients and overlook the asymptomatic carotid counterpart. Even if the alterations are only subtle, they can progress in time and lead to debilitating or fatal consequences if they go unnoticed. Carotid ultrasound screening is a non-invasive and cost-effective way to prevent these horrendous complications from happening.

#### P1553

##### Influence of diabetes mellitus and renal failure in the short-term mortality in patients hospitalized for heart failure.

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**Purpose:** Assess whether the presence of diabetes mellitus, renal failure ( $Cr > 1.5$  mg / dl) or both comorbidities increase mortality at 3 months in patients hospitalized for heart failure.

**Methods:** Observational prospective cohort study including a total of 1824 patients presenting to emergency departments in acute decompensated heart failure (acute decompensated heart failure and chronic heart failure). Sociodemographic features, cardiovascular risk factors, comorbidities, history of heart disease (ischemic cardiomyopathy, valvular, arrhythmia) and analytical and echocardiographic data were collected during emergency episode and hospital admission. Outcome variables were considered short-term mortality and readmissions in 3 months. Multivariate regression model was performed on the dependent variable mortality at three months after being hospitalized for the index episode.

**Results:** Of 609 diabetic patients died 71 (11.66%) and of 1215 non diabetic patients 154 died (12.67%),  $p = 0.53$ . Of the 366 patients with renal insufficiency died 81 (22.13%) and of 1403 patients without kidney failure died 140 (9.98%),  $p < 0.001$ . Of the 139 patients with diabetes and kidney failure died 27 (19, 42%) while of the 1630 without both comorbidities died 194 (11.90%),  $p = 0.01$  However, when performing the multivariate analysis of mortality at 3 months diabetes presents OR (CI 95%) 0.646 (0.370 to 1.129)  $p = 0.12$  sample OR Kidney failure (CI 95%) 3.115 (1.846 to 5.256)  $p < 0.0001$  and diabetes and kidney failure associated OR (CI 95%) 1,746 (0.783 to 3.891)  $p = 0.17$

**Conclusions:** 1. In our study, kidney failure has shown to be an independent factor of increased short-term mortality in patients hospitalized for heart failure. 2. Diabetes mellitus, in our study, is not associated with increased mortality to 3 months in this patient group

#### P1554

##### Left ventricular diastolic function in hypertensive patients with heart failure and preserved ejection fraction combined with rheumatoid arthritis

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**Background:** In a world that is aging and in which hypertension have an increasing prevalence, the proportion of patients with heart failure with preserved ejection fraction (HFpEF) is growing. HFpEF is an important cause of disability and hospitalization. There is strong evidence that rheumatoid arthritis (RA) affects the heart muscle and contributes to heart insufficiency. Left ventricular diastolic function is first impaired in both clinical entities. It would be useful to know the contribution of hypertension and RA in left ventricular diastolic function impairment and which is worse.

**Purpose:** The aim of our study was to assess the left ventricular diastolic function in patients with hypertension and hypertension combined with mild/moderate RA, both with preserved ejection fraction ( $FE \geq 45\%$ ), admitted in Internal Medicine Department.

**Methods:** The study included 23 patients with hypertension, with mean age  $54 \pm 10$  years, and 19 patients with hypertension and RA, mean age  $53 \pm 9$  years. All patients were women and had preserved ejection fraction ( $FE \geq 45\%$ ). Patients with diabetes, significant heart valve dysfunctions, ischemic heart disease and any unstable systemic disease were excluded. The main duration of hypertension was  $8.5 \pm 5$  years, and the mean duration of RA was  $5.6 \pm 4$  years. Transthoracic echocardiography was performed in all patients, including pulse Doppler transmitral flow. Diastolic left ventricular function was assessed by the following Doppler parameters: early (E) and late (A) peak velocities, E/A ratio, isovolumic relaxation time (IVRT), and deceleration time of E velocity (DT). Results There were significant differences between patients with hypertension and those with hypertension and RA. E/A ratio was  $1.2 \pm 0.4$  in hypertensive versus  $0.8 \pm 0.2$  in hypertensives with RA ( $p < 0.01$ ). IVRT was  $93.2 \pm 20.1$  ms in hypertensive patients versus  $109.6 \pm 25.8$  ms in patients

with hypertension combined with RA ( $p < 0.01$ ). As regarding DT, hypertensives had  $190 \pm 68.3$  ms and patients with hypertension and RA  $262.5 \pm 110.5$  ms ( $p < 0.01$ ). The remaining left ventricular parameters and systolic function did not differ between the two groups.

**Conclusions:** Hypertensive patients with heart failure with preserved ejection fraction combined with rheumatoid arthritis had a more severe impairment of left ventricular diastolic function than patients only hypertensive. It seems that RA worsens the prognosis of patients and may require additional therapeutic strategies.

### P1555

#### Incidence and predictors of long-term of acute kidney injury after transcatheter aortic valve implantation

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Acute Kidney Injury (AKI) after cardiac surgery is associated with increased mortality, but very few data exist on the occurrence of AKI associated with Transcatheter Aortic Valve Implantation (TAVI). The aim of this study was to determine the incidence and prognosis of AKI after percutaneous treatment in patients with aortic stenosis.

**Methods:** Between April-2008 and December 2015, 492 patients with severe aortic stenosis were treated with the CoreValve prosthesis. The AKI was defined according to the Valve Academic Research Consortium criteria, as the absolute increase in serum creatinine  $\geq 0.3$  mg/dl at 72 hours after percutaneous procedure. We excluded patients died during procedure.

**Results:** the incidence of AKI was 16.5% and none required renal replacement therapy. After implantation there was a slight improvement in renal function, baseline serum creatinine decreased from  $1.27 \pm 0.4$  mg/dl to  $1.17 \pm 0.4$  mg/dl,  $p = 0.001$ . In patients with AKI, the mortality at 30 days was 69.2% compared to 15.1% of patients without AKI, OR=12.7 (95% CI 3.85-42.4),  $p = 0.001$  and late mortality after a mean of  $34.3 \pm 23$  months was 20% in those patients with AKI compared to 14% without AKI,  $p = 0.098$ . In the multivariable analysis AKI was an independent predictor of cumulative total mortality HR 1.93 (95% CI 1.23-3.01),  $p = 0.006$ .

**Conclusions:** the incidence of AKI was associated with increase early mortality and also was a predictor of worse outcomes in the long-term follow-up

### P1556

#### The length of hospital stay in heart failure patients - how to know when to let go

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**Background:** Substantial decreases in heart failure (HF) hospital stay rates over time are consistent with reports from most European countries and North America. Prolonged hospitalization carries a risk for HF patients such as hospital-acquired infections, deep vein thrombosis, pulmonary embolism, depression, deconditioning of the body and for many other social, economic and medical problems.

**Purpose:** The aim of our study was to assess the average length of hospital stay in patients with acutely decompensated HF and the factors associated with the increased length of hospital stay

**Results:** During 3 months we included in our study 201 consecutive patients with acute HF; average age was  $71.55 \pm 10.35$  years and 60.7% were male. The average duration of HF was  $1.69 \pm 1.13$  years. The average length of hospital stay was  $2.43 \pm 1.89$  days. 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 a valvular disease. At admission, 55 patients (27.4%) had New York Heart Association (NYHA) class II, NYHA class III had 108 patients (53.7%) while 38 patients (18.9%) had NYHA class IV. Hospital duration was not significantly longer in patients with higher NYHA class. Patients with NYHA class II were hospitalized  $4.62 \pm 2.1$  days, those with NYHA class III:  $4.99 \pm 2.2$  days and with NYHA IV:  $4.53 \pm 2.25$  days. Also left ventricle ejection fraction (LVEF:  $37.4 \pm 13.7\%$ ) did not correlate with the length of hospital stay. Patients with HF and preserved ejection fraction had longer hospital stay compared to those with reduced ejection fraction, but not significantly ( $5.15 \pm 2.31$  vs.  $4.6 \pm 2.08$  days). A number of comorbidities, however, was associated with the average duration of hospitalization ( $p = 0.012$ ). Patients without co-morbidities (1.5%) had the shortest hospital stay (2 days) while those with 6 comorbidities (1.5%) were  $6.67 \pm 2.0$  days in the hospital.

**Conclusions:** The average stay in hospital in our HF patients was not associated with the NYHA class at the admission or with LVEF. However, the presence of comorbidities increased the length of hospital stay. This could be the consequence of lack of the interdisciplinary corroboration between health professionals with different medical specialities. The awareness of the presence of co-morbidities and the need

for multidisciplinary approach should take the high ground regarding the fragile heart failure patients.

### P1557

#### Effects of neuropeptide Y on coronary artery vasomotor tone

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**Background:** Patients with microvascular angina usually have a reduced coronary blood flow reserve. Neuropeptide Y (NPY) is a potent endogenous vasoconstrictor involved in modulation of coronary vasomotor tone and may play a role in microvascular angina. Methods. We compared the effects of NPY (0.2-1.0 pmol/kg, intracoronary) on the vasomotor response of proximal and distal segments of the coronary arteries in 7 patients with microvascular angina and left ventricular dysfunction (MALVD), 9 with chronic stable angina, and 9 control individuals. The coronary response to the administration of ergonovine was also assessed in 9 other patients with microvascular angina and normal LV function. Computerized coronary artery diameter measurements were carried out before (baseline) and after the administration of the vasoactive agents.

**Results:** Mean baseline coronary lumen diameters were similar in control, MALVD, and coronary artery disease patients. NPY constricted proximal coronary segments by  $8 \pm 2\%$ ,  $5 \pm 2\%$  and  $6 \pm 3\%$  and distal segments by  $14 \pm 2\%$ ,  $11 \pm 2\%$  and  $10 \pm 2\%$  in control, MALD, and coronary artery disease patients, respectively ( $p = NS$  between groups). In patients with microvascular angina, ergonovine constricted proximal coronary segments by  $7 \pm 1.5\%$  and distal segments by  $12.5 \pm 3\%$  ( $p = NS$  vs. NPY). During NPY administration four MALVD patients developed chest pain, ST segment depression, and a marked lengthening of the contrast medium run off, in the absence of epicardial coronary artery spasm. Control individuals and coronary artery disease patients did not experience chest pain, ST segment shifts, or lengthening of the run off during NPY administration. Ergonovine administration caused chest pain and lengthening of the contrast run-off, in the absence of epicardial coronary artery spasm, in one patient with microvascular angina and normal LV function.

**Conclusions:** Exogenous NPY causes mild epicardial coronary artery constriction which is similar in patients with non-cardiac chest pain, MALVD and coronary artery disease. Myocardial ischemia and marked lengthening of the contrast run off in response to NPY occurred in MALVD patients but not in control or coronary artery disease patients. An abnormal constrictor response to NPY at the microcirculation level could be the mechanism underlying the ischemic manifestations observed in patients with microvascular angina with LV dysfunction.

### P1558

#### Acute kidney injury is associated with cardiohepatic syndrome in patients with decompensated heart failure

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**Objective:** Liver and kidney dysfunction is frequently encountered in heart failure and related to worse prognosis. Over the last several years interdependent feedback mechanisms involving the heart, kidney and liver have been discussed. The aim of the study was to assess the prevalence of acute kidney injury (AKI) and abnormal liver function tests (LFTs) and their interrelations in acute decompensated heart failure (ADHF).

**Methods:** In 322 patients with ADHF (190 male,  $69.5 \pm 10.7$  years (M  $\pm$  SD), arterial hypertension 87%, myocardial infarction 56.5%, atrial fibrillation 65.5%, diabetes mellitus 41.6%, known chronic kidney disease 39.1%, chronic anemia 29.2%, ejection fraction (EF)  $37.6 \pm 12.6\%$ , EF  $< 35\%$  39.1%) alanine transaminase (ALT), aspartate transaminase (AST), direct and total bilirubin (DB and TB), alkaline phosphatase (AP), gamma-glutamyl transpeptidase (GGT) and international normalized ratio (INR) were measured on admission. LFTs were considered abnormal when levels exceeded local upper normal limit. Patients on warfarin were excluded from INR analysis. AKI was diagnosed based on KDIGO 2012 Guidelines. Mann-Whitney test and multivariate logistic regression analysis were performed,  $p < 0.05$  was considered statistically significant.

**Results:** Abnormal LFTs occurred in 274 (85.1%) patients. Increase of transaminases were detected in 68 (21.1%) patients (alone ALT/ alone AST/ both TA in 35.3, 26.5, 38.2% respectively), DB and/or TB in 264 (82%) patients (alone DB/ alone TB/ DB and TB - in 28, 0.8, 71.2% respectively), AP in 90 (27.9%) and GGT in 102 (31.7%) patients. Community-acquired AKI (CA-AKI) was diagnosed in 60 (18.6%) patients. Patients with versus without CA-AKI had higher levels of ALT ( $60 \pm 88$  vs  $29 \pm 26$  U/l,  $p < 0.05$ ), AST ( $52 \pm 45$  vs  $31 \pm 16$  U/l,  $p < 0.001$ ), TB ( $29 \pm 13$  vs  $25 \pm 15$   $\mu$ mol/l,  $p < 0.01$ ), DB ( $12 \pm 7$  vs  $9 \pm 7$   $\mu$ mol/l,  $p < 0.001$ ), GGT ( $157 \pm 117$  vs  $102 \pm 68$  U/l,  $p < 0.001$ ), AP ( $124 \pm 74$  vs  $112 \pm 88$  U/l,  $p < 0.05$ ), INR ( $1.49 \pm 0.42$  vs  $1.29 \pm 0.23$ ,  $p < 0.01$ ). Patients with vs without AKI had higher prevalence of increase of ALT (30 vs 12.3%,  $p < 0.001$ ), AST (33.3 vs 9.2%,  $p < 0.001$ ), TB (73.3 vs 56.2%,  $p < 0.05$ ) and INR (60.8% vs 43.8%,  $p < 0.05$ ). AKI was predictor for increase of ALT

(odds ratio (OR) 3.1, 95% confidence interval (CI) 1.6-5.9), AST (OR 4.9, CI 2.5-9.7), TB (OR 2.1, CI 1.2-4.0) and INR (OR 2.0, CI 1.0-3.9).

**Conclusions:** Abnormal LFTs occurred in 85.1%, CA-AKI - in 18.6% of patients admitted with ADHF. Patients with versus without AKI had higher prevalence of abnormal LFTs. In patients with ADHF increase of transaminases, total bilirubin and INR can directly contribute to AKI and vice versa.

#### P1559

##### Predictors of late 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 an alternative to surgical treatment in patients with severe aortic stenosis and high surgical risk, 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 2015, the CoreValve prosthesis was implanted in 500 patients with symptomatic severe aortic stenosis with deemed high risk.

**Results:** The mean age and the logistic EuroSCORE were 79.1 ± 7 years and 17.4 ± 11%, respectively. The implantation success rate was 99.8%. In-hospital mortality was 3.6%. The late mortality (beyond 30 days) was 19.2%. Survival at 1, 2, 3, 4, 5 and 6- years were 89.7%, 84.7%, 80.5%, 72.6, 63.02% and 40.76 % respectively, after a mean follow-up of 30.5 ± 20 months. The predictors of cumulative mortality were: Charlson index [HR 1.19 (95% CI 1.05-1.34), p = 0.006], coronary artery disease [HR 1.97 (95% CI 1.15-3.36), p = 0.012], extracardiac arteriopathy [HR 1.96 (95% CI 1.07-3.59), p = 0.029] and need of pacemaker after TAVI [HR 1.95 (95% CI 1.132-3.36), p = 0.016] and protective factors were a preserved left ventricular ejection fraction [HR 0.278 (95% CI 0.109-0.717) p = 0.008]

**Conclusions:** Survival during follow-up depends on the associated comorbidities and the complications of procedure

#### P1560

##### Total bilirubin increase is associated with congestion and hypoperfusion in acute decompensated heart failure

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**Objective:** Elevated total bilirubin (TB) is frequently reported in patients with heart failure and associated with worse prognosis. It is presumed that TB increase is related with predominantly right-heart dysfunction and congestion. We aimed to characterize TB increase in patients with acute decompensated heart failure (ADHF), as it is commonly encountered yet poorly defined.

**Methods:** In 322 patients with ADHF (190 male, 69.5 ± 10.7 years (M ± SD), arterial hypertension 87%, myocardial infarction 56.5%, atrial fibrillation 65.5%, diabetes mellitus 41.6%, known chronic kidney disease 39.1%, chronic anaemia 29.2%, ejection fraction (EF) 37.6 ± 12.6%, EF < 35% 39.1%) TB was measured on admission. TB increase was considered when serum level exceeded 21 µmol/l (local upper normal limit). Mann-Whitney test and multivariate logistic regression analysis were performed. P < 0.05 was considered statistically significant.

**Results:** Increase of TB occurred in 232 (72%) patients. Mean value of TB was 26.3 ± 14.5 µmol/l. Patients with versus without TB increase had higher levels of NT-proBNP (9510 ± 8046 vs 6102 ± 5607 pg/ml, p < 0.01), higher right ventricular diameter (36 ± 7 vs 32 ± 7 mm, p < 0.001), left ventricular end-diastolic volume (LV EDV) (59 ± 9 vs 55 ± 8 mm, p < 0.001), pulmonary artery pressure (47 ± 18 vs 59 ± 18 mm Hg, p < 0.001), heart rate (103 ± 29 vs 97 ± 29, p < 0.05), lower LV ejection fraction (36 ± 13 vs 40 ± 11%, p < 0.01), systolic blood pressure (134 ± 19 vs 142 ± 17 mm Hg, p < 0.001) and pulse pressure (52 ± 16 vs 59 ± 13 mm Hg, p < 0.001), higher prevalence of severe mitral regurgitation (47 vs 36%, p < 0.05) and tricuspid regurgitation (72 vs 21%, p < 0.001). TB increase was associated with signs of right-heart dysfunction/ congestion: jugular venous distension (44 vs 35%, p < 0.05), dilated inferior vena cava (77 vs 49%, p < 0.001) and portal vein (49 vs 26%, p < 0.05), echo-hydropericardium (30 vs 17%, p < 0.01), hydrothorax (48 vs 32%, p < 0.01), ascites (51 vs 21%, p < 0.001), hepatomegaly (79 vs 58%, p < 0.001) and with signs of left-heart dysfunction/ hypoperfusion - EF < 35% (50 vs 24%, p < 0.001) and SBP < 110 mm Hg on admission (14 vs 2%, p < 0.001).

**Conclusions:** TB increase occurred in 72% of patients with ADHF. The TB increase was associated with signs of right- and left-heart dysfunction.

#### P1561

##### We can predict the improvement of cheyne-stokes respiration with central sleep apnea in hospitalized heart failure patients

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**Purpose:** Cheyne-Stokes respiration with central sleep apnea (CSR-CSA) has been recognized as a prognostic factor in heart failure (HF) patients. Some studies reported that an optimal medical treatment (OMT) for HF including β-blockers suppressed CSR-CSA and also those treatments bring improvement of left ventricular (LV) ejection fraction (EF). However, we often find residual CSR-CSA despite the OMT. We conducted this study to evaluate the predictors for the improvement of CSR-CSA in hospitalized patients due to acute HF.

**Methods:** We studied hospitalized patients due to acute HF, and enrolled 25 HF patients with CSR-CSA (apnea-hypopnea index [AHI] ≥ 15/h and central apnea index [CAI] ≥ 5/h) evaluated by a fully-attended polysomnography just before discharge. After 3 months of the OMT, the sleep study, the echocardiography and blood test were performed again for all patients.

**Results:** Patient's characteristics at discharge were as listed: mean age, 62 years old; body mass index (BMI), 26.5; brain natriuretic peptide, 364 pg/ml; mean LV end-diastolic dimension, 62 mm; mean LVEF, 31%. On the whole, the OMT decreased AHI (46.6 ± 18.3/h to 34.8 ± 6.9/h, p = 0.05), CAI (16.3 ± 13.1/h to 7.8 ± 13.1/h, p < 0.05), and also obstructive apnea index (13.2 ± 15.8/h to 7.9 ± 7.5/h, p < 0.05). In 17 patients, CSR-CSA vanished accompanied by significant improvement of plasma BNP levels and LVEF after 3 months. By univariate analyses, BMI and relative wall thickness (RWT) at discharge were related to the improvement of CSR-CSA, but plasma BNP level, LVEF, LV mass index, severity of sleep apnea, and dose of β-blockers at discharge were not related to the improvement of CSR-CSA. Multivariate analysis revealed that BMI (odds ratio [OR], 1.68; 95% confidence interval [CI], 1.04 to 3.59; p < 0.05) and RWT (OR, 1.35; 95%CI, 1.08 to 2.15; p < 0.01) were independent determinants of the improvement of CSR-CSA accompanied by improvement of LVEF.

**Conclusion:** In hospitalized HF patients, greater BMI and RWT were the clinical predictors for the improvement of CSR-CSA accompanied by improvement of LVEF.

Determinants for the improvement of CSR-CSA (univariate and multivariate analyses)

	univariate analyses			multivariate analysis		
	OR	95% CI	p value	OR	95% CI	p value
age, yr	0.93	0.84 - 1.00	0.05			
BMI, kg/m <sup>2</sup>	1.54	1.12 - 2.43	< 0.01	1.68	1.04 - 3.59	< 0.05
BNP, pg/ml	0.75	0.51 - 1.00	0.053			
PNE, per 100 pg/ml	1.01	0.81 - 1.39	0.91			
AHI, /h	0.99	0.95 - 1.04	0.70			
OAI, /h	0.99	0.93 - 1.05	0.65			
CAL, /h	0.99	0.92 - 1.06	0.66			
LVEF, %	1.05	0.98 - 1.15	0.16			
LVd, mm	0.90	0.76 - 1.00	0.06			
LVDs, mm	0.94	0.85 - 1.02	0.15			
LVMI, g/m <sup>2</sup>	1.00	0.99 - 1.02	0.71			
RWT, per 0.01	1.39	1.12 - 2.08	< 0.01	1.35	1.08 - 2.15	< 0.01
dose of β-blockers, mg/dl	1.13	0.95 - 1.42	0.17			

#### P1562

##### Echocardiographic variations in pulmonary pressure, vascular resistances and biventricular hemodynamics during different phases of Cheyne-Stokes respiration in heart failure patients

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**Background and aim:** Cheyne-Stokes respiration (CSR) frequently occurs in patients with heart failure (HF), where not only has it proarrhythmic effects, but it also fosters negative hemodynamic consequences. We aim to study the echocardiographic changes associated with ventilatory instability in a group of HF patients with 24-hour CSR.

**Methods:** 7 HF patients (age 69 ± 11 years, left ventricular ejection fraction 23.5 ± 6.5%) underwent 24-hour cardiorespiratory screening for CSR and simultaneous echocardiographic and respiratory monitoring, via inductance plethysmography.

**Results:** All patients had 24-hour CSR (diurnal apnea-ipopnea index AHI 28 ± 16, nocturnal AHI 33 ± 10 events/hour). During CSR we found an increase in both systolic pulmonary artery pressure (sPAP) from hyperventilation to apnea (H 39.3 ± 11.1 versus A 45.7 ± 14.9 mmHg, p = 0.018). The same was found for pulmonary vascular resistances (PVR: H 3.7 ± 1.8 versus A 4.5 ± 2.2 wood units, p = 0.046). The increase in sPAP and PVR, was even higher comparing mid-hyperventilation with end-apnea (sPAP: 38.7 ± 11.8 versus 47.5 ± 15.3 mmHg, p = 0.017; RVP:



3.6 ± 1.7 versus 4.7 ± 2.3 wood units, p=0.028), as predictable from O<sub>2</sub>/CO<sub>2</sub> and chemoreflex kinetics. This was paralleled by a slight reduction in tricuspid annular plane systolic excursion from early-hyperpnea to late-apnea, (14.6 ± 3.4 versus 13.1 ± 2.8 mm, p=0.028), likely due to right ventricular afterload increase, and by mitral E velocity reduction from late-hyperpnea to late-apnea (105.8 ± 27.9 versus 97.6 ± 24.5 cm/s, p=0.046), likely due to left ventricular preload decrease.

**Conclusions:** In HF patients CSR, likely via recurrent hypoxia and hypercapnia cycles and chemoreflex mediated adrenergic discharge, may cause pulmonary vasoconstriction and an increase in pulmonary arterial pressure, with undesirable consequent changes in right and left ventricular preload-afterload (figure 1).

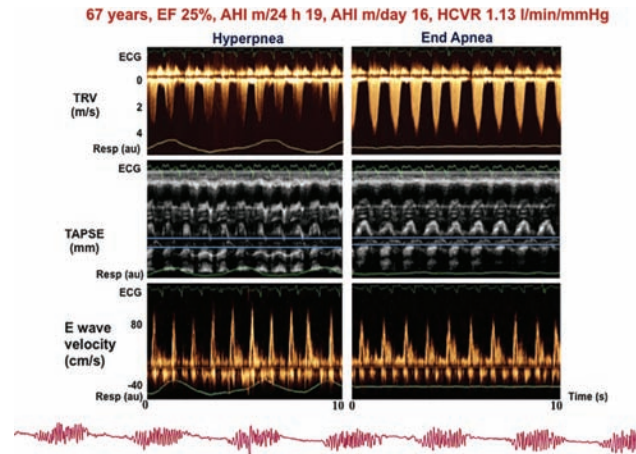


Figure 1

**P1563**

**Evaluation of the apnea-hypopnea index determined by the peripheral arterial tonometry device in patients with heart failure: results from multicenter study**

Philips-Respironics

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**Background:** Patients with heart failure (HF) frequently have sleep apnea (SA) and presence of SA is associated with poor clinical outcomes in patients with HF. Thus, assessment of SA is important for risk stratified care management of HF patients. However, polysomnography (PSG), the gold standard technique for the assessment of SA, remains costly, labor intensive, limited access especially for HF patients. Therefore, portable sleep study devices have been developed in order to increase accessibility and reduce costs of diagnosing and treating SA. One such device includes peripheral arterial tonometry (PAT) -based portable device. Although meta-analysis indicated that apnea-hypopnea index (AHI) determined by PAT device correlated significantly with those determined by PSG in the general population, there are no specific data regarding accuracy of AHI determined by the PAT device in patients with HF.

**Purpose:** The purpose of this study was to compare the AHI determined by the PAT device with the AHI derived from the PSG in patients with HF.

**Methods:** Patients undergoing overnight PSG in 5 centers, Juntendo University Hospital, Tokyo Medical University Hospital, Fukushima Medical University Hospital, University Hospital, University Hospital and Medical Center of the Medical University were enrolled. Overnight PSG was performed according to standard protocol/criteria using electroencephalogram, electrooculogram, submental and anterior tibialis electromyogram, electrocardiogram, airflow, chest and abdominal wall motion, body position and arterial oxygen saturation. PAT device was attached in addition to the full PSG set-up. All PSG recordings were sent to the core laboratory and scored centrally by one experienced registered PSG technician who was blinded to the results of PAT device. All PAT device recordings were also sent to the core laboratory but scored using automatic algorithm. The AHI derived from the PSG (AHI-PSG) and the AHI determined by PAT device (AHI-PAT) were obtained. The correlation between AHI-PSG and AHI-PAT and agreement of them were assessed separately in patients with and without HF.

**Results:** Overall, 120 patients including 91 without and 29 with HF were analyzed. Compared with patients without HF, those with HF were more likely to have diabetes (34% versus 16%, P=0.046) and coronary artery disease (41% versus 13%, P=0.002) and predominant central sleep apnea (59% versus 16%, P<0.001) despite similar AHI-PSG. There were strong correlations between AHI-PSG and AHI-PAT in both patients with and without HF (r=0.80, P<0.001 for those with HF and r=0.87, P<0.001 for those without HF). In addition, there was no interaction between presence or absence of HF and AHI-relationships (P=0.643)

**Conclusion:** AHI-PAT positively and strongly correlated with AHI-PSG. Strengthened by the blinded design, PAT device can be an important alternative to PSG for evaluating SA even in patients with HF.

**P1564**

**Hematocrit as a marker of short-term mortality and length of stay in hospitalised patients with congestive cardiac failure**

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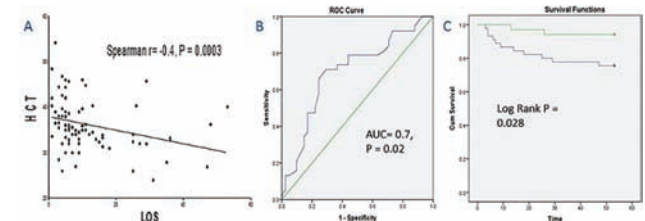
**Background:** OPTIMIZE-HF has identified predictors of in-hospital mortality but did not include markers of intravascular fluid status such as hematocrit (HCT). Get With the Guidelines study has concluded that stratifying patients for length of stay (LOS) is limited for heart failure.

**Purpose:** We sought to establish whether hematocrit would prove to be a useful predictor for short term mortality and length of stay in hospitalised patients with congestive cardiac failure (CCF).

**Methods:** A retrospective analysis of all consecutive patients who were admitted with diagnosis of CCF between September 2012 and August 2013. Patients were included using hospital coding database and only included if the primary diagnosis was CCF. Patients were divided into two groups: low HCT (<36% in females & <38% in males) and normal HCT. Statistical analysis was performed using SPSS 22.0.

**Results:** Total of 121 patients were identified with 79 patients met inclusion criteria. Of these, 45 (57%) had low HCT. Mean age was 77 ± 9, 57% females with median LOS of 7 days. There was no difference between low & normal HCT groups in terms of gender, co-morbidities, or ejection fraction. Normal HCT patients were younger with better renal functions, while low HCT group had longer LOS (16 versus 8 days, p=0.01) and higher mortality (23% versus 6%, p=0.028). There was a significant association between baseline HCT and LOS (Spearman r =-0.4, P=0.0003). ROC area under the curve was 0.7 (p=0.02) for HCT cut off of 36%. HCT was significant predictor of LOS on univariate (OR 0.87 CI 0.79-0.96, p=0.007) but not on multivariate regression analysis (OR 0.93 CI 0.62-1.39, p=0.73). Kaplan-Meier curves at eight weeks showed statistical significance (Log Rank p=0.028) between low & normal HCT groups.

**Conclusion:** HCT is a useful marker to predict LOS and short-term mortality for hospitalised patients with CCF. HCT is available to all patients with no extra costs for this beneficial test.



Figure

**P1565**

**Iron status in patients with chronic heart failure in an asian cohort**

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Iron deficiency is a common comorbidity in chronic heart failure which has unfavourable clinical and prognostic consequence. Studies regarding iron status in an Asian population has been sparse. The objective of this study was to look at iron status in patients with chronic heart failure in an Asian cohort and to look at its association with short term outcomes in patients with chronic heart failure.

**Method:**We enrolled 74 consecutive patients who attended the heart failure clinics in a General Hospital. Full iron studies were obtained from blood sample. Results - Total of 74 patients were recruited, sixty percent (n=44) were male. Mean haemoglobin 13.1 g/dl(SD+/-0.2), TSAT was 23%( SD+/-13), ferritin was 206microgram /L (SD+/- 23), TIBC was 57micromol/L (SD+/-1.7) and iron was 13.6 micromol/L (SD+/-0.8). TSAT distribution among NYHA I,II and III were

26.3%(SD+/-15.1), 29.4%(SD+/-13.9), 21.6%(SD+/- 9.8) and haemoglobin distribution among NYHA I,II,III were 13.3g/dl(SD+/-2.1), 13.2g/dl (SD+/-2.1) and 12.7 g/dl(SD+/-2.0) respectively (P = not significant). Survival rate at 6 months was 93% (n = 69). Haemoglobin (P = 0.02) and serum ferritin (P = 0.034) was associated with increase mortality whilst TSAT levels, serum iron and TIBC was not significantly associated with mortality at 6 months.

**Conclusions:** - In an Asian cohort patients with chronic heart failure, presence of anemia had an unfavourable outcome. Ferritin levels is also associated with mortality most likely due to underlying inflammatory process.

#### P1566

##### Left ventricular ejection fraction recovery associated to myocardial iron repletion in patients with heart failure treated with intravenous iron

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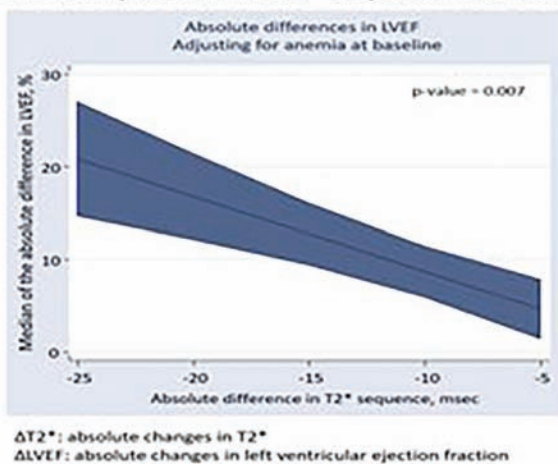
**Purpose:** In patients with heart failure with reduced ejection fraction (HFrEF), treatment with intravenous iron has shown to improve symptoms, functional capacity, and quality of life regardless of anemic status. Some authors have speculated myocardial iron repletion may explain, at least in part, this beneficial effects. Cardiac magnetic resonance (CMR) T2\* sequence is a well-considered technique for assessing myocardial iron content. Thereby, we aimed to evaluate whether T2\* sequence changes ( $\Delta T2^*$ ) after intravenous iron administration in HFrEF patients with iron deficiency (ID) and whether such changes correlate with simultaneous changes in left ventricular ejection function (LVEF).

**Methods:** We enrolled 8 patients with HFrEF, NYHA class  $\geq$ II and ID. All patients received a dose of 1000 mg of ferric carboxymaltose (FCM). CMR and blood laboratory tests were performed baseline and 43 days (IQR=35-48) after FCM administration. A partial correlation analysis and a quantile regression analysis ( $q = 0.5$ ) were performed.

**Results:** After intravenous administration of FCM, NYHA class improved in 50% of patients. T2\* decreased from a median of 39.5 (35.9-48) to 32 msec (32-34.5),  $p = 0.012$ . The median of LVEF showed a borderline increase [40 (36-44.5) to 48.5% (38.5-53)  $p = 0.091$ ]. In a bivariate correlational analysis,  $\Delta T2^*$  was highly correlated with changes in LVEF ( $\Delta LVEF$ ) ( $r = -0.747$ ,  $p = 0.033$ ). After controlling for anemia at baseline, the association between  $\Delta T2^*$  with  $\Delta LVEF$  persisted ( $r_{\text{partial}} = -0.865$ ,  $R2_{\text{partial}} = 0.748$ ,  $p = 0.012$ ). Likewise, in a quantile regression, per decrease in 1 unit of  $\Delta T2^*$  there was an associated increase in the median of LVEF by a factor of 0.81 ( $p = 0.007$ ) having the sample adjusted by anemia (Figure).

**Conclusion:** In a small group of patients with HFrEF and ID, myocardial iron repletion, as assessed by CMR, was associated to positive changes in LVEF.

#### Relationship between $\Delta T2^*$ sequence and $\Delta LVEF$



#### P1567

##### Improvement of parameters of heart failure after intravenous iron therapy in patients with defibrillator.

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**Purpose:** Iron deficiency (ID) is one of the main comorbidities seen in patients with advanced heart failure (HF) and can worsen the prognosis of the disease. Many studies have demonstrated that ID can worsen functional class, myocardial contractility, renal function, quality of life and prognosis in patients with heart failure. The aim of our study was to analyze the early clinical response based on HF parameters of the defibrillators (ICDs), after the administration of intravenous ferric carboxymaltose (FCM) in patients with chronic HF, systolic dysfunction and deficient iron stores.

#### METHODS

This was an observational, retrospective cohort study, which included 35 patients with HF and ID. Absolute ID was defined as ferritin  $< 100 \mu\text{g/L}$ , functional ID was defined as ferritin 100-299  $\mu\text{g/L}$  and transferrin saturation (TSAT)  $< 20\%$ . ID was calculated using the simplified Ganzoni formula. The parameters obtained by ICDs were the average daily activity, nocturnal heart rate, average daily ventricular premature beats, unsustained ventricular tachycardia, sustained ventricular tachycardia and the necessity of appropriate therapies. These data were compared at the time of iron administration and three months

#### RESULTS

Mean age was  $61.2 \pm 13.3$  years, and patients were predominantly male (68.6%). All had EF  $< 35\%$ ; 13 were ischemic. 21 patients had ICDs and 13 CRT-D. After three months of treatment, patients had clinical improvement based on an increased daily activity and reducing the number of premature ventricular contractions and night heart rate (Table 1).

**Conclusions:** Intravenous iron therapy improved functional status stage of patients with HF and ID based on objective parameters of ICDs

Table 1

Parameters	Before FCM	3 months post FCM	p
Daily activity, hour/day	$2.49 \pm 1.67$	$2.87 \pm 1.69$	$< 0.001$
PVC/hour	$153.13 \pm 237.03$	$93.25 \pm 142.25$	$< 0.01$
2-4 PVC/hour	$48.94 \pm 77.54$	$35.38 \pm 72.79$	$< 0.001$
$> 4$ PVC/hour	$7.28 \pm 35.06$	$0.21 \pm 0.79$	0.24
Average night ventricular rate, bpm	$70.63 \pm 12.37$	$67.68 \pm 10.49$	$< 0.001$

#### P1568

##### Iron deficiency and functional capacity in patients with advanced heart failure with preserved ejection fraction

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**Background:** Heart failure with preserved ejection fraction (HFpEF) is a highly prevalent syndrome characterized for an elevated morbimortality. Iron deficiency (ID) has emerged as a novel prognostic factor and therapeutic target in patients with heart failure with reduced ejection fraction (HFrEF); however, poor is known about the pathophysiological implications of ID in HFpEF. In this work we sought to evaluate whether standard parameters of ID were related to functional capacity in patients with HFpEF.

**Methods:** we prospectively studied a cohort of 40 patients with advanced HFpEF (74 years (66-77), 55% female, 50% NYHA III). Maximal functional capacity was evaluated with an incremental and symptom-limited cardiopulmonary exercise testing and was expressed as peak oxygen consumption (peakVO<sub>2</sub>). ID was defined as: ferritin  $< 100 \text{ mg/L}$  or ferritin 100-300  $\text{mg/L}$  with transferrin saturation (TSAT)  $< 20\%$ .

**Results:** The median (IQR) peakVO<sub>2</sub>, hemoglobin (Hb), ferritin and TSAT were 10 ml/min/kg (8.9-12.9), 13 g/dL (11.7-13.8), 94 mg/L (53-220), 19% (15-26), respectively. Anemia and ID were present in 15 (37.5%) and 28 (70%) patients, respectively. In a bivariate setting, log-peakVO<sub>2</sub> was negatively correlated with age, NT-proBNP, and E/E' ratio, while positively correlated with Hb, TSAT, estimated glomerular filtration rate (eGFR), tricuspid annular plane systolic excursion and ferritin (Figure 1). In a multivariable setting, age, resting heart rate, NT-proBNP, eGFR, E/E' ratio, Hb, TSAT and serum ferritin were retained as significant predictors for the mean peakVO<sub>2</sub> (82,3% of variability).

**Conclusion:** in patients with advanced HFpEF, standard parameters of ID were related to patient's functional capacity evaluated by peakVO<sub>2</sub>.

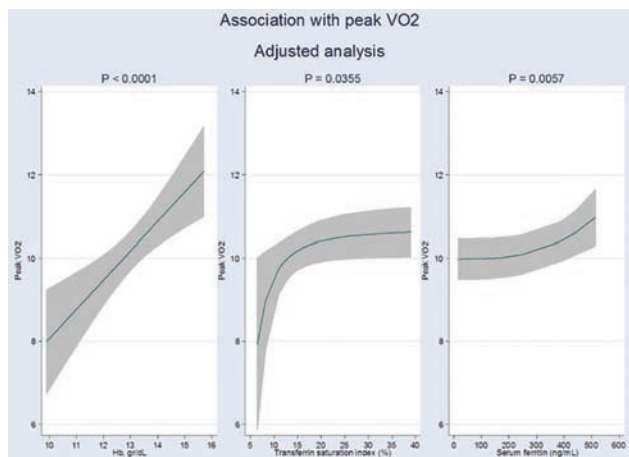


Figure 1

**P1569**

**Nonalcoholic fatty liver disease is associated with higher 1-year all-cause rehospitalization rates in patients admitted for acute heart failure**

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**Background:** Repeat hospitalization due to acute heart failure (HF) is a global public health problem that markedly impacts on health resource use. Non-alcoholic fatty liver disease (NAFLD) is an emerging risk factor for many heart diseases, including HF.

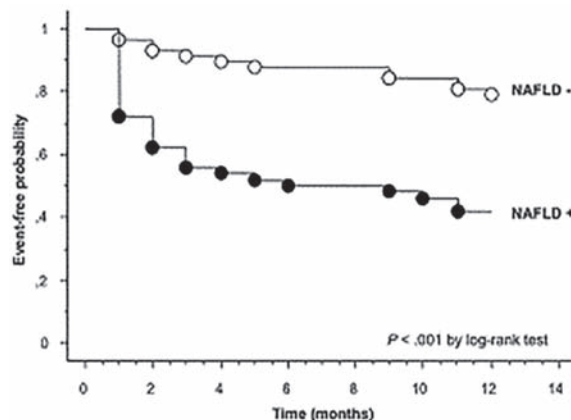
**Purpose:** We assessed whether NAFLD at hospital admission predicts 1-year re-hospitalization in patients with acute HF.

**Methods:** We enrolled all patients consecutively admitted for acute HF to our General Medicine Division during 2013 after excluding patients with acute myocardial infarction, severe heart valve diseases, malignancy, known liver diseases and those with volume overload related to extra-cardiac causes. NAFLD was diagnosed by ultrasonography. Primary outcome: 1-year all-cause re-hospitalization rate.

**Results:** Among the 107 patients enrolled in the study, patients who had been hospitalized during the follow-up period had significantly lower eGFR values and higher serum GGT and AST concentrations, they have a higher prevalence of atrial fibrillation, and were more treated with spironolactone than those not requiring re-hospitalization. At baseline, age, sex distribution, body weight, BMI, heart rate, systolic/diastolic blood pressure, plasma NT-proBNP levels, LV-EF, prior histories of diabetes, COPD, CHD/angina, peripheral artery disease, current use of ACE-inhibitors, sartans, beta-blockers, furosemide and amiodarone did not differ significantly between the two groups of patients. Notably, the prevalence of NAFLD at baseline was markedly higher in patients with re-hospitalization at follow-up (70.7% vs. 31.8%,  $P < .001$ ). Patients with NAFLD at baseline had markedly higher 1-year re-hospitalization rates than those without NAFLD (58% vs. 21% at 1 year;  $P < .001$  by the log-rank test) (Figure). Cox regression analysis revealed that NAFLD was associated with a 5-fold increased risk of re-hospitalization (adjusted-hazard ratio 5.56, 95% CI 2.46–12.1,  $P < .001$ ) after adjustment for multiple HF risk factors and potential confounders. In conclusion, NAFLD was independently associated with higher 1-year hospital readmission in patients hospitalized for acute HF.

Multivariable Cox regression models			
Cox Hazard Models	Hazard ratio	95% CI	P value
NAFLD (yes vs no) Unadjusted model	3.71	1.88-7.30	< 0.001
Adjusted model 1 (age and sex)	4.83	2.36-10.1	< 0.001
Adjusted model 2 (model 1+eGFR and GGT)	5.38	2.55-11.2	< 0.001
Adjusted model 3 (model 2+NT-proBNP, LV-EF, BMI, Diabetes, history of AF)	5.56	2.46-12.1	< 0.001

Factors independently associated with 1-year all-cause re-hospitalization rate in patients with acute AF at baseline.



Figure

**P1570**

**Determining risk of heart failure hospitalization and mortality using routine liver function tests.**

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**Background:** Deranged liver function has been demonstrated in both acute and chronic heart failure (HF) patients, but has always been considered as merely a sequel to HF itself. There has been recent interest in using parameters of liver function as markers of HF severity and prognosis, however the majority of analysis has been limited to patients in clinical trials only. We aimed to use a population-based database of an unselected cohort of HF patients to develop a risk prediction model based on liver function parameters to predict HF hospitalization and all-cause mortality.

**Methods:** We analyzed data from the BIOSTAT-CHF database which prospectively tracks patients with heart failure from a region in Scotland. Multivariable cox proportional hazard models were used to assess the prognostic impact of liver dysfunction on heart failure outcomes, while controlling for covariates like age, gender, treatment regime, previous history of myocardial infarctions, atrial fibrillation, diabetes, renal disease and CHF duration.

**Results:** Out of a total 1585 patients with a mean age of 73.6 (+/-10.6) years and mean HF duration 3.49 (+/-4.61) years, there were 401 (25.3%) HF hospitalizations and 329 (20.8%) deaths. Of the 6 liver function parameters, 4 were independent predictors of composite HF hospitalization or death. Per log unit reduction in serum albumin (ALB) showed increased hazards by 1.59 (95% CI 1.29 -1.97,  $p < 0.001$ ). Whereas per log unit increase in total bilirubin(TB), alkaline phosphatase(ALP) and gamma-GT(GGT) were associated with increasing hazards of the composite outcome by 1.63 (95% CI 1.25-2.13,  $p < 0.001$ ), 1.29 (95% CI 1.02-1.62,  $p = 0.030$ ) and 1.49 (95% CI 1.21-1.82,  $p < 0.001$ ) respectively. AST and ALT were not predictors of HF outcomes. We then developed a simplified 4-point risk scoring model using the above parameters which demonstrated increasing HF risk as the score increased, reaching a peak hazard of 5.52 (95% CI 3.48–8.76) in patients with the maximum score of 4 points.

**Conclusions:** Our findings demonstrate lower ALB, elevated TB, ALP and GGT are independent predictors of HF hospitalization or all-cause mortality among HF patients. Our simplified risk scoring model can be used as an easy-to-use tool to prognosticate HF patients.

**P1571**

**Model for end-stage liver disease excluding normalized ratio (MELD-XI) score as a measure of hepato-renal dysfunction in patients with decompensated heart failure**

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**Introduction:** The occurrence of hepato-renal dysfunction is important for the selection of patients to procedures such as heart transplant and ventricular assist-devices. We investigated the value of hepato-renal dysfunction in patients with decompensated heart failure.

**Methods:** We analyzed a cohort of 409 patients admitted for decompensated heart failure in a tertiary hospital dedicated to cardiology from August 2013 through December 2015; MELD-XI at hospital admission was determined in 312 patients



and categorized in quartiles; values were confronted with clinical characteristics and prognosis

**Results:** Mean age was  $55.3 \pm 15$  years and 254 (62.1%) patients were male; left ventricle ejection fraction was  $30 \pm 12$ ; 102 (24.9%) patients had ischemic heart disease, 97 (23.7%) Chagas' cardiomyopathy, 74 (18.1%) idiopathic dilated cardiomyopathy and 48 (11.7%) hypertensive disease. At admission BNP level was  $1486 \pm 1297$  pg/dL and creatinine  $1.96 \pm 1.2$  mg/dL. During hospital admission 45 (11%) patients were submitted to heart transplant and 128 (31.3%) died. The analysis of MELD-XI quartiles showed that increasing MELD-XI was associated with higher proportion of male patients (44.9% for first quartile, 56.4% for second quartile, 71.8% for third quartile, 71.8% for fourth quartile,  $P=0.01$ ), increasing age ( $49.6 \pm 15.1$  years,  $55.4 \pm 13.8$ ,  $52.7 \pm 15.5$ ,  $56.7 \pm 12.9$ ,  $P=0.01$ ), higher proportion of patients with ascites (14.3%, 23.1%, 31.2%, 38.5%,  $P=0.036$ ), higher proportion of patients with peripheral edema (45.5%, 64.1%, 70.1%, 59.7%,  $P=0.044$ ), higher proportion of patients with right ventricular dysfunction (26.9%, 43.6%, 53.8%, 47.4%,  $P=0.06$ ) and higher BNP levels ( $868 \pm 107$  pg/dL,  $1480 \pm 179$ ,  $1201 \pm 141$ ,  $1475 \pm 178$ ,  $P=0.013$ ). The rate of heart transplant decreased according to MELD-XI quartile (21.8%, 12.8%, 11.8%, 10.3%) and mortality increased (21.8%, 33.3%, 44.7%, 46.2%,  $P=0.021$ ). When MELD-XI score was analyzed in multivariable logistic regression model that included sodium, hemoglobin, blood pressure and heart rate at admission, BNP and ejection fraction, only blood pressure was associated with mortality (OR 0.977,  $P=0.001$ ).

**Conclusion:** Hepato-renal dysfunction is frequent in patients with heart failure especially in older male patients with right ventricular dysfunction. However, in the setting of decompensated heart failure, hemodynamic variables remain as more important markers of prognosis than organ damage.

#### P1572

##### Brain natriuretic peptide levels and echocardiography data of patients with acute myocardial infarction against the background of non-alcoholic steatohepatitis

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**Background:** Brain natriuretic peptide (BNP) level and echocardiography are the two most informative tests to evaluate the risk of future heart failure development in patients with ST-elevation myocardial infarction (STEMI). The presence of non-alcoholic steatohepatitis (NASH) can influence the prognosis of STEMI. The purpose of this study was to determine BNP levels and the dynamics of functional heart parameters in patients with STEMI accompanied with NASH. Methods. 76 patients with STEMI accompanied with NASH and 31 patients with STEMI without liver pathology were examined. Groups were comparable in age and gender. Cardiac ultrasonography was done to all patients on 3rd and 28th day after AMI. The amount of troponin, creatine phosphokinase, transaminases was determined in blood of all patients. BNP levels were assessed  $64 \pm 7$  hours after onset of chest symptoms. Also the data of liver ultrasound and liver biopsy were used to confirm the diagnosis of NASH.

**Results:** Patients with STEMI accompanied with NASH had the following dynamics of functional heart parameters from 3rd to 28th day: left ventricular enddiastolic volume (LVEDV) was slightly decreased (-2.9%;  $60.74 \pm 4.16$  mm), left ventricular endsystolic volume (LVESV) showed a tendency to increase (+14.8%;  $54.36 \pm 5.13$  mm) as well as ejection fraction (EF) +14.6%;  $45.39 \pm 2.82\%$ . However, the mentioned above changes weren't statistically significant. Patients with STEMI without liver pathology demonstrated significant decrease of LVEDV (-17.2%;  $54.08 \pm 3.97$  mm; = 0.031), as well as LVESV (-21.1%;  $39.49 \pm 3.25$  mm; = 0.042); EF increased to 28% ( $51.93 \pm 2.69\%$ ;  $p=0.007$ ). The analysis of indexes on 28th day showed increase of EF in both groups (70.36 % and 84.57% of patients respectively, = 0.048); decrease of contractile ability determined in 23.6% and 15.13% of patients respectively, = 0.042). Patients with STEMI accompanied with NASH demonstrated significantly higher levels of BNP compared to controls (749.25 pg/ml vs 435.18 pg/ml,  $p \leq 0.05$ ). Also, a positive correlation was found between BNP and LVESV ( $r=0.358$ ,  $p \leq 0.05$ ), BNP and peak troponin levels ( $r=0.452$ ,  $p \leq 0.05$ ) in such patients. **Conclusion.** Patients with STEMI accompanied with NASH had worse dynamics of functional heart parameters than the ones without liver pathology. These included insufficient improvement of left ventricular systolic function and its contractile ability, tendency to enlargement of left ventricular cavity. Together with significantly higher levels of BNP such changes may predict increased probability of the left ventricle dysfunction, heart failure development and poorer prognosis in patients with STEMI accompanied with NASH.

#### P1573

##### Urinary levels of new kidney biomarkers and risk of worsening renal function and mortality in patients with acute heart failure.

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**Background:** Increased urinary levels of cystatin C (uCysC), neutrophil gelatinase-associated lipocalin (uNGAL) and kidney injury molecule 1 (uKIM-1) are proposed as sensitive, early markers of renal tubular injury. We investigated their predictive value for the development of worsening renal function (WRF) and long-term outcomes in patients hospitalized with acute heart failure (AHF).

**Methods:** Urinary levels of CysC, NGAL, KIM-1 were measured using high sensitive immunoassay based on a single-molecule counting technology (Singulex, US) at baseline, days 1 and 2 in 132 patients with AHF (mean age:  $65 \pm 13$  years, male: 78 %). The concentration of the biomarkers was normalized to the creatinine in urine (ng/gCr for uKIM-1,  $\mu$ g/gCr for uNGAL and uCysC). WRF was defined as an increase  $\geq 0.3$  mg/dl in serum creatinine or a decrease  $>25\%$  in the glomerular filtration rate from the baseline value during hospital stay.

**Results:** WRF occurred in 28 (22%) patients and they had significantly higher levels of uNGAL at baseline (29.7 [10.3-45.7] vs. 13.1 [5.9-41.2],  $\mu$ g/gCr), at day 1 (24.6 [17.2-54.0] vs. 14.7 [6.3-31.6],  $\mu$ g/gCr), and day 2 (29.2 [16.3-114.3] vs. 18.7 [6.9-30.5],  $\mu$ g/gCr) (patients with vs without WRF, medians [interquartile range],  $p < 0.05$  in all comparisons). There were no differences in uKIM-1 and uCysC between groups. In the multivariable analyses elevated uNGAL at day 1 remained as independent predictor of WRF (1.53 [1.09-2.14],  $P=0.012$ ), with area under curve of 0.71 (0.60-0.82). During 1-year follow-up there were 36 (27%) deaths. WRF was not associated with mortality [ $P=0.94$ ]. After adjustment for other prognosticators, uNGAL at days 1 and 2 and uCysC at day 1 were independent predictors of mortality with hazard ratios of 1.36, 1.39 and 1.35, respectively ( $P < 0.05$  for all).

**Conclusions:** Elevated uNGAL measured at 24 hours after admission predicts WRF during hospitalization in patients with AHF. Elevated levels of uNGAL and uCysC could be used to identify patients at risk of poor outcome.

#### P1574

##### Effect of implementation of algorithm preventing loading in clinical practice before primary percutaneous coronary intervention on contrast-induced acute kidney injury

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**Background:** 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. In primary PCI we have limited time to assess the risk and preventing of CI-AKI. Therefore important to develop and implementation of algorithm preventing.

We performed a single-centre prospective study to determine the effect of implementation of algorithm preventing on the incidence of CI-AKI in patients with STEMI and primary PCI.

**Methods:** We used of historical control data for assessing of algorithm preventing CI-AKI in routine clinical practice. The study compared two groups of patients with ST-segment elevation myocardial infarction (STEMI) and primary PCI before and after implementation of algorithm preventing CI-AKI. In 1 Group - control group ( $n=33$ ) we used the routine prophylaxis CI-AKI: in patients with eGFR  $< 60$  ml/min/1.73m<sup>2</sup> received intravenous hydration of 0.9% saline solution of sodium chloride (NaCl) at a rate of 1.0-1.5 ml/kg/h before the PCI. In 2 group - prevent group ( $n=33$ ) we prevented CI-AKI according to the algorithm: patients with eGFR  $< 60$  ml/min/1.73m<sup>2</sup> and/or with Mehran risk score  $\geq 11$  received intravenous fluid administration hydration of 0.9% NaCl and N-Acetylcysteine (NAC): 0.9% NaCl  $\times$  500-1000 ml before PCI and 1 ml/kg/h post contrast administration with NAC 300 mg before PCI and 900 mg after PCI. Both groups were comparable in age ( $63 \pm 11$  and  $62 \pm 12$  years), comorbidity (hypertension 89 and 85%, chronic kidney disease 14 and 15%, diabetes mellitus 19 and 17%) and received therapy. CI-AKI was defined using 2012 KDIGO Guidelines. Isoosmolar contrast media iohexanol (Visipaque-320) or low-osmolar contrast media iohexol (Omnipaque-350) were used. Transradial access for PCI was used in 98% of patients. Mann-Whitney test and multivariate logistic regression analysis were performed.  $P < 0.05$  was considered statistically significant.

**Results:** The incidence of CI-AKI in intervention group was significantly lower than in the control group (20 and 11%,  $p < 0.05$ ).

**Conclusion:** Implementation of algorithm preventing of contrast-induced acute kidney injury significantly reduced the risk of CI-AKI in clinical practice in patient with STEMI and primary PCI.

## P1575

### To assess effect of ultrafiltration by peritoneal route on echocardiographic parameters in refractory congestive heart failure by two dimensional echo and tissue doppler imaging

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**Background:** - Ultrafiltration by peritoneal route is an effective alternative to conventional diuretic treatment for refractory heart failure. There are no direct studies demonstrating effect on Echocardiographic parameters.

**Purpose:** - 1. To assess the effect of ultrafiltration on echocardiographic parameters and TDI at baseline and three month post ultrafiltration 2. To determine the therapeutic role of ultrafiltration in improving patient clinical status; this is assessed by New York Heart Association (NYHA) functional class, Change in number of days of hospitalization 6 minute walk test.

**Methods:** The study population includes both outpatient who attended Heart failure clinic as well as inpatients admitted for heart failure. It was a non randomised observational study. The baseline data was collected at start and then after three months of ultrafiltration therapy. The collected data was entered and analyzed using Microsoft office window excel 2007 and SPSS version 16 (SPSS 16.0 for Windows, release 16.0.0. Chicago: SPSS Inc). We considered the association or difference to be significant when the p value was less than 0.05.

**Results:** 19 patients of refractory heart failure of various etiologies were recruited in the study. Out of 19 patients 16 were alive and undergoing CAPD at 3months. 19 study subjects were studied. EF (Ejection fraction) before the treatment was (35.4±6.6) which improved to (43.1±13.8) (P<0.01). RAVI (Right atrial volume index) before the treatment was (31.8±14.3) and improved to (28.3±14.9) (P=0.016). IVC diameter before the treatment was (2.27±0.44) at 3 months (1.8±0.68). PASP (Pulmonary artery systolic pressure) was compared before the treatment was 50.7±14.4 to post CAPD decreased (38.1±15.6)(P<0.01). There was significant decrease in duration of hospitalisation from (17.5±8.3) to (1.7±3.4) (p<0.0001). NYHA class III & IV significantly improved to NYHA class I & II pre 19 (100%) and post 3(17.6%) ultrafiltration (p<0.0001). There was highly significant increase in the duration of 6 minutes' walk test pre 58.52±47.6 and post 176.4±80.7 (p<0.0001) after ultrafiltration. Conclusion - Ultrafiltration was safe and associated with significant improvement in echoardiographic parameter. LV systolic function (ejection fraction) was improved; also there was reduction in LV dimension and volumes. We found ultrafiltration was associated with a substantial improvement in NYHA functional class, physical performance (6MWT), and with significant reduction rehospitalization days.

## P1576

### Biochemical determinants of worsening renal function after diuretic therapy for heart failure patients

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**Background** Diuretic therapy for worsening heart failure (HF) frequently leads to deterioration of renal function. How changes in serum substance(s) are associated with changes in renal function after diuretic therapy in HF patients, however, is unknown.

**Purpose:** We tested our hypothesis that changes in serum solute(s)/albumin are associated with the changes in the serum creatinine (SCr) level after diuretic therapy.

**Methods:** Data from 47 patients (32% men; 78.2±9.7 years) with mild-to-moderate HF that experienced a worsening episode of HF defined by ≥2 HF signs were analyzed. Each patient underwent conventional diuretic therapy and returned to stable HF status after therapy. Blood tests included measurement of hemoglobin (Hb), hematocrit (Ht), serum albumin, solutes, and serum b-type natriuretic peptide. The relative change in the plasma volume (%PV) from worsening HF to recovery was estimated as follows: 100 x {Hb (worse) x [1-Ht (recovery)]/[Hb (recovery) x [1-Ht (worse)]}-100.

**Results:** Among a total of 47 worsening HF events, the incidence of an increase and decrease in SCr was 40 (85%) and 7 (15%), respectively, after decongestive therapy. Changes in SCr negatively correlated with changes in sodium (Na) (r=-0.453, P=0.0014) and chloride (Cl) (r=-0.534, P=0.0001), and positively correlated with changes in BUN (r=0.621, P<0.0001), although changes in SCr did not correlate with changes in body weight (r=0.149, P=0.317) or %PV (r=-0.09, P=0.559). When divided into two groups by the median SCr, the group with increased SCr [SCr≥0.12mg/dL (range 0.12 to 1.31); n=24] exhibited a greater decrease in serum Na (-4.29±4.39 vs -1.39±3.93mEq, P=0.02) and Cl (-7.3±5.05 vs -1.4±3.44mEq, P<0.0001) after decongestive therapy compared with the group without increased SCr [SCr<0.12mg/dL; n=23], whereas the decrease in body weight and log BNP did not differ between the two groups. Multivariate logistic regression analysis demonstrated an independent association between the increase in SCr and the decrease in serum Na (OR: 0.145, 95% CI: 0.023-0.883, P=0.036) and Cl (OR: 0.134, 95% CI: 0.02-0.919, P=0.04) after decongestive therapy.

**Conclusions:** Deterioration of renal function defined by an increase in SCr after

decongestive therapy in worsening HF patients is associated with a decrease in the serum Na and Cl concentrations. Preservation of these solutes might be crucial toward maintaining renal function in patients under diuretic therapy for worsening HF.

## P1577

### Association between galectin-3 and worsening renal function

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**Background and aim of the study:** Galectin-3 (Gal-3) is a biomarker reflecting inflammation status and fibrosis which has been demonstrated to be related to both chronic heart failure (CHF) and renal dysfunction. The aim of this study was to evaluate the association between Gal-3 serum levels and worsening renal function (WRF) in a group of CHF outpatients.

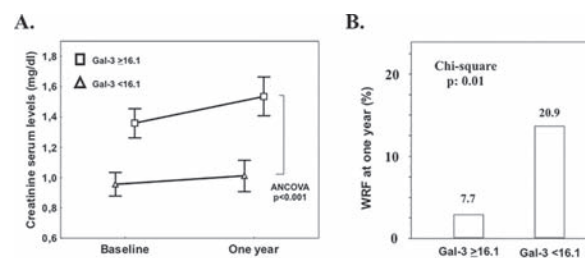
**Methods:** We enrolled 171 outpatients (81% males, 64±13 years, NYHA class 2.4±0.6, left ventricular ejection fraction, LVEF, 33±8%, GFR EPI 74±26 ml/min\*1.73 m<sup>2</sup>) with CHF (ESC criteria) due to left ventricular systolic dysfunction, in stable clinical conditions (>1 month) and in conventional therapy. All patients underwent a clinical evaluation, a routine chemistry and an echocardiogram. WRF was defined as an increase in serum creatinine of ≥0.3 mg/dl associated with a change >25% or a decrease in GFR>20% at 1 year follow-up.

**Results:** During follow-up, WRF was observed in 21 patients (12%). At baseline patients with WRF, when compared with those without WRF, showed significantly lower mean GFR values (63±27 vs. 73±25 ml/min\*1.73 m<sup>2</sup>, respectively; p: 0.03), but these differences further increased at 1 year (41±19 vs. 74±24 ml/min\*1.73 m<sup>2</sup>, respectively; at ANCOVA analysis p<0.001).

Patients with WRF, when compared to patients without, showed also significantly higher serum levels of Gal-3 (21.2±11.8 vs 15.1±5.5 pg/ml; p<0.001). At univariate logistic regression analysis Galectin 3 was associated with WRF occurrence (OR: 1.10; 95%CI: 1.04-1.17; p: 0.002) and this association remained significant (OR: 1.09; 95%CI: 1.01-1.19; p:0.038) after correction for the others univariate predictors, i.e. baseline GFR EPI, baseline central venous pressure >5 mm Hg and baseline logarithm of NT-proBNP.

At ROC curve analysis (AUC 0.65; 95% CI: 0.51-0.79) the best cut-off was 16.1 (with a sensitivity of 64% and a specificity of 64%). Panel A of the figure shows changes in creatinine serum levels according to this cut-off value of Gal-3. Patients with high Gal-3 showed greater baseline values, which further and significantly increased at one year (p<0.01 at ANCOVA analysis). Panel B shows the percentage of patients with one year occurrence of WRF according to Gal-3 cut-off.

In conclusion, our findings demonstrate the independent association between Gal-3 and worsening renal function in CHF outpatients. These results can be explained by the fact that Gal-3 reflects the pathophysiological status underlying both cardiac and renal dysfunction, thus strengthening the potential clinical usefulness of this biomarker in predicting the progression of cardiorenal syndrome in heart failure patients.



Figure

## P1578

### Markers of renal dysfunction in chronic heart failure

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**Introduction:** Kidneys are one of the most critical target organs in individuals with chronic heart failure (CHF). As CHF progresses, a significant number of patients develop renal dysfunction achieving a degree of chronic renal dysfunction.

**Objective:** to define and assess markers of renal dysfunction in chronic heart failure (CHF).

**Materials and methods:** A total of 132 subjects (mean-age 60,75±7,31 y.o.) with CHF NYHA functional class II, III with previous Q-wave myocardial infarction (MI) were assessed. Myocardial infarction was not older than 4,06±3,27 years. Mean

left ventricular ejection fraction (LVEF) was  $50.2 \pm 7.68\%$ . Patients with renal impairments and/or endocrine pathology were excluded from the study. Medical treatment: beta-blocking agents, ACE-inhibitors or angiotensin receptor blockers, aspirin, statins, and diuretics. All patients had general physical examination. Echocardiography was performed using Vivid-7 (GE, USA-Belgium) device with a sensor of 3.5 MHz. Biochemistry was obtained using Olympus analyzer: the level of cystatin was detected using Randox kits with the application of Olympus analyzer (normal between 0.57 and 1.05 mg/l), creatinine concentration was obtained using Beckman kits (normal 44.0-110.0  $\mu\text{mol/l}$ ). Glomerular filtration rate (GFR) by cystatin level based on the formula:  $\text{GFR (ml/min/1.73m}^2) = -4.32 + 80.35/\text{cystatin}$ . Urine microalbuminuria (MAU) was assessed using Olympus analyzer, microalbumin OSR 6167, urine alpha-microglobulin-1 (1) was obtained using direct enzyme-linked immunosorbent assay using monoclonal antibody pairs EIA-1 (normal not exceeding 10 mg/l).

**Results:** Urine, blood glucose, and enzyme levels were normal in all the subjects. Mean values of creatinine ( $99.80 \pm 11.67$   $\mu\text{mol/l}$ ) and cystatin ( $0.93 \pm 0.09$  mg/l) in the above-mentioned group were normal. However, higher creatinine was shown in 21.9% subjects, and higher cystatin was seen in 28% subjects. Mean GFR by creatinine and cystatin was below normal and accounted for  $83.72 \pm 12.78$  and  $85.65 \pm 11.87$  ml/min/1.73m<sup>2</sup>, respectively. Decreased GFR (from mild to moderate) defined by cystatin was seen in 62.1% subjects. Thus, most of the CHF subjects had evidence of chronic renal dysfunction. Moderately decreased GFR (by cystatin) was shown in 8.3% subjects. These patients had lesions of target organs with no clinical signs. Higher levels of 1 (14.4% subjects) and MAU (12.9% subjects) were also present. A correlation between cystatin and 1 was defined ( $r = -0.50$ ,  $p < 0.001$ ), as well as a negative correlation between LVEF and cystatin C ( $r = -0.54$ ,  $p < 0.001$ ). Conclusion: Thus, most of the subjects with CHF had signs of renal dysfunction with no clinical manifestations. It is obvious that cystatin, microalbuminuria and alpha-1-microglobulin may be considered as early markers of renal dysfunction in GFR that are associated with the development of systolic heart failure.

#### P1579

##### Renal resistance index and microalbuminuria as multiparametric approach to assess renal function in heart failure: prognostic aspects

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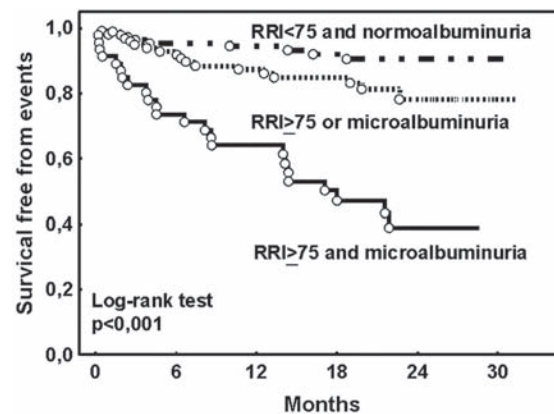
**Background:** In order to better evaluate renal function in chronic heart failure (CHF) patients, it has been suggested that microalbuminuria and the evaluation of renal blood flow, by renal resistance index (RRI), can integrate information obtained by glomerular filtration rate (GFR). The aim of the study was to evaluate the prognostic relevance of a multiparametric approach for the assessment of renal function in a group of CHF outpatients.

**Methods:** We enrolled 253 outpatients (81% males,  $64 \pm 13$  years, NYHA class  $2.3 \pm 0.6$ , left ventricular ejection fraction, LVEF  $33 \pm 10\%$ , GFR EPI  $69 \pm 27$  ml/min<sup>1.73 m<sup>2</sup></sup>) with CHF (ESC criteria) due to left ventricular systolic dysfunction, in stable clinical conditions (> 1 month) and in conventional therapy. In all patients, on the basis of pulsed Doppler peak systolic velocity and end diastolic velocity of segmental renal artery, RRI was calculated. Microalbuminuria was defined as the urinary albumin/creatinine ratio (UACR) of 30 to 299 mg/g. Patients with macroalbuminuria were excluded from the analysis. Creatinine serum levels were used to estimate GFR by EPI formula. During follow-up heart failure progression was defined as the occurrence of hospitalization and/or heart transplantation and/or death due to worsening of heart failure.

**Results:** During a mean follow-up of  $19 \pm 7$  months, in 56 patients heart failure progression occurred. At Cox univariate regression analysis a GFR <60 (HR 2.19; 95%CI: 1.25-3.81;  $p < 0.006$ ; C index 0.59), an RRI  $\geq 75$  (HR 3.83; 95%CI: 2.04-7.22;  $p < 0.001$ ; C index 0.65) and microalbuminuria (HR: 3.81; 95%CI: 2.18-6.67;  $p < 0.001$ ; C index 0.66) were all associated to heart failure progression. However, in a multivariate analysis including the three parameters only RRI >75 (HR: 2.99; 95%CI: 1.54-5.83;  $p < 0.001$ ) and microalbuminuria (HR: 2.99; 1.66-5.36;  $p < 0.001$ ), but not GFR <60 (HR: 1.15; 95%CI: 0.63-2.09;  $p < 0.65$ ) remained significantly associated to events.

When a score was computed, on the basis of the presence or not of a high RRI and of microalbuminuria, it was obtained a new parameter associated to events at univariate (HR 3.09; 2.10-4.56;  $p < 0.001$ ; C-index: 0.71) as well as at multivariate Cox regression analysis (HR: 1.14%CI: 54-1.72;  $p < 0.001$ ) after correction for age, NYHA class, LVEF and NT-proBNP. Moreover, the new parameter showed a significant incremental value when added to the multivariate model (free net reclassification index  $p < 0.001$ ). Figure shows Kaplan Meier curves of the three groups according to RRI  $\geq 75$  and/or microalbuminuria.

**Conclusions:** The combination of RRI and microalbuminuria allows to obtain an evaluation of renal function with a greater value in predicting heart failure progression. This can be explained by the fact that these parameters are more able to reflect the different pathophysiological mechanisms leading to the progression of heart failure and cardiorenal syndrome.



Figure

#### P1580

##### Cardiorenal relations in patients with prosthetic valve IE

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**Purpose:** To study the features of heart failure and kidney injury in patients with prosthetic valve (PV) infective endocarditis (IE).

**Material and methods:** 80 patients (50 men) with IE (Duke 2015) were included, of which 16 (12.8%) patients have PVIE (group 1) and 64 (51.2%) have native valve IE (group 2). We evaluated the anamnesis, echocardiogram, renal function (GFR, proteinuria, microscopic hematuria, serum Cystatin C, urinary KIM-1), heart failure (NYHA) rates and NT-proBNP levels, acute kidney injury (AKI, KDIGO 2012) and mortality rates. Early AKI was defined as AKI at the moment of hospital admission, AKI developed during hospitalization was considered as late AKI.

**Results:** The median age in the group 1 was 64 [58-67], in group 2 — 63 [54-69] years,  $p > 0.05$ . Groups did not differ by age, gender and comorbidity. Subacute IE prevailed in both groups [11 (68.8%) vs. 34 (53.1%),  $p > 0.05$ ], left ventricular EF mainly was preserved [ $53.8 \pm 8.7$  (39-69) vs.  $55.6 \pm 8.4$  (28-72),  $p > 0.05$ ]. In the group of PVIE condition was significantly more often associated with medical interventions [8 (50.0%) vs. 21 (32.8%),  $p < 0.05$ ] and characterized by multivalve involvement [7 (43.8%) vs. 4 (6.3%),  $p < 0.05$ ]. Heart failure was more severe in group 1 than in group 2 and more frequently presented by NYHA FC III/IV HF [13 (81.3%) vs. 33 (51.6%),  $p < 0.05$ ]; NT-proBNP median values were 3792 [649-4570] pg/ml vs. 1603 [584-4068] pg/ml, respectively,  $p < 0.05$ . Median GFR in group 1 was 41 [31-53] ml/min, in the group 2 — 55 [39-85] ml/min,  $p < 0.05$ . AKI occurred more often in group 1: in 11 (68.8%) vs. 30 (49.6%) patients,  $p < 0.05$ . The same was true for early [3 (18.8%) vs. 6 (9.4%),  $p < 0.05$ ] and late AKI [8 (50.0%) vs. 24 (36.5%),  $p < 0.05$ ]. Groups did not differ by incidence of urine laboratory changes [13 (81.3%) vs. 49 (76.6%),  $p > 0.05$ ]. In group 1 there were higher values of serum Cystatin C — 3.5 [3.0-4.8] vs. 2.0 [1.6-2.2] pg/ml ( $p < 0.05$ ), KIM-1 in urine — 2.8 [2.5-3.3] vs. 1.6 [1.5-1.7] ng/ml ( $p < 0.05$ ). In the group of PVIE prevailed Enterococcus spp. (n=6) and Staphylococcus spp. (n=4) presented by Staphylococcus epidermidis and Staphylococcus haemolyticus. Mortality rates were similar in both groups [5 (31.3%) and 20 (31.3%),  $p > 0.05$ ], but surgical treatment was performed more often in group 1 [6 (37.5%) vs. 4 (6.3%),  $p < 0.05$ ]. Conclusion: Prosthetic valve IE has stronger connection to medical interventions, is often associated with Enterococcus spp. and Staphylococcus spp. and characterized by more severe heart failure and higher frequency of AKI, higher NT-proBNP, Cystatin C and KIM-1 values.

#### P1581

##### Uncovering heart failure in stable chronic obstructive pulmonary disease

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**Background:** Heart failure (HF) is one of the major causes of death in chronic obstructive pulmonary disease (COPD) patients. Despite the fact, HF remains to be underrecognized and undertreated in COPD patients as clinical symptoms of both diseases frequently overlap and echocardiography is not routinely performed in COPD patients.

**Purpose:** The aim of our study was to assess the prevalence of HF in stable COPD patients.



**Methods:** The prospective cohort study included 120 patients with previously diagnosed COPD. In all patients spirometry and transthoracic echocardiography were performed. Patients were divided into four stages of COPD according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria.

**Results:** The overall HF prevalence was 28,3%:40% in GOLD stage IV, 30% in stage III, 26,7% in stage II and 16,7% in stage I. The prevalence of HF with preserved EF was 23,3%:16,7% in GOLD stage I, 26,7% in stage II, 23,3% in stage III and 26,7% in stage IV. The HF with reduced EF <45% was diagnosed in 6.7% of cases and was present only in severe stages of COPD (6.7% in stage III and 20% in stage IV).

**Conclusion:** The high prevalence of unrecognized HF highlights the need for echocardiography in COPD patients, especially in advanced COPD stages.

## P1582

### Small airways obstruction better predicts mortality risk than central airways obstruction in patients with stable heart failure and reduced ejection fraction

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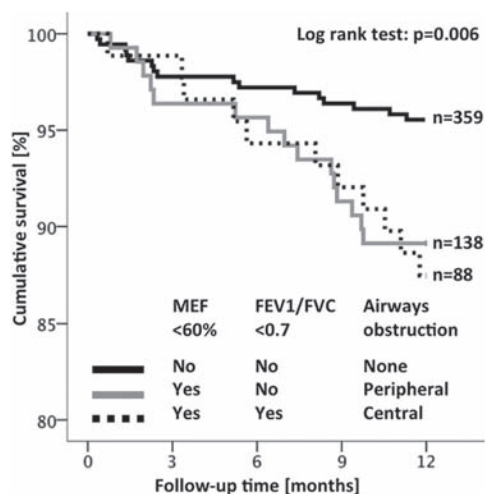
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**Background:** Impairment of pulmonary function increases symptom burden and mortality risk in heart failure (HF). Previous studies focused on the prognosis of a reduction in forced expiratory volume in the first second (FEV1), that is, central airways obstruction. By contrast, the prognostic effect of small airways obstruction as measured by the limitation of mid-expiratory flow (MEF) has not been investigated. We compared the prevalence and prognostic utility of central and small airways obstruction in patients with HF and reduced ejection fraction (HFrEF).

**Methods:** Spirometry was performed six months after hospitalization for cardiac decompensation in patients with HFrEF at discharge (left ventricular EF ≤40%). We measured the ratio of FEV1 and forced vital capacity (FVC) and the MEF at 50% of FVC. The cut-offs defining central and small airways obstruction were <0.7 for FEV1/FVC and <60% of predicted value for MEF, respectively.

**Results:** We included 585 patients (mean age 65 ± 12 years, 75% male). 359 (61%) patients had no expiratory flow limitation, 88 (15%) had a FEV1/FVC <0.70 (all of those subjects also showed a MEF reduction), and 138 (24%) patients exhibited only a reduced MEF. During the follow-up period of twelve months, 42 patients (7.2%) died. Figure 1 shows Kaplan-Meier plot of patients with i) no, ii) central, and iii) small airways obstruction. In univariable Cox regression, MEF <60% and FEV1/FVC <0.7 were associated with increased all-cause mortality risk (hazard ratios [95% confidence intervals]: 2.65 [1.42-4.94], p = 0.002, and 2.04 [1.02-5.05], p = 0.043, respectively). In a bivariable model including both parameters, only MEF <60% remained associated with increased mortality risk (2.51 [1.24-5.08], p = 0.010), but not FEV1/FVC <0.7.

**Conclusions:** Expiratory flow reduction in small airways is more common than central airways obstruction in HFrEF and seems a better predictor of increased risk of death as central airflow limitation.



Kaplan-Meier survival plot

## P1583

### Prolonged use (18 months) of tiotropium and indacaterol in patient with chronic heart failure due to coronary artery disease combined with chronic obstructive pulmonary disease

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**Purpose:** to compare clinical efficacy and safety of tiotropium and indacaterol prolonged (18 months) 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 81 patients (58 men and 23 women), aged 66.5 ± 4.3 years, with CHF classes II to III (New York Heart Association) combined with moderate to severe COPD (GOLD-2013) and with initial ejection fraction of the left ventricle (LVEF) less than 45%, were randomized to three groups - tiotropium (18 µg daily, n=29), indacaterol (150 µg daily, n=27) and tiotropium+indacaterol group (18/150 µg daily, n=25). Patients of all groups received the complex CHF treatment comprising diuretics, nebivolol, losartan, cardiac glycosides (subject to indications) and basic COPD therapy (inhalation corticosteroids). Echocardiography, exercise tolerance (6-min walk distance), 24-hour electrocardiography and blood pressure monitoring were assessed at baseline and every 6 months of treatment, respiratory function test was assessed at baseline, after 1 month and every 6 months. The quality of life was evaluated by MYHFQ, SGRQ and mMRC.

**Results:** after 18 months of therapy the improvement of clinical condition and quality of life were marked in all groups. In 1st, 2nd and 3rd group LVEF was increased by 4.2%, 5.0% and 8.8%, pulmonary hypertension decreased by 7.4%, 10.8% and 14.5%, episodes of silent myocardial ischemia decreased by 15.3%, 16% and 21.4%, 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 6.6%, 7.7%, and 12.1% accordingly. 6-min walk distance increased by 19.1%, 21.6% and 30.2% accordingly. Patients showed statistically significant and clinically meaningful reduction of SGRQ score (19.4%, 18.1%, 23.7%) and MYHFQ score (14.2%, 13.8%, 21.9%), significant improvements in mMRC dyspnea grade (23.1%, 22.2%, 27.5% respectively). All treatments were well tolerated.

**Conclusions:** the tiotropium and indacaterol 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 inhaled anticholinergic agent (tiotropium) and long-acting β-agonist (indacaterol) in patient with CHF due to CAD combined with COPD are similar. Combination of these drugs significantly enhances the positive effects of the prolonged therapy.

## P1584

### Right heart failure as a risk factor for exacerbation in patients with chronic obstructive pulmonary disease

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**Background:** Patients with Chronic Obstructive Pulmonary Disease (COPD) exacerbations have progressive and widespread vascular disease and not just respiratory. Heart Failure (HF) is common in patients with COPD, with a prevalence of 10-40%, and is implicated in a considerable number of exacerbations, morbi-mortality and hospitalization. It is estimated that the prevalence of HF undiagnosed in patients presented at emergency services is 20.9%. However it is unknown the role of Right Heart Failure (RHF) on exacerbations in patients with COPD.

**Aim:** Determine whether the RHF is an independent risk factor for COPD exacerbation.

**Materials and Methods:** A retrospective cohort study was performed in patients diagnosed with COPD from the Instituto Nacional de Enfermedades Respiratorias "Ismael Cosío Villegas" between 2009 - 2015. COPD was diagnosed based on FEV1 / FVC <0.7. Patients with bronchial hyperreactivity or asthma attack were excluded. X2 and independent t-test were performed in order to contrast the differences between the groups with and without exacerbation. Multiple regression analysis was made in order to assess the risk of exacerbations in patients with ICD adjusting for confounding variables.

**Results:** Were studied 250 patients diagnosed with COPD, age mean 72.22 ± 10 years, 48% were men, from them 105 (42%) presented exacerbations. The differences between subjects with or without exacerbations were: RHF (63.9% vs. 58.8%, p = 0.66), PAH (7.6% vs 1.6%, p = 0.04), pneumonia (24.2% vs. 51.4%, p = 0.001) thyroid disease (1.1% vs. 10%, p = 0.01). No differences in sex, age, GOLD, diabetes, HAS, dyslipidemia, cancer, diastolic or systolic HF between the two groups

were observed. Adjusting for age, sex, hemoglobin, hematocrit, leukocytes, pneumonia, asthma, hypertension, diabetes, systolic or diastolic HF, patients with Right HF have 5.78 (HR: 5.78; 95% CI 1.13 - 29.49) times the risk of developing COPD exacerbation.

**Conclusion:** In COPD patients, RHF is an independent risk factor for exacerbations develop, consequently its diagnosis and treatment are essential to prevent complications and / or hospitalizations.

#### P1585

##### Trastuzumab-induced cardiomyopathy: a retrospective observational study assessing the prevalence, characteristics and outcomes over 3 years. a single center experience in the eastern province of Saudi

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**Background:** The field of cardio-oncology is rapidly growing. Treatment-related cardiotoxicity has been of a significant concern in the management of breast cancer patients. There are well-established reports on the cardiotoxic effects of anthracyclines and trastuzumab in breast cancer. However, there is scarce data to describe its prevalence in the Eastern Province of Saudi Arabia.

**Purpose:** To better understand the prevalence of trastuzumab-induced cardiomyopathy in our population and the characteristics of the patients that develop this complication along with reversibility of specific type of cardiomyopathy.

**Methods:** A retrospective observational study was conducted to looking at consecutive patients that received trastuzumab from January 1st, 2012 up to September 30th, 2015 in a single tertiary oncology center in the Eastern province of Saudi Arabia. The patients' baseline characteristics were obtained from chart review and a detailed review of serial echocardiographic studies was gathered. Those with reduction of Ejection Fraction (EF), defined as an EF of less than or equal to 50%, were identified and a careful review of their medications and cardiac biomarkers was done. Serial measurements of EF for those who experienced a decline in EF were captured to assess the percentage of myocardial recovery.

**Results:** A total of 302 patients received trastuzumab in the pre-specified time period in our center. Out of the 302 patients, 71 patients developed trastuzumab induced cardiomyopathy as defined earlier. This constitutes 23.5% of the population studied. Out of those affected, the mean age was  $48.3 \pm 10.9$  years. 46.4% were hypertensive and 18.30% were diabetic. Out of the 71 patients who developed cardiotoxicity, 55 recovered leaving 22.5% of the population with residual LV dysfunction. However only two patients had persistently significant LV dysfunction defined as an EF of <45%. From the 71 patients with trastuzumab induced cardiomyopathy, 23.4% were initiated on ACE-I/ARB and 20.59% were instituted on beta blockers. As for the biomarkers, BNP was requested in f cases and Troponin was requested in m cases. Out of all requested troponins, only one patient had a value above the 99th centile. As for the BNP, h were above elevated, defined as a value greater than or equal to 100— . g% of those elevated BNP's correlate to those cases with persistent LV dysfunction.

**Conclusion:** The prevalence of Herceptin induced cardiotoxicity in our population was 23.5% over 3 years. Almost half of these patients were hypertensive and 18.3% were diabetic. 74.3% of these patients recovered, but only 2.8% had significant residual LV dysfunction. Elevation in BNP closely correlated to persistent LV dysfunction. Given the data listed above, we have initiated a pathway by which the population at risk of cardiotoxicity are identified and initiated on an ACE I/ARB at the time of, or even prior to, starting trastuzumab.

#### P1586

##### Factors associated with cancer chemotherapy-induced cardiomyopathy: a cumulative case-control study

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**Objective:** To determine the factors associated with the occurrence of cancer chemotherapy-induced cardiomyopathy. Design: Retrospective study. Setting: Pay and charity patients of our Medical Center in Philippines. Patients/Participants: All newly diagnosed cancer patients who underwent chemotherapy, 18 years old and above seen from January 2009 to December 2014. Patients who had cardiomyopathy prior to study period or who have had cardiomyopathy prior to study period or who have had cardiomyopathy prior to having cancer; pregnant patients and patients who were diagnosed with coronary artery disease by coronary angiogram were excluded.

**Results:** Among the risk factors studied (age, gender, body surface area, type of cancer, stage of cancer, left ventricular ejection fraction before chemotherapy and presence or absence of comorbidity), gender is the only significant risk factor associated with cancer chemotherapy-induced cardiomyopathy with an odds ratio of 10.6 (95% CI 3.07, 36.65) with a p value of 0.00001, which is statistically significant. Thus, male is 10.6 times more likely to develop cardiomyopathy compared to female.

**Conclusion:** Gender is significantly associated with the occurrence of cancer chemotherapy-induced cardiomyopathy. Specifically, males are 110.6 times more likely to develop cardiomyopathy than females.

## VALVULAR HEART DISEASE(DIAGNOSIS, MANAGEMENT AND INTERVENTIONAL THERAPIES)

#### P1587

##### Permanent pacemaker implantation after a new fully repositionable device for trans-catheter aortic valve implantation; impact on left ventricular function and myocardial deformation.

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**Background:** Fully repositionable trans-catheter aortic valve devices (TAVI) facilitate precise positioning and minimise paravalvular regurgitation. However, the occurrence of some periprocedural complications remains a concern, and the need for permanent pacemaker implantation (PPI) after the procedure is frequent. Very few data exist on the clinical, myocardial deformation and left ventricular ejection fraction impact of PPI after second-generation TAVI procedure.

**Methods:** A total of 20 consecutive patients with symptomatic severe aortic stenosis undergoing TAVI with fully repositionable devices were included.

**Results:** Mean age was 80.6 years, 65% were female and 70% were New York Heart Association functional class III/IV. Eight patients (45%) required a PPI within the first 30 days after TAVI. The average hospital stay for TAVI procedure was 9 days, with no differences between the PPI and no PPI groups ( $p=0.3$ ). After a mean follow-up of 12 months, a total of 3 patients (15%) either had died or required a rehospitalization for heart failure, with no differences between the PPI and no PPI groups (8.3% versus 25%; Fisher's exact: 1.045;  $P=0.31$ ). Left ventricular ejection fraction decreased slightly in the overall population at 12-month follow-up (from  $60.29 \pm 10.9\%$  to  $57.57 \pm 11\%$ ). But a small improvement in myocardial deformation by global longitudinal strain (GLS) was observed over time by mean (from  $-16.05 \pm 4.1\%$  to  $-16.53 \pm 4.8\%$ ), with no differences between PPI and no PPI groups ( $-15.02\%$  versus  $-18.42\%$ ; T-student:  $-1.15$ ;  $P=0.28$ ).

**Conclusions:** PPI after a new fully repositionable device for trans-catheter aortic valve implantation remains a frequent complication, but it was not associated with any increase in cardiovascular death or rehospitalization for heart failure after a follow-up of 12 months. Indeed, myocardial deformation by GLS increased in the overall population over time.

#### P1588

##### The effects of TAVI on arterial stiffness and ventricular-arterial coupling

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**Background:** transcatheter aortic valve implantation (TAVI) is a percutaneous intervention for patients affected by severe aortic stenosis not suitable for cardiac surgery, typically the eldest. The ageing process itself is responsible of vascular and ventricular stiffening. Arterial stiffness and ventricular-arterial coupling (VAC) are independent prognostic factors in patients suffering from heart failure (HF).

**Purpose:** we aimed at evaluating arterial stiffness and VAC before and early after TAVI.

**Methods:** 20 patients scheduled for TAVI were enrolled. Within 3 day before and at least 3 day after the procedure they underwent radial artery applanation tonometry to evaluate central blood pressures and augmentation index (AIx@75), and transthoracic echocardiography to calculate the aortic elastance (Ea), the end-systolic left ventricular elastance (Ees) and their ratio, namely VAC.

**Results:** mean age was  $82 \pm 8$  years. 12 (60.0%) were male. Functional aortic valve area was  $0.7 \pm 0.2$  cm<sup>2</sup>, peak gradient  $82 \pm 26$  mmHg and mean gradient  $49 \pm 17$  mmHg. Hemodynamic parameters are reported in Table 1. After TAVI there was a great improvement in AIx@75. Moreover, a tendency to amelioration was found for central blood pressures, stroke volume, Ea, Ees and VAC, without statistical significance.

**Conclusion:** TAVI is associated with an early improvement in arterial stiffness and a tendency to better central hemodynamics and VAC. Considering the prognostic role of these factors in patients with HF, TAVI is of growing importance under different points of view.

Table 1

Variable	Before TAVI	After TAVI	p
Aortic SBP (mmHg)	117 ± 20	113 ± 19	0.4
Aortic DBP (mmHg)	71 ± 12	66 ± 10	0.1
Aortic MAP (mmHg)	88 ± 14	89 ± 12	0.1
Aortic PP (mmHg)	46 ± 15	47 ± 13	0.8
Alx@75 (%)	33 ± 16	23 ± 12	0.005
Stroke volume (mL)	76 ± 21	85 ± 30	0.2
Ea (mmHg/mL)	1.6 ± 0.6	1.5 ± 0.5	0.5
Ees (mmHg/mL)	1.8 ± 0.9	1.9 ± 0.8	0.8
VAC	1.0 ± 0.4	0.9 ± 0.3	0.3

SBP=systolic blood pressure; DBP=diastolic blood pressure; MAP=mean arterial pressure; PP=pulse pressure; Alx@75 augmentation index corrected for 75 bpm; Ea=aortic elastance; Ees=end-systolic left ventricular elastance; VAC=ventricular-arterial coupling

**P1589**

**Mitral regurgitation severity correlates with symptoms and extent of left atrial dysfunction: effect of mitral valve repair**

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**Background:** Severe mitral regurgitation (MR) causes left ventricular (LV) and left atrial (LA) volume overload, and atrial fibrillation (AF). The aim of the study was to assess the relationship between MR severity, symptoms and LA structure and function, and their response to mitral valve repair (MVR).

**Methods and Results:** Global peak atrial longitudinal strain (PALS) was evaluated in 37 patients with severe symptomatic MR and preserved LVEF (60 ± 4.6%) before and 3 months after MVR and was compared with values from 30 age- and gender-matched controls. Before surgery, compared with controls, global PALS was reduced and indexed LA volume was increased (p < 0.0001 for both) and fell after MVR (p = 0.001 and p = 0.05, respectively). After surgery, LVEF and longitudinal strain (LS) reduced (p = 0.05 and p < 0.001, respectively) and LV mass (LVM) regressed (p < 0.0001). Before surgery, LA volume correlated modestly with end-diastolic volume (R = 0.51, p = 0.01); effective regurgitant orifice area (EROA) correlated strongly with PALS (R = -0.69, p < 0.001) and modestly with LVLS (R = 0.54, p = 0.01); and NYHA class correlated strongly with PALS (R = -0.69, p < 0.001) and EROA (R = 0.60, p < 0.001), modestly with LA volume (R = 0.51, p = 0.04), but not with LVLS (R = 0.23, p = ns). LA volume was the strongest predictor of global PALS reduction (p < 0.001) and indexed LVM of LA volume reduction (p < 0.001) after MVR while global PALS was the main predictor of post-operative AF (p < 0.001).

**Conclusions:** In patients with severe MR, symptoms correlate with EROA as does LA PALS, which itself predicts the occurrence of post-operative AF and is determined by LA volume.

**P1590**

**Adverse events in operated and non-operated patients with severe aortic valve stenosis**

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**Background/Introduction:** Aortic valve replacement (AVR) in patients with severe aortic valve stenosis (SAVS) provides considerable improvement of survival and quality of life. Postoperative adverse events are not negligible, but little is known about the total burden when compared with patients refused for AVR. Purpose: To report adverse clinical events one year following AVR and one year after refusal for AVR, in patients with SAVS. Methods: Of 480 patients with SAVS evaluated for AVR, 389 underwent operation (OP) and 91 were declined operation (NON-OP). Mean (SD) age was 74 (10) and 81 (9) years, and percentage women was 41 and 52 for OP- and NON-OP respectively. Counting one year from the operation day, or time of evaluation for non-operated patients, all available medical records were reviewed. The outcomes of interest were predefined as clinically relevant. Results: See table. Conclusion: This study demonstrates a significant number of adverse events among OP patients, but not being operated for SAVS is associated with significantly more myocardial infarctions, new hospital admissions as well as significantly increased one-year mortality. These results advocate AVR in patients with SAVS.

Frequencies of adverse clinical events

	OP, n = 389	NON-OP, n = 91	p-value	
	During postoperative stay	One year	One year	
One-year mortality, n (%)	-	22 (6)	17 (19)	< 0.01
Myocardial infarction, n (%)	4 (1.1)	6 (1.5)	9 (9.9)	< 0.01
Stroke, n (%)	14 (3.5)	27 (6.9)	3 (3.3)	0.2
Transient ischemic attack, n (%)	2 (0.5)	9 (2.3)	0	0.1
New permanent pacemaker, n (%)	1 (0.2)	26 (7)	6 (7)	0.9
Endocarditis, n (%)	1 (0.2)	11 (2.8)	2 (2.2)	0.7
Myocarditis, n (%)	4 (1.0)	5 (1.2)	0	0.3
Pneumonia, n (%)	65 (17)	82 (21)	12 (13)	0.09
Urinary tract infection (UTI), n (%)	24 (6.2)	38 (9.8)	8 (9)	0.8
Wound infection, n (%)	11 (2.8)	22 (5.7)	1 (1.1)	0.3
Minor bleeding, n (%)	29 (7.1)	-	-	-
Major bleeding, n (%)	23 (5.7)	-	-	-
Post-operative hospital stay, median days (SD)	10 (9)	-	-	-
At least one hospitalization, % patients	-	52	54	0.7
Overnight hospitalizations, median days (IQR)	-	6 (11)	14 (18)	< 0.01
Hospital contacts, total number (rate/patient)	-	382 (0.98)	99 (1.09)	< 0.01

SD = standard deviation, p-value compares one year results in OP vs NON-OP

**P1591**

**Low cardiac output syndrome after aortic valve replacement in 2045 elderly patients**

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**Background:** Low cardiac output syndrome (LCOS) is one of the most lethal hospital complications after aortic valve replacement. If modifiable predictors can be identified, postoperative outcome might improve.

**Purpose:** Identification of modifiable predictors for LCOS. Methods: A retrospective file study of 2045 patients was performed, in whom a diseased aortic valve was replaced by a bioprosthesis. Of these, 1124 were males and 513 were over 80. The mean age was 76 ± 6 years. Concomitant CABG was performed in 1243 patients. For 36 preoperative and 10 operative variables, a chi-square test was performed to examine their effects on LCOS. The significant variables were entered in a stepwise logistic regression, to identify the independent predictors. Results: LCOS was diagnosed in 110 patients, which was fatal in 51% of the cases. Need for urgent valve replacement is the most dominant predictor. LCOS is also associated with a prolonged stay in the intensive care unit (p < 0.001), pulmonary complications (p < 0.001), increased need for transfusion (p = 0.007), ventricular arrhythmias (p = 0.012) and delirium (p = 0.015). Conclusion: Need for urgent valve replacement is the most dominant modifiable predictor for postoperative LCOS. This points to an exhaustion of compensatory mechanism of the left ventricle to maintain an adequate circulation. This could be prevented by removing timely the pressure burden of the stenotic valve. Once symptoms develop, surgery should not be delayed. Except for the choice for a Carpentier-Edwards pericardial valve, there are no other modifiable predictors.

**P1592**

**Magnesium orotate improves health-related quality of life after surgical valve replacement**

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**Purpose:** Successful surgical intervention in valvular heart disease has been shown to prolong and improve quality of life. We aimed to evaluate postoperative



health-related quality of life (HRQoL) in patients following metabolic magnesium orotate therapy.

**Methods:** 100 patients (aged  $56.2 \pm 3.5$  years, 62 males, 35% concomitant SCAD) 2–4 weeks after surgical aortic (n=58) and mitral (n=42) valve replacement by mechanical prostheses were randomized 1:1 to receive either conventional therapy (vitamin K antagonists, ACEIs/ARBs, beta-blockers, diuretics, MRAs, statins and digoxin) or magnesium orotate (500 mg t.i.d.) added to standard treatment. HRQoL was assessed at baseline and 12 months using the Short Form (SF-36 v.1) Health Survey.

**Results:** There were no significant differences between magnesium orotate and control groups at baseline. Patients reported poor postoperative HRQoL. In both groups, SF-36 scores substantially rose after follow-up. Magnesium orotate patients had significant higher improvements in HRQoL over time compared to controls. One patient died in the control group (p = 0.63).

**Conclusions:** Mechanical valves patients commonly suffer from severe HRQoL impairment. Long-term magnesium orotate, added to conventional treatment, greatly improves HRQoL. The results provide support for nonsteroidal anabolic magnesium orotate as an additional therapy for patients with heart valve prostheses.

Health-related quality of life			
SF-36 scales	Baseline mean scores (SE)	1-year % change from baseline	
Control (n = 50)	Magnesium orotate (n = 50)	Control (n = 49)	Magnesium orotate (n = 50)
Physical Functioning	42.1 (2.5)	41.7 (2.4)	+ 45.3 + 87.5**
Role-Physical Functioning	38.3 (3.2)	39.4 (3.5)	+ 36.4 + 78.2**
Bodily pain	37.5 (2.4)	38.0 (2.7)	+ 56.2 + 122.3***
General Health	35.3 (3.5)	35.7 (3.6)	+ 82.5 + 135.4**
Total Physical Health	43.5 (2.4)	42.8 (2.5)	+ 52.1 + 95.3**
Vitality	29.3 (1.5)	28.7 (1.7)	+ 103.2 + 164.8***
Social Functioning	25.4 (1.3)	26.3 (1.3)	+ 135.8 + 183.8**
Role-Emotional Functioning	32.9 (2.1)	33.5 (2.2)	+ 108.3 + 142.2*
Mental Health	31.4 (1.8)	30.8 (1.7)	+ 89.4 + 168.3***
Total Mental Health	29.8 (1.7)	28.7 (1.8)	+ 92.7 + 175.1***
Total SF-36 score	35.6 (2.4)	36.8 (2.2)	+ 68.4 + 121.5**

\*p < 0.05, \*\*p < 0.01, \*\*\*p < 0.001 differences between control and magnesium orotate groups.

### P1593

#### Improvement of left ventricular function beyond ejection fraction in patients undergoing percutaneous mitral valve repair

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**Aims:** Long-standing mitral regurgitation (MR) causes chronic volume-overload leading to left ventricular (LV) enlargement and remodeling. The objective of this study was to investigate the effect of LV remodeling on LV function after percutaneous mitral valve repair (PMVR).

**Methods and Results:** 66 heart failure patients with moderate-to-severe MR undergoing PMVR underwent speckle-tracking echocardiography (STE) at baseline and at six-months follow-up. Despite no notable improvement in LV ejection fraction (LVEF;  $43.3 \pm 14.6\%$  vs.  $44.5 \pm 14.9\%$ , p = 0.163) study patients provided an increase in effective forward stroke volume (SV) determined by means of PW Doppler in left ventricular outflow tract ( $63.4 \pm 37.1$  ml vs.  $76.2 \pm 35.1$  ml, p < 0.001) implying an improvement of global cardiac performance.

In our study we differentiated 35 patients with LV remodeling and 31 patients without (LVN). LVN patients showed preserved LV function with higher baseline LVEF ( $50.9 \pm 12.2\%$  vs.  $35.2 \pm 12.7\%$ , p < 0.001) and LV global longitudinal strain (GLS)

than LVR patients ( $-13.8 \pm 3.5\%$  vs.  $-9.9 \pm 4.5\%$ , p < 0.001) indicating better myocardial contractility. Most importantly, we noted a salient amelioration in GLS following PMVR in LVN patients ( $-13.8 \pm 3.5\%$  vs.  $-16.3 \pm 3.8\%$ , p < 0.001) whereas no improvement was observed in LVR group ( $-9.9 \pm 4.5\%$  vs.  $-9.9 \pm 5.1\%$ , p = 0.936).

**Conclusion:** In patients with chronic MR PMVR results in increased SV, which remains undetected by means of conventional echocardiographic parameters. STE describes significant reverse remodeling in patients undergoing PMVR demonstrating that patients with preserved LV geometry show notable improvement in terms of LV contractile function.

### P1594

#### Influence of atrial fibrillation on heart remodelling and severity of heart failure at patients with mitral valve disease

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**Purpose:** To evaluate the influence of atrial fibrillation on heart remodelling at patients with mitral valve disease after valve replacement. Methods: 95 patients (mean (SD) age  $57.4 \pm 9.6$  years) with mitral valve disease (isolated mitral stenosis (MS) – 40 patients, isolated mitral regurgitation (MR) – 48 patients, combined valve lesion – 7 patients) who underwent mitral valve replacement. Atrial fibrillation (AF) before valve replacement has 65 patients (permanent – 39 patients, paroxysmal and persistent – 26 patients). Before and 12 months after valve replacement patients underwent transthoracic echocardiography and 6-minute walk test (MWT). Results: At baseline the size of the left atrium was greater in patients with AF  $57.6 \pm 6.4$  mm and  $49.2 \pm 5.3$  mm, respectively. At 12 months after surgery in patients with atrial fibrillation there was a significant (p < 0.05) decrease in the size of the left atrium from  $49.2 \pm 5.3$  mm to  $41.4 \pm 4.1$  mm. In patients with AF, such changes were not observed. Also in the second group there was a significant (p < 0.05) decrease in the size of the left ventricle (LVESD and LVEDD). In the first group these parameters also were unchanged. At month 12 it was significant improving (p < 0.05) in 6-minute walk test distance in both groups: from  $186.6 \pm 89$  m to  $339 \pm 80$  m at patients with AF and from  $227.5 \pm 74$  m to  $457 \pm 91$  m at patients without AF.

**Conclusions:** The absence of atrial fibrillation positively affects on parameters of cardiac remodeling at patients with mitral valve disease 12 months after valve replacement. The presence of AF in patients with mitral valvular disease does not significantly affect the positive dynamics of the 6-minute test 12 months after valve replacement.

Table 1

	1 groupe (with AF)		2 groupe (without AF)	
Pre-operative	12 month	Pre-operative	12 month	
LA (mm)	$57.6 \pm 6.4$	$51.5 \pm 4.9$	$49.2 \pm 5.3^*$	$41.4 \pm 4.1^*$
LVESD (mm)	$36.3 \pm 6.1$	$37.1 \pm 5.4$	$40.5 \pm 5.8^*$	$32.6 \pm 4.9^*$
LVEDD (mm)	$53.9 \pm 7.2$	$50.4 \pm 6.9$	$58 \pm 6.3^*$	$48.3 \pm 5.3^*$
EF (%)	$55.8 \pm 8.6$	$51.7 \pm 7.3$	$58.5 \pm 7.6$	$60 \pm 7.3$
LVM (g)	$166.1 \pm 25.8$	$152.2 \pm 23.9$	$180.2 \pm 25.3$	$153.2 \pm 22.5$

\* - p < 0.05 vs baseline LA – left atrium; LVESD - end systolic dimension of left ventricular; LVEDD - end diastolic dimension of left ventricular EF – ejection fraction LVM - Left Ventricular Mass

### P1595

#### Is there any difference in interplay between kidney and heart after TAVR or SAVR?

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**Background:** Data on acute and chronic cardio-renal syndromes in patients undergoing aortic valve replacement are scarce.

**Purpose:** To compare influence of AKI on 6-month cardiac and kidney performance in the elderly with severe aortic stenosis (AS) undergoing surgical or transcatheter aortic valve replacement (SAVR or TAVR). Methods. Eighty over 70-year-old consecutive patients with severe symptomatic AS undergoing SAVR (n=40) or TAVR (n=40) were enrolled in prospective, observational single-centre study. Thirty-five patients in each group attended 6-month follow-up visit. AKI was defined based on VARC-2 criteria.

**Results:** AKI was more prevalent after SAVR compared to TAVR (72.5% vs 47.5%;  $p=0.022$ ) despite higher baseline eGFR ( $p=0.01$ ), younger age ( $p<0.001$ ) and lower logistic EuroSCORE ( $p=0.001$ ). Baseline NTproBNP levels and left ejection fraction (LVEF) were similar between the groups but NYHA class was lower in TAVR ( $p=0.004$ ). To assess the influence of AKI occurrence patients were divided into 4 subgroups: SAVR/AKI SAVR/nonAKI TAVR/AKI TAVR/nonAKI. Baseline LVEF, NTproBNP levels and NYHA class were comparable between AKI and nonAKI subgroups in both SAVR and TAVR. eGFR was lower in AKI subgroups compared to correspondent nonAKI ones. After procedure NTproBNP increased ( $p=0.042$ ) only in SAVR/AKI patients. Thus, at discharge median NTproBNP values were higher in SAVR/AKI compared to SAVR/nonAKI patients ( $p=0.003$ ; Figure 1B). At the follow-up SAVR/AKI patients improved NYHA class ( $p<0.001$ ) and reduced NTproBNP (both  $p<0.012$ ), however median NT-proBNP levels remained higher in SAVR/AKI vs SAVR/nonAKI ( $p=0.006$ ; Figure 1B), along with tendency for higher median NYHA class (1 IQ 0 vs 1 IQR 1;  $p=0.056$ ). Neither NYHA class nor NTproBNP values were affected by AKI in TAVR (Figure 1A). NYHA class improved in both TAVR subgroups (both  $p<0.002$ ). AKI occurrence did not lead to significant reduction of eGFR in neither group (Figure 1A and 1B).

**Conclusions:** AKI affected NTproBNP levels only after SAVR. The effect persisted for 6 months. AKI occurrence did not alter chronic kidney function in neither therapeutic group.

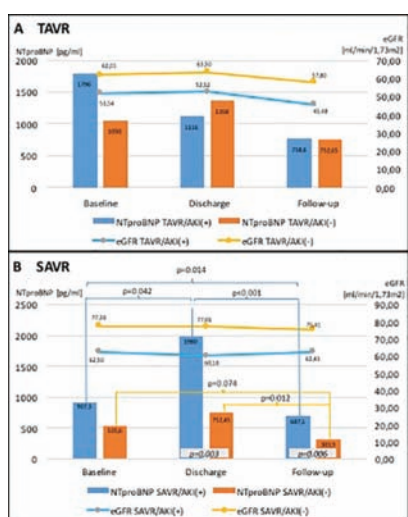


Figure 1. Comparison of NTproBNP and eGFR changes between AKI and nonAKI patients after (A) TAVR and (B) SAVR.

**P1596**

**Calcium-phosphate metabolism disturbances and quality of life in patients with significant mitral regurgitation.**

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**Purpose:** There are several factors connected with quality of life (QL) in patients with valvular heart disease (VHD). Though new ones are still researched. In recent years trials indicated vitamin D (25(OH)D3) and other calcium-phosphate (Ca-P) metabolism parameters and its disturbances as potential new factors influencing QL. Taking under consideration frequency of Ca-P metabolism disturbances and frequency of VHD in general and cardiovascular population we assessed the extent of Ca-P metabolism disturbances in this population and their influence on QL.

**Methods:** 99 consecutive patients hospitalized in our Department 07-09.2013 were included in the study. Inclusion criteria were: age>18, significant mitral regurgitation (MR) assessed with TTE(vena contracta>3mm, effective orifice area>0.2 cm<sup>2</sup>, MR volume>30ml/s). EQ-5D,SF-36 and MacNew QL Questionnaires (MNQLQ) were used to assess health-related QL (HRQL). Results We included 39 patients with severe and 60 with moderate MR (39.9% and 60.6% accordingly, average (avg) age 73.2yrs, 33.3% female). There were no significant differences in anthropometric measures between 2 studied groups. Avg serum Ca level corrected by albumin was 3.2mmol/L in both groups, avg serum Ca ionized level

corrected by pH was 1.06mmol/L in severe MR group and 1.05mmol/L in moderate MR group, avg serum P level was 3.6mmol/L and 3.4mmol/L in severe MR and in moderate MR group accordingly ( $p=0.055$ ), avg 25(OH)D3 level was 17.7ng/ml in severe MR group and 14.9ng/ml in moderate MR group. Additionally avg daily urinary P excretion was 37.2g/24 hours and 29.08g/24 hours in moderate and in severe MR group respectively and avg PTH level was 72.04pg/ml and 71.8pg/ml accordingly. We ascertained presence of Ca-P metabolism disturbances in population with significant MR, but with no significant differences in groups divided according to MR severity. There was significant negative correlation between parathormone (PTH) level and HRQL in 3 domains assessed with MNQLQ ( $(\rho)=(-0.242);(-0.243)$  and  $(-0.255),p=0.018;0.018$  and  $0.013$  for Global, Physical and Social domains respectively). Additionally we found significant correlation between the presence of abnormal PTH level itself and scores gained in 3 HRQL domains assessed with MNQLQ ( $4.34 \pm 1.26$  and  $3.76 \pm 1.30, p=0.031; 4.17 \pm 1.44$  and  $3.49 \pm 1.38, p=0.027; 4.48 \pm 1.44$  and  $3.81 \pm 1.39, p=0.019$  for Global, Physical and Social domains respectively).

**Conclusions:** There are significant Ca-P disturbances in population with significant MR. Those disturbances result in significantly worse QL. Further studies are needed to assess importance of those findings.

**DEVICES / CRT / ICD**

**P1597**

**Could one-year effect of cardiac resynchronization therapy on hemodynamic parameters evaluated by impedance cardiography be predicted ?**

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**Background:** Impedance cardiography (ICG) is a plethysmography technique for non-invasive measurement of hemodynamic parameters.

**Purpose:** the aim was to find out if ICG can be an useful in assessment of cardiac resynchronization therapy (CRT) efficacy.

**Methods:** A single-center, prospective study included 26 patients with chronic HF (92.3% male,  $65.5 \pm 9.4$  years, 42.3 % NYHA class II, 57.7% NYHA class III, 15.4% with atrial fibrillation, 61.5%, ischemic etiology of HF) qualified to CRT implantation. In all patients CRT were optimized in perioperative period. ICG was performed twice: one day before CRT implantation (before CRT) and 9-12 months post-implantation (after CRT).

**Results:** There was a significant improvement in some hemodynamic parameters in patients after CRT implantation (Table). In 8 patients (30,8%) a significant increase (defined as more than one standard deviation change) in stroke volume was observed. In 16 patients (61,5%), the changes were not significant and only 2 patients had deterioration of hemodynamic parameters (fall over one standard deviation in SV). Efficacy of treatment (defined as no heart failure worsening measured by ICG) was observed in 24 patients (92,3%). No significant differences in baseline demographics, clinical and echocardiographic parameters were found between 8 responders in comparison with the remaining 18 patients.

**Conclusion:** One-year efficacy of CRT in patients with heart failure can be demonstrated by ICG. No baseline demographics, clinical or echocardiographical data were able to predict the one-year response.

Hemodynamic parameter	before CRT	after CRT	p
Heart rate (HR) / bpm	65 ± 7,1	63,4 ± 8	p=ns
Stroke volume (SV) / ml	66,6 ± 10,3	76,2 ± 18,7	0,029
Cardiac output (CO) / l/min	4,3 ± 0,7	4,8 ± 1,1	0,056
Cardiac index (CI) / l/min/ m <sup>2</sup>	2,2 ± 0,4	2,4 ± 0,6	0,074
Left Ventricular Ejection Time (LVET) /ms	276,2 ± 55,9	304 ± 63,9	0,028
Systemic vascular resistance (SVR) / dyn·s/cm <sup>5</sup>	1552,8 ± 235,3	1631 ± 407	p=ns
Systemic vascular resistance index (SVRI) / dyn·s/cm <sup>5</sup> / m <sup>2</sup>	3103,8 ± 541,1	3249,9 ± 802,2	p=ns
Left cardiac work index (LCWI) / kg/m	2,4 ± 0,6	2,9 ± 1	0,016
End-diastolic filling ratio (EDFR)	77,5 ± 21,1	72,6 ± 16	p=ns

Comparison of hemodynamic parameters in patients before and one-year post CRT-implantation

## P1598

### FDA expedited access pathway enables staged approval opportunity for baroreflex activation therapy for heart failure with reduced ejection fraction: the BeAT-HF trial

This study is funded by CVRx, Inc., Minneapolis, Minnesota, USA.

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**Background:** Baroreflex activation therapy (BAT) improves quality of life, functional status, exercise capacity and biomarkers in patients with heart failure with reduced ejection fraction (HFrEF). Phase II randomized, controlled results also indicate BAT may reduce HF hospitalization. While these findings secured European regulatory approval, in the United States it is commonly necessary to improve outcomes. This may not only increase time to approval but also pre-market costs of clinical development to >100 million Euros. Thus, FDA initiated a program to accelerate approval of novel therapies targeting an unmet need for life-threatening conditions, the Expedited Access Pathway (EAP). The EAP allows initial approval using surrogate and intermediate endpoints with post-approval demonstration of improved outcomes. Motivated by strong Phase II results, coupled with the unmet need, FDA worked with the sponsor and clinical steering committee to design a trial within the EAP.

**Purpose:** To describe BeAT-HF, a 2-phase, prospective, randomized trial of BAT in HFrEF.

**Methods:** The overall objective of BeAT-HF is to demonstrate that BAT reduces HF hospitalization and cardiovascular mortality. At least 480 HFrEF patients will be randomized to guideline-directed medical therapy (GDMT) or BAT+GDMT. The first study phase includes the initial 264 patients followed for 6 months. Improved 6-minute hall walk distance, quality of life from the Minnesota Living with HF Questionnaire and NT-proBNP will suffice for pre-market approval submission if the probability of meeting the outcomes endpoint is trending positive, with an associated indication for HFrEF symptom relief. At the end of the first phase, accrued events will be analyzed to determine if sample size adjustment is required. Following enrollment completion events will be monitored until the outcomes endpoint is determined. Improved outcomes will result in a supplemental indication for the general treatment of HFrEF with commensurate labeling. The adaptive design is guided by a Bayesian approach with the final sample size determined by predictive probability with observed effect sizes at pre-specified interim analyses.

**Conclusion:** Based on favorable Phase II results of BAT in HFrEF and the unmet need of the population, a unique collaboration with FDA, taking advantage of the Expedited Access Pathway and using an innovative adaptive trial design has produced the BeAT-HF trial for possible US regulatory approval. The trial allows for staged approval of BAT, first for symptom relief and later for outcomes improvement. Enrollment is to begin early in 2016.

## P1599

### A local network for refractory cardiogenic shock

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**Background:** Veno-Arterial Membrane Oxygenation (VA-ECMO) represents a therapeutic option in patients with refractory cardiogenic shock (RCS).

**Purpose:** Only a restricted number of centers have technical capabilities for implanting VA-ECMO and for management of this support, so it is necessary to create a local network for patients with RCS. We report on the initial experience of our ECMO referral center for patients with RCS. **Methods:** We analyzed our ECMO data registry for RCS, particularly we considered 9 patients with RCS treated with VA-ECMO, consecutively transferred by peripheral hospitals to our Intensive Cardiac Care Unit (ICCU). A multidisciplinary team assessed indications and the suitable setting of ECMO implantation.

**Results:** In our population (6 male, median age 54.7 years) the most frequent etiology of RCS was acute coronary syndrome (55.5%). 4 patients (44.4%) implanted VA-ECMO in the peripheral centers and after on-site stabilization, they were transferred to our hospital with no adverse events (median distance 38 Km). Other 5 patients were directly transferred to our ICCU and there treated with VA-ECMO. All 9 patients survived at discharge, their length of stay in ICCU median was 19 days. After discharge 7 patients showed a complete recovery, one patient underwent to cardiac transplantation (CT) effectively, one patient died while waiting for CT because of cerebral haemorrhage. The survival rate after 30 days was 88.9% and all survival showed a good neurological outcome (cerebral performance category scale 1-2).

**Conclusions:** In our series, the survival rate of RCS patients supported by VA-ECMO is high (100% during ICU, 88.9% after 30 days) and the neurological outcome is good. Our data support that a network for RCS is needed to transfer safely patients in well-experienced center.

Sex	Age	Etiology	Site ECMO implantation	Length of ECMO (days)	ICCU LOS (days)	Evolution
Female	74	Takotsubo	ICCU	7	22	Recovery
Female	57	ACS	Cath lab	3	27	Recovery
Male	42	STEMI	ICCU	4	4	CT
Male	59	STEMI	ICCU	3	3	Death CT
Male	52	STEMI	Spoke	4	20	Recovery
Male	33	Electrical storm	Spoke	2	15	Recovery
Female	49	Thyroid storm	ICCU	3	17	Recovery
Male	57	ACS	Spoke	5	53	Recovery
Male	72	DCM	Spoke	3	18	Recovery

LOS=length of stay, ACS=acute coronary syndrome, STEMI=ST-elevation myocardial infarction DCM=dilated cardiomyopathy

## P1600

### Long-term survival and predictors of mortality in patients supported with a left ventricular assist device as destination therapy

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**Background:** Left ventricular assist devices (LVADs) represent an established therapeutic option for patients with end-stage heart failure (HF). Due to the paucity of cardiac allografts, LVADs are increasingly used as destination therapy.

**Purpose:** To study the long-term outcome and identify predictors of mortality in patients who underwent implantation of a continuous flow LVAD as destination therapy in a single, tertiary teaching hospital.

**Methods:** All patients who underwent implantation of a continuous flow LVAD with the indication of destination therapy during the period 1/2006-12/2015 were included in the analysis. We recorded the baseline characteristics and the long-term outcome, and performed univariate analysis to identify predictors of 1-year mortality.

**Results:** Thirty four patients (mean age 53±11 years) underwent implantation of a continuous flow LVAD as destination therapy during this period. Twelve percent of the patients were female; 59% suffered from ischemic cardiomyopathy. Mean values of New York Heart Association class, left ventricular ejection fraction (LVEF), cardiac index and BNP were 3.9±0.5, 23.2±5.7%, 1.9±0.5 L/min/m<sup>2</sup> and 1494±1319pg/ml. Only 32.5% and 14.7% of the patients tolerated administration of a b-blocker and an ACE inhibitor/ARB prior to implantation, while mean daily dose of furosemide was 554±404mg. Predicted 1-year survival based on the Seattle Heart Failure Model was 40%.

Peri-operative mortality was 8.8%. Survival rates at 1, 3 and 5 years were 81.3%, 44% and 29.2%, respectively. The longest observed survival exceeds 8.5 years from LVAD implantation. In univariate analysis, the baseline characteristics that correlated with 1-year mortality were female sex (HR: 7.1, p=0.025), non-ischemic cardiomyopathy (HR: 8.5, p=0.05), INTERMACS profile (HR: 0.28, p=0.032), LVEF (HR: 1.17, p=0.043) and systolic arterial pressure (HR: 0.79, p=0.04).

**Conclusion:** The implantation of a continuous flow LVAD impressively increases the survival of patients with end-stage HF. Identification of factors that affect the long-term outcome of these patients will enable selection of the most suitable candidates for chronic mechanical support.

## P1601

### Single center long term results of mechanical circulatory support in the netherlands

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**Background:** Prevalence of heart failure (HF) increases. Despite improvement in medical therapy it has a poor prognosis (1 year mortality 26% in patients aged ≤ 75 years). In end-stage HF refractory to medical therapy mechanical circulatory support (MCS) improves survival and quality of life. Nowadays, continuous-flow left



ventricular assist devices (cf-LVADs) are most often implanted. In The Netherlands, duration on MCS has increased because of an increasing waiting list for heart transplantation due to lack of donor hearts. Consequently, experience is built on longer term support. We present the long term results from our hospital.

**Purpose:** To provide insight in long term mechanical circulatory support.

**Methods:** Of all patients (pts) who received MCS between March 2006 and January 2016, data were prospectively collected in a central database, including baseline clinical characteristics as well as complications defined according to INTERMACS. Data were extracted for statistical analysis.

**Results:** 203 cf-LVADs were implanted in our hospital. 67 pts were transplanted and 7 pts explanted. Actuarial survival at 5 years is 68% (figure 1). Death was most often caused by neurological complications and sepsis. Gastro-intestinal bleeding and intracerebral complications (hemorrhage and stroke) both occurred 0.15 times per patient year. Twenty-seven replacements were performed, most often due to pump thrombosis or technical defects.

**Conclusion:** MCS in patients with end-stage HF has a 5-year survival of 68%. It is a promising therapy that might be a good alternative for heart transplantation in selected patients. However, further optimization of the therapy as well as management of long term complications is required.

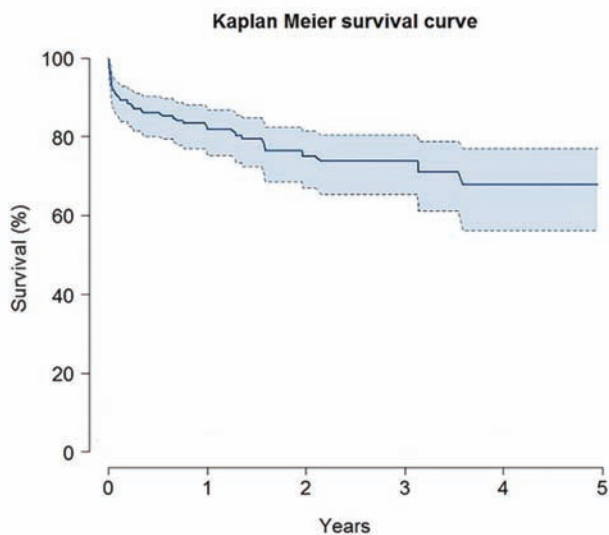


Figure 1. Kaplan Meier curve

**P1602**

**Evolution of mitral regurgitation in Berlin Heart EXCOR LVAD patients less than 10kg**

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**Background:** Left ventricular assist device (LVAD) is an important treatment option for bridging pediatric patients to heart transplant. LVAD allows left ventricular (LV) unloading with an improvement in mitral regurgitation (MR). However, a significant MR may persist in some patients with LVAD.

**Purpose:** The aim of this work is to evaluate the evolution of mitral regurgitation in pediatric patients less than 10Kg undergoing LVAD implantation.

**Methods:** Echocardiographic data of 15 pediatric patients less than 10Kg undergoing Berlin Heart EXCOR LVAD implantation were retrospectively collected before implantation and one, three and six months after LVAD to asses LV unloading and MR evolution.

**Results:** HF etiology was idiopathic dilated cardiomyopathy (79%) and non compacted LV myocardium (21%). Mean time of LVAD staying was 115.45 ± 84.33 days. The incidence of MR was in 8 patients at the baseline and 4 patients at the three and six months follow up. At the univariate analysis of patients with and without significant MR at the implantation, age, mitral valve annulus, left atrial size and vena contracta were predictive for residual significant MR after LVAD implantation. LV unloading provided by the LVAD was more evident till the first month follow-up and decreased at the three and six months follow up. Nine patients (60%) were successfully transplanted, two (13%) are still on LVAD and four (26%) died for major complication.

**Conclusion:** MR persistence is a possible complication also in pediatric LVAD recipient. The possibility of concomitant valve surgery is controversial, especially in low weight children. A patient-tailored LVAD setting optimization could potentially improve the haemodynamic benefits of LVAD and, in particular, LV unloading and MR.

Parameters	Baseline	1 month	3 months	6 months
Weight (Kg)	6.0 ± 1.9	6.5 ± 1.9	7.4 ± 2.0	7.9 ± 1.9
Left Atrium (mm)	25.4 ± 8.9	16.8 ± 3.7	19.4 ± 6.2	19.3 ± 5.8
Left Ventricular End Systolic Volume (ml)	46.5 ± 22.4	12.7 ± 10.4	24.3 ± 14.6	28.3 ± 17.3
Left Ventricular End Diastolic Volume (ml)	55.1 ± 23.2	18.9 ± 11.1	34.4 ± 17.6	40.6 ± 23.6
Mitral Valve Anulus (mm)	18.1 ± 6	15.3 ± 2.6	17.4 ± 5.4	18.6 ± 5.2
Vena Contracta (mm)	2.2 ± 0.9	1.9 ± 0.8	2.4 ± 1.0	3.0 ± 1.6
Right Ventricular Fractional Area Change	34.1 ± 9.7	34.1 ± 9.7	41.2 ± 13.6	36.0 ± 18.3

Evolution of echocardiographic parameters

**P1605**

**Soluble ST2 levels in end-stage heart failure and during LVAD support**

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**Background:** The interleukin 33 (IL-33)/suppressor of tumorigenicity 2 (ST2) pathway might play an important role in the progression of heart failure (HF) and is related to cardiac fibrosis. Although the exact source of the ST2 protein is not clarified, increased serum levels (sST2) are associated with adverse outcome in HF. In this study sST2 measurements were performed sequentially in patients with end-stage heart failure, before and after LVAD support. Furthermore we analyzed whether sST2 levels during HF were related to clinical parameters. Method: Serial serum measurements of sST2 were performed in EDTA plasma prior to LVAD and 1, 3 and 6 months after LVAD-implantation in 38 patients, using the high-sensitive Presage ST2 assay. Several clinical factors were analyzed for their relation with sST2 levels.

**Results:** sST2 levels were significantly elevated in end-stage HF just before LVAD implantation (74.2 ng/ml (IQR 54.7 -116.9; normal < 30 ng/ml) and decreased substantially during LVAD support, to 29.5ng/ml (IQR 24.7-46.6)(p< 0.001), normalizing in most patients. This normalization was complete at 3 months post-LVAD. The variation in sST2 levels at baseline could not be correlated to any of the clinical factors tested (gender, HF etiology, duration of HF, right ventricular function and renal function).

**Conclusion:** LVAD support results in a significant drop in sST2 levels with normalization within 3 months post implantation. This suggests that even in patients with end-stage HF, sST2 may be used as a biomarker to monitor therapy. The great variance in sST2 levels at baseline cannot be explained by differences in gender, HF etiology or duration, right ventricular function and renal function.

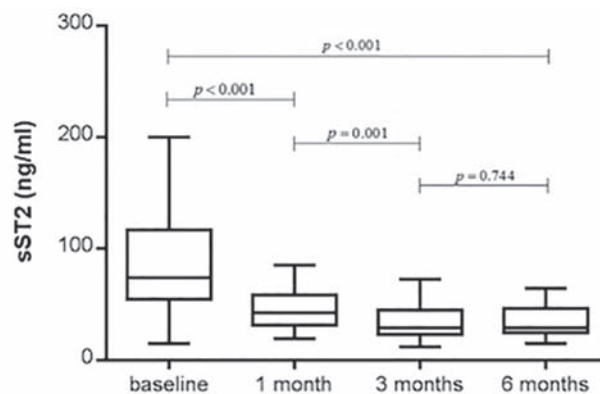


Figure 1. Boxplot showing median sST2 levels during LVAD support with IQR (25-75%), p < 0.05 was considered significant.

## P1606

**Hemodynamics during ramp testing predicts functional capacity in patients supported with continuous-flow left ventricular assist devices (CF-LVADs).**

The Danish Heart Foundation.

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**Background and Purpose:** Ramp studies- measuring changes in cardiac parameters as a function of serial pump speed modulations - are increasingly being used as an indicator of device function in CF-LVAD patients. The ability to predict functional status, quality of life (QOL) and survival from ramp studies, however, remains unexplored.

**Method:** Hemodynamic changes as a function of serial pump speed increase ( $\Delta$ rpm) were measured by right heart catheterization at the time of routine examination. Measures were undertaken at baseline pump speed (Ramp-base) followed by incrementally increasing pump speed steps until reaching maximal pump speed (Ramp-high). Ramp-high was decided bedside based upon left ventricular dimensions and/or septal shift. Finally pump speed was decreased to a minimum of support or to the point of aortic valve opening (Ramp-low). Subsequently functional capacity, QOL and survival were assessed. Results Eighty ramp tests were performed in 44 CF-LVAD patients. Changes in pump speed, cardiac output (CO) and pulmonary capillary wedge pressure (PCWP) are shown in Table 1. Functional status was evaluated in 70% (31/44). Average 6-MWT was 312  $\pm$  220 m, NYHA I-II/III-IV (70/30%) and activity scores Very low-Low/Moderate-Very high (55/45%). Decrease in PCWP per  $\Delta$ rpm was related to better NYHA classification; NYHA I-II vs III-IV,  $-0.29 \pm 0.15$  vs  $-0.09 \pm 0.16$  mmHg/rpm\*10<sup>-2</sup> ( $p = 0.007$ ) as well as to activity score; Very low-Low vs Moderate-Very-high,  $-0.16 \pm 0.16$  vs  $-0.31 \pm 0.16$  mmHg/rpm\*10<sup>-2</sup> ( $p = 0.02$ ). Changes in CO per  $\Delta$ rpm was correlated to measures of QOL. Ramp tests did not predict survival. Conclusion Hemodynamic changes during ramp studies are associated with measures of functional capacity and QOL. Hence such tests could potentially identify patients in risk of failure to thrive during CF-LVAD support.

Table 1

	Ramp-low	Ramp-base	Ramp-high	Difference Ramp-low to Ramp-high	$\Delta$ Change/ $\Delta$ rpm
Pump Speed	8,609 $\pm$ 518	9,605 $\pm$ 362	10,573 $\pm$ 555	1,964 $\pm$ 584 ( $p < 0.001$ )	NA
CO (l/min)	4.9 $\pm$ 1.2	5.5 $\pm$ 1.2	6.0 $\pm$ 1.4	1.1 $\pm$ 1.0 ( $p < 0.001$ )	0.6 $\pm$ 0.6 ml/min/rpm
PCWP (mmHg)	14.5 $\pm$ 7.3	10.8 $\pm$ 6.7	8.7 $\pm$ 6.1	-5.8 $\pm$ 6.1 ( $p < 0.001$ )	-0.28 $\pm$ 0.19 mmHg/rpm*10 <sup>-2</sup>

Hemodynamic changes in response to pump speed modulations. Abbreviations: CO, cardiac output; PCWP, pulmonary capillary wedge pressure.

## P1607

**Health care utilization, QOL and user satisfaction using the heart failure risk score (HFERS): insights from the TRIAGE-HF Trial**

Medtronic

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**Background:** TRIAGE-HF was a Canadian prospective observational post-market study to evaluate the performance and usability of the heart failure risk status (HFERS) feature. HFERS integrates device diagnostics to generate a dynamically updated risk status (low, medium or high) which has been previously demonstrated to correlate with 30 day probability of HF hospitalization.

**Purpose:** During the TRIAGE-HF trial, HFERS was introduced to HF care providers to better understand how HFERS and HF diagnostics were incorporated into "real life" workflow and patient management strategies. Study objectives included measurements of healthcare utilization (HCU), changes in HF related QOL, and user satisfaction.

**Methods:** TRIAGE-HF enrolled 100 patients with HF and a wireless CRT-D/ICD device followed for 8 months. All-cause HCUs were collected and included HF-related HCUs and HF-related hospitalizations. QOL was measured by MLWHF scores at baseline and study exit and compared using a one-sample t-test. A 9 question user satisfaction survey was completed by clinical care providers at study end.

**Results:** Patients enrolled were mostly male (78%), with a mean age of 66.9  $\pm$  11 years and NYHA class II/III symptoms (82%). Mean EF was 31.1  $\pm$  12.3%. 83% were on ACE-i/ARB and 95% on a  $\beta$ -blocker. A total of 96 HCUs were reported during the study with an annualized rate of 1.5 HCU/patient/year. 26 HCUs

were HF-related with an annualized rate of 0.4 HCU/patient/year. 13 HCUs were HF-related hospitalizations consistent with an expected rate of 0.2 HF hospitalizations/patient/year. MLWHF scores demonstrated a non-significant trend towards improvement (32.8  $\pm$  21 vs 30.0  $\pm$  21.6,  $p = 0.19$ ). A total of 91 user surveys were completed mostly by nursing staff (81%). HFERS was reported as easy to interpret by 96%, allowed quick triage of patients (85%) with 37% reporting HFERS led to better patient care. However, satisfaction rate for overall clinical utility of HFERS was in the range of 20 - 40%.

**Conclusion:** TRIAGE-HF demonstrated no impact on HCU, possibly because the protocol did not mandate clinical actions upon HFERS review. User surveys revealed that HFERS is easy to interpret by nursing staff and it scored well on its ability to triage at-risk patients. This may allow HF clinic staff to reduce the frequency of in person follow up visits. However, the satisfaction rate for overall clinical utility of HFERS was low and may be because device patients are a small subset of the overall HF population and hence the specific value of a device feature may be diluted.

## P1608

**Patient's satisfaction about remote monitoring system of cardiac implanted electronic devices**

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**Introduction:** Overall satisfaction and acceptance of patients about remote monitoring (RM) of cardiac implanted electronic devices (CIEDs) was assessed in several studies. Currently, no validated questionnaires are available to be applied to RM.

**Purpose:** To evaluate patient's satisfaction of RM by a self-made questionnaire in our institution.

**Methods:** We used a self-made questionnaire designed to investigate five different aspects strictly connected to patient's acceptance and satisfaction of RM: 1) the overall satisfaction, 2) the completeness of the information provided by staff, 3) the difficulty of use of the equipment of RM, 4) the psychological impact of RM and 5) the impact on the lifestyle of the patient. All items allowed only one answer choosing among five options.

**Results:** The questionnaire was given to 207 patients followed by RM. 100% of all the administered questionnaire items were answered. Regarding overall satisfaction, the survey showed that 97% of patients judged very satisfactory the service, and 95% of patients said they received a complete and exhaustive initial training. The 98% of patients had no difficulty in using the equipment. The 90% of patients percent of patients received a sense of security by the transmitter, while only 60% of patients improved their lifestyle.

**Conclusions:** Patients show high level of satisfaction and acceptance of RM suggesting its proper usefulness in daily practice.

## P1609

**CHF therapy guided by pulmonary artery pressure monitoring: does baseline right heart catheterization predict outcome?**

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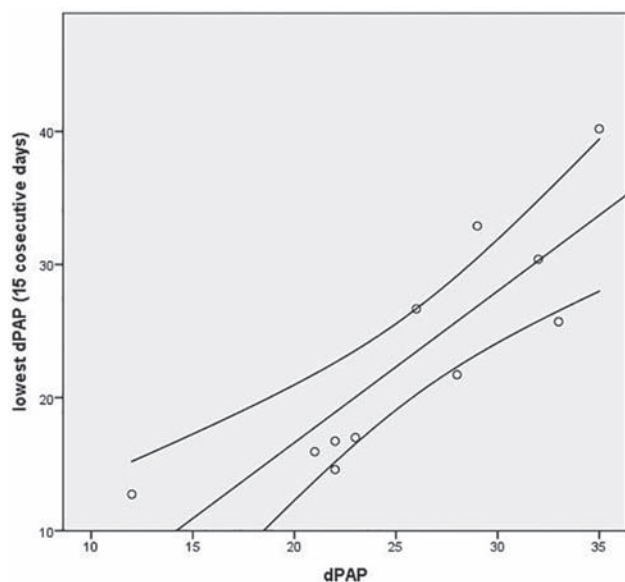
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**Background:** Remote monitoring of Pulmonary Artery Pressure (PAP) and haemodynamic guided optimization of therapy are effective in reducing events in Chronic Heart Failure (CHF). The improvement in prognosis is correlated to the decrease of diastolic PAP, with a target of 20 mmHg or less. The purpose of our study was to verify whether any baseline haemodynamic parameter could predict the degree of the maximum PAP reduction obtained by sensor guided therapy Methods. In 2015 11 CHF patients (Age 71  $\pm$  9; EF 27  $\pm$  4; NYHA III) underwent pulmonary artery catheterization, haemodynamic study and PAP sensor implant. PAP tracings were transmitted daily. For three months (observation period) CHF specialists were blinded to PAP transmissions (no medical intervention was guided by PAP). Afterwards, therapy was adjusted on PAP, according to CHAMPION study workflow (active phase).

**Results:** Baseline haemodynamics: Cardiac Index (CI) 2.0  $\pm$  0.57 L<sup>2</sup>/m<sup>2</sup>; Systolic PAP(sPAP) 58.6  $\pm$  14.5 mmHg; Diastolic PAP(dPAP) 25.7  $\pm$  6.6 mmHg; Pulmonary Wedge Pressure (PWP) 26.4  $\pm$  6.0 mmHg; TransPulmonary gradient (TPG) calculated as mean PAP-PWP 13.8  $\pm$  3.6 mmHg. During active phase the lowest stable (average of 15 consecutive days) dPAP was 23.1  $\pm$  8.7 mmHg ( $p < 0.001$  vs. baseline). Lowest dPAP was significantly correlated with baseline dPAP ( $r = 0.869$ ;  $p = 0.001$ ) and with TPG ( $r = 0.712$ ;  $p < 0.01$ ).

**Conclusions:** In a population of NYHA class III CHF patients with advanced hemodynamic impairment, sensor guided therapy was associated to significant decrease of dPAP. The lowest dPAP was directly correlated to baseline dPAP, suggesting that the benefit of this approach might be limited in patients with very high baseline filling pressures. Pulmonary vascular disease might be involved in the non reversibility of pulmonary hypertension, as suggested by the correlation of lowest dPAP and

baseline TPG.



#### P1610

##### Changes in left ventricular ejection fraction after primary prevention ICD implantation and its correlation with appropriate ICD shocks

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**Background:** Left ventricular ejection fraction (LVEF) lower than 35% is a key criterion in determining eligibility for implantable cardioverter defibrillator (ICD) for primary prevention (PP) in patients (pts) with chronic systolic heart failure (HF). Although HF pts may experience an improvement in LVEF after PP ICD implantation (particularly after CRT-D implantation), it is unknown whether LVEF improvement affects subsequent risk for sudden cardiac death (SCD).

**Aim:** The aim of our study was to assess the changes in LVEF after ICD implantation and the implication of this parameter on ICD shocks.

**Methods:** We analysed the data of 99 HF pts referred for PP ICD implantation between 2010 and 2014 (mean age: 63.4 ± 9.9 years, male: 75.8%, ischaemic: 56.6%, NYHA: 2.4 ± 0.8, LVEF: 26.0 ± 5.8%), who received their devices according to current guidelines (CRT-D: 80 pts, ICD: 19 pts). Every pts got optimal medical therapy at least 3 months before device implantation. The change in LVEF was assessed 6 months after device implantation. The occurrences of ICD shock was observed during the follow-up (mean: 31.5 ± 12.7 months) of the pts.

**Results:** 6 months after ICD implantation LVEF improved at least 5% in 73 pts (73.7%). 35.4% (35 pts) had an LVEF improvement to above 35%. During follow-up 31 pts died and we observed appropriate ICD shocks in 12 pts and inappropriate ICD shocks in 6 pts. Among pts with LVEF improved above 35% there was no appropriate ICD shocks at all, in contrast with the 12 pts with appropriate ICD shocks observed in the group of pts with LVEF < 35% six months after device implantation (p=0.0072).

**Conclusion:** Remarkable number of pts has an improvement in LVEF after PP ICD implantation. It seems that the improvement in LVEF reduces the risk of appropriate ICD shocks. To avoid unnecessary implantations we should identify HF pts with baseline LVEF < 35% who benefit most from ICD therapy by determining additional markers predicting the risk of SCD more specifically than LVEF alone.

#### P1611

##### Cardiac implantable defibrillator in primary prevention: predictors of appropriate therapy

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**Background:** Prophylactic implantable cardiac defibrillator (ICD) therapy (Rx) has been shown to improve survival in some conditions. Finding the predictors of appropriated ICD Rx can be helpful in medical management of patients (pts) with ICD as well as improve pts' selection at first. Our aim was to describe clinical profile of pts with ICD for primary prevention (PP) and to evaluate the predictors of appropriate ICD Rx and the predictors of poor outcome.

**Methods:** We reviewed the data of ICD implantation from a tertiary centre between June 2012 and December 2014. Of 134 pts, we included 62 pts, who had left ventricular (LV) systolic dysfunction and were referred for ICD implantation for PP. Appropriate ICD Rx was defined as occurrence of ATP or shock triggered by ventricular arrhythmia at first event.

**Results:** Mean age was 62.5 ± 10.4 years and 83.9% were males. More than 90% pts had at least 1 cardiovascular (CV) risk factor. The diagnosis was dilated cardiomyopathy (DC) in 50%, ischemic cardiomyopathy in 41.9% and valvular heart disease in 6.5% of the cases. The echocardiography (echo) before implantation showed a mean ejection fraction (EF) of 23.2 ± 6.8% and a mean LV end-diastolic dimension of 66.2 ± 10.8 mm. During a mean 20.0 ± 8.2 months of follow-up (FU), 32.3% pts had auricular fibrillation/flutter (AF) and 56.5% had non-sustained ventricular tachycardia (NSVT). Only 13 pts received appropriate ICD Rx (40% ATP alone and 60% ATP followed by shock or shock alone). The main trigger for appropriate ICD Rx was ventricular tachycardia. Appropriate ICD Rx occurred in mean 10.3 ± 6.9 months after implantation. Fifteen pts were admitted for CV causes and 5 pts died during FU. No clinical or echo feature of pts before ICD implantation was associated with appropriate ICD Rx, whereas NSVT was an independent predictor of appropriate ICD Rx (OR 11.4, p=0.02). Alcoholic DC, AF and shock of any cause during FU were associated with admissions for CV causes. Appropriate ICD Rx was associated with admissions as well. In our cohort, only alcoholic DC was predictor of CV death (66.7% vs. 10.2%, p=0.04).

**Conclusions:** In this study, ICD implantation for PP occurred mainly in male pts. Half of pts had DC. The mean EF was lower than 25% and most pts had LV dilatation. Many pts had NSVT and this was a strong predictor of appropriate ICD Rx. AF and shock of any cause was predictor of hospitalization. Interestingly, alcoholic DC was associated with admissions and CV death.

#### P1612

##### Gap between guidelines and clinical practice in device implantation in heart failure patients: insights from HEARTS registry

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**Background and Objectives:** Patterns of implantable cardioverter-defibrillator (ICD) and cardiac resynchronization therapy (CRT) use in patients with Heart Failure (HF) vary by geography, and data from developing countries are limited. Therefore, our aim was to identify the gap in the application of device implantation guidelines for acute on chronic systolic heart failure patients in Saudi Arabia. Design and Setting: We used data from the heart function assessment registry trial in Saudi Arabia (HEARTS) to explore the rate of device implantation. In consecutive cohort admitted in 18 governmental hospitals with heart failure between October 2009 and December 2010.

**Results:** Of 1664 patients with acute on chronic systolic heart failure enrolled in the HEARTS registry, 227 (13.64%) have undergone a past ICD/CRT, 148 (8.9%) patients with ICD and 79 (4.7%) patients with CRT. 1437 (86.36%) patients did not go through an ICD or a CRT. From 71 VT/VF patients who are required to have an ICD only 10 (14%) patients received an ICD therapy. 223 patients have a left bundle branch block and 35 (15.6%) of those patients received an ICD/CRT device. From 831 patients with LVEF < 30%, 170 (20.5%) went through a past ICD/CRT.

**Conclusion:** Since a large number of whom required an ICD/CRT did not receive a device, a gap in the application of ICD/CRT devices had been identified. The estimated ICD/CRT implant rate is lower than what has been reported in many developed countries, further studies are required to establish the reason behind this.

#### P1613

##### Cardiac rehabilitation programs in left ventricular systolic dysfunction: do these programs reduce the number of patients requiring an implantable cardioverter defibrillator?

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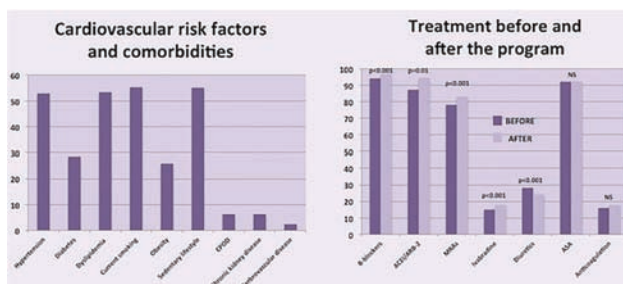
**Introduction:** Cardiac rehabilitation programs (CRPs) in left ventricular systolic dysfunction (LVSD) patients (p.) provide optimal medical treatment (OMT), close monitoring, exercise and counselling. Implantable cardioverter defibrillators (ICDs) should be considered in symptomatic p. and a left ventricular ejection fraction (LVEF) ≤ 35% despite OMT. CRPs represent a favourable scenario for a suitable stratification and optimal selection of these p.. Our purpose was to describe the population with LVEF ≤ 35% in our program and to analyse predictors for an ICD implantation in these p..

**Methods:** We made an observational retrospective study including p. with LVSD admitted to a CRP between 2006 and 2015. Physical training, OMT, medical counselling and smoking cessation support, were supplied for 8 to 10 weeks. LVEF was assessed before and after the program using TTE. Functional capacity (FC)



was tested before and after the CRP in accordance with the NYHA Classification, besides a treadmill stress test (TST). Exercise capacity (EC) was reported in METs. **Results:** A total of 206 p. were included, mean age  $57.6 \pm 12.3$  years, male 89.8%. Baseline characteristics are shown in graphic 1. The 89.8% of these p. had a recent acute coronary syndrome. After the CRP, an ICD was implanted in 35 p. (17%). Regarding medical therapy, the number of p. receiving B-blockers, ACEi/ARB2, MRAs and ivabradine was higher after the CRP ( $p < 0.01$ ). Not significant differences according to sex, age, cardiovascular risk factors (CVRF) and comorbidities were found among p. requiring or not an ICD. The use of diuretics was superior in p. requiring an ICD before (48.6% vs 20.4%;  $p = 0.002$ ) and after CRP (26.5% vs 12.6%;  $p = 0.047$ ), no differences were found with any other treatment. The NYHA class before the program was I 44.7%, II 48%, III 6.7%, IV 0.6%. After CRP NYHA improved: I 73.2%, II 25.6%, III 1.2% ( $p < 0.001$ ). Referring to TST, medium METs before CRP were  $6.2 \pm 2.8$  and after were  $9.8 \pm 2.7$ . Mean LVEF were  $29.5 \pm 5.6$  before and  $41.8 \pm 10.3$  after. Patients requiring an ICD had both worst functional class before and after CRP ( $p = 0.005$ ,  $p = 0.002$ ; respectively), and lower LVEF before ( $27.6 \pm 6.8$  vs  $30.5 \pm 4.6$ ;  $p = 0.02$ ) and after CRP ( $30.8 \pm 7.8$  vs  $44.8 \pm 8.7$ ;  $p < 0.001$ ), as well as less METs at the beginning ( $5.2 \pm 2.8$  vs  $6.6 \pm 2.6$ ;  $p = 0.012$ ) and the end of the program ( $8.6 \pm 2.9$  vs  $10 \pm 2.7$ ;  $p = 0.02$ ). Considering p. with  $LVEF \leq 35\%$  and NYHA II-III, differences were found before and after the program (55.3% vs 14.5%;  $p < 0.001$ ), which modifies the indication for an ICD implantation along the CRP.

**Conclusions:** CRPs are a valuable tool to properly select candidates to an ICD. CRPs improve FC, optimize medical therapy and increase LVEF. No differences in CVRF and comorbidities among p. requiring or not an ICD were found. However, these p. had less LVEF and worst FC and EC at the beginning of the CRP, besides a minor improvement of these parameters within the program. The proportion of p. with ICD indication decreases after the CRP is completed.



CVRF, comorbidities and treatment

#### P1614

##### Predictive factors of death and appropriate ICD shock in primary prevention: analysis with a competing risk model.

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**Background:** The indication of ICD implantation for primary prevention of sudden death could be optimized with a prognostic tool that identifies those patients who will die without an appropriate ICD shock (AIS) and those ones who will have a first AIS. Our purpose is the development of a competing risks predictive model (Fine-Gray) and the evaluation of its predictive accuracy.

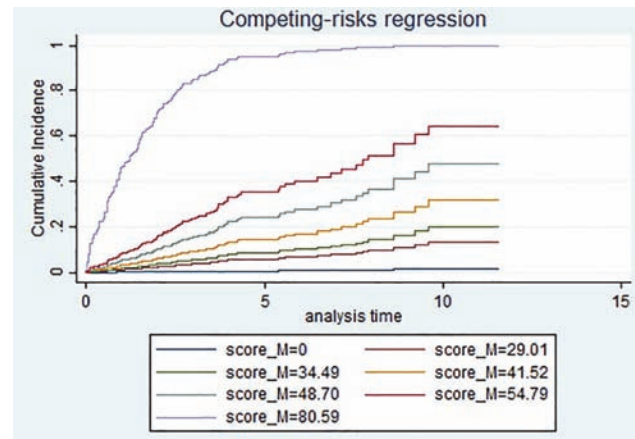
**Methods:** Multicenter national level cohort study of 1171 patients with ICD for primary prevention with this clinical profile: 81 % male, mean age 62 y. (30 % over 70 y), ischemic 55 %, complete revascularization 29 %, LVEF  $< 25\%$  51 %, NYHA 3-4 39 %, serum creatinine  $> 2$  mg/dl 4 %. In univariate study we determined the cumulative incidence function for death without AIS and Pepemori's test. In multivariate analysis we built a Fine-Gray regression model, calculated a risk score of death without AIS and stratified the cohort population by its value. We calculated the predictive accuracy of the model with Harrell's c index. Then we calculated pseudo-values and estimated the potential years of life lost as a function of the selected covariates. We also built a predictive model of first AIS.

##### Results

The incidence rate of death without AIS was 4.22 /100 person-years (155 p) and first AIS 3.94/100 p-y (145 p). The predictive model of death without AIS included age  $> 70$  y, LVEF  $< 25\%$ , NYHA 3-4, COPD, serum creatinine  $> 2$  mg/dl, previous admission because of heart failure, malignant neoplasm, dyslipemia, previous implanted pacemaker, male sex, digoxin treatment, ischemic cardiomyopathy and

indication of resynchronization therapy (Harrell's c index 0.76 corrected 0.75 95%CI 0.72-0.80). The model of first AIS included creatinine  $> 2$  mg/dl, arterial hypertension, malignant neoplasm, antidiabetic treatment and complete revascularization (Harrell's c index 0.66 corrected 0.65 95% CI 0.62-0.70).

**Conclusions:** Mortality without first AIS can be predicted reasonably with a questionnaire of clinical variables. We can establish different groups of risk of death without AIS according to the value of death risk score. The prediction of first appropriate shock is, so far, unreliable.



Death risk score

#### P1615

##### Ultrasound-guided venous access for PMK and ICD. randomised trial.

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In the light of increasingly stringent recommendations of companies of anesthesiology and intensive care units to use approaches vascular eco-guided we wanted to evaluate the safety and efficacy approach to the axillary vein methodically drove to the eco system leads to stimulation and cardiac defibrillation. After disinfection of the skin in the region clavicular and preparation of the sterile field was used a sterile covers for cardiac probe that was previously coated with sterile gel. To improve visualization of the images and reduce the air-skin interface probe cover was used saline. Deliberately not sterile gel was used to reduce the costs of the procedure. The operator right-handed wielding the probe with the left hand and the syringe with the needle with your right hand. It identified the anatomical region extrathoracic axillary vein was pricked after local anesthesia in the area of interest, with Seldinger technique. The progression of the needle was guided by ultrasonography. The puncture was possibly carried out two or three times depending on the type of plant programmed. After a learning period of the echo-guided technique were enrolled 90 patients in which consecutive, randomly 1:1, was chosen the initial approach (echo or subclavian). If in a maximum time of 5 minutes the first approach failed in the cannulation is passed to the second approach. In the learning period of about three months the frequency of failure is lower than 30%. In the period of enlistment randomized, the frequency of success at the first attempt of the approach echo is comparable with that for subclavian (42/45, 93.3% vs. 43/45, 95.6%). Are not reported to the system and major events in the postoperative period. Are registered minor events such as dislodgment during the procedure and / or raising the threshold post-procedure to be comparable in the two groups (Eco: 2.2% vs 6.7% Subclavian). The proposed technique appears to be effective and safe as the classical technique for subclavian, also presents the advantage of being free from risk of pneumothorax and breaking of leads. Ratings on a follow-up in the medium and long term are in place to assess their reliability. Studies with an adequate number of patients would be desirable to confirm our preliminary results.

#### P1616

##### The effectiveness of implantable cardioverter-defibrillator in preventing sudden cardiac death in patients with chronic heart failure.

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**Introduction:** Chronic heart failure is one of the leading cause of mortality all over the world. Its optimization and therapy is one of the priority task in cardiology.

**Purpose:** To analyze the own results of implantable cardioverter-defibrillator in preventing sudden cardiac death (SCD) in patients with chronic heart failure.

**Materials and Methods:** 47 patients received implantable cardioverter-defibrillator (ICD) from 2010 to 2014. Among them are 27 men (average age  $51 \pm 3.7$  year) and 20 women (average age  $49 \pm 2.5$  year). 32 patients with myocardial infarction, 14 patients with dilated cardiomyopathy and 1 patient with idiopathic ventricular tachycardia also received ICD. 9 patients with CHD had a permanent form of atrial fibrillation, they received a single-chamber implantable cardioverter-defibrillator. Other patients received dual-chamber device. Control inspection, testing and reprogramming was in terms of ICD in 3.6 and 12 months after the initial implantation or after the triggering device. Complications were not during and after operation period.

Results Triggering the ICD reported in 11 patients. 5 patients had unmotivated triggering as cardioversion and defibrillation in response to atrial fibrillation with high conduction of impulses to the ventricles. After selection of antiarrhythmic therapy with amiodorane hydrochloride (in 3 patients), digoxinum (in 1 patient), bisoprololol (in 2 patients), and the correction parameters discrimination tachycardia ICD, repeated episodes of unwanted discharges were not observed. The remaining 6 patients had antithetically triggering ICD in one case, and in 5 cases had defibrillation with discharge to 34J.

**Conclusions:** Implantable cardioverter-defibrillator has been reducing the number of deaths from life-threatening tachycardias in patients with high risk of SCD. Timely correction of the ICD parameters, with additional features of supraventricular tachycardia discrimination, appropriate treatment of the underlying heart disease may reduce the number of unwanted alarms ICD and improve the quality of patients' lives.

#### P1617

##### Possibilities of cardiac resynchronization therapy and ablation of the atrioventricular junction in patients with heart failure and atrial fibrillation

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**Purpose:** to explore the effectiveness of cardiac resynchronization therapy (CRT) in combination with ablation of atrioventricular junction (AV-ablation) in patients with chronic heart failure with NYHA functional class III or IV (III-IV FC CHF), ejection fraction (EF) <35%, QRS duration  $\geq 120$  ms and permanent atrial fibrillation. Methods. The study involved 55 patients who underwent CRT and AV-ablation. Examination was carried out at baseline, in 6 and 12 months after surgery, and included general clinical tests, determination of the level natriuretic peptide (NT-proBNP), myocardial dyssynchrony, transthoracic echocardiography and the 6-minute walk test.

**Results:** No significant changes in clinical tests were revealed. The level of NT-proBNP decreased from 7954 pg/ml at baseline to 3476 pg/ml by the 6 month and to 1228 pg/ml by the 12 month ( $p < 0.05$ ). In a year after the surgery presystolic aortic delay decreased from  $175.6 \pm 4.8$  ms to  $157.8 \pm 7.2$  ms ( $p < 0.05$ ). Interventricular dyssynchrony reduced from  $175.6 \pm 4.8$  ms to  $169.4 \pm 5.7$  ms after 6 months and to  $157.8 \pm 7.2$  ms after 12 months ( $p < 0.05$ ). Atrioventricular dyssynchrony was not measured. End-diastolic volume (EDV) decreased from  $345.2 \pm 32.4$  ml to  $316.5 \pm 28.7$  ml by the 6 month and to  $31.8 \pm 34.6$  ml by the 12 month ( $p < 0.05$ ). At baseline end-systolic volume (ESV) was  $285.4 \pm 30.4$  ml. After 6 months it was  $243.6 \pm 28.7$  ml, after 12 months it was  $235.7 \pm 30.2$  ml ( $p < 0.05$ ). EF increased from  $24.6 \pm 2.5\%$  to  $30.1 \pm 2.4\%$  by the 6 month and to  $31.2 \pm 1.8\%$  by the 12 month ( $p < 0.05$ ). At baseline mitral regurgitation (MR) was  $3.6 \pm 1.2$ ; after 6 and 12 months it became  $3.1 \pm 1.3$  and  $2.7 \pm 1.2$  ( $p < 0.05$ ). The 6-minute walk test revealed an increase of distance from 152 m to 326.7 m by the 6 month and to 358.4 m by the 12 month, respectively ( $p < 0.05$ ). Conclusion. CRT in combination with AV-conjunction ablation is an effective method of treatment in patients with III-IV FC CHF (NYHA), EF <35%, permanent atrial fibrillation, QRS duration  $\geq 120$  ms. The treatment resulted in the decrease of NT-proBNP level, ESV, EDV, the degree of MR and the increase of EF, a distance of the 6-minute walk test.

#### P1618

##### Unfavourable outcome after the upgrade of an implantable cardioverter defibrillator to cardiac resynchronisation therapy

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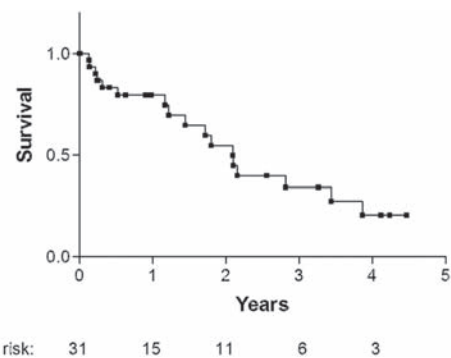
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**Background:** Cardiac resynchronization therapy (CRT) improves survival in selected patients with heart failure (HF). As the potential survival benefit of CRT performed as an upgrade from a previously implanted cardioverter defibrillator (ICD) has not been explored, we evaluated total mortality after CRT upgrade in this context.

**Methods and Results:** A total of 31 patients (27 male, mean age:  $63.7 \pm 9.6$  years)

with structural heart disease underwent CRT device implantation as an upgrade of a previously implanted single or dual chamber ICD between 2004 and 2015 at our Institute. The indication for ICD implantation was prophylactic based on the MADIT II or SCD-HeFT criteria (in 13 patients) or secondary prevention after a sustained ventricular arrhythmia (in 18 patients). Mean left ventricular ejection fraction (LVEF) was  $29.9 \pm 7.8\%$  and mean NYHA status was  $2.4 \pm 0.8$  at the time of ICD implantation. No indication for CRT was present in any of these patients at the time of ICD implantation. CRT upgrade was performed after a mean follow-up of  $3.9 \pm 2.9$  years based on the following indications: widening of the QRS complex (from  $108 \pm 20$  to  $158 \pm 24$  msec.) in 24, decreasing LVEF (from  $41.5 \pm 2.1$  to  $26.5 \pm 2.1\%$ ) in the presence of LBBB in 2, and an increase in the need for right ventricular stimulation (burden > 40%) in 5 patients. A significant reduction in the QRS width after CRT upgrade (from  $160.3 \pm 26$  to  $130.3 \pm 23$  msec.,  $p < 0.001$ ), an improvement in NYHA class (from  $3.1 \pm 0.8$  to  $2.5 \pm 1.0$ ,  $p = 0.16$ ) and an increase in the mean LVEF (from  $27.6$  to  $33.3\%$ ,  $p = 0.049$ ) was observed including 4 patients (13%) who demonstrated an increase in LVEF above 10 % at the 1-year follow-up. 17/31 patients (55%) died during a mean follow-up of  $19.0 \pm 16.6$  months after CRT upgrade (Figure). No statistically significant prognostic factor of survival was found among the patients' baseline data by using the Cox proportional hazard model.

**Conclusion:** Despite a marked reduction in QRS width and a modest improvement in LV EF, mortality remains high after CRT upgrade in this patient cohort. This would argue for an earlier administration of alternative treatment modalities (assist device, heart transplantation) in HF patients who demonstrate QRS widening, a significant decrease in the LV EF or a need for ventricular stimulation.



Kaplan-Meier survival curve

#### P1619

##### The influence of cardiac resynchronization therapy on prognosis and functional status of blood circulatory system at patients with mild chronic heart failure

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**Purpose:** to study the influence of cardiac resynchronization therapy (CRT) on tolerance to physical loading (TPL), aerobic capacity and predictors of pure prognosis at patients with the chronic heart failure (CHF) according to spiro Bicycle Ergometry Test (spiroBET).

**Methods:** We studied 13 patients with CHF NYHA Class II, sinus rhythm, duration of QRS  $\geq 130$  ms and a dyssynchrony according to echocardiography (EchoCG). Implantation of CRT and treatment of CHF were carried out according to ESC Guidelines (2013). TPL was measured in the conditions of spiroBET using Schiller AG AT-104 ErgoSpiro equipment. We used Bruce protocol. Efficiency of CRT was estimated according to EchoCG: increase of ejection fraction  $\geq 5\%$  was regarded as "responder" (R); <5% - "non-responder" (NR).

**Results:** Improvement of myocardial contractility in 12 months after implantation of CRT we found at 8 (62%) from 13 patients, they made R Group, another 5 (38%) made NR Group. The age of patients of R Group and NR Group was similar -  $58.6 \pm 9.8$  and  $57.5 \pm 8.8$  years, respectively ( $> 0.05$ ). In 12 months after implantation of CRT EF was  $38.5 \pm 13.8\%$  in R Group and  $21.0 \pm 10.9\%$  - in NR Group,  $< 0.05$ . We also found significant improvement of TPL in R Group in comparison to NR Group - maximal achieved loading was  $72.3 \pm 24.9$  Wt and  $33.3 \pm 9.1$  Wt correspondingly ( $< 0.05$ ). Improving of myocardial contractility in R Group brought to increase not only TPL but also to augmentation of maximal oxygen consumption in comparison to NR Group - is taped  $8.5 \pm 4.2$  and  $7.3 \pm 4.9$  ml/kg/min., respectively,  $< 0.05$ . Earlier (Sujayeva V.A., 2013) we found that TPL < 50Wt in combination with level <20% from age expected were strong predictors of 1 year mortality in patients with CHF (sensitivity 100%, specificity 82%). The most important result of 12 month CRT was disappearance of above mentioned predictors in patients of R group. It means that implantation of CRT leads not only to improvement of prognosis but also to decrease of requirement of heart transplantation in patients with CHF.

**Conclusions:** at patients with CHF NYHA Class II efficiency of CRT in 12 months was 62%. In group of responder along with improvement of global myocardial contractility we found increasing TPL, maximal oxygen consumption, improve of prognosis and decrease of requirement of heart transplantation.

#### P1620

##### Cardiac resynchronization therapy alters serum lipids profile in patients with chronic heart failure - results of the pilot study.

Annual grant for Young Scientists 2014, Club 30-Polish Cardiac Society  
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**Introduction:** Cardiac resynchronization therapy (CRT) leads to reversal of the processes occurring in the course of development of the heart failure. The molecular basis of lack of response to CRT in a group of about 20-30% of chronic HF patients remain unknown.

**Aim:** The use of metabolomics to identify changes in the blood metabolites profile, occurring as a result of cardiac resynchronization therapy.

**Methods and Results:** We prospectively studied 15 optimally treated patients with stable chronic HF (M=93%, 63.8 ± 11.7 years, BMI 27.5 ± 2.9 kg/m<sup>2</sup>, 53% ischemic etiology, QRS duration 174.7 ± 24.5 ms, left ventricular ejection fraction—LVEF 19.9 ± 5.5%, NYHA class II/III 27/73%) who had indications for CRT listed in current ESC CHF guidelines. Acute and chronic inflammatory diseases (rheumatoid arthritis, diabetes mellitus, asthma) were excluded. All of the enrolled patients were assessed clinically, biochemically, echocardiographically and functionally on baseline and 6 months after device implantation. Fasting serum samples were collected and fingerprinted by liquid chromatography-mass spectrometry (LC-QTOF-MS). Depending on the data distribution, paired t-test or Wilcoxon signed rank test were used and solely statistically significant metabolites (p < .05) were selected to draw

**Conclusions:** Identification of significant features was performed based on custom library with accurate mass and retention time of more than 100 metabolites. 66% (n = 10) of enrolled patients responded positively to the CRT. Six months after CRT implantation there were significant reduction in the width of QRS complex (mean 175 vs 147 ms, p = .01), increase in LVEF (20 vs 28%, p = .00) and decrease in LV end-diastolic diameter (LVEDd; 6.98 vs 6.41 cm, p = .00). We observed also higher level of sphingosine-1-phosphate (+30 ± 11%, p = .014), lysophosphatidylethanolamine - LPE 16:0 (+26 ± 8%, p = .021), LPE 18:1 (+32 ± 14%, p = .028), hexadecenoyl carnitine (+72 ± 51%, p = .034) and decrease in hydroxysphingosine (-40 ± 21%, p = .040). Higher baseline level of LPE 18:1 was correlated with lower endsystolic/-diastolic baseline volume of left ventricle (LVEsV, LVEDv; r = -.59; r = -.65, respectively) and lower LVEDd (r = -.61). Those who responded positively to CRT had higher median intensity of LPE 18:1 than those who had no benefits from the therapy (0.78 vs 0.46, p = .02).

**Conclusions:** Serum metabolites profile changes in the course of CRT especially in terms of lipids (sphingolipids, phospholipids). LPE 18:1 seems to be associated with echocardiographic parameters and positive response to cardiac resynchronization therapy.

#### P1621

##### Analysis of strain in CRT patients with mild systolic dysfunction and LBBB: the miracle EF cohort

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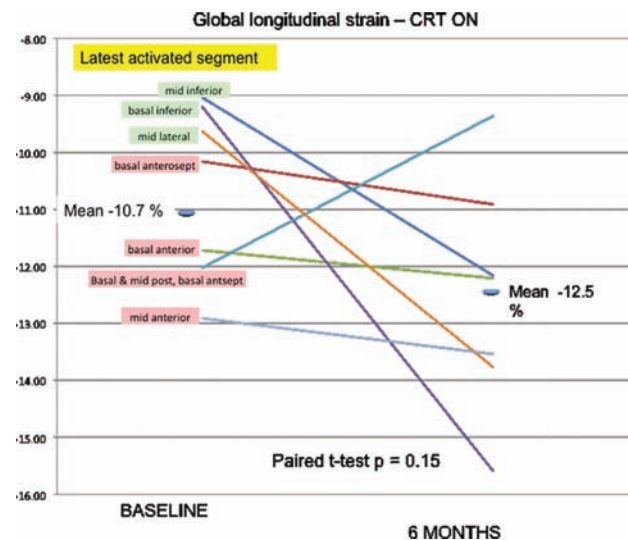
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**Background:** MIRACLE EF attempted to test the hypothesis that heart failure (HF) patients with LVEF 36-50% and left bundle branch block (LBBB) might benefit from cardiac resynchronization therapy (CRT). Although the study was halted for lack of enrollment, we analyzed the effect of CRT on global and regional longitudinal strain (GLS).

**Methods:** Major inclusion criteria were LVEF 36% to 50%, QRS > 130 ms, and LBBB morphology. Patients were randomized 2:1 to treatment with CRT-P vs. Control (implanted, LV lead turned OFF). Speckle tracking analysis was performed on all patients with matched 6-month studies utilizing commercial software GLS measurements were compared within groups over time with a paired t-test and the change in GLS measurements were compared between groups with a two-sample t-test. Results In the control group there is no discernible change in GLS at 6 months, with a mean GLS of -9.7 at both time points (p = 0.99; n = 3). Latest activated segment was non-anterior in all three patients. In contrast, for the CRT patients, mean GLS improved from -10.7 to -12.5 (p = 0.15; n = 7), though it was not

statistically significant. There was no detectable difference between randomization groups in the change in mean GLS from baseline to six months (p = 0.37; n = 10). Further, those with the greatest improvement in GLS demonstrated latest activation in the non-anterior segments.

**Conclusions:** In HF patients with moderate systolic dysfunction and LBBB, CRT may improve GLS, most notably in those with non-anterior latest activating segments.



#### P1622

##### Left ventricular rotational dyssynchrony before cardiac resynchronization therapy: a step forward into ventricular mechanics.

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**Background:** Systolic Heart Failure (HF) patients show impaired left ventricular (LV) rotation and twist. In patients undergoing Cardiac Resynchronization Therapy (CRT) the significance of pre-implant LV rotational timing between different ventricular regions is unknown.

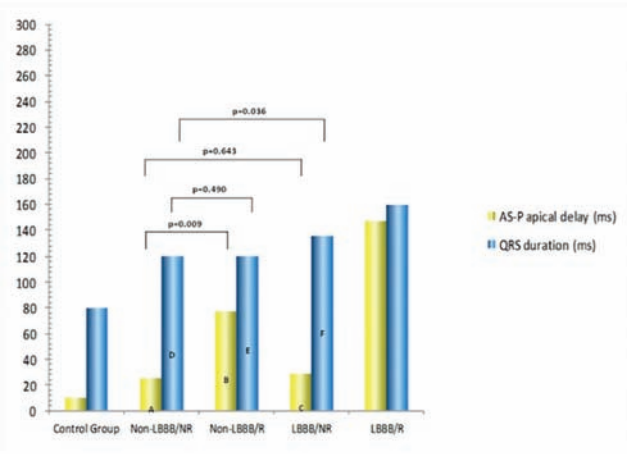
**Purpose:** in the present study we aimed at 1) thoroughly evaluating, in healthy subjects and in HF patients with severe systolic dysfunction and prolonged QRS, who were eligible for CRT, the baseline LV rotational mechanics, also assessing rotational timing of each different LV segment, and 2) investigating whether the presence of a specific pattern of rotational dyssynchrony may be associated with echocardiographic response after CRT application.

**Methods:** By 2-dimensional speckle-tracking echocardiography, baseline peak apical and basal rotation, peak twist, and time-related parameters, such as delays between opposite segments at base and apex, were assessed in 55 CRT patients and 11 healthy subjects.

**Results:** At 6 months, 30 (54%) patients were echocardiographic responders. LV rotation and twist had no association with response. All time-related parameters were significantly altered in CRT patients, as compared to control group. Maximum basal and apical segments delay, and anteroseptal-posterior (AS-P) delays at base and apex, were longer in responders than in non-responders (p < 0.05 for all), regardless of the presence of left bundle branch block (LBBB) and QRS duration (Figure). At multivariable analysis, apical AS-P delay resulted independently associated with response [OR: 1.022 (1.007-1.038); p = 0.004]. A cut-off value of 97.5 ms for apical AS-P delay predicted response with 96% specificity and 57% sensitivity (AUC = 0.83). Magnitude of LV reverse remodeling was significantly related to apical AS-P delay (p = 0.001).

**Conclusion:** In HF patients eligible for CRT, LV rotational timing is altered. Dyssynchrony in rotational mechanics shows a specific pattern in responders regardless of the presence of LBBB. Apical anteroseptal-posterior rotational delay is independently associated with LV reverse remodeling.





Apical AS-P delay, QRS and response.

## DIURETICS AND FLUID STATUS MANAGEMENT

### P1623

#### Heart failure with preserved ejection fraction: does the intra-venous diuretic treatment duration matter?

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**Background:** Heart failure with preserved ejection fraction (HFpEF) is a prevalent disease among hospitalized patients. However, its prognosis and optimal medical treatment are still poorly defined.

**Purpose:** To assess the impact of intravenous (IV) diuretic therapy duration on prognosis in patients with HFpEF.

**Methods:** We enrolled a total of 317 consecutive admissions due to acute heart failure to either the cardiology ward or the coronary intensive care unit of a single center between January 2012 and December 2013. Of those, 55% were excluded due to reduced ejection fraction (<50%), 9% due to severe valvular heart disease and 12% due to misclassification of the episode (not due to acute heart failure). A total of 34 patients (12.5%) were included. We registered and analyzed the clinical variables as well as short (in-hospital mortality) and long time follow-up (mortality and heart failure [HF] re-admission rate). The mean follow-up time was 25 ± 15 months.

**Results:** Mean age was 79 ± 9 years, with female gender predominance. Hypertensive cardiopathy was the most common etiologic factor (46%). Atrial fibrillation, ischemic heart disease and moderate valvular disease were present in 71%, 21% and 64% of the patients, respectively. Of note, non-cardiovascular morbidity had a high prevalence. Mean nt-pro-BNP at admission was 7650 ± 8078 pg/dL and mean hospital stay was 8 ± 8 days. In-hospital mortality rate was 14.7%; mortality and HF re-admission rates during follow-up were respectively 37.9% and 55.9%. In-hospital mortality was associated with a longer duration of IV diuretic therapy (13 ± 12 vs 5 ± 4 days, P < 0.01). IV diuretic therapy duration of less than three days had a sensitivity of 100% for the outcome of in-hospital survival (area under the curve of 0.74).

**Conclusions:** Our data showed that patients admitted for HFpEF were older, had an important burden of cardiovascular and non-cardiovascular morbidity and a significant number of events during follow-up. Remarkably, the need for a shorter duration (<3 days) of IV diuretic therapy seemed to be a clinical marker of good prognosis.

### P1624

#### Blood purification in end-stage heart failure: a study in 16 patients

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**Background:** End-stage heart failure ultimately leads to cardiorenal syndrome, in which control of the patient using pharmacological therapy or a device for cardiac resynchronization therapy (CRT) becomes difficult. For patients with refractory heart failure, fluid removal through hemodialysis (HD) or recently continuous ambulatory peritoneal dialysis (CAPD) may be used. We reviewed the effectiveness of each of these filtration methods in the treatment of end-stage heart failure.

**Subjects and Methods:** We treated 7 patients with end-stage heart failure with CAPD and 9 patients with HD (Cr=2.8 ± 1.3; Age 71.3 ± 10.8 years; non-ischemia=8/16 patients; ejection fraction (EF) 34.7 ± 15.0%; New York Heart Association [NYHA] 3/4=8/8 patients; device implantation 10/16 patients). We compared the clinical outcomes of these patients. Results At the end of the observation period, 3 out of 7 patients treated with CAPD survived while 2 out of 9 patients treated with HD survived. The mean survival time of the patients treated with CAPD was 204.4 ± 177.4 days while that of those receiving HD treatment was 184.6 ± 243.2 days (P = 0.6198). Although there was not a significant difference, the CAPD group had a better outcome. Better outcomes were also observed in the CAPD group with other indexes such as body weight (BW), NYHA, days and number of hospitalizations. For both groups, the prognosis of the patients was poor if they were unable to be discharged from the hospital within 30 days after the introduction of the treatment. Meanwhile, compared to the HD group, the CAPD group had a lower rate for both EF (CAPD 28.3 ± 17.5% vs HD 40.3 ± 13.1%; P = 0.14) and systolic blood pressure (SBP) (CAPD 105.9 ± 24.0mmHg vs HD 120.1 ± 35.6mmHg; P = 0.49) at the time of introduction of the treatment. Although 2 shunt failures were observed for the HD group, no complications were seen for the CAPD group and the treatment was conducted safely.

**Conclusions:** CAPD not only has a lower risk of complications but also appears to be a better choice compared to HD as a treatment method for end-stage heart failure and cardiorenal syndrome patients with low blood pressure and low heart function.

### P1625

#### What are predictive factors for body weight loss in patients with acute decompensated heart failure added an oral aquaretic, tolvaptan ?

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**Background:** Tolvaptan is an aquaretic agent and has been used for fluid management in patients with acute decompensated heart failure (ADHF). However, it remains unclear what are predictive factors for body weight (BW) loss following administration of tolvaptan in patients with ADHF.

**Purpose:** The purpose of this study was to identify predictive factors for BW loss in patients with ADHF treated with tolvaptan.

**Methods:** This is a single-center, prospective, and observational study. Forty-two consecutive patients with ADHF were enrolled. Tolvaptan was administered at a dose of 15 mg/day for 3 days in addition to standard heart failure medication. Water intake was not restricted during this study. BW was measured before and 3 days after the administration of tolvaptan. Measurement of multiple biomarkers and echocardiographic parameters were performed before the administration of tolvaptan. 72h-Urine volume (UV) was measured. Patients were divided into 2 groups: responders and non-responders. The definition of responders to tolvaptan was based on more than 2% decrease in BW in 3 days.

**Results:** The decreases in BW were 4.4 ± 1.7% in responders and 0.3 ± 0.5% in non-responders. Total UV tended to be larger in responders compared with non-responder (6125 ± 2097 ml vs. 5131 ± 1998 ml, p = 0.08). There were no significant differences in baseline serum and urinary sodium levels, plasma osmolality, and echocardiographic parameters between 2 groups. Estimated glomerular filtration rate (eGFR) was significantly higher in responders than non-responders (56 ± 17 ml/min vs. 41 ± 15 ml/min, p < 0.05). There were significant differences in serum potassium and serum glucose levels. Multivariate analysis revealed that eGFR was the independent predictive factor for responders (OR; 0.90, 95 % CI; 0.77-1.06, p < 0.05). Receiver operating characteristics analysis identified eGFR 43 ml/min/1.73m<sup>2</sup> as the optimal cut-off point for the prediction of responders (AUC 0.84 with sensitivity of 0.64 and specificity of 0.74).

**Conclusion:** eGFR before the administration of tolvaptan might be the predictive factor for more than 2% BW loss in patients with ADHF treated with tolvaptan.

### P1626

#### Discontinuation of diuretic therapy is safe in accurately selected patients with chronic heart failure and severely reduced ejection fraction: a prospective cohort study in the outpatients setting

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**Introduction:** long-term diuretic therapy in patients with heart failure with reduced ejection fraction (HFrEF) portends unknown and likely non benign side effects. Our hypothesis is that diuretics can be safely suspended in well selected, asymptomatic patients with chronic HFrEF once adequate neuro-hormonal blockage has been accomplished.

**Purpose:** To evaluate independent predictors of diuretics withdrawal (DW) in patients with chronic HFREF from our outpatient's clinic.

**Methods:** Two hundred and sixteen consecutive patients with HFREF (left ventricular ejection fraction (LVEF) =  $26 \pm 6$  %) were enrolled. Clinical evaluation, N-terminal pro brain natriuretic peptide (NT-proBNP) level as well as standard 2D and Doppler echocardiogram were performed every six months for a median follow-up period of 18 month. Patients for which DW was not recommended based on clinical judgment were included in the Non-Withdrawal (NW) group, N = 169 (78%), while patients where diuretic discontinuation was considered safe were included in the withdrawal (W) group, N = 21 (10%). N = 26 (12%) patients had no diuretics at baseline. Patients with recent (i.e. <30 days) admission for acute HF, recent (< 180 days) myocardial revascularization and/or resynchronization therapy, congenital heart disease or more than mild valve disease were excluded.

**Results:** Baseline factors positively associated with DW included: younger age (OR 1.05; 95% p = 0.04), NT-proBNP < 550 ng/L, (OR 3.82; p = 0.005). Among echocardiographic parameters, LV end-diastolic diameter < 60 mm (OR 5.34; p = 0.0005), end-diastolic indexed volume (OR 3.25; p = 0.02), left atrial indexed volume  $\leq 33$  ml/mq (OR 3.53; 95% p = 0.009), tricuspid annular plane systolic excursion (TAPSE)  $\geq 20$  mm (OR 5.78; p = 0.001) were positively related to DW. Baseline factors negatively associated with DW included: body mass index  $\geq 25$  (OR 0.25; p = 0.005), arterial hypertension (0.11; p = 0.01), implantable cardioverter defibrillator (ICD) carrier (0.22; p = 0.002), LVEF  $\leq 30$ % (0.33; p = 0.02). According to multivariable logistic analysis TAPSE  $\geq 20$  mm, and NT-proBNP < 550 ng/were the only independent predictors of DW (ROC AUC = 0.76). In the W group no patients required diuretic resumption, no episode acutely decompensated HF and no NT-proBNP modification (p = 0.27) occurred afterwards.

**Conclusions:** Diuretic therapy can be safely discontinued in patients with chronic HFREF, in particular when NT-proBNP level is < 550 ng/L and TAPSE is > 20 mm. Further studies enrolling a bigger study sample with extended follow-up are warranted to confirm our preliminary report.

#### P1627

##### Influence of clinical severity on the association of loop diuretic dose with mortality in patients with heart failure: insights from the unite-hf registry

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**Introduction:** Higher loop diuretic doses have been associated with increased mortality in patients (Pts) with heart failure (HF) but less is known about the influence of clinical severity on the long term risk of this therapy.

**Purpose:** To test the influence of clinical severity on the association of loop diuretic dose with mortality in Pts with HF predominately due to systolic dysfunction.

**Methods:** The relationship between loop diuretic dose, clinical severity and mortality was investigated in the UNITE-HF Registry, a prospective, observational HF study. Total daily doses of loop diuretics at baseline were converted to milligram equivalents of furosemide (Furo mgEq). Clinical severity was categorized by median LVEF ( $\geq 28$ % versus <28%) and NYHA class (1-2 versus 3-4) at baseline. Loop dose (continuous and categorical) and the risk of death during follow-up (relative to Pts not on loop diuretic) was assessed in all Pts and in clinical subgroups. Risk models were adjusted for predictors of mortality.

**Results:** This cohort (n = 1303) was 37% female, 37% African American, with mean ( $\pm$  SD) age of  $58 \pm 14$  years, creatinine  $1.43 \pm 1.26$  and LVEF of  $31 \pm 15$ . Loop diuretics were taken at baseline in 83% of Pts with median dose 40 mgEq/day (lower quartile <25, upper quartile > 120). There were 676 deaths during  $6.6 \pm 3.7$  years of follow-up. Mortality was significantly related to loop diuretic dose (continuous) for all study Pts (adjusted HR 1.06 95% CI 1.05-1.08, p < 0.0001 per 20 mgEq). In Pts with higher LVEF, larger doses of loop diuretic were weakly associated with increased mortality. In contrast, there was a strong association between increasing loop dose and increasing mortality in Pts with lower LVEF. NYHA class did not alter the association of loop diuretic dose with mortality.

**Conclusion:** Increasing loop diuretic dose was associated with higher mortality in this retrospective observational analysis of Pts with HF. LVEF but not NYHA class influenced the adverse association of increasing loop dose with mortality.

#### Loop dose and death by clinical severity

Furo mgEq Quartiles	Lower 25%	Mid 50%	Upper 25%
Clinical Group	HR (95% CI) P	HR (95% CI) P	HR (95% CI) P
LVEF $\geq 28$ NYHA 1-2*	0.43 (0.19-0.97) 0.042	1.15 (0.67-1.93) 0.597	1.51 (0.76-3.01) 0.242
LVEF $\geq 28$ NYHA 3-4**	0.79 (0.50-1.06) 0.497	0.90 (0.56-1.44) 0.661	1.24 (0.74-2.07) 0.418
LVEF < 28 NYHA 1-2†	1.01 (0.42-2.43) 0.979	1.79 (0.91-3.51) 0.090	3.25 (1.50-7.04) 0.003
LVEF < 28 NYHA 3-4‡	0.99 (0.47-2.10) 0.979	2.10 (1.21-3.67) 0.009	2.91 (1.61-5.24) <0.001

Risk relative to No Loop at baseline. Analysis is adjusted for final clinical predictors model. P Values for Linear Trend Test within each clinical group  
\*0.0487, \*\*0.3633, †0.0009, ‡<0.0001.

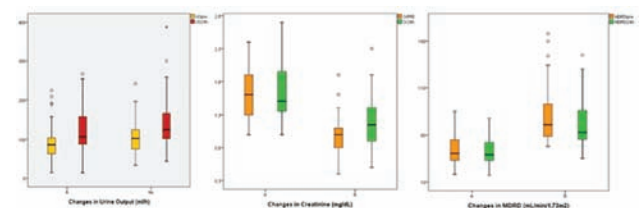
#### P1628

##### Diuretic resistance and chronic renal disease, how to face it?

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**Purpose:** Diuretic resistance (DR) (defined as reduction of efficacy of loop diuretics seen as weight gain and lower diuresis) is still a challenge in daily clinical practice. The relationship between chronic kidney disease (CKD) (known as MDRD less than 60 mL/min/1.73m<sup>2</sup>) and DR is a common scenario that limits the treatment, making the use of thiazides controversial. Our aim is to study the utility and safety of the combination of thiazides (HTZ) and amiloride associated with loop diuretics, in patients who developed DR and had CKD. METHODS A retrospective study of all patients with DR admitted for DHF treated with the combination of amiloride (5 mg) and HTZ (50 mg) was made. Two groups were created according to their basal glomerular filtration rate [MDRD (mL/min/1.73m<sup>2</sup>)], (Group A <60 mL/min/1.73m<sup>2</sup> basal, and group B >60 mL/min/1.73m<sup>2</sup> basal). Evaluation of sodium, potassium (mEq/L), creatinine (Cr) (mg/dL) and glomerular filtration rate by MDRD in plasma was made at 24 hours and at discharge. The rate of diuresis (mL/h) and weight (kg) was evaluated at 24 and 48 hours after initiating treatment. RESULTS Eighty two patients were included (52 male) with a mean age of  $74 \pm 9$ . Ischemic and valvular heart disease were the most prevalent cause of HF (41% vs 26%). Both groups (A and B) had 41 patients. Diuresis increased significantly at 24 hours and 48 hours in both groups (figure 1) which correlated with a corresponding significant weight loss at 24 hours (Group A:  $73 \pm 19$  vs  $66 \pm 18$  and Group B:  $71 \pm 13$  vs  $70 \pm 14$ , p < 0.05). Not statistically significant changes of Cr at 24 hours were found (figure 1) neither of MDRD (figure 1). None of them developed electrolytic disturbances. DISCUSSION Our study shows that the combination of loop diuretics, thiazides and potassium sparing diuretics, is an effective and safe treatment for diuretic resistance, regardless CKD, being an option in DR.



Diuresis, Creatinine and MDRD basal/24h

#### P1629

##### Mortality and rehospitalization data from diuretic therapy with effective doses of oral torasemide and furosemide in treatment of patients with exacerbation of chronic heart failure (DUEL-CHF) trial

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**Background:** Torsemide is a loop diuretic that may have a more favorable side-effect profile, particularly with regards to its influence of potassium. There are limited data on its efficacy when compared to furosemide in the management of patients with decompensated chronic heart failure (CHF).

**Purpose:** to compare efficacy and safety therapy with furosemide and torsemide in patients hospitalized for an acute decompensation of CHF

**Methods:** Patients with NYHA II-IV CHF, hospitalized for an acute decompensation, were randomly (2:1) assigned to either torsemide (T) 20 mg/day or furosemide (F) 80 mg/day plus to conventional therapy. They were subsequently followed for 180 days. The primary endpoint was time to compensation based on the elimination of symptoms (clinical assessment scale dynamics, VAS dynamics and optimal reduction in body weight). Secondary endpoints included safety, worsening of renal function and number of 30 days rehospitalisation and 180 days mortality and CHF hospitalization. The study was carried out in 30 clinical centers in 23 Russian cities.

**Results:** 470 pts from 18 to 75 years were included (n = 143, LVEF < 40%, mean 32,6%) and preserved (n = 184, LVEF > 50%, mean 56,9%). T was more effective and 95% vs 86% (p < 0,01) reach optimal elimination of symptoms up to 6 day (vs 10 days with F). Clinically meaningful side effects were much lower in T group 0,3% vs 4,1% (p < 0,001). Worsening of renal function (increased creatinine > 0,3 mg/dl) appears only in 1,2% in T vs 4,2% in F treated patients. After 180 days 13/144 (9%) died in F vs 19/326 (5,8%) T group (p=0,23) and 41/144 (28,5%) was rehospitalised due to worsening of CHF vs 50/326 (15,4%), p = 0,0014 in F and T groups, respectively. The risk of combine endpoint was lower in T group (21,2% vs 37,5%, =0,0004)

**Conclusion:** Non-intensive therapy with oral diuretics is well tolerated and does not cause deterioration of either renal function or electrolyte balance. Compensation was seen without complications in most patients with CHF and with lower rates of readmission. Torasemide had advantages over Furosemide on the time to CHF compensation, a degree of clinical improvement and achievement of complete compensation with a significantly lower rate of adverse events and rehospitalizations.

**P1630**  
**Hyponatremia in acute heart failure: relationship with congestion and outcome**

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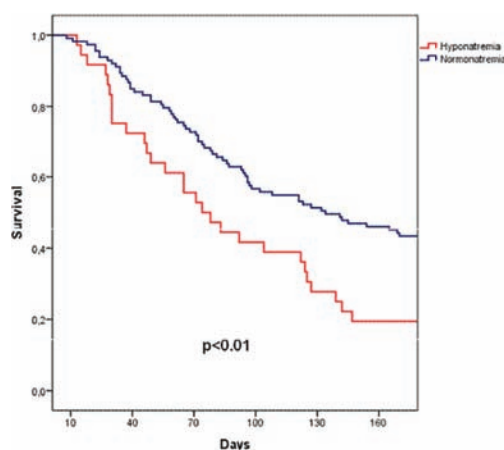
**Background:** Hyponatremia is the most common electrolyte disorder in clinical practice in patients submitted to loop diuretic treatment. The prognostic importance of hyponatremia in heart failure (HF) patients is well-recognized. However the clinical determinants of hyponatremia in AHF are not well understood.

**Purpose:** The aims of this study are: 1- to investigate the link among hyponatremia and congestion in HF patients; 2- to evaluate prognostic influence of hyponatremia considering renal function and diuretics received.

**Methods:** In this study, we enrolled 164 patients admitted to our department with diagnosis of acute HF (performed by B-type natriuretic peptide [BNP] levels more than 400 pg/ml, echocardiography and chest-ray). We performed a systematic assessment of congestion (pulmonary rales, jugular venous distension, third heart sound, peripheral edema and hepatomegaly: one point for each sign) as well as laboratories (BNP, creatinine, blood urea nitrogen [BUN], sodium, potassium) at admission and at discharge. The mean daily dose of loop diuretic infusion was also calculated. Hyponatremia was defined as admission sodium levels lower than 135 mEq/L. Patients were followed for six months for death or re-hospitalization due to cardiovascular causes.

**Results:** Of 164 patients, only 151 completed the follow-up. Of these, 36 patients presented with hyponatremia. Univariate predictors included congestion score  $\geq 3$  points (50 patients) p=0.009, and higher loop diuretic dosage (250  $\pm$  125 mg vs 125  $\pm$  50 mg p < 0.001). Hyponatremic patients had a higher composite of re-admission or death over 180 days of followup (72% vs 55% p < 0.05). Cox regression analysis showed that hyponatremia was significantly related to poor outcome also after adjustment for congestion, CKD, age and other baseline variables (Univariate HR: 1.87 [CI:1.21-2.91]; p = 0.005. Multivariable HR: 1.64 [CI: 1.02-2.65]; p = 0.04). Kaplan Meier survival plot confirmed these findings (see Figure).

**Conclusions:** Hyponatremia on admission is associated with greater degrees of pulmonary and systemic congestion and higher diuretic usage after admission. Baseline hyponatremia is an independent predictor of death or hospitalization after discharge after controlling for degree of congestion, renal function, and other baseline variables. Future strategies that specifically address initial hyponatremia upon admission are warranted in attempts to reduce re-admission and death.



**P1631**  
**Increase of HF re-admission rate by chronic administration of tolvaptan for the tolvaptan non-responders.**

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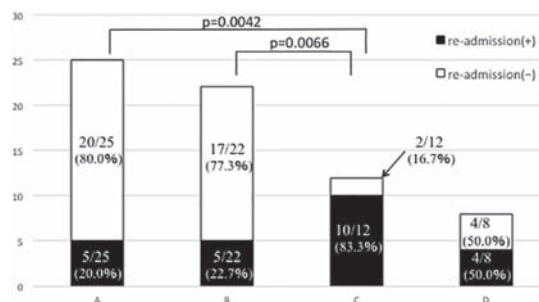
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**Background:** Tolvaptan is a novel water diuretic which exerts its diuretic effect via selective vasopressin type-2 receptor inhibition and subsequent renal collecting duct aquaporin-2 suppression. The usefulness of tolvaptan in acute decompensated heart failure (HF) was demonstrated in EVEREST trial, whereas those in chronic HF was unfavorable. However, another report showed the possible usefulness of tolvaptan administration for the chronic HF patients who preserved urine aquaporin-2 synthesis and trafficking. The efficacy of tolvaptan administration for the patients in chronic phase of HF was not fully understood.

**Purpose:** To investigate the efficacy of tolvaptan administration in chronic HF.

**Methods:** 67 patients who had acute decompensated HF treated by tolvaptan from April, 2014 through March, 2015 were enrolled in this retrospective observational study. Responder was defined as the patient whose urine volume was increased after tolvaptan administration. We divided the patients into four groups as follows: group A as for the responders who continued tolvaptan administration after discharge (n = 25); group B as for the responders who ceased tolvaptan administration after discharge (n = 22); group C as for the non-responders who continued tolvaptan administration after discharge (n = 12); and group D as for the responders who ceased tolvaptan administration after discharge (n = 8). Four groups were compared with regard to all-cause mortality and the rate of HF re-admission during observation period. The deviation among four groups were analyzed by chi-square test. Comparison between groups were analyzed by Fisher's exact test adjusted using Bonferroni method. P < 0.05 considered significant. Results There were significant deviation in all-cause mortality (chi-square test, p = 0.0476) and HF re-admission rate (chi-square test, p = 0.0008) among group A, group B group C, group D (all-cause mortality were 0.0% (0/25), 4.6% (1/22), 25.0% (3/12), 12.5% (1/8); and HF re-admission rate were 20.0% (5/25), 22.7% (5/22), 83.3% (10/12), respectively). The significant difference were found in HF re-admission rate comparing between group A and C (p = 0.0042), and group B and C (p = 0.0066).

**Conclusions:** It was demonstrated that non-responder and continuous administration of tolvaptan would be harmful combination with high HF re-admission rate.



Comparison of HF re-admission rate



## P1632

**Ambulatory intravenous diuretic heart failure unit: 18 months experience**

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**Background:** Heart failure (HF) with fluid overload requires intravenous diuretic therapy that may need to be given over a long and costly admissions to hospital. We established an ambulatory intra-venous diuretic therapy unit for heart failure (AID-HF). We present our experience in the last 18 months.

**Methods:** We replaced 4 beds with chairs in one of the wards, trained the ward nurses in the principles of heart failure management. The patients who were no longer in pulmonary oedema, who were mobile and otherwise ready to return home apart from peripheral oedema with or without ascites were invited to be admitted to AID-HF. Those who consented were admitted daily for intravenous (iv) diuretics given over 2-6 hours/day while monitoring their weight, blood pressure and renal function. The patients were discharged when the oedema became limited to below the knees, and they tolerated the switch to oral diuretics. Care was provided by the HF specialist nurses supported by the ward nurses, the HF cardiologists and a junior doctor in HF. Data are collected on the patients' background, the days of attendance as a marker of hospitalisation days saved, the patients' re-admission to hospital, their chance of re-admission into the service within 1 month.

**Results:** There were 77 patients admitted to AID-HF unit between June 2014 and December 2015. Of these patients, 61 patients (79%) were 50-80 years of age, and 67 patients (87%) were males. HF with reduced ejection fraction was the diagnosis in 49 patients (64%). All the patients had a degree of pulmonary hypertension and/or right ventricular impairment with or without tricuspid regurgitation. Re-admission to the AID-HF unit affected 25 patients (33%), and 8 patients (10%) had more than one re-admission. In addition, 16 patients (21%) were hospitalised from the AID-HF unit. The mean length of attendance is 11 days with a median of 7 days. In total, the patients attended the AID-HF unit on 888 days which are the total hospital days saved.

**Conclusion:** Ambulatory intravenous diuretic therapy is feasible in advanced heart failure even in high risk patients and could possibly result in health economic savings.

## DRUG THERAPY, OTHER

## P1633

**Assessment of the use of ESC heart failure guideline recommended therapy among patients followed at a heart failure outpatient clinic participating in the ESC Heart Failure long-term Registry**

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**Background:** In the large randomized, controlled trials which proved the favourable effect of neurohormonal antagonists on the outcome of chronic systolic heart failure (HFREF), the proportion of patients receiving the target doses (TD) of these drugs reached about 60-70%. Contrary to that, in observational studies, even in the whole cohort of the recently published ESC Heart Failure Long-term (EORP) Registry the proportion of patients receiving TD of these drugs was significantly lower.

**Aim:** To assess the proportion of patients receiving the ESC guideline recommended treatment in the patient cohort (PC) suffering from HFREF followed at our heart failure outpatient clinic (HFOC) participating in the EORP Registry.

**Patients and methods:** We analysed the data of 154 consecutive ambulatory patients with HFREF followed at our HFOC (LVEF: 34.6 ± 10.3%; NYHA: 1.7 ± 0.8; blood pressure: 119.3 ± 19.2/68.3 ± 11.1 mmHg; ischemic etiology: 57.1%; diabetes: 31.8%; hypertension: 68.2%; atrial fibrillation: 32.4%; male: 79.8%; age: 66.7 ± 13.3 years; eGFR: 52.1 ± 22.5 ml/min/1.73 m<sup>2</sup>) at the time of inclusion to the EORP Registry and one year later. The majority of the patients was managed at our HFOC for more than one year before the inclusion.

**Results:** Treatment at baseline were: ACEi/ARB in 95.4% (at TD: 55.1% of pts of PC), beta-blocker (BB) in 97.4% (at TD – 62.3% of pts) and mineralocorticoid receptor antagonists in 77.2%. Resynchronization therapy (CRT-P/CRT-D) was used in 32.4% and ICD was implanted in 17.5%. Contrary to the whole EORP cohort, our pts were younger, had slightly lower LVEF, better mean NYHA class, and higher percentage of prior coronary artery disease. At one-year follow up the proportion of patients receiving TD of an ACEi/ARB and a BB increased slightly (59.8% and 65.8%, respectively) contrary to the data of the whole EORP registry. In total, 57.1% of pts were suitable for ICD, and 78.4% of them had already undergone the implantation, while 40.2% fulfilled the criteria for CRT-P/CRT-D and 90.3% had already have the device. One-year survival of our ambulatory PC was 90.3%.

**Conclusions:** Although the worldwide rate of patients receiving the cornerstone

neurohormonal antagonist regime of HFREF has increased within the last years, the proportion of pts receiving the target doses of these drugs is still moderately low. Follow up of HFREF patients at a HFOC, and the effort and motivation to optimize the treatment by specialists can make it possible to reach the doses of neurohormonal antagonists that is similar to that were used in the large landmark heart failure trials.

## P1634

**Long-term follow up of hospitalized patients with systolic heart failure undergoing early treatment with beta-blockers more ivabradine: a randomized study**

The authors claim to have received an unconditional grant from Servier F Francisco Jose Hidalgo Lesmes<sup>1</sup>; M Anguita Sanchez<sup>1</sup>; JC Castillo Dominguez<sup>1</sup>; S Rodriguez Diego<sup>1</sup>; L Pardo Gonzalez<sup>1</sup>; M Ruiz Ortiz<sup>1</sup>; D Mesa Rubio<sup>1</sup>; M Delgado Ortega<sup>1</sup>

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**Background and aims:** Heart rate (HR) seems to have prognostic value in patients with heart failure and depressed ejection fraction (HF-dEF) in sinus rhythm. HF guidelines recommend to obtain a HR < 70 bpm, but it is not well known if the way in which this target is reached affects outcomes. The aim of our study was to analyze the effect or early administration of ivabradine added to betablockers (lv+BB) versus only betablockers (BB) on heart rate and outcomes in this kind of patients. Methods.- The effect of two different protocols, lv+BB or only BB during hospitalization, in patients with HF-dEF, sinus rhythm, HR>70bpm and left ventricular ejection fraction (LVEF) < 40% was evaluated in a comparative, randomized study. HR at 28 days after discharge was the primary end-point. HR, LVEF, NYHA class, BNP levels and clinical outcomes at 1 year were also analyzed. In the lv+BB group, ivabradine was started at 24 hours after admission.

**Results:** Sixty-two consecutive patients who met inclusion criteria were included, 30 in the lv+BB group and 32 in the BB groups. Mean age was 66.2 ± 15.4 bpm in the lv+BB group, and 67.7 ± 12.3 bpm in the BB group (p=0.68). The LVEF was 29.8 ± 7.5% in the lv+BB group and 29.9 ± 6.1% in BB group (p=0.6). Both groups were homogeneous in terms of gender, blood pressure and HR at admission, BNP levels, renal function and drug therapy with diuretics, ACEi or ARA and ARM too. Ivabradine dosage at discharge was 5 mg/12 hours in 18 patients and 7.5 mg/12 hours in 12 patients. Betablockers dosage at discharge and at 1 year follow up was similar in both groups. HR at 28 days after discharge was significantly lower in the lv+BB Group (64.3 ± 7.5 vs 70.3 ± 9.3 bpm; p=0.01). HR at 1 year remained lower in the lv+BB group (61.84 ± 5.5 vs 68.47 ± 9.3 bpm; p=0.01). LVEF at discharge was similar in both groups (32.9 ± 8.7 vs 31.9 ± 6.1%), but significantly higher at 1 year in the lv+BB group (48.2 ± 17.2 vs 41.8 ± 10.2%; p=0.002). There were no differences in BNP levels at 1 year (404 ± 200 vs 368 ± 113 pg/ml; p=0.9), as well as the proportion of patients in NYHA class III or IV (16 vs 21.5%). There were no differences in clinical events (re-hospitalizations or death) at 1 year. Mortality was 16.7% in the lv+BB and 12.5% in the BB group. No severe adverse effects related to drugs were noted.

**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. This drug protocol also decreased HR at 1 year and seems to improve systolic function without differences in BB doses.

## P1635

**Comparison of perindopril-amlodipine and losartan-amlodipine combinations in the management of hypertension in patients with metabolic syndrome**

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**Background:** Metabolic syndrome (MS) is a condition linking insulin resistance, dyslipidemia, hyperglycemia, and hypertension that increases the risk of developing diabetes, cardiovascular disease, and subsequent cardiovascular morbidity and mortality. High blood pressure is considered one of the key features of metabolic syndrome. It is a very prominent feature of the metabolic syndrome, present in up to 85% of patients.

Aim of the study was to compare the efficacy and tolerability of perindopril 4 mg + amlodipine 5 mg combination (P+A) versus losartan 50 mg + amlodipine 5 mg (L+A) combination in patients with MS.

**Material and Methods:** We investigated 84 hypertensive patients with metabolic syndrome with mild-to-moderate arterial hypertension not adequately controlled by a monotherapy with ACE inhibitors or calcium channel blockers or ARB entered this work, randomized, parallel-group study. After a two week placebo run-in, all patients with sitting diastolic blood pressure (DBP) > 95 mmHg and/or sitting systolic (BP) > 160 mmHg were randomized to receive either P+A (42 patients) or L+A (42 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 P+A were, respectively, 1.9 and 2.6 mmHg lower than those obtained with L+A (both  $p < 0.002$ ). The response rate in the L+A group (90.6%) was better than that observed in the P+A group (88.4%,  $p = 0.01$ ). The incidence of adverse events was similar with the 2 treatment groups (14.2% vs. 16.6%,  $p < 0.02$ ).

**Conclusions:** These data suggest a higher antihypertensive efficacy of the fixed combination L 50 mg + A 5 mg as compared with P 4 mg + A 5 mg. Further investigations are required with a large amount of patients.

### P1636

#### How do we use anticoagulation therapy in the era of novel drugs - results of FIRST II registry

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**Background:** Patients with need of anticoagulative treatment (ACT) are substantial part of daily clinical practice. Clinical and risk assessment, especially in the era of novel anticoagulative drugs, (NOAC) is yet not well known.

**Purpose:** To compare patients with indication for ACT, their clinical and pharmacological profile and to assess their risk for bleeding.

**Methods:** Compared were patients with atrial fibrillation/flutter (group AF,  $n = 650$ ) to patients with valve prosthesis (group P,  $n = 14$ ), acute pulmonary embolism (group PE,  $n = 80$ ) and deep venous thrombosis (group VT,  $n = 71$ ) who were hospitalized at university cardiology centre during the study period of May 2013 to May 2014.

**Results:** Patients with AF were the oldest (71.4 years), PE population the youngest (65.9,  $p = 0.001$ ). Patients with PE presented with better renal function (estimated creatinine clearance 67.8 vs. 58.3 ml/min in AF group,  $p < 0.05$ ). VT patients had the lowest BMI (27.3 vs. 28.9 in AF population,  $p < 0.05$ ) and higher incidence of myocardial infarction in the history (29.6% vs. 18.8% AF group,  $p < 0.05$ ). AF patients suffered more by hypertension (82.5%), diabetes mellitus (31.5%) and heart failure (30.9%) when compared to PE subgroup (56.3%, 13.8% and 6.3% respectively,  $p < 0.05$ ). NOAC were used more frequently in PE and VT population (25.0 and 19.7% respectively, AF in 15.2%,  $p < 0.05$ ). Warfarin was used dominantly in P and AF indication (85.7 and 70.9% vs. 57.5 and 49.3% in PE and VT group). Rest of the patients used low molecular weight heparin. Patients with AF and in the P group had higher risk of bleeding when assessed by HAS BLEED score (2.2 and 2.1 points vs. 1.6 and 1.8 in PE and VT group,  $p < 0.05$ ).

**Conclusion:** Patients with AF are older, present with higher incidence of comorbidities (especially hypertension, diabetes, heart failure, renal dysfunction) and have the highest risk of bleeding when ACT is used. Warfarin is used dominantly in AF indication, while NOAC in the indication of PE and VT.

### P1637

#### Cardioprotective effects of long-term high-dose therapy with atorvastatin in patients with STEMI in the prevention of chronic heart failure

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**Objective:** to study the dynamics of the characteristics of the global contractility, the structural parameters of the myocardium of the left ventricle (LV) in patients with acute myocardial infarction with ST segment elevation (STEMI) against the backdrop of 24 weeks of treatment with different doses of atorvastatin.

**Methods:** The study included 46 patients with STEMI, confirmed by the ECG data, level of troponin I, CK-MB. An obligate criterion was the presence of hemodynamically significant stenosis of only one coronary artery based on the results of coronary angiography. Patients were randomized into two groups. The group C (control) included 26 people who received atorvastatin at a dose 20 mg/day. Group A consisted of 20 patients with STEMI, treated with atorvastatin 80 mg/day. Comparison groups were matched by sex, height, BMI, office blood pressure values. Lipid-lowering therapy was started in the first 24-96 hours from the onset of the disease. Initially, at 7-9 day from the beginning of the STEMI and at 24 weeks of treatment all patients underwent echocardiography using ultrasonic device MyLab90 (Esaote, Italy). Computer analysis was performed using the XStrain™ software with evaluation of the following parameters: global longitudinal strain (GLS), circular strain (GCS) and radial strain (GRS). Among the traditional echocardiographic parameters the index of end-diastolic volume (EDV index) and ejection fraction (EF) have been analyzed.

**Results:** According to the two-dimensional Strain in the group C the baseline value of the global deformation were the following: GLS -  $-14.9 \pm 7.6\%$ , GCS -  $-20.2$  (12.9; 25.0)%, GRS -  $29.7$  (25.4; 40.0)%; the follow-up, respectively,  $-16.8 \pm 5.9\%$ ,  $-21.1 \pm 7.5\%$  and  $32.3 \pm 11.4\%$  ( $p > 0.05$ ). In group A no significant dynamic of global

Strain parameters have been revealed as well. The baseline values of GLS was  $-17.2 \pm 5.3\%$ , GCS -  $-18.3 \pm 8.3\%$ , GRS -  $37.2 \pm 13.5\%$ ; after 24 weeks of treatment  $-17.0 \pm 4.9\%$ ,  $-19.7 \pm 5.0\%$  and  $34.0 \pm 9.6\%$  ( $p > 0.05$ ). While in the group C an increase of EDV index has been revealed from  $47.2 \pm 8.2$  ml/m<sup>2</sup> to  $58.0 \pm 7.9$  ml/m<sup>2</sup> ( $p < 0.05$ ). In patients treated with atorvastatin 80 mg, the dynamic of this parameter was the following: 7-9 hours -  $52.0 \pm 6.7$  ml/m<sup>2</sup>, 24 weeks -  $48.0 \pm 9.1$  ml/m<sup>2</sup> ( $p > 0.05$ ). Initial values of the EF in the control group were  $56.11 \pm 11.9$ , follow-up -  $56.0 \pm 9.7$  ( $p > 0.05$ ); patient of comparison group -  $54.5 \pm 10.0\%$  and  $58.6 \pm 8.7\%$ , respectively ( $p < 0.05$ ).

**Conclusions:** The 24-weeks of treatment with different doses of atorvastatin in patients with STEMI was not accompanied by deterioration of the deformation characteristics of the left ventricle. An increase of LV end-diastolic volume in the group treated with 20 mg of atorvastatin has been revealed. High-dose statin therapy was accompanied by a significant increase in LVEF.

### P1638

#### Mineralocorticoid receptor antagonists improve quality of life in patients with systolic heart failure highly treated with neurohormonal inhibitors: a propensity-score matching analysis

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**Background:** Mineralocorticoid receptor antagonists (MRA) constitute a cornerstone of therapy in patients with heart failure with reduced ejection fraction (HFrEF), as they improve significantly long-term outcome. However, their effect on quality of life (QoL) in the current HFrEF populations who are highly treated with neurohormonal inhibitors has not been clarified.

**Purpose:** We sought to assess the effects of MRA therapy on QoL along with exercise capacity, neurohormonal activation and central hemodynamics in chronic HFrEF patients highly treated with neurohormonal inhibitors

**Methods:** We analyzed retrospectively a cohort of 120 stable chronic HFrEF patients (57% male, NYHA class II or III, mean left ventricular ejection fraction,  $28 \pm 5\%$ ). We compared quality of life between patients receiving or not MRA using propensity-score matching. Kansas City Cardiomyopathy Questionnaire (KCCQ) functional and summary scores were used for QoL evaluation. Six-min walked distance (6MWD), B-type natriuretic peptide concentration (BNP) and mitral E/e' ratio were also assessed.

**Results:** Of 120 patients, 106 (88%) were on MRA therapy. In addition, 114 patients (95%) were receiving angiotensin converting enzyme inhibitors or angiotensin II receptor blockers and 117 (97%) beta-blockers. Therapy with MRA was associated with significantly better KCCQ functional and summary scores [average treatment effect (ATE), 0.16, 95% confidence interval (CI): (0.13, 0.18),  $p < 0.001$  and 0.13, 95% CI: (0.11, 0.14),  $p < 0.001$ , respectively]. In addition, MRA therapy was associated with significantly lower BNP [ATE, -135.46, 95% CI: (-245.61, -25.31),  $p = 0.016$ ] and mitral E/e' ratio [ATE, -3.59, 95% CI: (-4.56, -2.62),  $p < 0.001$ ], but not with significantly longer 6MWD [ATE, 10.43, 95% CI: (-16.20, -37.07),  $p = 0.443$ ].

**Conclusion:** In chronic HFrEF patients highly treated with neurohormonal inhibitors, MRA was associated with better QoL, along with improved central hemodynamics and neurohormonal activation.

### P1639

#### Ivabradine in the treatment of severe left ventricle systolic dysfunction in very elderly patients

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**Introduction:** Congestive heart failure (CHF) is a common syndrome, especially in advanced-age patients. Ivabradine has shown to be beneficial in the treatment of CHF with left ventricle systolic dysfunction (LVSD). However, there are still very few available data regarding its usage and efficacy in very elderly patients (PT). Thus, we aim to describe our experience with respect to ivabradine and elderly population.

**Methods:** Since January 2008 to December 2013 we prospectively collected data (in a single third level hospital) from PT with LVSD (ejection fraction (EF) < 35% and  $\geq 75$  years of age. We included clinical, electrocardiographic and echocardiographic variables. We performed prospective follow-up with clinical history and phone calls.

**Results:** We finally included 802 PT. The mean age was 82.03 years ( $SD \pm 4.95$ ) and 66.2% were male. Only 7% of the total population was on Ivabradine (51 PT) with a mean age of 80.13 years ( $SD \pm 4.03$ ) in this subgroup, being 70.6% of them males. 70.6% of them had hypertension, 39.2% diabetes mellitus, 56.9% dyslipidemia, 27.5% chronic renal injury, 31.4% chronic obstructive pulmonary disease (COPD) and 13.7% cerebrovascular disease. The mean EF was 26.9% ( $SD \pm 6.4$ ) with ischemic origin in 76.7% of the total. There were no side effects in this Ivabradine-subgroup. In 2 PT, ivabradine was removed to start in beta-blockers

(BB), not considered initially due to history of asthma in one of them, and intolerance in the other one. Nevertheless, up to 43.1% of the subgroup was receiving both Ivabradine and BB without complications. The main cause of patients who did not receive BB was the presence of COPD. After a mean follow up period of 36.5 months (SD  $\pm$  18.06), up to 37.3% of the PT were admitted due to an episode of CHF and up to 39.2% of them died. PT in Ivabradine treatment had a significant reduction in the heart rate as compared with those non receiving Ivabradine (78.8 versus 69.8 bpm, respectively;  $p=0.05$ ) and a significant increase in the mean EF in those receiving Ivabradine during the follow up period (26.9 versus 34%;  $p=0.05$ ). We also detected an improvement in the NYHA functional class in the Ivabradine-subgroup during the follow up (1.8 versus 1.6;  $p=0.05$ ).

**Conclusions:** Ivabradine might have clinical benefit in very elderly patients with severe left ventricular systolic dysfunction and congestive heart failure. In addition, it has a good profile of tolerance and safety in our population. We suggest that further trials should be performed in this a common specific subgroup of patients.

#### P1640

##### The effects of ivabradine on diastolic function in patients with decompensated systolic heart failure

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**Premises and purpose:** In patients with heart failure and reduced ejection fraction (HFREF) diastolic function also has an important prognostic value. The objective of this study was to assess the influence of ivabradine on diastolic function in patients with decompensated HFREF.

**Material and methods:** This prospective study recruited 42 consecutive patients (32 males, 10 females) admitted for decompensated heart failure, with LV systolic dysfunction, sinus rhythm and resting heart rate  $>70$  b/min, treated according to current guidelines in whom ivabradine therapy was initiated (in hospital or in the first week after discharge). Echocardiographic data on systolic and diastolic function (LV ejection fraction, indexed LV endsystolic and enddiastolic volumes – iESV and iEDV, mitral E velocity, E/A ratio, e' velocity, E/e' ratio, E deceleration time, left atrial volume) were measured at baseline and after 6 months of ivabradine therapy.

**Statistics:** data were expressed as mean  $\pm$  standard deviation or percentages, comparisons between baseline and follow-up data were done with Student's paired t test.

**Results:** Study group consisted of 35 P in whom both baseline and 6 month data were available (1 P died, 3 P did not tolerate ivabradine, 1 P presented atrial fibrillation during follow-up with subsequent interruption of ivabradine, 2 P lost to follow-up). Mean age was 60  $\pm$  12 years, heart failure etiology was ischemic in 19 P (54%), 11 P (31%) had diabetes, 15 P (43%) had left bundle branch block, 7 P (20%) had COPD. Associated heart failure therapy consisted of ACE inhibitors/ARBs in 26 P (74%), betablockers in 33 P (94%), furosemide in 33 P (94%), spironolactone in 29 P (82%). Mean ivabradine dose at 6 months was 10.8  $\pm$  3 mg/day. After 6 months LV ejection fraction increased from 26  $\pm$  8 to 31  $\pm$  8% ( $p=0.007$ ), LV volumes decreased (iEDV from 93  $\pm$  25 ml/m<sup>2</sup> to 87  $\pm$  27 ml/m<sup>2</sup>- $p=0.1$ , iESV from 69  $\pm$  23 ml/m<sup>2</sup> to 61  $\pm$  24ml/m<sup>2</sup>-  $p=0.02$ ). Diastolic parameters under ivabradine therapy showed improvement after 6 months: E velocity decreased from 83  $\pm$  23 cm/s to 77  $\pm$  22 cm/s ( $p=0.1$ ), E/A ratio decreased from 1.9  $\pm$  1.2 to 1.3  $\pm$  1.02 ( $p=0.009$ ), e' velocity increased from 5.5  $\pm$  1.7 cm/s to 7.2  $\pm$  1.6 cm/s ( $p=0.0009$ ), E/e' ratio decreased from 14.7  $\pm$  5 to 11  $\pm$  4 ( $p=0.0003$ ), EDT increased from 165  $\pm$  56 ms to 190  $\pm$  68 ms ( $p=0.1$ ) and left atrial volume decreased from 38.6  $\pm$  13 to 35.4  $\pm$  11 ml/m<sup>2</sup> ( $p=0.2$ ). Readmissions due to HF aggravation were noted in 5 P (14%).

**Conclusions:** In patients with decompensated HFREF, well treated with guideline recommended medical therapy, association of ivabradine, besides the beneficial effects on systolic function, seems to improve also left ventricular diastolic function parameters.

#### P1641

##### Risk of heart failure related to non - ergot derived dopaminergic agonists in Parkinson disease. A meta-analysis of randomized controlled trials

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**Background:** Parkinson's disease (PD) is a neurodegenerative disorder caused by the disruption of dopaminergic neurotransmission in the basal ganglia. Levodopa is currently the most effective agent used in the treatment of PD. Even though dopaminergic agonists(DAs) are less effective than levodopa as treatment regimen, they are associated with lower risks of dyskinesia and motor fluctuation. This has caused the wide-scale application of DAs in the early stages of PD in order to postpone the use of levodopa, or as an add-on treatment to reduce levodopa dosages. With regard to the more recently developed non-ergot-derived DAs

such as pramipexole and ropirinoles, a number of randomized controlled trials(RCTs) and observational studies have reported a clear, albeit nonsignificant, trend to the increase in the risk of heart failure and cardiovascular events associated with the use of non-ergot DAs, especially in the case of the pramipexole.

**Purpose:** Thus we decided to carry out a systematic review and meta-analysis of RCTs related to the use of non-ergot DAs in patients with PD. Our primary endpoints were all-cause mortality and cardiovascular events.

**Methods:** Systematic searches were performed in Pubmed, Embase and Clinical-Trial.gov up to June 2015. Eligibility for inclusion in the meta-analysis was based on the following: RCTs of non-ergot DA use in PD patients, trials exceeding three months in duration, more than ten participants in each arm of the intervention, and the availability of outcome data pertaining to mortality and cardiovascular events. Both fixed and random effects models were used to assess the risk of mortality associated with the use of non-ergot DAs. The effect size was expressed as relative risk (RR) of non-ergot DA versus placebo on overall mortality and cardiovascular events (including any cardiovascular events, major adverse cardiovascular events and heart failure). Results Thirteen trials (5215 PD patients) were comprised in our analyses of mortality rates and 24 RCTs(6734 patients) were considered to evaluate cardiovascular events. Overall, the use of non-ergot DAs was associated with a risk of death lower than that associated with placebo use (RR: 0.53; 95% CI: 0.30-0.96). Moreover, the use of non-ergot DAs was not associated with increased risk of cardiovascular events(RR: 0.87; 95% CI: 0.56- 1.37), including myocardial infarction, stroke, and heart failure.

**Conclusions:** The use of non-ergot DAs was shown to modestly reduce overall mortality without increasing the risk of cardiovascular events, including heart failure. Further research is warranted to assess the potential risks and benefits concerning therapy with non-ergot DAs by analyzing large population-based data.

#### P1642

##### Ivabradine treatment for chronic heart failure in clinical practice is associated with reductions in symptoms and hospitalizations with improved quality of life, independent of beta blocker dose

Study supported by Servier Germany  
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**Background & Objectives:** Ivabradine is recognized in current treatment guidelines of chronic heart failure (CHF). We aimed to evaluate the symptomatic effectiveness, tolerability, effect on quality of life (QoL) of ivabradine in CHF patients treated in clinical practice, with a special focus on hospitalizations over a 12-month period.

**Methods:** In this non-interventional study heart rate (HR), heart failure symptoms and medication were documented at cardiologist level in outpatients with CHF. The frequency of heart failure hospitalizations during the study period was compared with an internal control period of 12 months prior to study start. Patients with indication for ivabradine treatment were eligible (NYHA class II-IV, sinus rhythm, HR  $\geq 75$  bpm). Therapy with ivabradine twice daily was initiated for a duration of 12 months, with possibility of dose adjustment. QoL was evaluated by the EQ-5D patient questionnaire. A descriptive statistical analysis was performed, with stratification according to beta blocker (BB) dose categories (i.e.,  $<50\%$ ,  $50-99\%$  or  $\geq 100\%$  of recommended target dose).

**Results:** A cohort of 767 CHF patients (mean age 65.5  $\pm$  11.4 years, 23%  $\geq 75$  years; 57% male) was recruited. Median follow-up was 11.9 months. 61% of patients had ischemic etiology of CHF. Hypertension (81%) and dyslipidemia (50%) were the most prevalent comorbidities. Concomitant medication at baseline: 65% BB (Metoprolol 42%, Bisoprolol 41%, Nebivolol 8%, Carvedilol 8%), ACEI/ARB 86%, diuretics 60%, aldosterone antagonists 21%, aspirin 59%, statins 59%.

Follow-up information after 1 year of treatment was available in 90% of all patients. Ivabradine (mean daily dose 11.3 mg) was associated with reduced HR by 14-18 bpm in all three categories of BB dose. The absolute percentage of patients with NYHA III classification was reduced by 25%, 33% and 31% in patients with  $<50\%$ ,  $50-99\%$  or  $\geq 100\%$  of BB target dose, respectively, whereas the percentages in NYHA class I substantially increased ( $p < 0.0001$  for changes).

Compared to the 12 months prior to ivabradine treatment percentages of patients with any hospitalization for heart failure were significantly reduced during the study period in all three BB subgroups: from 19% to 5%, from 31% to 6%, and from 29% to 3%. QoL (EQ-5D score) improved by 20%, 26%, and 19%, respectively ( $p < 0.0001$ ). Mean BB doses remained stable during the trial. Adverse drug reactions, potentially related to ivabradine use, occurred in 3.4% of all patients.

**Conclusion:** In this cohort of CHF outpatients treated by cardiologists, ivabradine was associated with reductions in heart failure symptom burden and frequency of CHF-related hospitalizations, independent of concomitant BB dose. QoL consistently improved in all BB subgroups. These effects were accompanied by good general tolerability of the drug.



## METABOLISM / DIABETES MELLITUS / OBESITY

## P1643

**Diastolic dysfunction in lipotoxic myocardial damage by patients with obesity**G Galina Chumakova<sup>1</sup>; O Gritzenko<sup>2</sup>; N Veselovskaya<sup>2</sup><sup>1</sup>Altay State Medical University, Barnaul, Russian Federation; <sup>2</sup>Research Institute for Complex Issues of Cardiovascular Diseases, Kemerovo, Russian Federation

The risk of lipotoxic myocardial damage is significantly increases in patient with obesity. Visceral obesity is characterized by impaired lipid metabolism, which leads to "overload" cardiomyocytes lipids that contribute to initiation of apoptosis that leads to myocardial fibrosis and heart failure.

**Purpose:** To identify risk factors for lipotoxic myocardial remodeling and explore features of remodeling heart in patients with obesity.

**Materials and**

**Methods:** Was included 48 patients (43,8 ± 5,2) with common obesity. Patients has obesity I-III degree, BMI 33,86 ± 4,23 kg / sq.m. From the study were excluded patients with diabetes, hypertension, coronary heart disease. All patients measured the thickness of epicardial adipose tissue (EAT), end-diastolic and end-systolic volume, size of LA, end-diastolic size of RV, diastolic dysfunction by echocardiography and determined the level of metabolic risk factors and free-fatty acid (FFA). Was allocated 2 groups: Group 1 with obesity and EAT more than 7 mm (26), Group 2 with obesity and EAT less 7mm (22).

**Results and discussion:** In Group 1 higher level of glucose (4,2 ± 0,2 and 5,7 ± 0,4 mmol/l in group 1 and 2 respectively, p = 0,004), level of insulin in group 1 was 7 ± 0,3 mcEd/ml, in group 2 - 16 ± 0,7 mcEd/ml (p = 0,02), higher level of unsaturated FFA in group 1 than in group 2 (0,2 ± 0,01 and 0,8 ± 0,1 respectively, p = 0,003), level of TG was 0,9 ± 0,1 mmol/l and 1,5 ± 0,2 mmol/l respectively in group 1 and 2 (p = 0,04) and level of VLDL was higher in group 1 than in group 2 (2,2 ± 0,2 mmol/l and 3,5 ± 0,3 mmol/l respectively, p = 0,002). Evaluation of remodeling of left ventricular was made and it was found that end-diastolic volume and end-systolic volume in group 1 were significantly higher than in group 2 (73,2 ± 4,3 ml and 46,7 ± 3,5 ml respectively p = 0,02). In addition, patients in Group 1 with a 7mm EAT has more size of the LA - 44,42 ± 4,89 mm and end-diastolic RV size - 29,41 ± 3,52 mm than patients in Group 2 (p = 0.001). In group 1, diastolic dysfunction (DD) type 1 is determined in 28.5% of patients in group 2, 14% of patients.

**Conclusion:** Obesity significantly increases the risk of myocardial lipotoxic. This risk increases in visceral adiposity patients. Myocardial fibrosis and heart failure are causes lipotoxic myocardial damage. Markers of lipotoxic myocardial damage are increased level of FFA, TG and VLDL.

## P1644

**Type II diabetes mellitus and its early effects on the heart: an echocardiographic study**R Petroni<sup>1</sup>; M Di Mauro<sup>1</sup>; V Porretta<sup>1</sup>; N Borrelli<sup>1</sup>; S Romano<sup>1</sup>; M Penco<sup>1</sup><sup>1</sup>University of L'Aquila, cardiology, L'Aquila, Italy

**Introduction:** Diabetes mellitus (DM) is a chronic disease characterized by elevation of blood glucose levels with multi organ damage, steadily increasing and burdened with a high mortality. It was estimated that in 2000 the prevalence of DM was around 2.8 % of the world population and that in 2030 will reach 4.4% with a parallel increase in cardiovascular risk

**Purpose:** to identify early myocardial changes in order to choose the best treatment and to establish the correct follow-up of these patients

**Materials and methods:** eighteen consecutive patients suffered from Type II Diabetes Mellitus (mean age 50 ± 4; mean BMI 32,7) referred to our center were enrolled. All these patients were submitted to an echocardiographic evaluation. All the obtained data were compared with a population of eighteen patients without Type II Diabetes Mellitus but similar in age and gender. We evaluated both systolic and diastolic parameters (diameter, volumes, functional parameters) for right and left ventricle. Results For right ventricular parameters the following significant differences were observed: Tricuspid Annular Plane Systolic Excursion (TAPSE) was significantly lower in diabetic patients (p<0,05); right ventricular end-systolic and end-diastolic volume and right atrium area were higher in diabetic patients (p<0,001); E/A ratio and deceleration time of E wave (DTE) were altered in diabetic patients (p<0,05) and Doppler tissue imaging-derived peak systolic velocity (S') was lower (p=0,002). For left ventricular parameters the following significant differences were observed: Left ventricular end-systolic volume, end-diastolic volume and left atrium area were significantly higher in diabetes patients (p<0,001). E/A and E/E' ratio were altered in diabetic patients more than in normal patients (p<0,001 and p=0,02), and Doppler tissue imaging-derived peak systolic velocity (S') was lower (p=0,001) in diabetic patients. Conclusion Echocardiographic parameters demonstrate that type II diabetes mellitus leads to a very early damage of the heart muscle. Variation of speed contraction may be the first sign of this damage and changes in intraventricular volumes the consequence. These observations are very important

to establish in which kind of type II diabetic patients we must optimize therapy in order to prevent or slow the progression to a full-blown heart disease.

## P1645

**The differences between various obesity indices in predicting clinical severity and prognosis of acute myocardial infarction**Z Babic<sup>1</sup>; M Marko Mornar Jelavic<sup>2</sup>; H Pintaric<sup>3</sup><sup>1</sup>University Hospital "Sestre Milosrdnice", Coronary Care Unit, Zagreb, Croatia;<sup>2</sup>Health Center Zagreb - East, Center for Internal Medicine and Dialysis, Zagreb, Croatia;<sup>3</sup>University Hospital "Sestre Milosrdnice", Cardiac Catheterisation Laboratory, Zagreb, Croatia

**Introduction:** Measurement of anthropometric parameters is a primary method for diagnosing obesity. Central obesity measures are stronger predictors of CVD risk than overall obesity.

**Purpose:** To investigate the differences between various obesity indices in predicting clinical severity and prognosis of acute ST-elevation myocardial infarction (STEMI).

**Methods:** We included 250 acute STEMI patients treated with primary percutaneous coronary intervention. They were classified into two groups (with/without obesity, according to obesity indices: overall - body mass index (BMI) vs central - body adiposity index (BAI), conicity index (Cindex), visceral adiposity index (VAI), waist circumference (WC), waist-to-hip (WHR) and waist-to-height ratio (WHtR)) which were analyzed by baseline (medical history and demography), severity (clinical presentation, laboratory, echocardiography, coronary angiography and in-hospital complications) and prognostic parameters (major adverse cardiovascular events (MACE) and sick leave duration (SLD) during 12-month follow up).

**Results:** Of the total of 250 patients, there were 72 (28.8%) patients with overall obesity. Central obesity has 24 (10.3%), 202 (80.8%), 114 (52.8%), 149 (59.6%), 222 (88.8%) and 81 (32.4%) patients with very high BAI, Cindex > 1.25/1.18, WC ≥ 102/88 cm, WHR ≥ 0.90/0.85 and WHtR ≥ 63/58, respectively. Very high BAI (adjusted for BMI < 30.0 kg/m<sup>2</sup>) increased the risk of dyspnea, Cindex > 1.25/1.18 (adjusted for WHtR ≥ 63/58) of total in-hospital complications, WHR ≥ 0.90/0.85 of significant proximal/middle coronary segments stenosis and Gensini score ≥ 20, and WHtR ≥ 63/58 (adjusted for hyperglycemia) of heart failure (p < 0.05). The number of significantly stenosed coronary arteries increased the risk of total MACE (p < 0.05).

**Conclusions:** Several central obesity indices are superior to BMI in predicting acute STEMI severity (clinical presentation, in-hospital complications, severity of coronary disease), while the others (VAI, WC) have no influence on it. They all have no influence on prognosis (MACE and SLD).

## P1646

**Using the modified seattle angina questionnaire for patients with heart failure and metabolic syndrome after percutaneous intervention for assessment the effectiveness of treatment.**NV Chumachenko<sup>1</sup>; LS Kholopov<sup>1</sup>; VN Bondar<sup>1</sup><sup>1</sup>Odessa National Medical University, Odessa, Ukraine

**Background:** Patients with coronary artery disease and metabolic syndrome (MS) after percutaneous coronary intervention (PCI) for acute coronary syndrome without ST-segment elevation (ACS nST) have a very high risk of the further development of heart failure (HF), due to significant signs of severe microvascular inflammation and endothelial dysfunction. Assessment of subjective condition of the patient is an important diagnostic component for a quick solution of necessity of in-depth examination and treatment strategies correction. The purpose of the work: to evaluate the information content of "Modified Seattle Angina Questionnaire for Patients with MS after PCI" (MSAQ) in the presence of HF.

**Methods:** 94 patients (M 61, F 33) took part in the research; average age 65.6 ± 6.1 year; all of them either in clinical routine, or in connection with health aggravation. They were clinically tested especially for determination of asymmetric dimethyl-L-L-arhynyn (ADMA) and N-terminal prohormone of brain natriuretic peptide (NT-proBNP) of plasma. Patients filled in Personal Health Questionnaire Depression Scale (PHQ-8) and MSAQ.

**Results:** Patients with the results from 81 to 100% of questionnaire MSAQ (n = 26) were considered as an effective treatment group I, 61-80% (n = 49) - the group II - group of medium effectiveness of treatment and less than 60% (n = 19) - the III group of ineffective treatment. The average period after PCI was 15.1 ± 1.2 months and didn't differ between groups. In the group III there has been distinguished a big percent of patients independently visiting hospital on the occasion of health aggravation, 73.5% against 50.0% and 16.7% in group II and I. Verasiously big indices of ADMA were observed in the III group (0.74 ± 0.21, mmol / L) and the II group (0.65 ± 0.08, mmol / L) compared with group I (0.61 ± 0.09 mmol / L), (p < 0.05); and NT-proBNP: 814.1 ± 71.3 pg / mL, 730.7 ± 65.1 pg / mL, 534.1 ± 52.2 pg / mL, (p < 0.05) for III, II and I group, respectively. Patients demonstrated high indices of the left ventricular systolic function (measured by Simpson) in group I (50.1 ± 5.9, %) and II (49.2 ± 5.24, %), compared with III group (43.1 ± 3.8, %), (p < 0.05), respectively.

**Conclusions:** Designed "MSAQ" conveys multicomponent aspects for diagnosing of comorbid patients. It can be useful as an accessible screening method for evaluating the effectiveness of treatment for patients with HF and MS after PCI.

#### P1647

##### Nutritional assessment and prognosis in hospitalized patients with acute heart failure

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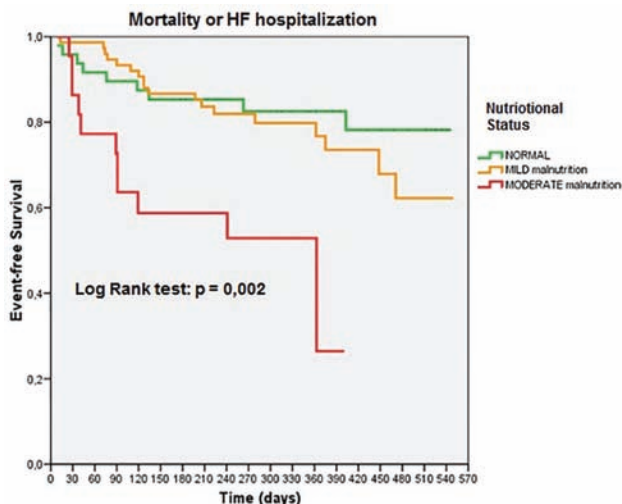
**Background:** Malnutrition is common in hospitalized patients with heart failure (HF) and may predict adverse outcomes. The relationship between nutritional status and outcomes in HF has been only partially studied.

**Purpose:** Our objective was to measure the relationship between assessment of nutritional status (CONUT method) and long-term prognosis (hospital admission for HF or mortality) in patients hospitalized for acute HF.

**Methods:** We analyze 145 patients (mean age 69,6 years, 61% men) admitted to a cardiology service for acute HF, 54 with previous HF hospitalization (37%), 112 with hypertension (HTA) (77%); 67 diabetic (DM) (46%); 135 class III or IV NYHA (93%), and 39 ischemic etiology (26,9%), with mean left ventricular ejection fraction (LVEF) 42,7%. Nutritional status was measured with the CONUT method, a validated measure of nutritional status based on laboratory test (albumin; cholesterol; lymphocytes) analysed during hospitalization. Patients were classified as normal, mild, moderate or severely malnourished, and followed prospectively in a HF clinic.

**Results:** Forty eight patients (33%) have normal nutritional status; 75 mild malnourished (52%); and 22 moderate malnourished (15%). There were no severely malnourished patients. Age, sex, history of HTA or DM, NYHA class, LVEF or ischemic etiology among de 3 groups there were no statistically different. Previous hospitalization for heart failure was more frequent in moderate malnourished patients (55%), than in mild malnourished (45%) and well nourished (17%) patients ( $p < 0,01$ ). After a mean follow-up of 327 days, 19 patients died (13%) and 27 had a HF hospitalization (19%). In well nourished group 9 patients (19%), in mild malnourished group 18 patients (24%) and in moderate malnourished group 11 patients (50%) presented an event (death or HF hospitalization). The analysis by Kaplan-Meier curves and log rank test shows that these differences are statistically significant.

**Conclusion:** Malnutrition is common in patients hospitalized for HF and determines a poor prognosis especially in its more advanced forms.



KM curves (HF hospitalisation/Mortality)

#### P1648

##### Effect of liraglutide on myocardial glucose uptake and blood flow in non-diabetic heart failure patients

The present study was funded by an unrestricted grant from Novo Nordisk A/S  
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**Introduction:** Liraglutide is a glucagon-like peptide-1 (GLP-1) receptor agonist that is used for treatment of type 2 diabetes (T2D) and obesity. Liraglutide may protect the heart against ischemia-reperfusion injury. The effect in chronic heart failure (HF) patients is undetermined. However, animal studies have shown improvement in mitochondrial and vascular function, and an increase in myocardial glucose uptake (MGU) during GLP-1 infusion that may be beneficial in HF. The present study is a sub-study of the LIVE study investigating the effect of liraglutide on left ventricular systolic function in patients with chronic HF.

**Purpose:** We investigated the effect of liraglutide treatment on MGU and myocardial blood flow (MBF) in non-diabetic patients with HF and reduced ejection fraction (LVEF<45%) (HFrEF).

**Methods:** 36 patients with HFrEF (LVEF 33 ± 8 %) and no known T2D were enrolled and randomized 1:1 in a double blinded design to receive either 1.8 mg liraglutide or placebo once daily for 24 weeks. Global MBF during rest, myocardial flow reserve (MFR) and MGU were quantified by H<sub>2</sub>O-PET and FDG-PET at baseline and follow-up. MGU was measured during an oral glucose tolerance test (OGTT) to reflect daily oral intake in a standardized setup.

**Results:** Two patients in each group dropped out, and 32 patients completed the study. Compared with placebo, liraglutide treatment reduced HbA1c levels (mean difference between groups: -3 ± 1 mmol/mol,  $p = 0.03$ ) and the 2-hour peak glucose level during OGTT (mean difference between groups: -2.1 ± 0.7 mmol/l,  $p = 0.006$ ). MGU was similar at baseline in the groups (liraglutide: 0.26 ± 0.08 mmol/g/min; placebo: 0.26 ± 0.10 mmol/g/min), and the change between baseline and follow-up did not differ between groups (mean difference between groups: 0.01 ± 0.04 mmol/g/min,  $p = 0.69$ ). MBF (liraglutide: 0.75 ± 0.18 ml/min/g; placebo: 0.78 ± 0.16 ml/min/g,  $p = 0.51$ ) and MFR (liraglutide: 2.70 ± 1.12; placebo: 2.48 ± 1.04,  $p = 0.55$ ) were similar at baseline, and the change during the study did not differ between the groups (MBF mean difference between groups: 0.03 ± 0.06 ml/g/min,  $p = 0.60$ ; MFR mean difference between groups: -0.21 ± 0.29,  $p = 0.48$ ).

**Conclusion:** Despite an improvement in HbA1c levels and lowering of glucose levels during an OGTT, the GLP-1 analogue liraglutide does not affect global MGU, MBF or MFR in non-diabetic HF patients. Whether the effect of liraglutide is different in patients with diabetes and HFrEF needs to be investigated.

#### P1649

##### The significance of diabetes mellitus on left ventricular function and heart rate variability in patients with stable angina

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**Background/Introduction:** Coronary patients with diabetes are at high risk of cardiovascular events. Echocardiographic parameters of left ventricle function and heart rate variability (HRV) are used to identify coronary patients at risk for cardiovascular event or death.

**Purpose:** The aim of this study was to assess the significance of diabetes mellitus on left ventricular function and heart rate variability in patients with stable angina.

**Methods:** The study included 135 patients with stable angina, who were in the sinus rhythm without AV blocks or branch blocks (average age 57.4 years) and 35 subjects without cardiovascular disease (average age 51.1 years), that were in the control group. Patients with stable angina were divided into two subgroups: 49 patients were with diabetes mellitus, and 86 were without diabetes. There was no significant difference in age or sex between two subgroups of patients. In all subjects echocardiographic examination and 24-hour ECG recording were performed. From the holter record, the analysis of the heart rate variability was performed by software. Four parameters of the time domain heart rate variability were assessed: SDNN, SDANN, RMS-SD and NN>50ms.

**Results:** The study has shown that patients with stable angina had significantly lower values of left ventricular ejection fraction (LVEF: 60.2 ± 9.4 vs 70.5 ± 4.8%,  $p < 0.001$ ), and significantly higher values of left ventricular end-systolic diameter (LVESd: 35.2 ± 6.2 vs 30.4 ± 3.5mm,  $p < 0.001$ ) and left ventricular end-diastolic diameter (LVEDd: 53.4 ± 6.2 vs 50.9 ± 4.2mm,  $p < 0.01$ ), as well as higher degree of left ventricle diastolic dysfunction, in comparison to the control group ( $p < 0.05$  for ratio E/A and  $p < 0.02$  for Dt). Patients with stable angina and diabetes had significantly lower values of LVEF (55.1 ± 8.3 vs 63.4 ± 10.2%,  $p < 0.001$ ), and significantly higher values of LVESd (37.8 ± 5.3 vs 33.4 ± 6.0mm,  $p < 0.001$ ) and LVEDd (55.4 ± 5.3 vs 52.3 ± 5.8mm,  $p < 0.005$ ), as well as 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). Patients with diabetes also had significantly lower values of followed parameters of HRV (94.5 ± 21.7 vs 118.9 ± 24.9ms,  $p < 0.001$  for SDNN; 85.8 ± 17.3 vs 103.4 ± 20.6ms,  $p < 0.001$  for SDANN; 28.1 ± 9.3 vs 36.5 ± 11.5ms,  $p < 0.001$  for RMS-SD and 5.9 ± 4.7 vs 11.8 ± 9.3,  $p < 0.001$  for NN>50ms) in comparison to those without diabetes.

**Conclusions:** The study demonstrated that patients with stable angina and without diabetes have better left ventricle systolic and diastolic function and significantly higher values of HRV parameters in comparison to those with diabetes.

#### P1650

##### Diabetes and treatment as predetermining factors of heart failure in patients with STEMI

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**Background and purpose:** Heart Failure (HF) is a major complication in patients with ST-Elevation Myocardial Infarction (STEMI). In outpatients, Diabetes Mellitus (DM) is an independent risk factor, increasing the risk twofold to fivefold for HF development compared to non diabetic patients. In acute coronary syndromes, diabetic patients are more prone to develop HF. Revascularization therapies have changed tremendously the mortality and morbidity in patients with STEMI. Our purpose is to determine the impact of DM and treatment on in-hospital development of HF in patients with STEMI.

**Methods:** In this study were included 629 patients, admitted in our hospital with STEMI within the first six hours, in the period between September 2012 and November 2015. They were treated with conservative therapy, thrombolysis or with primary percutaneous coronary intervention (PPCI). For all the enrolled patients, data about DM, smoking habit, age, gender, race, hypertension and the type of Myocardial Infarction (MI) were registered, and they were observed during hospitalization regarding HF development. Determination of HF was done with the Framingham criteria.

**Results:** In total 629 patients were followed up, out of which 194 patients (30.8%) had DM. HF was present in 191 patients (30.3%), 87(45.5%) of which were diabetics. They developed HF 2.6 fold compared to those without diabetes (OD:2.59,CI95%,1.61-3.39). There was a statistically significant correlation between age and HF(72.04+/-10.93 years old vs. 63.21+/-11.99 years old,  $P < 0.001$ ); also between gender and HF(47.23% females vs. 24.46% males,  $P < 0.001$ ). The patients treated with conservative therapy were 6.8 fold risked to develop HF compared to patients treated with PPCI (OD:6.78,CI95%,2.78-16.03); while patients treated with thrombolysis were 2.9 fold risked to develop HF compared to those treated with PPCI (OD: 2.89,CI%,1.83-4.55).

**Conclusion:** Diabetes Mellitus and conservative treatment are important predetermining factors of in-hospital development of HF in patients with STEMI. Also gender and age were found to be statistically significant risk factors for the occurrence of HF.

## HEART FAILURE IMAGING

#### P1651

##### Impact of fibrosis extent on left ventricular deformation: application of 3D wall motion tracking technology in hypertrophic cardiomyopathy

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**Background:** Hypertrophic cardiomyopathy is characterized by myocardial hypertrophy, disarray of the muscle fibers and fibrosis. Fibrosis is associated with loss of ventricular function and worse prognosis. The decrease myocardial deformation parameters, namely global longitudinal strain, has been related to the presence and extent of myocardial fibrosis.

**Aim:** To evaluate the impact of the extent of left ventricular fibrosis (number of segments with fibrosis) in the myocardial deformation parameters in patients with HCM.

**Methods:** Single-center, retrospective, study including patients with HCM who underwent three-dimensional echocardiography (3D Echo) with 3D Speckle tracking technology and cardiac Magnetic Resonance (MRI). Obtained global myocardial strain values for each component: global longitudinal strain, global circumferential strain, global radial strain and area tracking. Myocardial fibrosis extension was defined according to the number of segments with late enhancement in cardiac MRI. For statistical comparison between groups, patients were divided into 3 groups: no fibrosis (0 segments); mild extensive fibrosis  $\leq 2$  segments, moderate or very extensive fibrosis  $\geq 3$  segments affected). Statistical analysis: Spearman correlation coefficient and comparison of means between groups with non-parametric tests; defined statistical significance at  $p < 0.05$ .

**Results:** 19 patients were included, mean age  $62.4 \pm 10.4$  years; 52.6% were male. The mean LVEF assessed by 3DEcho was  $59.1 \pm 7.3\%$ ; the mean left ventricular mass was  $103.5 \text{ g} / \text{m}^2$  (MRI). From the total patients, 16 had late enhancement cardiac MRI, mean of  $3.3 \pm 2.8$  segments affected by fibrosis. More frequently affected segments were the septal basal segments. There was no statistically significant correlation between the number of segments affected by delayed enhancement and

LVEF ( $p = 0.6$ ) or ventricular mass ( $p = 0.56$ ); and global longitudinal strain values ( $r = 0.03$ ,  $p = 0.9$ ), global circumferential strain ( $r = 0.4$ ;  $p = 0.008$ ), global radial strain ( $r = 0.14$ ,  $p = 0.54$ ) and area tracking ( $r = 0.02$ ;  $p = 0.8$ ). When analyzed groups (no fibrosis vs mild extensive fibrosis vs extensive fibrosis) also statistically significant differences were not found.

**Conclusion:** In this group of patients with HCM, there was no correlation between the number of segments with evidence of fibrosis and ventricular function and deformation parameters, which may be related to the small sample size. Additional studies are needed, particularly with quantitative evaluation of mass/% of myocardial fibrosis that may have a better correlation with the parameters of ventricular function and overall strain.

#### P1652

##### Correlation between wall motion score and global longitudinal strain.

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**Background:** Global longitudinal strain (GLS) allows evaluation of the longitudinal function of the left ventricle (LE) and to distinguish the global and regional deformation. On the other hand the wall motion score (WMS) is a visual subjective score of radial contractility. Together they present a more complete evaluation of global and regional function in ischemic patients.

**Aim:** This study aims to correlate GLS and WMS and to interpret their role in establishing the prognosis in these patients.

**Methods:** Reviewed echocardiograms performed since February 2013 to July 2014. The exams that allowed performing longitudinal strain with speckle tracking (ST-E) in 3 apical windows (4 chamber, 2 chamber and 3 chamber) were selected. The patients with 3 or more LV segments unable to be analysed by ST-E were excluded. From this selection resulted a sample of 138 patients. A minimum follow up of 365 was performed. As endpoints were selected cardiovascular hospitalization (stroke, heart failure, acute coronary syndrome) and death. Statistical analysis in SPSS 20, using T student test, Spearman correlation and linear regression.

**Results:** In the sample ( $n = 138$ ) 81,9% were males. The mean age was  $64,36 \pm 14,37$  years, being that 21,0% were older than 80 years and 28,3% were younger than 55 years. The patient with STEMI were 54,7%, the patient with NSTEMI were 41,6% and the patients with unstable angina were 3,7%. The mean ejection fraction was 53,49%, the mean GLS was  $-13,88$  and the mean WMS 1,296. A bivariate correlation was performed between GLS and WMS and showed a strong correlation (Pearson coefficient 0,668,  $p < 0,001$ ; Rsquare 0,449,  $p < 0,001$ ). Linear regression was performed successfully with statistic significance ( $p < 0,001$ ). The GLS and WMS did not correlated with hospitalization or death at 3, 6 e 12 months. Total mortality was different in the follow up according to GLS (alive 14,138, death 11,520,  $p = 0,048$ ), but not to WMS ( $p = 0,108$ ).

**Conclusions:** This study was able to correlate successfully GLS and WMS, with a strong correlation. The GLS was better predicting death during the follow up of this study.

#### P1653

##### Assessment of left ventricular mass in hypertrophic cardiomyopathy by three-dimensional echocardiography

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**Introduction:** Left ventricular (LV) mass is an important prognostic indicator in hypertrophic cardiomyopathy (HCM). Although LV mass can be easily calculated using conventional echocardiography, it is based on geometric assumptions and has inherent limitations in asymmetric left ventricles. Three-dimensional echocardiographic techniques may provide a more accurate evaluation method in this context.

**Purpose:** Compare three-dimensional echocardiography technique (3DEcho) with two-dimensional echocardiography (2DEcho) in evaluation for left ventricular mass compared to cardiac magnetic resonance imaging (cardiac MRI) in patients with HCM.

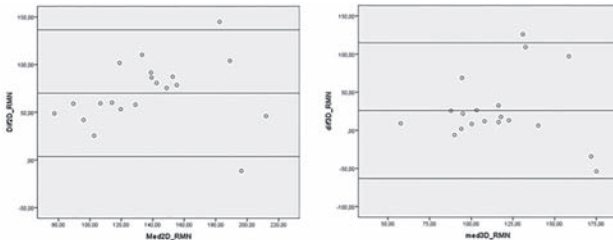
**Methods:** Single-center study, including patients with HCM who underwent 2D, 3D echocardiography and cardiac MRI. For mass calculation the following formulas were used: 2DEcho mass =  $0.8 [1.4 (PWT + LVlDd + SWT) - LVlD3] + 0.6$ ; 3D Echo: mass =  $1.5 * \text{Volume myocardial diastolic} / (\text{myocardial diastolic volume within the epicardial contour} - (\text{diastolic ventricular volume}))$ . We compared the results of left ventricular mass calculated by Echo 2D and 3D, using as reference values obtained by cardiac MRI. The degree of agreement between methods was assessed using the Bland-Altman analysis.

**Results:** 20 patients were included in the analysis of left ventricular mass by 2DEcho and MRI; 1 patient excluded from the three-dimensional analysis by poor acoustic window. The mean age was  $61.15 \pm 11.2$  years; 55% were male. The mean left ventricular mass (global and indexed to body surface area) were



lower when measured by MRI ( $191.7$  g,  $103.5 \pm 38.3$  g / m<sup>2</sup>), and the values obtained by 3DEcho ( $236.6$  g,  $129.4 \pm 37.0$  g / m<sup>2</sup>) were most approximate to MRI compared to those obtained by 2DEcho ( $317$  g,  $172.1 \pm 42.8$  g / m<sup>2</sup>). There was no significant difference in mean ventricular mass obtained by MRI and 3DEcho ( $p=0.068$ ). Figure 1 corresponds to the Bland-Altman analysis of agreement between the 2DEcho-MRI and 3DEcho-MRI in assessment of left ventricular mass.

**Conclusion:** Assessment of left ventricular mass by 3D echocardiography is a practical method and results closer to those obtained by cardiac MRI than 2DEcho in patients with HCM, and thus can provide a more accurate assessment of ventricular mass, especially in cases asymmetric ventricular hypertrophy. The 2D echocardiography tends to overestimate the ventricular mass in these patients.



#### P1654

##### Echocardiography in dyssynchrony assessment and factors related to its severity

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The role of mechanical dyssynchrony (MD) in the selection of patients suitable for CRT is not well-established and still a matter of debates in current guidelines.

**Aim:** To compare the value of 2D- and 3D-echo in the diagnosis of intraventricular dyssynchrony (IVD) and to identify factors related to its severity.

**Methods:** 164 patients (110 men,  $54.8 \pm 10.1$  yrs) with left bundle branch block (LBBB) on the ECG were enrolled into the study. 52 of them (31,7%) had dilated, and 19 (11,6%) ischemic cardiomyopathy; 43 patients (26,2%) had a history of previous myocardial infarction and/or myocardial revascularization; 43 (26,2%) had hypertension as a primary diagnosis, and the remaining 7 (4,2%) had no clinical manifestations of any CVD (idiopathic LBBB). 53 patients had  $EF < 30\%$ ; 70 patients had  $EF 31-49\%$ ; 41 patient had  $EF \geq 50\%$ . IVD was examined by 2D-, and 3D-echo. The presence of IVD on 2D-echo was demonstrated by the the septal to posterior wall motion delay (SPWMD), obtained from M-mode in the parasternal long axis (SPWMD  $> 130$  ms). 3D-echo: time to minimum systolic volume (Tmsv) and its dispersion (Diff.) for each segment of LV were analyzed. Parameters of IVD were calculated for 5 positions.  $Tmsv > 12\%$  was considered as a criterion of IVD.

**Results:** 2D-echo allowed detecting IVD accurately in only 40% of patients with LBBB, mainly due to the presence of severe wall motion abnormalities (a-, hypo-, dyskinesia), and inability to obtained an adequate echo image. 3D-echo revealed IVD in 87% of the total cohort of patients with LBBB. The incidence of IVD in patients with  $EF < 30\%$  was 95.4%, but only 14.8% in patients with  $EF > 50\%$ . Multiple linear regression analysis was used to identify factors associated with the severity of IVD. Twenty six parameters were analyzed altogether. The severity of TMSV Sel-SD (the maximum value of dyssynchrony between randomly selected segments) was related to the distance of 6-minute walk test ( $p=0.006$ ), and the points score of the the Minnesota questionnaire ( $p=0.05$ ). LVEF was the only predictor of TMSV 16-SD severity (all segments except the apex of LV,  $p=0.006$ ), TMSV 6-SD (dyssynchrony between the basal segments of LV,  $p=0.001$ ), and it showed a tendency for TMSV Sel-SD as well ( $p=0.055$ )

**Conclusions:** 3D-echo reveals IVD in 87% of patients with LBBB, with the incidence of 95.4% in patients having  $EF < 30\%$ . EF value, and signs of CHF determined the severity of IVD.

#### P1655

##### Utility of myocardial deformation analysis in the heart failure

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**Introduction:** Heart failure (HF) has become one of the most important health problems worldwide. Around 50% of patients with chronic HF have preserved ejection fraction (HFpEF). Current diagnostic criteria lack of accuracy, thus HFpEF is probably overdiagnosed. The aim of this study is to assess the diagnostic and prognostic role of the myocardial deformation analysis (MDA) measured by echocardiography in a group of patients with HFpEF vs. reduced EF (HFrEF).

**Material and methods:** A cross-sectional and prospective study was performed to evaluate the differential aspects of HFpEF vs. HFrEF with regard to MDA. We included 81 consecutive patients admitted for an acute decompensation of HF. Patients with intraventricular conduction disorders, valvular prostheses or pacemakers were excluded. Patients were followed-up for 180 days.

Results MDA showed statistically significant differences in all its parameter when comparing both populations. The longitudinal deformation of the left ventricle (LV) was higher among HFpEF as compared to HFrEF ( $-12.79\%$  vs  $-9.18\%$ ;  $p < 0.05$ ). Strain rate was also higher in HFpEF in its 3 dimensions: longitudinal ( $-1.46$  vs  $-1.26$ ;  $p < 0.05$ ), radial ( $21.9$  vs  $17.3$  / s,  $p < 0.05$ ) and circumferential ( $-15.3$  vs  $-10.4$  / s,  $p < 0.05$ ). The ability of MDA to discriminate between HFpEF and HFrEF was optimal (ROC curve: 0.808). Strain rate circumferential systolic was a good predictor of cardiac event as well (OR 2.20 (95% CI 1.16 to 4.20;  $p=0.02$ ). It was associated with an increase to suffer from an adverse event during follow-up (ER visits, readmission or death).

**Discussion:** MDA, measured by 2D-echocardiography, is an emerging technique, with a potential new role in HF diagnosis and prognosis assessment. MDA has an optimal power to discriminate between HFpEF and HFrEF. Hence it may be a new useful tool in the diagnosis of HFpEF, especially in patients with borderline decrease of EF. In our experience MDA has proven to be, as well, good predictor of cardiac events in HF irrespective EF. This is especially important in HFpEF due to the lack of good echocardiographic prognostic markers among such patients.

**Conclusions:** MDA may help to improve the accuracy of HFpEF diagnosis. In addition functional abnormalities found in main parameters of MDA help identifying a group of patients with higher risk of complications during follow-up. We, thus, suggest including MDA as a routine test in every patient with HF irrespective of EF.

#### P1656

##### Assessment of right ventricular systolic and diastolic parameters in pulmonary sarcoidosis

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**Background:** The clinical manifestations of cardiac involvement are seen in about 5% of sarcoidosis patients however the incidence of cardiac involvement is higher in autopsy series. About 14% of patients with pulmonary sarcoidosis (PS) without known cardiac involvement had diastolic dysfunction.

**Purpose:** Herein we aimed to determine the role of parameters of RV systolic and diastolic function in PS patients without evidence of cardiac symptoms.

**Methods:** Our study population consisted of 28 patients with grades 1 to 4 PS and 24 healthy subjects. This study was a clinical prospective cohort study.

**Results:** RVEDA was found to be significantly higher in PS group ( $p=0.032$ ). RVFAC and TAPSE were statistically lower in PS group as compared to the control group ( $p < 0.001$ ). However, PASP was significantly higher in PS group ( $p=0.003$ ). The tricuspid E velocity and E/A ratio were detected to be significantly lower in PS group ( $p=0.025$  and  $0.009$ , respectively), while the tricuspid A velocity and MPI were found to be significantly lower in the control group ( $p=0.034$  and  $0.007$ , respectively).

**Conclusions:** Early detection of cardiac involvement in PS is crucial because of increased morbidity and risk of sudden cardiac death. RV diastolic Doppler parameters, tissue Doppler MPI, RVFAC and TAPSE are practical and cheap techniques in diagnosis of cardiac involvement in PS.

table 1

Parameters	Sarcoidosis patients n=28	Control group n=24	P value
Age, years	40.22 ± 11.92	37.57 ± 5.20	0.640
Gender, F/M	15/13	13/11	0.435
BMI, kg/m <sup>2</sup>	25.29 ± 2.4	24.75 ± 2.0	0.35
LVEF, %	64.14 ± 2.55	65.80 ± 2.40	0.260
Mitral E wave (cm/s)	78.6 ± 16.0	90.0 ± 12.8	0.01
Mitral A wave (cm/s)	72.2 ± 20.1	62.3 ± 9.0	0.04
Mitral E/A ratio	1.07 ± 0.32	1.2 ± 0.36	0.03
RVEDA, cm <sup>2</sup>	25.25 ± 9.20	20.57 ± 7.33	0.032
RVFAC, %	44.96 ± 6.19	51.47 ± 5.34	< 0.001
TAPSE, cm	1.92 ± 0.24	2.43 ± 0.40	< 0.001
PASP, mmHg	32.54 ± 5.84	24.36 ± 3.78	0.003
Tricuspid E (cm/s)	55.25 ± 7.84	60.19 ± 5.71	0.025
Tricuspid A (cm/s)	50.62 ± 15.76	44.61 ± 5.26	0.034
Tricuspid E/A ratio	1.18 ± 0.27	1.36 ± 0.16	0.009
MPI	0.48 ± 0.08	0.43 ± 0.04	0.007

The clinical and echocardiographic data of the PS and control group.

### P1657

#### Interatrial septal tissue doppler time intervals in patients with heart failure

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The purpose of our research was to study the changes in interatrial septal (IAS) TDI parameters in patients with Heart Failure (HF).

**Material and Methods:** We studied 45 patients with II-IV NYHA functional class systolic HF (I gr.) 90 normal persons (II gr) and 90 patients with Arterial Hypertension and Coronary Artery Disease but without HF (III gr). IAS TDI was registered from apical 4-chamber view. All patients were in sinus rhythm. We measured maximal systolic (s), early diastolic (e) and late diastolic (a) velocities.

**Results:** There was significant difference in IAS TDI velocity parameters between patients with and without HF. The s velocity was lower in persons with HF (I gr - 5.2 ± 1.8 cm/sec, II gr - 7.0 ± 1.7 cm/sec, III gr - 7.0 ± 1.8 cm/sec). The e (I gr - 4.6 ± 1.6 cm/sec, II gr - 8.7 ± 2.5 cm/sec, III gr - 6.4 ± 2.0 cm/sec) and a velocities (I gr - 6.4 ± 2.4 cm/sec, II gr - 7.4 ± 1.9 cm/sec, III gr - 8.2 ± 2.1 cm/sec) also were lower in persons with HF.

**Conclusion:** There are prominent changes in IAS TDI velocity parameters in patients with systolic left ventricular HF which were significantly lower in systolic HF group than in persons without HF.

### P1658

#### Insights into cardiovascular alterations after pre-eclampsia: a 2D strain echocardiographic study

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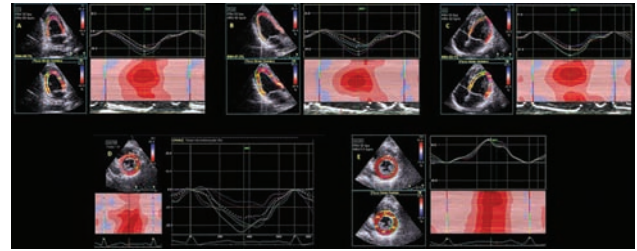
**Background:** Pre-eclampsia (PE) is characterized by a subsequent higher cardiovascular (CV) risk. Previous studies demonstrated the persistence of left ventricular (LV) dysfunction after this syndrome.

**Purpose:** We aimed at evaluating myocardial 2D strain and LV torsional mechanics after pregnancies complicated by early-onset (EO) or late-onset (LO) PE.

**Methods:** 30 pregnancies complicated by EOPE, 30 with a previous LOPE and 30 controls were retrospectively selected from our electronic database and evaluated by echocardiography 6 months to 4 years after delivery using speckle-tracking imaging. All the study cohort was free from any CV risk factor. Multivariate regression was run to test the association between gestational age (GA) at PE onset and 2D strain parameters.

**Results:** 2D strain and torsional parameters suggested a subclinical impairment in LV systole in the EOPE group which also showed a slight alteration in right ventricular (RV) function. Multivariate regression confirmed a positive correlation of GA at PE onset and echocardiographic alterations at long term.

**Conclusions:** Women with a history of EOPE and free from CV risk factors showed a persistent subclinical contractile impairment involving the whole heart, if compared to LOPE and healthy controls. This is responsible of their predisposition to CV diseases and Heart failure.



### P1659

#### Myocardial work efficiency in heart transplanted patients

Health Research Fund of Central Denmark Region and the Danish Heart Association

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**Aims:** Myocardial work efficiency (MWE) is a well established measure of left ventricular function closely linked to the oxidative myocardial metabolism. MWE may be influenced by fibrosis and reduced perfusion. Hence, MWE assessment could provide new insight to the reduced physical capacity seen in heart transplanted (HTx) patients. We sort to evaluate the clinical significance of alterations in MWE during exercise in HTx patients.

**Methods:** Sixty-four HTx patients underwent comprehensive 2D and 3D echocardiographic assessment of graft function at rest and during symptom-limited, semi-supine exercise test. Cardiac allograft vasculopathy was assessed by 2D quantitative coronary angiography and coronary flow velocity reserve (CFVR) assessment by Doppler echocardiography. We calculated a rejection score based on previous acute cellular rejection episodes. Rate pressure product (RPP) was calculated as mean arterial blood pressure x stroke volume estimated from left ventricular (LV) outflow tract x heart rate. MWE was calculated as RPP / LV mass estimated from 4D full volume echocardiography. Furthermore, we calculated rate systolic pressure product (RSPP) as systolic blood pressure x stroke volume estimated from left ventricular (LV) outflow tract x heart rate.

**Results:** At rest MWE was 3.0 ± 0.9. We found no relation between MWE at rest and NYHA functional class (r=-0.15, p=0.23), exercise capacity (r=0.03, p=0.80), CFVR (r=0.09, p=0.49), severity of CAV (r=-0.10, p=0.45), or rejection score (r=-0.16, p=0.20).

At peak exercise MWE was 7.3 ± 2.2. The change in MWE (ΔMWE) correlated significantly with NYHA functional class (r=-0.40, p<0.01), exercise capacity (r=0.43, p<0.01), CFVR (r=0.35, p<0.05), and severity of CAV (r=-0.28, p=0.05). No relation between rejection score and ΔMWE was seen (r=-0.21, p=0.15).

We found slightly better correlations using MWE based on RSPP: NYHA functional class (r=-0.46, p=0.001), exercise capacity (r=0.54, p<0.0001), CFVR (r=0.37, p<0.01), severity of CAV (r=-0.35, p<0.05). No relation between rejection score and ΔMWE based on systolic blood pressure was seen (r=-0.18, p=0.21).

**Conclusions:** MWE during exercise was moderately correlated with NYHA functional class, exercise capacity, and vasculopathy burden, whereas MWE at rest was not. Hence, exercise MWE may provide new insight to the reduced physical capacity seen in HTx patients.

### P1660

#### Reproducibility and value of quantitative computed tomography to diagnose heart failure in patients with non-ST-elevation myocardial infarction

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**Background:** Assessing pulmonary congestion from cardiac CT images in patients is poorly investigated. Animal models have showed Quantitative CT (QCT) is correlated to pulmonary congestion and we therefore hypothesized it also has potential to improve a diagnosis of heart failure in patients with non-ST-elevation myocardial infarction (NSTEMI)

**Purpose:** To test if QCT assessed from cardiac-CT images in patients with NSTEMI can differentiate between patients and without a clinical heart failure (HF).

**Methods:** Patients were identified from a previously examined cohort of 371 patients with NSTEMI who underwent 64-slice cardiac-CT. Two groups were defined: A HF group defined as Killip class>1 within 5 days prior to CT, at least 1 significant stenosis on coronary angiogram, and LVEF <45%. A control group was defined as Killip class 1, no stenosis on angiogram, and LVEF >55%. Patients with inappropriate image quality, signs of emphysema or pneumonia were excluded.

**Results:** 25 patients (12 HF, 13 control) were identified from the previously examined cohort of 371 patients. 15 patients fulfilled the criteria for the HF group. 3 were excluded because of incomplete lung delineation, bullae and pneumonia. 30 patients fulfilled the criteria for the control group. 17 were excluded because of incomplete lung delineation (n=12), motion artifacts (n=2), bullae (n=2) and pneumonia (n=1). Mean lung density was significantly decreased in the HF group (-732 ± 31 vs -653 ± 48, p < 0.0001). The ROC area under the curve was 0.93 (0.84-1.00). The Intra observer variability and inter observer variability (CV) among examiners was 0.8 % and 0.6 % respectively.

**Conclusion:** QCT is highly reproducible, objective and accurately discriminates NSTEMI patients with and without overt heart failure.

#### P1661

##### Cardiac magnetic resonance: diagnostic and therapeutic impact on suspected acute coronary syndrome with near normal coronary angiography

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**Background and purpose:** A subset of patients with suspected acute coronary syndrome (ACS) undergoing coronary angiography have non-significant coronary stenosis. The clinical guidelines available are not well-defined regarding the diagnosis, therapeutic and outcome in this setting. The goal of this study was to investigate the diagnostic role of cardiac magnetic resonance (CMR) and its implications in defining therapy and prognosis.

**Material and methods:** This study was based on a retrospective analysis of 109 consecutive patients presenting to a tertiary centre with a clinical diagnosis of ACS and normal or near normal coronary arteries on angiography, in a 7-year period (2007-2014). All patients were referred to CMR, performed in a 3 T scanner. Clinical, radiological and therapeutic data was collected from the electronic clinical process and registered in a uniform base.

**Results:** Mean age at admission was 52.3 ± 16.9 years and 52.3% were females. At least one known cardiovascular risk factor was identified in 82.6% of the patients, hypertension being the most frequent (45.9%). At presentation, dynamic ST-T segment changes were registered in 37.0% of the cases and mean troponin I was 12.0 ± 36.2 ng/ml. Besides chest pain, fever or other infectious features were referred by 25 of the patients and an emotional stress event was identified in 21 cases. A completely normal coronary angiography was identified in 85.2%. The mean left-ventricular ejection fraction was 50.1% estimated by echocardiography and 56.1% calculated by CMR. CMR was diagnostic in 78.7% of the cases studied. Myocarditis was the most frequent diagnosis (38.9%), followed by stress cardiomyopathy (15.7%) and myocardial infarction with normal coronary arteries (14.8%). Delayed-enhancement and edema were present in 63.0% and 35.2% of the exams, respectively, and correlated significantly with the CMR diagnosis (p < 0.05). At discharge, all patients with CMR diagnosis of ACS were on antiplatelet therapy. On the other hand, this therapy was suspended in 47 patients because other diagnosis was established. The CMR diagnosis correlates significantly with antiplatelet suspension at release (67.7% vs 31.3%, p = 0.008). During a mean 3-year follow up time, 3 non-cardiac deaths and 6 hospital readmissions for cardiac reasons were registered.

**Conclusions:** Suspected ACS with non-significant coronary artery disease is a very heterogeneous entity. CMR may contribute to better establish etiologic diagnosis in this setting, helping in adjusting antiplatelet therapy. More studies are needed in order to define the best diagnostic and therapeutic approach.

#### P1662

##### Left ventricular diastolic function with cardiac magnetic resonance imaging in systemic sclerosis patients

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**Background:** Cardiac impairment frequently occurs in systemic sclerosis (SSc) patients and is often clinically silent until the late stages of the disease. The early diagnosis of cardiac involvement by certified non-invasive methods such as cardiac magnetic resonance imaging (CMR) may favor prompt initiation of adequate treatment and consequently improve prognosis. Phase-contrast cardiovascular magnetic resonance (PC-CMR) studies performed on small groups of patients compared to healthy controls suggested the ability of PC-CMR to assess LV diastolic function in agreement with echocardiography.

**Purpose:** In the present study we sought to assess the ability of PC-CMR to detect sub-clinical left ventricular (LV) diastolic parameters in patients with SSc.

**Methods:** Thirty-five consecutive SSc patients (48 ± 13.6 years, 22 women) were enrolled in a prospective CMR-based study and compared against thirty-five healthy volunteers with similar demographic characteristics. All subjects underwent standard echocardiographic and CMR examinations to assess LV and RV systolic and diastolic function. Transmitral flows and LV myocardial PC-CMR images were analyzed by an operator blinded to clinical data using Argus Flow. PC-CMR was used to estimate: 1) early trans-mitral and trans-tricuspid (E) and atrial (A) peak filling flow-rates (ml/s) and filling volume (FV), 2) deceleration time (DT), isovolumic relaxation time (IVRT), and 3) early myocardial longitudinal (E') peak velocity.

**Results:** PC-CMR diastolic parameters were reproducible, as reflected by low coefficients of variation, and were found to be independently associated to LV remodelling, assessed by LV mass to end-diastolic volume ratio and to myocardial wall thickness (p < 0.01). Although the LV systolic function was preserved, LV diastolic function parameters were impaired. Reasonable correlations were found between CMR and echocardiography-derived parameters of diastolic dysfunction. Mitral flow velocities (E wave: r = 0.38, p = 0.001; A wave: r = 0.32, p = 0.006) and particularly the E/A ratio (r = 0.61, p < 0.0001) measured by CMR correlated well with the corresponding echocardiography measurements, as did the mean value of lateral mitral annular myocardial velocities (E' wave: r = 0.59, p < 0.001).

**Conclusions:** SSc patients without cardiovascular symptoms rarely exhibit LV systolic dysfunction, whereas LV diastolic function impairment occurs frequently. Such parameters, which were shown to be reproducible and consistent, might be useful for a fast and reliable characterization of diastolic function in patients referred for CMR. Early identification of such changes in the asymptomatic stages of the disease by CMR may improve the overall prognosis of SSc patients.

## BIOMARKERS

#### P1663

##### Biomarkers and drugs prescription before discharge in patients hospitalized with acute heart failure

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**Purpose:** To evaluate the association between the number of prescribed drugs at discharge with levels of biomarker's panel of myocardial stress and injury, renal dysfunction and fluid overload, at admission and discharge in patients (pt) hospitalized with acute heart failure (AHF)

**Methods:** Between 01-Feb and 30-Jun 2014, 144 pt hospitalized with AHF were prospectively included. At admission and discharge, serum levels of creatinine, NT-pro brain natriuretic peptide (NT proBNP), high sensitive troponin T (hsTnT), carbohydrate antigen 125 (CA125) and urine levels of neutrophil gelatinase-associated lipocalin (NGAL) were determined. According with the number of drugs with proved benefit in morbidity and mortality in heart failure (betablockers [BB]; angiotensin converting enzyme inhibitors or angiotensin receptor blocker [ACE/ARB] and mineralocorticoid receptor antagonist [MRA]) prescribed before discharge, patients were classified in group 1 (G1: 0-1 drugs); 2 (G2: 2 drugs) or group 3 (G3: 3 drugs) results.

**Results:** Mean age was 68 ± 13 years, 35% were women and 35% has ischemic aetiology, with mean ejection fraction of 45% ± 38. At discharge, 39 (27.1%) were classified as G1, 53 (36.8%) as G2 and 52 (36.1%) as G3. One-year free rehospitalization for AHF survival was for G1, G2 and G3, 36; 60 and 69%, respectively (p = 0.003). The comparison is shown in table 1.

**Conclusion:** The number of evidence-based drugs used at discharge after AHF hospitalization was associated with the long-term outcome. Patients who receive 0-1 drug at discharge have a worse biomarkers profile at admission, which deteriorated during hospitalization, and it was related with poor prognosis

Biomarker	Measurement	G1 (mean ± SD)	G2 (mean ± SD)	G3 (mean ± SD)	p
Creatinine (mg/dl)	Admission	2.12 ± 1.26	1.25 ± 0.68	1.17 ± 0.4	< 0.001
	Discharge	19822 ± 16020	10200 ± 13300	12545 ± 13232	0.006
Nt proBNP (pg/ml)	Admission	18854 ± 15872	26846 ± 10303	7880 ± 11028	< 0.001
	Discharge	70.4 ± 68	45 ± 51	41 ± 62	0.051
Hs-TnT (ng/l)	Admission	102.7 ± 160	41.2 ± 47	29 ± 27	< 0.001
	Discharge	147 ± 196	114 ± 159	163 ± 178	ns
CA125 (U/ml)	Admission	142 ± 201	97 ± 152	128 ± 165	ns
	Discharge	30 ± 52	29 ± 71	12.5 ± 27	ns
NGAL (ng/ml)	Admission	154 ± 247	35 ± 76	24 ± 53	< 0.001
	Discharge				



## P1664

**Soluble ST2 in heart failure patients using a point-of-care-testing system**

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**Introduction:** Soluble ST2 (sST2; suppressor of tumorigenicity 2) is a member of the IL-1 receptor family. ST interferes with the signal cascade of IL-33/ST2, which inhibits the cardioprotective effects of IL-33. ST2 is therefore classified as a novel biomarker for heart failure patients, which might provide additive information as compared to natriuretic peptides.

**Purpose:** Investigation of ST2 levels in various clinical settings of heart failure patients with diverse clinical presentations and brain natriuretic peptide (BNP) levels.

**Methods:** sST2 measurements were performed using a point-of-care-testing (POCT) analysis system (Aspect Reader; bestbion dx) in serial heart failure patients in addition to clinical routine workup. The sST2 values were obtained employing 35 µl EDTA plasma in Aspect-Plus POCT cassettes within a processing time of 20 minutes per sample.

**Results:** sST2 values were measured in n=17 heart failure patients (age: 66±4.3 years; men: 76%) with known or newly diagnosed heart failure, and in n=10 control patients (age: 55±5.6 years, men: 80%; healthy volunteers: n=4; coronary artery disease patients without heart failure and LVEF > 50%: n=6). The range of sST2 values in all measurements was 12.5-250 ng/ml. The range of BNP-values was 29-16,601 pg/ml. Heart failure patients presented significantly higher sST2 values compared to controls (100.4±81.5 versus 35.5±21.0 ng/ml; p=0.021). Heart failure patients presenting with acute decompensated heart failure (ADHF) and NYHA functional class IV (n=4) had significantly (p<0.0001) higher sST2 values (224.9±50.1 ng/ml) compared to controls, and to patients with chronic heart failure NYHA I-III (62.1±38.3 ng/ml). There was no significant association between sST2 and BNP (p=0.21). In n=2 patients presenting with Takotsubo cardiomyopathy (TTCM), a substantial decrease of sST2 by 70% was observed within 8 days after the initial evaluation, accompanying the resolution of TTCM under heart failure medication.

**Conclusions:** These data confirm the practicability of sST2 measurements by POCT in serial heart failure patients, revealing a broad range of sST2 values, available within 20 minutes processing time. They indicate an additional value of ST2 for biomarker based evaluation of heart failure patients as compared to BNP values, with emphasis on ADHF and NYHA functional class IV. Preliminary serial data on TTCM patients indicate the dynamics of sST2 in the evolution of heart failure.

## P1665

**Cystatin C and global longitudinal strain in patients with chagas disease: just a marker of kidney function?**

COLCIENCIAS and RED CHAGAS COLOMBIA. BIOCHAGAS project, code 501453730398, CT 380-2011.

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**Purpose:** Cystatin C (CysC) is an inhibitor of the cysteine protease constantly produced by all nucleated cells and is freely filtered by the glomerulus, due to its low molecular weight (13kDa). In patients with Chronic Heart Failure (CHF) is an independent predictor of adverse events (death, myocardial infarction, stroke) even after adjusting for traditional risk factors and BNP. Global Longitudinal Strain (GLS) has proven to be a sensitive marker of myocardial dysfunction, allowing to discriminate between patients with cardiac events and those with a better prognosis. In the present study, the correlation between the levels of CysC and GLS in patients with chronic chagas disease was determined, which has not been previously reported in the literature.

**Methods:** Analytical cross-sectional study. Patients older than 18 years with chagas disease were included. Those patients with uncontrolled hypertension, diabetes, history of coronary artery disease and valvular disease were excluded. The GLS was established by speckle tracking electrocardiography and blood levels of CysC were determined, both measures were taken the same day. A descriptive analysis was performed, the correlation between the GLS and CysC was evaluated by scatter plot and Spearman's rank correlation coefficient. Finally, a multiple linear regression analysis adjusted by sex, age and GFR was performed.

**Results**

A total of 100 patients were analyzed, 55% (55/100) were men; the mean age was 61 years (SD±12 years); the median and interquartile range of LVEF was 42% (Q1=27; Q3=56), of CysC was 1.14 mg / L (Q1=0.91, Q3=1.37); of GLS was -12.6% (Q1=-17.8; Q3=-8.1); 40% (40/100) of the patients had a GFR < 60 mL / min / 1.73 m<sup>2</sup>. A positive correlation between GLS and CysC values (rho=0.579, p=0.000) was established; on the other hand, CysC and LVEF presented a

negative correlation (rho=-0.639, p=0.000). Finally, an association between GLS and CysC (β=6.079, p=0.032) was established; as well as between LVEF and CysC (β=24,324; p=0.000), both models adjusted by sex, age and GFR.

**Conclusions:** In patients with Chagas cardiomyopathy, CysC showed a moderate positive correlation with the GLS, and a moderate negative correlation with LVEF, suggesting a potential utility as a marker of myocardial dysfunction in this setting. Remarkably, when evaluating the association of the CysC and the GLS on a linear regression model adjusted for age, sex and GFR it remained significant, suggesting that CysC is a marker of early myocardial dysfunction even in patients with preserved renal function.

## P1666

**Galectin-3 and ST-2: association with inflammation and renal dysfunction in patients with chronic heart failure**

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**Purpose:** To evaluate the connection between plasma level of galectin-3, ST-2 and biomarkers for inflammation and renal dysfunction in patients with chronic heart failure (CHF).

**Methods:** 167 patients (age, 64,4±3,8 years) with documented prior myocardial infarction, were included in the study. Patients were divided into 3 basic groups according functional class (FC) CHF (NYHA). 1 group (n=56) - patients with II FC CHF, 2 - 67 patients with III FC, and 3 group (n=44) - IV FC. There was valued the level of galectin-3, ST-2 and cystatin-C by immunoassay analysis. The estimated glomerular filtration rate (e-GFR) was calculated using the Modification of Diet in Renal Disease (MDRD) equation. Biomarkers for inflammation included hs-CRP, interleukin-6 (IL-6). All statistical analysis was performed with Statistica 6.0. Continuous variables were described by median. Comparisons of continuous variables were performed using Mann-Whitney, U-test. Spearman's rank correlation coefficient was calculated to measure dependence between two variables.

**Results:** Galectin-3 values increased in parallel with the clinical severity of CHF (NYHA classification): II FC - 9.8 ng/ml, III FC - 18.6 ng/ml, the highest levels being reached in class IV patients 34,1 ng/ml. We observed significant difference between groups (p < 0,001). The level of hs-CRP in patients with CHF was 1,8; 3,3 and 6,5 mg/l. We also demonstrated a significant positive correlation between galectin-3 and hs-CRP in groups: r1=0,573, p=0,00085; r2=0,784, p=0,00001; r3=0,687, p=0,00007. We found a significant increase in the level of IL-6 in the 1st (7,8 pg/ml), 2nd (17,7 pg/ml) and 3d (38,9 pg/ml) groups. We observed a positive correlation between levels of galectin-3 and IL-6 in all groups of patients (r1=0,546, p=0,0001 and r2=0,746, p=0,00002; r3=0,615, p=0,00005.) The levels of ST-2 in the 1st, 2 and 3 groups were 22,58, 26,27, 36,7 ng/l accordingly. The correlation analysis showed the following significant correlations: ST-2 correlated with NYHA FC (r=0,35; =0,009), with concentration of hs-CRP (r=0,33; =0,006) in the cohort of observed patients. We also found an increase in the level of cystatin-C: 1800, 2800, 4600 pg/ml accordingly with a significant difference between groups (p<0,05). Strong correlations were also observed between galectin-3-cystatin C (r1=0,61, r2=0,64, r3=0,72, p<0,01.) and galectin-3-GFR (r1=-0,49, r2=-0,57, r3=-0,72, p<0,01.).

**Conclusion:** The plasma levels of galectin-3, ST-2 in patients with CHF were closely connected with indicators of inflammation and renal dysfunction beyond NYHA functional class.

## P1667

**Salivary biomarkers related to cardiovascular parameters during physical effort challenge in menopausal women**

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**Background:** Changes in autonomic nervous system and hypothalamus pituitary adrenal axis activity have been related to different challenges, like physical exercise or emotional stress. Salivary alpha-amylase and salivary cortisol are non-invasive, reliable biomarkers, potentially available for the evaluation of this 2 systems respectively. Our purpose was to examine whether variations of cardiovascular parameters during cardio-pulmonary effort test are related to salivary alpha-amylase and salivary cortisol response in menopausal women.

**Methods:** 30 postmenopausal women (15 hormone replacement therapy users and 15 never treated) were recruited and salivary biomarkers were measured in a rest day (at awake, 12:00, 17:00, 20:00) and in the day with the effort test (at the same hours and an additional sample 30 minutes after the effort test). During cardio-pulmonary effort test systolic and diastolic blood pressure and electrocardiogram were monitored. The effort session consisted by a 3 - min warm - up phase at 10 W, followed by a ramp effort phase increasing 10 W/minute. Heart rate was measured and reported at baseline, during the effort and at 1 and 2 min during recovery and

heart rate reserve was calculated as the difference between the heart rate at maximum effort and heart rate at rest. The total diurnal salivary alpha-amylase and cortisol production were calculated using the trapezoidal method. We used SigmaPlot 11 for statistical analysis, applying repeated measures ANOVAs and multiple linear regression analysis for salivary alpha - amylase and cortisol as independent and cardiovascular parameters as dependent variables.

**Results:** Postmenopausal women using hormone replacement therapy exhibited a cardiorespiratory functional capacity that was significantly ( $p < 0,05$ ) higher than that of non-users. In the rest day, treated women had significantly decreased daily production of alpha amylase ( $487 \pm 93$  vs  $575 \pm 82$ ,  $p < 0,05$ ) which increased significantly after effort ( $581 \pm 64$  vs  $487 \pm 93$ ,  $p < 0,05$ ). Multiple linear regression analysis revealed significantly correlations between systolic blood pressure and daily production of salivary cortisol in the effort day ( $r = -0,537$ ,  $p = 0,025$ ), diastolic blood pressure baseline and salivary alpha-amylase daily production in the rest day ( $r = 0,132$ ,  $p = 0,015$ ), salivary cortisol and maximal heart rate ( $r = 0,805$ ,  $p = 0,03$ ).

**Conclusions:** The influences of physical stress on autonomic nervous system could be detected using the salivary biomarkers and the values are related to cardiovascular parameters in menopausal women.

#### P1668

##### Mid-regional pro-adrenomedullin as a prognostic indicator of 1-year mortality after acute heart failure. MOLITOR substudy.

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**Background:** Adrenomedullin (ADM) is a vasodilatory peptide hormone with potent hypotensive effects. It is expressed in many different tissues, including myocardium and endothelium. Its plasma levels are elevated in patients with chronic heart failure (HF) and increase with disease severity. Mid-regional pro-ADM (MR-proADM) is a stable and reliable surrogate marker for ADM release.

**Aim:** The aim of our study was to investigate the predictive role of MR-proADM on 1-year mortality in patients admitted to hospital due to acute HF and to compare it with N-terminal pro-brain natriuretic peptide (NT-proBNP) which is an established diagnostic/prognostic marker in this setting.

**Methods:** We included 168 patients, age  $68.18 \pm 9.9$  years, 70.8% being males, 83.7% having HF with reduced ejection fraction (HFrEF). Patients were followed for 1 year after acute HF.

**Results:** Median MR-proADM levels at admission and after 1 year of follow up were:  $1.12$  (0.88-1.53) /  $1.01$  (0.81-1.22) nmol/L,  $p = n.s.$  Median NT-proBNP concentrations at admission and after 1 year of follow up were:  $2870$  (1240-7542) /  $969.6$  (428.5-2212) pg/mL,  $p < 0.001$ . We found significant correlation between NT-proBNP at admission with left ventricle ejection fraction- LVEF ( $33.57 \pm 12.49\%$ ) ( $\rho = -0.370$ ,  $p < 0.01$ ) and with MR-proADM ( $\rho = 0.483$ ,  $p < 0.01$ ). NT-proBNP measured after 1 year correlated with MR-proADM ( $\rho = 0.521$ ,  $p < 0.01$ ) but not with LVEF ( $36.89 \pm 12.57\%$ ) measured at that time. 37 patients (22%) died during one year. Median MR-proADM and NT-proBNP values at admission in patients who died compared to survivors were:  $2.09$  (1.35-3.4) vs.  $1.09$  (0.80-1.67) nmol/L,  $p < 0.001$  and  $14493.5$  (3470-25223.0) vs.  $3350.5$  (1044.0-8414.0) pg/mL,  $p < 0.001$ .

**Conclusions:** In our patients, MR-proADM concentration did not significantly change 1 year after acute HF. However, patients who died during 1 year had significantly higher concentrations of this marker at hospital admission. We found a significant correlation between MR-proADM with NT-proBNP in acute HF and in a stable phase of the disease. Unlike NT-proBNP, levels of MR-proADM did not correlate with LVEF. Although little is known about the role of ADM in HF, it seems that MR-proADM has similar predictive properties compared to NT-proBNP for 1 year all-cause mortality in acute HF.

#### P1669

##### The impact of biological variability on biomarker monitoring.

British Heart Foundation Pump Priming Grant (RE/08/003)  
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**Background:** NTproBNP is an established marker for diagnostic and prognostic use in heart failure patients. Evidence for serial monitoring to predict decompensation has, however, been mixed. This has, in part, been ascribed to its high biological variability, with weekly reference change values of 49% to 92%. We examined the biological variability of four novel biomarkers, sST2, galectin-3, apelin and mid-regional pro-adrenomedullin (MRproADM), and compared this with the ability of changes in serial concentrations to predict cardiovascular (CV) admission.

**Purpose:** To assess the relationship between biological variability and serial monitoring.

**Methods:** 50 patients with stable chronic heart failure due to LV systolic dysfunction and on optimum doses of prognostically indicated medications were studied. Mean age 67.3 years (SD 11.568), 82% male. Mean LVEF 30.7%. Patients were followed for a period of 6 months with clinical review and blood samples drawn at baseline and 6 months. Biological variability was assessed by the variables of intra-individual coefficient of variability (CVi) and reference change value (RCV). Receiver Operating Characteristic (ROC) analysis and area under curve (AUC) was used to assess the ability of percentage change and absolute change in biomarker concentrations to predict CV admission.

**Results:** Results for each biomarker at the 6-month end-point are shown in table 1. All novel biomarkers examined demonstrated lower biological variability than NTproBNP. Despite this, only galectin-3 showed significant ability to predict CV admission over the 6-month study period.

**Conclusion:** Our results suggest there is no relationship between biological variability and the monitoring ability of biomarkers. The value of using biological variability as a discriminator for using particular biomarkers for monitoring is unclear, and candidate markers should not be targeted on this basis alone.

#### Biological variability and ROC analyses

	Mean CV <sub>i</sub>	RCV (%)	AUC % change	AUC Absolute change
NTproBNP	46.02	128	0.571 ( $p = 0.553$ )	0.579 ( $p = 0.511$ )
sST2	16.41	47	0.734 ( $p = 0.052$ )	0.734 ( $p = 0.052$ )
Galectin-3	18.13	51	0.803 ( $p = 0.012$ )	0.807 ( $p = 0.011$ )
Apelin	10.19	30	0.571 ( $p = 0.553$ )	0.417 ( $p = 0.490$ )
MRproADM	18.93	54	0.506 ( $p = 0.962$ )	0.546 ( $p = 0.700$ )

NTproBNP = N-terminal pro-natriuretic peptide, sST2 = soluble suppression of tumorigenicity 2, MRproADM = mid-regional pro-adrenomedullin, AUC = area under curve, RCV = reference change value, CV<sub>i</sub> = inter individual coefficient of variability

#### P1670

##### Combining collagen type I-related biomarkers identifies a malignant phenotype of myocardial fibrosis in hypertensive heart failure

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**Background:** Myocardial fibrosis present in heart failure (HF) is the result of variable alterations in the quality (e.g. degree of collagen cross-linking; CCL) and quantity (i.e. collagen deposition; CD) of collagen, mainly collagen type I. Myocardial fibrosis contributes to the impairment of cardiac function and some studies suggest that it may have an impact on clinical outcome.

**Purpose:** To evaluate whether the combination of circulating biomarkers of myocardial CCL and CD identifies myocardial fibrosis phenotypes with distinct clinical outcomes in HF patients of hypertensive etiology. Since cross-linked collagen is more resistant to degradation a decrease in the ratio between the carboxy-terminal telopeptide of collagen type I (CITP) and matrix metalloproteinase-1 (MMP-1; CITP:MMP-1) has been shown to reflect increased collagen cross-linking. On the other hand, the carboxy-terminal propeptide of procollagen type I (PICP) has been proven to associate with the extent of myocardial CD.

**Methods:** Endomyocardial biopsies and blood samples from 38 patients (small cohort) and blood samples from 203 patients (large cohort) with clinical HF were analysed. Myocardial CCL and CD were assessed by histological methods. Serum PICP, CITP and MMP-1 were determined by ELISA.

**Results:** Compared with controls, patients from the small cohort exhibited increased ( $P < 0.001$ ) CCL and CD. CCL was above the upper limit of normality of control subjects (CCL+) in 71% of the patients and was normal (CCL-) in the remaining 29%. All patients presented CD values above the upper limit of normality, therefore, the severity of CD was established according to its median value (6.87%) in HF patients: non severe fibrosis (CD-) for values below the median and severe fibrosis (CD+) for patients above it. Using ROC curves a CITP:MMP-1 cut-off  $\leq 1.968$  and a PICP cut-off  $\geq 110.8$  ng/mL were selected to identify CCL+ and CD+, respectively. Participants from the large cohort were categorized in 4 subgroups based on the presence or absence of high CCL and severe CD considering the biomarker levels defined by the above thresholds: 37 (18.2%) patients presented CCL-CD-, 52 (25.6%) presented CCL-CD+, 56 (27.6%) presented CCL+CD- and 58 (28.6%) presented CCL+CD+. Compared to CCL-CD-, the adjusted hazard ratios for a composite end-point of HF hospitalization or cardiovascular death over 4 years were 1.11 ( $P = 0.79$ ) in CCL-CD+, 1.99 ( $P = 0.07$ ) in CCL+CD- and 2.18 ( $P < 0.05$ ) in CCL+CD+ ( $P$  for trend  $< 0.01$ ). In addition, the categorization based in CCL plus CD yielded significant ( $P < 0.05$ ) integrated discrimination and net reclassification improvements for the mentioned outcome.

**Conclusion:** The combination of serum C1P:MMP-1 ratio and PICP identifies patients with hypertensive HF and a malignant phenotype of myocardial fibrosis. The poor outcome associated with the concurrence of high CCL and severe fibrosis supports the necessity of a therapy targeting these alterations in this subgroup of patients.

### P1671

#### Estimated plasma volume as a determinant of heart failure hospitalization: TREAT-HF data

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**Background:** In heart failure patients, assessing presence and severity of congestion is of paramount importance but not always easy. In this regard a new method for non-invasive plasma volume measurement might be helpful. However, to our knowledge there is no data regarding the importance of estimated plasma volume (ePV) in the out-patient heart failure setting.

**Purpose:** The aim of this study was to assess the importance of ePV in predicting heart failure related hospitalization in an out-patient cohort of heart failure patients.

**Methods:** TREAT-HF (Turkish Research Team-Heart Failure) is a network of 16 heart failure centers in Turkey. Herein, we evaluated combined cohort of 2013-2014 and 610 patients who had data for calculating ePV were included into the study. Strauss formula was used to calculate ePV (ePV:  $[1 - \text{hemotocrit}] / [\text{hemoglobin} \times 0.01]$ ).

**Results:** Mean age of the cohort was  $60.7 \pm 13.8$  years (430 male, 180 female). In a median follow-up of 15 months, 439 of 610 patients were hospitalized for heart failure however 171 of them were not. Patients who were hospitalized for heart failure had higher ePV ( $5.29 \pm 1.47$  vs  $4.57 \pm 1.22$ ,  $p < 0.001$ ), were older ( $62.8 \pm 13$  vs  $58.7 \pm 13.6$ ,  $p < 0.001$ ), had higher systolic pulmonary artery pressure ( $43.8 \pm 14.9$  vs  $39.8 \pm 16.3$ ,  $p < 0.015$ ), lower left ventricular ejection fraction ( $31 \pm 8.4$  vs  $32.7 \pm 7.7$ ,  $p < 0.014$ ), higher creatinine level ( $1.44 \pm 0.7$  vs  $1.13 \pm 0.5$ ,  $p < 0.001$ ), lower hemoglobin level ( $12.2 \pm 2.1$  vs  $13.4 \pm 2$ ,  $p < 0.001$ ), lower hemotocrit level ( $38 \pm 5.9$  vs  $41 \pm 5.9$ ,  $p < 0.001$ ) and had more patients with NYHA class 3-4 (79% vs 65%,  $p < 0.001$ ). In univariate analysis ePV, age, NYHA class 3-4, creatinine, systolic pulmonary artery pressure, ejection fraction and hemoglobin were predictors of heart failure related hospitalization. However in multivariate analysis only age, NYHA class 3-4 and ejection fraction were independent predictors of heart failure related hospitalization.

**Conclusion(s):** In the setting of out-patient heart failure cohort although ePV was helpful, it was not an independent predictor of heart failure related hospitalization. Prospective outcome studies evaluating the role of ePV in heart failure are warranted.

### P1672

#### Galectin-3 serum levels are not associated with left ventricular remodeling in chronic heart failure outpatients

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**Background and aim of the study:** Galectin-3 (Gal-3) is an emerging biomarker which has been demonstrated to be related to inflammation status and fibrosis, two conditions that play a key role in ventricular remodeling in patients with chronic heart failure (CHF). The aim of this study was to evaluate the relationship among Gal-3 serum levels and left ventricular (LV) remodeling in a group of CHF outpatients.

**Methods:** We enrolled 152 outpatients (83% males,  $64 \pm 13$  years, NYHA class  $2.3 \pm 0.6$ , left ventricular ejection fraction, LVEF,  $32 \pm 8\%$ ) 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 at baseline and at one year. Ventricular remodeling was determined assessing changes of left ventricular end diastolic volume (LVEDV), left ventricular end systolic volume (LVESV) and left ventricular ejection fraction (LVEF), calculated using Simpson's rule. Progression of ventricular remodeling was defined as an increase in LVESV  $> 15\%$  at one year follow-up.

**Results:** At one year follow-up, 18 patients (12%) showed progression of ventricular remodeling. As shown in the table, patients with left ventricular remodeling showed, at baseline, a greater NYHA class, larger LVESV, lower LVEF and higher NT-proBNP serum levels. At one year LVESV further increased in patients with left ventricular remodeling and LVEF further decreased. No differences were found when baseline Gal-3 serum levels were considered.

**Conclusions:** Our findings demonstrate the Gal-3 serum levels are not associated with left ventricular remodeling in a population of patients with CHF and reduced ejection fraction. Further studies should assess the existence of other prominent mechanisms in determining Gal-3 prognostic role in these patients.

Variable	Pts without ventricular remodeling	Pts with ventricular remodeling	p
Baseline NYHA	2.2 ± 0.6	2.6 ± 0.5	0.034
Baseline LVESV	108 ± 46	142 ± 46	< 0.001
One year LVESV	102 ± 43	182 ± 54	< 0.001
Baseline LVEF	33 ± 8	26 ± 6	< 0.001
One year LVEF	35 ± 8	24 ± 7	< 0.001
Baseline NT-proBNP*	1703 ± 2823	2758 ± 3745	0.007
Baseline Gal-3	15.8 ± 7.1	15.3 ± 6.2	0.773

LVESV: left ventricular end-systolic volume; LVEF: left ventricular ejection fraction; Gal-3: Galectin-3. \*after logarithmic transformation

### P1673

#### Clinical value of cystatin-c levels in elderly patients with chronic heart failure preserved ejection fraction independent of renal function

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**Background:** The association between renal dysfunction and increased mortality has been reported in patients with chronic heart failure. Cystatin C, a novel endogenous marker of glomerular filtration rate, has been reported as more sensitive to detect renal insufficiency than creatinine, but its usefulness in elderly patients with heart failure with preserved ejection fraction (HFpEF) is less well defined.

**Methods:** We studied consecutive 98 Japanese HFpEF patients older than 80 years of age (42 males,  $84.1 \pm 3.2$  years, all serum creatinine levels were  $< 1.1$  mg/dl, NYHA II-III, LVEF  $> 50\%$ ). We measured circulating levels of cystatin C, C-reactive protein, norepinephrine (NAD), B-type natriuretic peptides (BNP), and cytokine (interleukin(IL)-1beta, IL-6, and tumor necrosis factor(TNF)-alpha). None had evidence of unstable angina, chronic inflammatory disease, collagen disease, or cancer at the time of evaluation. Patients were followed up for an average of 24.1 months, and 19 of 98 patients had cardiac and non-cardiac death.

**Results:** The mean ( $\pm$ SD) serum concentrations of cystatin C were  $1.24 \pm 0.22$  ng/dl. Patients with events had significantly higher cystatin C, NAD, uric acid, BNP, and IL-6. By multivariate Cox proportional hazard analysis, cystatin C and IL-6 were significant predictors for death in those patients.

**Conclusions:** These findings indicate that cystatin C measurement provides additional prognostic information in those elderly patients with HFpEF independent of renal function

### P1674

#### Pre-discharge high sensitivity cardiac troponin T predicts heart failure rehospitalisation and cardiac death in non-ischaemic acute heart failure: Marker of residual congestion?

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**Background:** High sensitivity cardiac troponin T (hs-cTnT) in patients with acute heart failure without clinically apparent myocardial ischemia is related to myocardial injury and maybe useful for prognostication. We sought to examine the value of hs-cTnT at the time of discharge in predicting 30-day rehospitalisation and cardiac death.

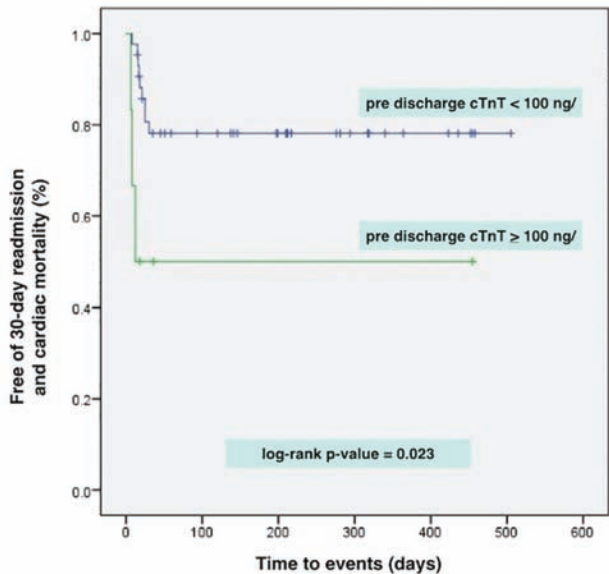
**Methods:** Fifty-one hospitalised patients with non-ischemic acute heart failure (49% men; mean age  $70 \pm 14$  years) from October 2014 to December 2015 were studied. Hs-cTnT was measured and echocardiography was performed at the time of discharge. Patients were followed over a median time of 4.5 months (interquartile range, 0.6, 10.5 months) for heart failure rehospitalisation and cardiac mortality. A multivariate Cox regression analysis was performed to identify associations with events.

**Results:** Heart failure rehospitalisation was found in 10 patients (20%), and 3 patients (6%) had cardiac death. HF rehospitalisation and cardiac death was associated with pre-discharge hs-cTnT (hazard ratio 1.002; 95% CI 1.001-1.003) independent of YALE CORE HF readmission score (calculated from 20 parameters of history, physical examination, laboratory and echo results). There was modest association between pre-discharge hs-cTnT and medial E/e' ( $R = 0.32$ ,  $p = 0.025$ ).



Predischarge hs-cTnT of > 100 ng/L identified the subgroup of highest risk for 30-day rehospitalisation and cardiac death.

**Conclusion:** Predischarge hs-cTnT, marker associated with LV filling pressure, is an independent predictor of heart failure rehospitalisation and cardiac death in patients with non-ischemic acute heart failure.



KM Curve as stratified by hs-cTnT

#### P1675

##### The prognostic value of red cell distribution width and markers of inflammation in acute decompensated heart failure

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**Background:** Red cell distribution width (RDW) and markers of inflammation are considered to be risk predictors in patients with acute decompensated heart failure (ADHF). Their relative significance and associations haven't been, nevertheless, thoroughly investigated.

**Purpose:** We aimed to evaluate the role of RDW together with inflammatory markers in predicting short-term major adverse cardiovascular events in ADHF patients.

**Methods:** Consecutive patients hospitalized with ADHF [n = 49; 51% male, median age 76 (68-80) years old, LVEF 49% (29-58%)] were included. RDW, NT-proBNP, erythrocyte sedimentation rate (ESR), high-sensitivity C-reactive protein (hsCRP), and interleukin-6 (IL-6) were measured within 48 hours of admission. The composite primary end-point was the occurrence of major adverse cardiovascular events (total mortality, MI, stroke, cardiovascular hospitalisations, urgent revascularization) during the median follow-up period of 111 (109-113) days. The association of aforementioned markers with the primary outcome was tested in ROC-curve analysis and univariable Cox regression with subsequent adjustment for significant predictors and possible confounders in multivariable analysis. Correlation was estimated with the use of Spearman's rank correlation coefficient (rho).

**Results:** On admission 31 (63%) patients had NYHA class 3, and another 18 (37%) class 4 heart failure. Average RDW values on admission were 15,4% (14,7-17,1%). The primary endpoint occurred in 29 (59%) patients; 12 (25%) participants died during follow-up. RDW values > 15,35% [relative risk (RR) 10,49, 95% CI 3,86-28,56, p<0,001], hsCRP > 10,11 mg/l (RR 10,24, 95% CI 2,42-43,36, p=0,002), IL-6 > 19,3 pg/ml (RR 2,73, 95% CI 1,31-5,72 p=0,008), and NT-proBNP > 4075 pg/ml (RR 7,18, 95% CI 2,99-17,24 p<0,001) were associated with the primary outcome in univariate analysis. ESR (p=0,965), total WBC count (p=0,063) and neutrophil-to-lymphocyte ratio (p=0,266) did not play a significant role. In multivariate analysis after adjustment for HF severity NT-proBNP (RR 3,77, 95% CI 1,42-10,05, p=0,008) still predicted the primary endpoint, and association of RDW with outcomes became borderline significant (RR 3,25, 95% CI 1,00-10,69, p=0,050). RDW correlated with hsCRP (rho=0,655, p<0,001), IL6 (rho=0,477, p<0,001), lymphocyte count (rho=-0,307, p=0,030) and NT-proBNP (rho=0,610, p<0,001).

**Conclusions:** RDW values correlated positively with markers of inflammation and independently predicted short-term negative outcomes in patients with ADHF. However, its prognostic significance is relatively weak in comparison to NT-proBNP.

#### P1676

##### Haemoglobin - a simple biochemical variable in prediction of in-hospital mortality in heart failure patients

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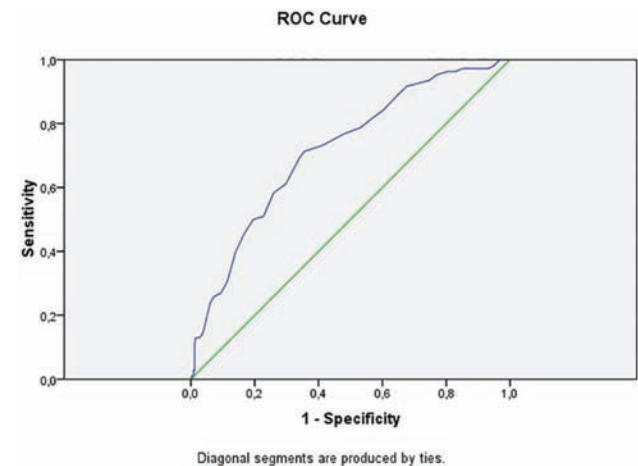
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**Aim of the study:** identifying predictors of in-hospital mortality in heart failure patients.

**Methods:** 451 patients admitted to ICCU with symptomatic HF were analyzed for: age, gender, co-morbidities, anemia, renal failure, parameters: heart rate, systolic and diastolic BP, Hgb, sodium, BUN, creatinine, ejection fraction (based on which patients were divided in PEF-HF and REF-HF), and calculated GWTG-HF score (Get with the Guidelines-HF risk score). Statistical analyze: descriptive, t-test, Chi square, uni and multivariate logistic regression, ROC Curve.

**Results:** mean age 69,9 ± 10,8, of 201(44,6%) f. and 250(55,4%) m. included. Presence of co-morbidities: Afib 41,0%; COPD 23,5%; DM 41,5%; HTA 71,6%; CAD 41,2%; preexisting-HF 34,8%; CRF 12,0%. Mean EF 42,5 ± 10,5% (26,1% with PEF-HF, and 73,9% with REF-HF). A total of 108 (23,9%) cardiac deaths were registered (IHD group), with the highest mortality rate during the first 48 hours (67,6%) of all. Univariate predictors: Afib: beta 0.383, p=0.085, exp(B) 1.466; HTA: beta -0.751, p=0.001, exp(B) 0.472; CRF: beta 0.819, p=0.007, exp(B) 2.268; DBP: beta -0.034, p=0.000, exp(B) 0.967; SBP: beta -0.017, p=0.000, exp(B) 0.983; sodium: beta -0.040, p=0.028, exp(B) 0.961; anemia: beta 0.951, p=0.000, exp(B) 2.588; Hgb: -0.190, p=0.000, exp(B) 0.827; creatinine: beta.248, p=0.000, exp(B) 1.282; BUN: beta.016, p=0.001, exp(B) 1.016; EF(%): beta -0.048, p=0.000, exp(B) 0.953; reduced EF: beta 0.989, p=0.000, exp(B) 2.687. In multivariate analyze four independent predictors identified: ejection fraction (beta -1.034, p=0.004), DBP (beta -0.032, p<0.000), BUN (beta 0.021, p<0.000) and Hgb (beta -0.119, p<0.039). Patients with REF-HF had significantly higher mortality rate in comparison with PEF-HF (OR 2.687, p=0.000). Mean GWTG-HF score was 39.5 ± 9.9 (37.7 ± 9.4; 45.3 ± 9.7; p 0.000, non-IHD vs IHD pts). It had excellent discriminate function (ROC Curve: Area under the Curve.718, p< 0.000 (CI.663-.772) (image 1), in predicting IHD.

**Conclusion:** It seems reasonable to include Hgb - a simple biochemical marker, in GWTG-HF score and increase its predictive value.



ROC Curve of IHD with GWTG-HF score

#### P1677

##### Cardiovascular biomarkers and severity of dyspnea predict readmission and death in patients hospitalised for acute dyspnea

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**Background:** Patients with acute dyspnea is a large heterogeneous patient group with high mortality and readmission rates. Risk assessment of in-patients is crucial for optimizing treatment and length of stay.

**Purpose:** To investigate the prognostic value of cardiovascular biomarkers and clinical characteristics for readmission and death in patients hospitalized for acute dyspnea.

**Methods:** We studied 65 dyspnea patients at a general internal medicine ward and followed them for 6 months. Death or readmission was considered as the combined endpoint. Measurements and

**Results:** A cardiovascular risk score of inflammatory and vascular stress biomarkers was related to the endpoint and adjusted for clinical characteristics by using Cox proportional hazard models (adjusted for sex, age, saturation, respiratory rate and CRP). The parameters were divided into tertiles and the bottom tertile was used as the reference group. The biomarkers Tissue-type plasminogen activator (tPA), Prolactin (PRL), Tumor necrosis factor receptor superfamily member 6 (FAS) and C-C motif chemokine 3 (CCL3) were independently significant and combined into a risk score. Each SD increment of the score conferred a hazard ratio (HR) of 2.03 (1.34-3.05)  $P=0.001$ . The top tertile conferred a HR of 2.81 (1.25-6.32)  $P=0.01$ . High severity of dyspnea (by modified NYHA-class) was also associated with worse outcome HR=2.68 (1.03-7.02)  $P=0.041$ .

**Conclusion:** Dyspnea level and a score of tPA, PRL, FAS and CCL3 predict 6-month death and readmission in patients hospitalised for acute dyspnea and may be used to optimise hospital care.

#### Cardiovascular risk biomarker score \*

	HR (95 % CI)	P	HR (95% CI) P-trend		
			Tertile 1	Tertile 2	Tertile 3
per 1 SD increment					
Biomarker score	2.03 (1.34-3.05)	0.001	REF (1.0)	1.58 (0.68-3.67)	2.81 (1.25-6.32) 0.01
Modified NYHA-class	NA	NA	M-NYHA class 2 REF (1.0)	M-NYHA class 3 1.73 (0.72-4.12)	M-NYHA class 4 2.68 (1.03-7.02) 0.041

\* adjusted for age, sex, respiratory rate, saturation and C-reactive protein. Biomarker score of tPA, PRL, FAS and CCL3. M-NYHA; modified NYHA-class. Dyspnea severity derived from the New York Heart Association (NYHA) Functional Classification.

#### P1678

##### Prognostic impact of C-reactive protein level on admission in patients with acute decompensated heart failure

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**Background:** C-reactive protein (CRP) level on admission has been related with the prognosis of several cardiovascular diseases such as acute coronary syndrome. Although admission CRP level was associated with in-hospital mortality in patients with acute decompensated heart failure (ADHF), association between admission CRP level and long-term mortality in patients with ADHF remains to be clarified.

**Methods:** A cohort of 1684 consecutive patients admitted to the cardiac intensive-care unit from 2007 to 2011 was studied. Among them, patients with acute coronary syndrome and neoplasms were excluded, and then patients with ADHF were divided into 5 groups based on quintiles of admission CRP level. Association between admission CRP level and long-term mortality was assessed by multivariable Cox proportional analysis including other independent variables which showed  $<0.1$  in univariable analyses.

**Results:** Overall, 527 patients were assessed. There were 142 deaths (27%) during a median follow-up of 2.0 years. In the multivariable analysis, hazard ratio (HR) increased with admission CRP levels in a significant dose-dependent manner for mortality ( $p$  for trend=0.045). Multivariable analysis also showed a significant relationship between admission CRP level, when treated as a natural logarithm-transformed continuous variable, and increased mortality (HR, 1.18;  $P=0.023$ ).

**Conclusion:** In patients with ADHF, admission CRP level is associated with increased risk of long-term mortality.

#### P1679

##### Prognostic value of biomarkers and co-morbidities in patients with acute heart failure: one year follow up

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**Purpose:** To evaluate the prognostic value of biomarkers B-type natriuretic peptide (BNP), troponin I (TnI) and high-sensitivity C-reactive protein (hsCRP) and co-morbidities on one-year mortality in patients with acute heart failure (AHF).

**Methods:** A total of 124 patients (pts) (70.69 ± 9.76 years, 76 male) who were admitted to intensive care unit due to signs and symptoms of AHF were enrolled in the study. During the first 24 hours after admission, values of both standard biochemical parameters as well as of BNP, TnI and hsCRP were determined.

In all pts echocardiography examination was performed and data on existing co-morbidities (chronic renal failure, cerebrovascular insult, myocardial infarction, angina pectoris, hypertension, peripheral arterial disease, diabetes mellitus, chronic obstructive pulmonary disease, depression) were collected. After discharge clinical one year follow-up was performed. All medical therapy was documented, and for this analysis, we focused on mortality.

**Results:** During one year follow up 37(29.8%) pts died. Value of serum BNP was higher in the group of non-survivors compared to the group of survivors (13538.84 ± 5078.32 vs 7184.84 ± 3876.95 pg/mL,  $p<0.001$ ), as well as value of TnI (3.26 ± 11.94 vs 1.07 ± 2.72 ng/ml,  $p=0.402$ ) and hsCRP (15.10 ± 13.21 vs 13.02 ± 16.04 mg/L,  $p=0.140$ ).

By applying Cox regression analysis the most important predictors for one year mortality were: BNP (HR 1.000, CI 1.000-1.000,  $p<0.001$ ), hypotension at admission (HR 7.226, CI 3.692-14.143,  $p<0.001$ ), left bundle branch block (HR 5.708, CI 2.746-11.863,  $p<0.001$ ), presence of chronic renal failure (HR 3.780, CI 1.943-7.356,  $p<0.001$ ), left ventricular ejection fraction (HR 0.925, CI 0.889-0.962,  $p<0.001$ ), right ventricular systolic pressure (HR 1066, CI 1.043-1.089,  $p<0.001$ ), the size of left atria (HR 1.052, CI 1.025-1.081,  $p<0.001$ ). Weaker, but significant predictors of mortality were: TnI (HR 1.042, CI 1.011-1.074,  $p<0.007$ ) ventricular arrhythmias (HR 2.115, CI 1.099-4.071,  $p<0.025$ ), depression (HR 2.602, CI 1.346-5.029,  $p<0.004$ ) left ventricular end-diastolic diameter (HR 1.056, CI 1.022-1.091,  $p=0.001$ ) and the presence of diastolic dysfunction (HR 2.946, CI 1.048-8.383,  $p<0.041$ ).

**Conclusion:** Our results showed that in patients with acute heart failure the most significant influence on one-year mortality out of biomarkers had level of BNP and TnI, and out of co-morbidities chronic renal failure and depression. Level of BNP and chronic renal failure stood out as the strong predictors of one-year mortality.

#### P1680

##### Neutrophil-to-lymphocyte ratio is a better marker for progression of renal dysfunction than neutrophil gelatinase associated lipocalin in heart failure

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**Background:** Neutrophil gelatinase-associated lipocalin (NGAL) is a biomarker for tubular kidney injury and inflammation. Previous studies have shown that high NGAL values in acute and chronic heart failure patients are associated with worse functional capacity, and adverse clinical outcome. The aim of the present study was to assess the utility of serum NGAL level to predict progression of kidney disease in heart failure patients with reduced ejection fraction (HFrEF).

**Methods:** Serum NGAL levels and markers of inflammation [hs-CRP, neutrophil-to-lymphocyte ratio (NLR)] were assessed from venous blood samples of 121 patients with chronic HFrEF. Primary endpoints were progression of kidney dysfunction (defined as a decline in eGFR category accompanied by a  $>=25\%$  decrease in eGFR from baseline), and composite of all-cause mortality and re-hospitalization.

**Results:** Data for follow-up eGFR was available for 85 patients during a median 16 months follow-up period, and progression of kidney disease was detected in 28 patients (33%). In univariate analysis, baseline functional class, NT-proBNP, hs-CRP, NGAL, and NLR were significantly higher, baseline eGFR, hemoglobin and albumin were significantly lower in patients with worsening kidney function. In Cox regression analysis, NLR [Exp(B)=1.374,  $p=0.001$ ] and hs-CRP [Exp(B)=1.148,  $p=0.019$ ] were independent predictors of worsening kidney function. Composite endpoint could be assessed in all patients [observed in 68 patients (56%)]. Signs of right heart failure in the initial visit [Exp(B)=0.465,  $p=0.010$ ] and hs-CRP [Exp(B)=1.077,  $p=0.024$ ] were the two independent predictors for all-cause mortality and re-hospitalization.

**Conclusion:** Simple markers of systemic inflammation (i.e. NLR and hs-CRP) are better predictors for progression of kidney dysfunction and for composite of all-cause death and rehospitalization than serum NGAL levels.

#### P1681

##### The effect of early increases of alanine aminotransferase on mortality in cardiogenic shock: the CardShock study

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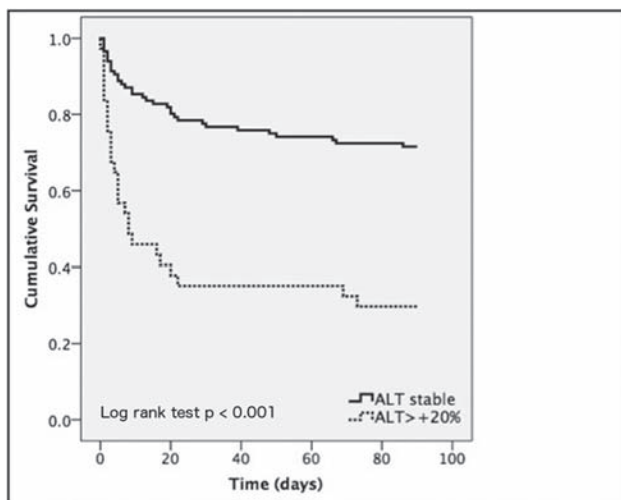
**Purpose:** To assess the prognostic value of early alanine aminotransferase (ALT) changes in cardiogenic shock patients.

**Methods:** Serial blood sampling (12h intervals for 24 hrs after study enrolment) was performed in 156 patients enrolled in the prospective multicenter CardShock study.

ALT levels were analyzed in a central laboratory. Associations of ALT levels with clinical data and outcomes were analysed using SPSS statistical software.

**Results:** Patients were on average 66 years old, and 26 % were women. The etiology of cardiogenic shock was mainly acute coronary syndrome, comprising 80% of the patients in the cohort. Mean systolic blood pressure was 77 mmHg (standard deviation 12 mmHg), and median lactate 2,5 mmol/l (interquartile range 1,6-5,1 mmol/l). The overall 90-day mortality was 42,0%. An increase in ALT of over 20% within 24 h of enrolment (ALT > +20%) was observed in 24% (38/156) of patients. ALT > +20% was associated with signs of hypoperfusion (higher lactate, oliguria, lower left ventricular ejection fraction, with p-values of <0.001, 0.02 and <0.01, respectively). ALT > +20% was also associated with a lower cardiac index (p < 0.01 for time points 24h, 36h and 48h after study enrolment) and a higher CVP (p < 0.01 for time points 12h and 24h after study enrolment). ALT > +20% was associated with an over two-fold increase in mortality compared with those with stable ALT (72% and 31%, respectively, p < 0.001) with a univariate Cox proportional hazard ratio of 3.7 (95% CI 2.2-6.3, p < 0.0001) for death at 90 days. In multivariate analysis adjusting for the initial level of ALT, highest TnT level within 24 hrs and the change in lactate levels within 24 hrs in addition to the risk factors included in the previously published CardShock risk score, the association remained statistically significant (HR 2.9, 95% CI 1.6-5.5, p = 0.001), showing that a greater than 20% increase in ALT levels within 24 h was strongly associated with 90-day mortality (Figure 1).

**Conclusions:** An increase in ALT of +20% or more within 24h is strongly associated with mortality and an independent predictor of 90-day mortality in cardiogenic shock.



Kaplan-Meier survival curves

#### P1682

##### Significance of soluble ST2-receptor and NT-proBNP concentrations in acute decompensated heart failure patients long-term risk stratification

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**Background:** sST2 and NT-proBNP concentrations are strong predictors for of the adverse long-term prognosis in pts with ADHF.

**Purpose:** to evaluate the significance of sST2 and NT-proBNP concentrations in risk stratification in patients (pts) with ADHF in one year follow-up period.

**Methods:** In our study were included 159 pts with ADHF III-IV FC NYHA. Blood samples to determine NT-proBNP, sST2, hsTnT, NGAL and galectin-3 concentrations were collected at the admission and at discharge from the hospital, and after 3, 6 and 12 months of follow-up. The primary end point was total cardiovascular events that included cardiovascular (CV) death and hospitalization due to HF.

**Results:** At admission all pts had elevated biomarker concentrations: NT-proBNP 3615,5(1578,0;6289,3) pg/ml, sST2 60,49(41,95;92,87)ng/ml, and at discharge: NT-proBNP 2165,5(982,7;4221,2)pg/ml and sST2 38,43(24,67;63,72)ng/ml. During 1-year follow-up (mean 277 ± 115 days) 54 pts (33,96%) had CV events. Biomarker concentrations in low risk pts (without CV events) were significantly lower compared with high risk pts (with CV events): at the admission NT-proBNP 2819 (1233;4912,7)pg/ml vs 5215,5 (3010; 8768,5)pg/ml, p < 0,0001; sST2 53,64(37,04;72,35)ng/ml vs 72,07(59,27;117,75)ng/ml, p < 0,0001; and at discharge from the hospital NT-proBNP 1439 (753,3;2604,5)pg/ml vs

3358 (1623,7;5432,7)pg/ml, p < 0,0001; sST2 31,28(21,68;48,00)ng/ml vs 60,19(37,25;98,35)ng/ml, p < 0,0001. At the discharge from the hospital NT-proBNP and sST2 concentrations had the most predictive capacity relatively the primary end point during 1-year follow-up: AUC=0,726 (0,637-0,816), <0,0001, sensitivity 75%, specificity 58,1% and AUC=0,768 (0,682-0,854), <0,0001, sensitivity 75,5%, specificity 64,3% respectively. Lack of NT-proBNP and sST2 concentrations decrease below 1696pg/ml and 37,8ng/ml was associated with the highest risk of CV events (OR 4,1(1,91-9,01), p < 0,0001 and OR 5,89(2,66-13,08), p < 0,0001, respectively). Changes of sST2 concentration during the period of pts hospitalization have had prognostic significance, AUC=0,696 (0,596-0,796), p < 0,0001. At the same time, insufficient degree of sST2 concentrations reduction during the period of hospitalization ( $\Delta$  % < 26,9%) have had the worst short-term and long-term prognosis (OR 3,68 (2,05-6,64), p < 0,0001).

**Conclusion:** The values of soluble ST2-receptor over 37,8ng/ml and NT-proBNP over 1696pg/ml at the discharge from the hospital reflects the adverse long term prognosis in patients with ADHF. sST2 concentration was an independent predictor of adverse prognosis in the multivariate analysis.

#### P1683

##### Risk-stratifying biomarkers to predict new onset HFpEF: potential roles for BNP, hsTroponin and galectin-3

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**Introduction:** The future prediction of new onset heart failure with preserved ejection fraction (HFpEF) is an important component of disease prevention strategies. HFpEF is characterised by progressive onset of cardiac remodelling and ventricular dysfunction providing opportunities to detect these disease manifestations earlier and therefore enabling timely intervention. Based on HFpEF pathogenesis, potential biomarker candidates in the future prediction of new onset HFpEF include natriuretic peptides, high sensitivity Troponins, and galectin-3. The purpose of this study was to investigate the utility of these biomarker candidates in predicting new onset HFpEF in asymptomatic, event-free patients with CVD risk-factors.

**Methods:** The study population consisted of 90 patients selected from within the longitudinal STOP-HF study (Ireland) which comprises asymptomatic patients with CVD risk factors. Thirty of these patients developed HFpEF over time, and were propensity matched 2:1 by age and sex to a cohort that did not develop HFpEF (n = 60) over a similar time period. BNP, hsTroponin I, and galectin-3 were quantified in all patients at two time points. Median time between measurements was 1.2 years. In the new onset HFpEF cohort, all analyses were done before the event, and median time between follow-up measurement and future HFpEF event was 1.6 years. Results Biomarker analysis of hsTroponin I and BNP at baseline and follow-up were statistically significant predictors of future new onset HFpEF, whereas galectin-3 at follow-up only was a significant predictor. A logistic regression model indicated that unadjusted biomarker combinations could significantly predict future HFpEF using both baseline (AUC 0.77 [0.68,0.87]) and follow-up data (AUC 0.86 [0.79,0.94]). NRI between adjusted models indicate that it is not necessary to take account of patient medications at 80% sensitivity. A simple clinical prediction rule to approximate the probability of future HFpEF development within the next 1-2 years was developed. Low and high risk was determined using BNP and galectin-3, with hsTroponin I being required to differentiate the intermediates. Applying this rule to the follow-up dataset yields sensitivity and specificity values of 83% and 71%, respectively. Discussion We provided evidence for the utility of BNP, hsTroponin I, and Galectin-3 in the prediction of future HFpEF in asymptomatic event-free populations with CVD risk-factors. Validation of our biomarker combination models and clinical prediction rule in an independent population is required.

#### P1684

##### NT-proBNP, ST2 and Galectin3: a multiparametric approach based on biomarkers to predict the risk of heart failure progression

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The aim of this study was to evaluate the possible integration of information carried by NT-proBNP, Galectin-3 (Gal-3) and ST-2 in order to better stratify the risk of heart failure progression in a group of outpatients affected by chronic heart failure (CHF)

**Methods:** We enrolled 215 outpatients (81% males, 64 ± 13 years, NYHA class 2.3 ± 0.6, left ventricular ejection fraction, LVEF, 33 ± 10% with CHF (ESC criteria) due to left ventricular systolic dysfunction, in stable clinical conditions (>1 month) and in conventional therapy. Plasma levels of NT-proBNP (mean 2447 ± 4018



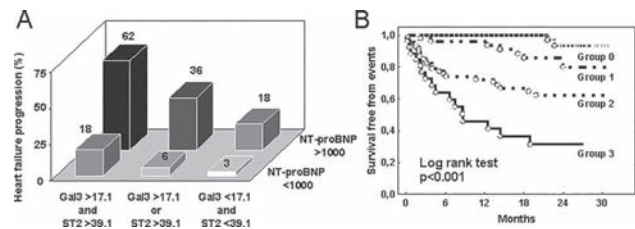
pg/ml), Gal-3 (mean 15.6±7.1 pg/ml) and ST2 (mean 41.9±21.6 pg/ml) were assessed. During follow-up heart failure progression was defined as the occurrence of hospitalization and/or heart transplantation and or death due to worsening of heart failure.

**Results:** During a mean follow-up of 16±10 months, 48 patients showed heart failure progression.

At Cox univariate regression analysis NT-proBNP ( after log transformation HR 10.9; 95%CI: 4.44-26.9; p < 0.001), Gal-3 (HR 1.05; 95%CI: 1.02-1.08; p < 0.001; C index 0.66) and ST-2 (HR: 3.51; 95%CI:1.9-5-6.35; p < 0.001; C index 0.66) were all associated to heart failure progression. However, accuracy of NT-proBNP (C-index 0.79) was greater than those observed for Gal-3 (C-index 0.66) and ST2 (C-index 0.66). At ROC curves for one year events, the best cut-offs observed were 1000 for NT-proBNP (sensitivity 94% and specificity 58%), 17.1 for Gal-3 (sensitivity 66% and specificity 67%) and 39.1 for ST-2 (sensitivity 69% and specificity 70%). Although less accurate in predicting events, when combined to NT-proBNP, ST2 and Gal-3 were able to better discriminate patients with and without events (free NRI p: 0.019 for Gal-3 > 17.1 and p < 0.001 for ST-2>39.1). In a Cox multivariate analysis, when the information concerning the presence of a high ST-2 and/or Gal-3 was added to that related to the presence or not of a high NT-proBNP, a significant association with events was found for ST-2/Gal-3 (HR 2.07;95%CI:1.35-3.16;p: 0.001).

Panel A of figure shows the risk of heart failure progression according to the presence or not of high NT-proBNP and of high ST-2/Gal-3. In panel B Kaplan Meier curves for events according to the number of altered biomarkers (none, one, two or three) are shown.

**Conclusions:** Our findings demonstrate that combination of Gal-3, ST2 and NT-proBNP is able to identify patients with the highest risk of heart failure progression. This can be due to the fact that these biomarkers can integrate each other because reflect different pathophysiological substrates leading to heart failure worsening.



**P1685**

**Biomarkers of oxidative stress and heart failure**

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**Aim:** of the study was to evaluate association between biomarkers of oxidative stress and development of heart failure in patients with coronary artery disease (CAD).

**Methods:** Patients treated because of CAD were analyzed for their demographic, LV functional, risk factors, biochemical variables: lipids, DM variables, Hgb, and markers of oxidative stress: oxidative stress markers: malondialdehyde and total hydroperoxides, and antioxidant enzymes: superoxide dismutase, catalase and glutathione peroxidase. They were divided in two groups: preserved and reduced EF (EF ≥40 or < 40%). Statistical analyze: descriptive, t-test, Chi square test, correlation, uni and multivariate logistic regression analyze. Significance was determined at level of 0.05.

**Results:** 134 pts. 94(70,1%) males and 40(29,9%) females at mean age of 64,3±11,2 years were analyzed. 99(73,9%) had A presence of REF-HFS, and 35(26,1%) had CCAD. 62,2% of pts. had HTA, 38,1% HLP, 33,6% DM, 59,7% were active or past smokers, 11,9% had anemia. Mean EF was 50,9±10,2%, 45,5% had reduced EF (< 40%). Mean values of all of the markers of oxidative stress are presented in Table 1. Statistically significant difference existed only for MDA. We found significant positive association with univariate logistic regression only for MDA and HF (beta.228, p=0,008), same result was confirmed when we took ACS as selection variable (beta.197, p=0,050), but statistical significance wasn't found in CCAD patients (beta.305, p=0,074). Significant association was found between age and MDA (beta=.177, p=0,041), especially with HF as selection variable (beta =.356, p=0,005), and HP (beta.155, p=0,074).

**Conclusion:** Chronic heart failure, regardless of etiology, is associated with abnormalities of a range of markers of oxidative stress, we managed to find significant

association for one of them - malondialdehyde. Also, it seems that there is an age dependency, we registered significantly higher levels of MDA and total HP in older patients with CAD and HF.

Table 1. Mean values of oxidative stress

OS marker	EF 0/1	N	mean ± SD	p
MDA	0 1	73 61	31,85 ± 7,17 36,73 ± 13,35	0,008
Total HP	0 1	73 61	281,83 ± 66,14 289,46 ± 73,99	0,530
SOD	0 1	73 61	106,39 ± 94,33 139,19 ± 131,67	0,096
CAT	0 1	73 61	63,13 ± 43,40 59,27 ± 36,55	0,583
GPX	0 1	73 61	6,39 ± 4,94 5,94 ± 6,80	0,759

Legend: OS-oxidative stress; 0- EF>40%; 1-EF < 40%; MDA-malondialdehyde; HP-hydroperoxides; SOD- superoxide dismutase; CAT-catalase; GPX- glutathione peroxidase.

**P1686**

**Some aspects of the effect of coenzyme Q10 on inflammatory processes, remodeling and functional status of endothelium in chronic heart failure**

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**Aim:** To evaluate the effect of coenzyme Q10 on biomarkers associated with inflammatory processes, remodeling and functional status of the endothelium of patients with chronic heart failure (CHF) in functional NYHA class II-III.

**Method:** 108 patients, with class II-III CHF and a history of myocardial infarction, were entered into the study. The patients were randomized into two groups: group I which received coenzyme Q10 at a dose 120 mg/day over 3 months in addition to the standard optimal treatment; and group II who received the standard optimal treatment only. All patients were tested at the start of the study and again at 3 months for blood serum levels of the following: galectin-3, ST2, high sensitivity C-reactive protein (hs-CRP), N-terminal pro B-type natriuretic peptide (NT-proBNP), circulating endotheliocytes (CEs), matrix metalloproteinases-9 (MM-9). Endothelial dysfunction was evaluated by peripheral arterial tonometry (PAT). All patients had an echocardiogram (Echo-CG) performed at the start of the study and again at 3 months.

**Results:** At 3 months, patients in both therapy groups showed clinical benefits of treatment for their CHF. Patients in group I showed a decrease of left ventricular diastolic and systolic end volumes and an increase of the ejection fraction. Both groups of patients showed a decline of hs-CRP-concentration in comparison with initial testing: group I from 3.4 (1.8; 6.7) mg/L to 1.5 (0.8; 3.0) mg/L (< 0.05), and group II from 3.85 (2.15; 8.70) mg/L to 1.35 (0.73; 3.4) mg/L (< 0.05). Over the same period of 3 months the concentration of galectine-3 decreased from 19.22 (10.88; 43.50) ng/ml to 16.76 (9.92; 34.50) ng/ml only in group I, and levels of ST-2 decreased from 75.11 (63.36; 100.43) ng/ml to 54.02 (48.84; 86.79) ng/ml (< 0.05) only in patients of group I; in group II patients ST-2 concentration was unchanged. The level of NT-proBNP during therapy was significantly decreased in both groups. Using the Wilcoxon rank-sum test, paired comparisons of MM-9concentration made in depended samplings decreased in group I patients. After 3 months of therapy the level of CEs (<0.05) decreased in both groups. According to the PAT data the reactive hyperemia index (RHI) increased in both groups: in group I patients from 1.38 (1.14; 1.50) to 1.87 (1.39; 2.57) and in group II from 1.33 (1.22; 1.50) to 1.44 (1.33; 1.74). However, only group I patients showed an increase in the median value of RHI of more than 1.67 over the 3 months of treatment.

**Summary:** Adding coenzyme Q10 to the standard treatment of patients with CHF with a history of myocardial infarction, led to progress in the management of post myocardial infarction remodeling according to Echo-CG findings, with improvement of endothelium function, decrease in inflammatory activity and fibrosis development, as evidenced by changes in the level of biomarkers associated with these processes.

**P1687**

**Neutrophil to lymphocyte ratio - an independent predictor of mortality in patients with heart failure**

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**Background:** Neutrophil to lymphocyte ratio (NLR), a marker of inflammation, was initially used as a prognostic factor in infectious and neoplastic diseases. Recently, NLR was associated with increased morbidity and mortality in different cardiovascular diseases.

**Purpose:** Our aim was to validate the prognostic utility of NLR in predicting 3-year survival in heart failure (HF) patients and to determine a cut-off level for this biomarker.

**Methods:** We retrospectively analyzed data from all adult HF patients admitted to our clinic during a two year period (after excluding those with acute coronary syndromes, pulmonary embolisms, readmissions and in hospital mortality). Survival was determined at 3 years after hospital discharge for each subject.

**Results:** Our sample consisted of 424 patients with a mean age of 69.47 ± 11.06 years and female predominance (56.97%). Median NLR was 2.66 (interquartile range 1.92; 3.65). 3-year survival was 77.07%. Surviving patients had a median NLR of 2.44 (1.81; 3.31) compared to 3.65 (2.83; 5.77) in non-survivors ( $p < 0.0001$ ). All-cause mortality increased proportionally to the NLR quartiles from 7 (6.66%) patients in the lowest quartile to 48 (45.28%) patients in the highest quartile ( $p$  for trend  $< 0.0001$ ).

In ROC curve analysis, NLR predicted all-cause mortality with an AUC of 0.753 (95% CI 0.709 - 0.794),  $p < 0.0001$  and a Youden index associated criterion of NLR  $> 2.76$  with a sensitivity of 78.4% and specificity of 62%. We therefore established the cut-off level at 3. Patients with a NLR  $> 3$  had a fatality OR of 5.33 (95% CI 3.24 - 8.77),  $p < 0.0001$ .

In multivariate analysis, NLR  $> 3$  was an independent predictor of all-cause mortality with an OR of 2.86 (95% CI 1.58 - 5.15),  $p < 0.0001$ , alongside the ejection fraction, NYHA class IV, potassium and hemoglobin levels. In this model, the NT pro-BNP no longer remained an independent predictor.

The all-cause mortality prediction model using NLR  $> 3$ , increased NT-pro BNP, ejection fraction, NYHA class IV, age, potassium and hemoglobin trended towards outperforming the NT-pro BNP level alone with a ROC curve of 0.837 (95% CI 0.793 - 0.882) versus 0.804 (95% CI 0.755 - 0.853),  $p = 0.07$ .

**Conclusions:** NLR  $> 3$  is an independent prognostic factor for 3-year all-cause mortality in heart failure patients. Using this easily available, cost-efficient biomarker alongside the already validated parameters increases the accuracy of fatality prediction in these patients.

#### P1688

##### Combining natriuretic peptides and 1, 25-dihydroxyvitamin D testing improves the predictive value for cardiovascular death in heart failure

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**Background:** B-type natriuretic peptides (BNP) and N-terminal pro-BNP (NT-proBNP) are reference biomarkers in heart failure (HF). A growing body of evidence supports the role of vitamin D and parathyroid hormone in cardiac remodeling and HF worsening. However, the prognosis value of the 1,25-dihydroxyvitamin D (1,25(OH)<sub>2</sub>D), the most potent active metabolite of vitamin D, remains to be investigated.

**Purpose:** We therefore evaluated a multimarker strategy based on the combination of 1,25(OH)<sub>2</sub>D and natriuretic peptides measurement to predict cardiovascular (CV) death.

**Methods:** 170 HF patients (females  $n = 36$ ; males  $n = 134$ ; NYHA II-IV; mean age: 67 years; etiology: ischemic  $n = 119$ , dilated cardiomyopathy  $n = 51$ ; median LVEF: 24%) were included in this study. The primary outcome (PO) was CV death. Circulating levels of BNP, NT-proBNP and 1,25(OH)<sub>2</sub>D were determined with automated immunoassays.

**Results:** Serum levels of 1,25(OH)<sub>2</sub>D decreased markedly with HF severity. Medians were 33.3 pg/mL for NYHA-II patients, 23.4 pg/mL for NYHA-III, and 14.0 pg/mL for NYHA-IV patients ( $p < 0.001$ ). The NT-proBNP to 1,25(OH)<sub>2</sub>D and the BNP to 1,25(OH)<sub>2</sub>D ratios were also significantly related to HF severity. Over a mean follow-up of 4 years, 106 out of 170 patients reached the PO. Cox proportional hazard modeling revealed that the ratios were strongly predictive of CV death. In ROC analysis, the area under the curve (AUC) for CV death for NT-proBNP/1,25(OH)<sub>2</sub>D and BNP/1,25(OH)<sub>2</sub>D ratios were respectively 0.769 and 0.782 (higher than BNP (AUC 0.744) and NT-proBNP (AUC 0.730)).

**Conclusions:** In heart failure, the ratios between natriuretic peptides and 1,25(OH)<sub>2</sub>D strongly and independently predict cardiovascular mortality and are more efficient than single natriuretic peptides testing. These simple new tools contribute to a more personalized management of heart failure patients.

#### P1689

##### Comparing baseline, admission and discharge natriuretic peptide levels (NT-proBNP) during admissions for acute decompensated heart failure: insights for a relative approach in guided treatment

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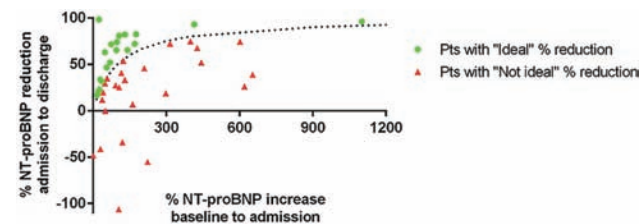
**Background:** In a previous study, we demonstrated that either an absolute or relative natriuretic peptide (NT-proBNP) discharge target may be used to guide treatment during admissions for acute decompensated heart failure (ADHF), as both can predict survival and readmissions. A  $> 30\%$  relative NT-proBNP reduction during admissions seems to be an attractive target for most patients, in which

the admission level is the first available measurement. Another approach may be an NT-proBNP reduction back to 'stable' baseline levels. We explored the relative changes in NT-proBNP levels in ADHF patients at baseline, admission and discharge, to better understand the proposed relative discharge target of  $> 30\%$  reduction in NT-proBNP.

**Methods:** Our study population comprised ADHF patients admitted between Dec 2004 and Dec 2008 in our academic hospital in whom admission and discharge NT-proBNP levels were available. In addition, an NT-proBNP measurement was available during stable condition within  $< 12$  months before admission at the outpatient HF clinic. We assessed the relationship between percentage NT-proBNP increase from baseline to admission, and the percentage NT-proBNP reduction from admission to discharge. Patients achieved an "ideal percentage reduction" when they attained their baseline NT-proBNP levels at discharge. We compared percentages of patients attaining "ideal percentages reduction" between patients attaining  $> 30\%$  vs  $< 30\%$  NT-proBNP reduction at discharge.

**Results:** A total of 44 patients (median age 70 (57-76), 57% males) were studied. Median percentage NT-proBNP increase from baseline to admission was 106% (48-220%). Median percentage NT-proBNP reduction from admission to discharge was 40% (20-72%). In 19 patients (43%), an NT-proBNP reduction below or at baseline levels was attained at discharge (Figure). Patients with an NT-proBNP reduction of  $\leq 30\%$  at discharge were significantly less often at baseline levels at discharge compared to patients with an NT-proBNP reduction of  $> 30\%$  at discharge (3/17 patients (18%) vs. 16/27 patients (59%),  $p = 0.01$ )

**Conclusion:** Admissions for ADHF are accompanied by a median increase of 106% in NT-proBNP from baseline levels, but with a wide variation of increases. At discharge, 43% of ADHF patients attain their baseline NT-proBNP level again. A discharge level of  $> 30\%$  NT-proBNP reduction indicates that 3/5 of patients reach baseline NT-proBNP levels.



#### P1690

##### Diagnostic utility of cardiac biomarkers in discriminating takotsubo syndrome from acute myocardial infarction

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**Introduction:** Takotsubo syndrome (TS) has a clinical and echocardiographic presentation similar to acute myocardial infarction (AMI), especially anterior AMI. Ideally the differential diagnosis should be done early and preferably non-invasively. However, in the majority of patients, TS is not recognized until cardiac catheterization reveals typical wall motion abnormalities in the absence of significant coronary artery disease. In TS the rise in serum troponin seems to be disproportionately low relative to the extent of cardiac dysfunction, which may be useful in the differential diagnosis.

**Purpose:** To test the ejection fraction/troponin I (EFT) index and the NT-proBNP/troponin I (BNPT) index as non invasive methods to identify the TS.

**Methods:** We have included 49 patients with TS and 49 patients with anterior AMI (34 AMI with ST elevation and 15 AMI without ST elevation) matched by left ventricular ejection fraction (LVEF) (mean = 36.5 ± 7.4%) and age (mean = 66.7 ± 9.1 years). We calculate the EFT and BNPT indexes and their receiver operator characteristic (ROC) curves to evaluate the discriminatory power.

**Results:** We observed a female predominance in patients with TS (81.6% vs 22.4%,  $p < 0.001$ ), with no difference in relation to the cardiovascular risk profile. The troponin I peak was lower in TS (median = 2.4, IQ 1.4 - 5.1 vs 44.4 IQ 5.6 - 134.0 ng/ml,  $p < 0.001$ ), but the NT-proBNP levels were higher (median = 5542, IQ 2849 - 8753 vs 1324, IQ 801 - 1959 pg/ml,  $p < 0.001$ ).

In TS both indexes were higher (EFT: median = 14.6, IQ 5.5 - 24.1 vs 0.92, IQ 0.22 - 6.27,  $p < 0.001$ ; BNPT: median = 1721, IQ 718-4595 vs 37.5, IQ 13.7 - 147.3,  $p < 0.001$ ). After analyzing the ROC curves, it was found that both indexes showed good discriminatory power for TS (EFT: area under the curve (AUC) = 0.859,  $p < 0.001$ ; BNPT: AUC = 0.930,  $p < 0.001$ ).

**Conclusion:** In our population, the profile of cardiac biomarkers identified the patients with TS among patients presenting with anterior AMI. The construction of models based on cardiac biomarkers may be a useful tool in the non invasive diagnosis of TS, which is particularly important when coronary angiography is not risk-free for the patient.

NURSING

P1691

**The effect of guided web-based cognitive behavioral therapy on patients with depressive symptoms and heart failure- a randomized controlled trial**

The Swedish Heart and Lung Association, Region Östergötland, the Medical Research Council of Southeast Sweden

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**Background:** Depressive symptoms, and the associated coexistence of symptoms of anxiety and decreased quality of life (QoL), are a common problem in patients with heart failure (HF). However, treatment strategies for depressive symptoms in patients with HF still remain to be established. Cognitive behavioral therapy (CBT) and its Internet-based version as guided self-help CBT programs (ICBT) have shown good effects in the treatment of depression, but ICBT has not previously been evaluated in patients with HF and depressive symptoms.

**Objective:** The aims of this study were to: (I) evaluate the effect of a nine-week ICBT program on depressive symptoms in patients with HF; (II) to assess factors associated with the change in depressive symptoms; and (III) to investigate the effect of the ICBT program on cardiac anxiety and QoL.

**Methods:** Fifty participants were included and randomized into two treatment arms: ICBT or an online moderated discussion forum (DF). The Patient Health Questionnaire -9 (PHQ-9) was used to measure depressive symptoms, the Cardiac Anxiety Questionnaire (CAQ) was used to measure cardiac-related anxiety, and the Minnesota Living with Heart Failure questionnaire (MLHF) was used to measure QoL. Data were collected at baseline and at the nine-week follow-up.

**Results:** In the ICBT group, depressive symptoms (M=10.8 vs. M=8.6, P=.02) and cardiac anxiety in the subscale of fear (M=1.55 vs. M=1.35, P=.04) improved significantly. QoL improved in the ICBT group by 6 points in the total score and 2.4 points in the physical factor, but this was not significant (P=.09 and P=.12). In the DF group, only a small reduction in the level of depressive symptoms was detected (M =10.6 SD=5.0, vs. M=9.8 SD=4.3, P=.36). Despite improvement in the ICBT group this was not significantly different compared to the DF group (ANCOVA analyses: depressive symptoms, P=.21; cardiac-related anxiety subscale of fear, P=.22; QoL total scale score, P=.09 and physical factors, P=.07). In the ICBT group, the number of logins to the web-portal correlated significantly with improvement in depressive symptoms (P=.02), whereas higher age (P=.01) and male sex (P=.048) were associated with less change in depressive symptoms.

**Conclusions:** Guided ICBT adapted for persons with HF and depressive symptoms can potentially reduce depressive symptoms, cardiac anxiety and increased QoL, but is not statistically superior to participation in an online discussion forum.

P1692

**Social support and adherence to the therapy in patients with heart failure: a systematic review**

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**Purpose:** To systematically review trials, examining the role of social support to the adherence to the therapy of patients with heart failure (HF).

**Methods:** A systematic search of Pubmed, Cumulative Index to Nursing and Allied Health Literature (CINAHL) and Cochrane Library, was performed to locate relative randomized controlled trials (RCTs). Search was done from the beginning of December 2015 until the end of December 2015. "Heart failure", "Social support", and "adherence to therapy" were used as key words in various combinations using the word "AND". The tool "related articles" of the Pubmed was also used. Inclusion and exclusion criteria were pre-specified. Quality assessment was done by two reviewers separately. The search yielded eight RCTs.

**Results:** HF patients whose family member followed the low sodium diet (LSD) were 1.6 times more adherent than those, whose family member did not follow the LSD. Patients whose spouse did not adherence the LSD were found to have 804 mg more sodium excretion than those whose spouse was adherent to the LSD (p = 0.012) and 1139 mg more sodium excretion than those who had a non-spousal family member that was adherence to a LSD (p = 0.015). The family partnership intervention and the patient-family member education reduced the urine sodium at 4 months and family partnership intervention differed from usual care at 8 months (p = 0.016). Dietary sodium was found to be decreased from baseline to 4 months for both, patient-family member education (p = 0.04) and family partnership intervention (p = 0.018). Medication adherence was not found to be different among groups. The level of social support was related to the level of self-care and the patients with high

level of support stated better self-care (p = 0.003). The Reciprocal Peer Support and Nurse Care Management groups had no differences in the improvement in 6-month measures, either on HF quality of life or social support. Many HF patients stated that support for exercise was very meaningful and appreciated from family and friends.

**Conclusions:** Family members' education and encouragement to follow LSD may be beneficial for the self-care of patients with HF. The role of partner, family or social support is also found to be important for patients' participation in physical activity and exercise.

P1693

**The effect of therapeutic education on self-care in patients with heart failure and implantable cardioverter defibrillator: study protocol for a randomised controlled trial**

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**Background:** Therapeutic education has been shown to improve the quality of life of patients with hearth disease. However little is known about the effects of a therapeutic education on self-care in patients with heart failure(HF) during the follow-up period after the implantation of implantable cardioverter defibrillator (ICD). This study aims to examine the effect of a nursing educational intervention to improve self-care in HF patients with ICD.

**Methods/Design:** A multicenter, double-blind, parallel-group randomized trial will be conducted in Italy. A sample size of 128 patients hospitalized for an ICD implantation due to an arrhythmia and/or ischemia will be randomly assigned to the intervention or control group. Intervention group will be undergo to the educational intervention during the first follow-up (10 days from Implantation) and at 3,6,12 months after. The intervention will be focused on:1) pharmacological adherence, weigh monitoring, how routinely do about diet, smoking, alcohol, job and sex; 2) signs of dyspnea, how to identify the edema through the fovea, how to recognize rapid weight gain, appetite loss, fatigue, asthenia, insomnia, mental confusion; 3) recognition the symptoms of inflammation of the surgical site of implantation. For each control (3, 6, 12 months), the patient will undergo an electrocardiogram. Additionally, between one follow-up visit and another, patients will be undergone to the execution of blood tests, Brain Natriuretic Peptide (BNP), renal function, indices of hepatobiliary stasis and serum protein parameters (creatinine, blood count, ast, alt, albumin, total serum protein).The primary outcomes will be: Self-care levels, measured by Self-Care Heart Failure Index, SCHFI v 6.2 and Quality of life perception measured using a Visual Analogic Scale from 0 to 100. The secondary outcomes are adverse events measured using: incidence of Emergency Department visits and/or hospitalizations at 12 months; mortality rate at 180 days after ICD implantation and infection rate in the ICD device pocket.Randomization is computer-generated, with allocation concealment by opaque sequentially numbered sealed envelopes.Patients and professionals outside of the research team are blinded to group assignment.

**Discussion:** We expect participants to be compliant with the intervention and therapeutic education to be effective, satisfying and money-saving.

Educational intervention	
Items	Actions
1) Appropriate lifestyles	1) how adhering to the therapy such as how weigh yourself and how routinely do about diet, smoking, alcohol, job and sex will be explained and shown;
2) Early recognition of signs/prodromal symptoms of HF	2) signs of dyspnea will be illustrated; how to identify the edema through the pitting edema, how to recognize rapid weight gain, loss of appetite, fatigue, asthenia, insomnia, mental confusion, will be shown;
3) Early recognition of signs of inflammation of the ICD-pocket	3) recognition the symptoms of inflammation (hyperpyrexia, heat, pain, redness and swelling) will be taught even with images illustrating the signs;
4) Good management of the device	4) how to manage the presence of device will be explained simulating multiple situations: use of metal detectors, air travel, use of electronic devices, access to diagnostic imaging services (as PET and MRI)

P1694

**Sodium intake by patients with chronic heart failure in relation to hospitalisation for chronic heart failure.**

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**Introduction:** Sodium restriction is frequently advised for patients with chronic heart failure (CHF) despite the gap of evidence relating to this lifestyle advice.



The European Society of Cardiology (ESC) advises to avoid an excessive intake of salt. The World Health Organisation advises a salt intake of 2 grams per day. Previous studies on dietary salt restrictions are often done in combination with a fluid restriction, therefore it is not clear which intervention (the salt or fluid restriction) is responsible for the

**Results:** In studies based on only a dietary salt restriction, the salt intake was measured via questionnaires or estimated in 24 hours urine collections by a single portion of urine which are both not very reliable. The golden standard for measuring the sodium intake, is to collect 24 hour urine. The result of these studies are variable.

**Purpose:** The purpose of this study is to investigate the effect on hospitalisation of sodium intake in patients with CHF in functional New York Heart Association (NYHA) class I – III. Primary endpoint is hospitalisation for CHF.

**Methods:** In this observational study 30 patients were included, 10 in each NYHA class I – III. Sodium intake was measured by collecting 24 hour urine at baseline, 6 months and 12 months. A blood sample was taken (including N-terminal pro-Brain Natriuretic Peptide (NT-proBNP), NYHA class was determined, medication use was asked, quality of life was measured by the Minnesota Living With Heart Failure Questionnaire, and feeling of thirst was measured by a Numeric Rating Scale. During the follow-up visits at 6 months and 12 months, hospitalisation for CHF was also asked.

**Results:** The majority of the patients was male (90%). Mean age was 66.9 ± 12.3 years (mean ± SD). (Table 1.) Unto January 2016 (92% of the follow up, which ends in February) 2 patients have withdrawn from the study. Four patients (13%) were hospitalised for CHF of which 3 of them (10%) had <90 mmol sodium in 24 hour urine (is <2 gram salt intake). All were in NYHA class III. Of these 4 patients 2 died and one has withdrawn from the study. On the other hand there were 5 patients (17%) which had <90 mmol sodium in 24 hour urine but were not hospitalised for CHF (2 in NYHA class II and 3 in NYHA class III).

**Conclusion:** In this small observational study, the preliminary results shows no difference in a low salt intake (<2 gram/day) in relation to hospitalisation for CHF. More research is needed with a greater number of patients.

N	Male	Female	Mean age ± SD	Age: range
30	90%	10%	66.9 ± 12.3	37-90 y/o

Baseline characteristics

#### P1695

##### The role of heart failure nurses in the up-titration of sacubitril/valsartan (LCZ-696)

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**Background:** Heart failure (HF) nurses (HFN) are the most implicated professionals in HF programs. A recent European survey has shown that 85% of HFN have been trained specifically in HF, nearly 75% of them up-titrate angiotensin converter enzyme inhibitors (ACEI), diuretics and beta-blockers and about 50% up-titrate angiotensin receptors blockers (ARB) and mineralocorticoid receptor antagonists. The standard requirements for an up-titration program are: HFN training, appropriate protocols developed by the HF team, a previous prescription of the drug by HF physicians and their availability for consultation. LCZ 696 is a new drug that has demonstrated to reduce the risk of cardiovascular death and hospitalization of chronic HF patients, with NYHA class II-IV and reduced left ventricular ejection fraction. It should be expected a worldwide prescription of this drug in these patients.

**Purpose:** To design a protocol for HFN up-titration of LCZ-696

**Methods:** review of the evidence based literature, the rules of the European Medicine Agency (EMA), European Public Assessment Report (EPAR) summary for the public and risk-management-plan-summary for Sacubitril/Valsartan and finally, the trademark's dosing and titration guide.

**Results:** The protocol describes how HF nurse could up-titrate LCZ696. On the first visit the physician prescribes the drug, establishes the maximal doses and points out the titration step-up. HFN explains the patient and his relatives the aim of titration, reviews all the pharmaceutical treatment ensuring that ACEI or ARB are not included, recommends the timing for the control of blood pressure (BP) and heart rate, gives a contact phone number and schedules next visit with control of renal function and electrolytes after 2-4 weeks, according to the physician's prescription. On the next visits HFN will check BP and laboratory tests, analyzing the tolerance of the drug, increasing the doses following physician's plan to reach the maximal doses prescribed and tolerated. Special attention will be paid to adverse effects like angioedema, hypotension, hyperkalemia, cough, dizziness and impairment of renal function. In case of detection of any abnormality or doubts, HFN should contact the cardiologist to make decisions about the best therapeutical approach.

**Conclusion:** The application by HFN of a consensus protocol for LCZ696

up-titration will facilitate HF patients to safely reach the target doses with a reduction in the number of medical visits.

#### P1696

##### Healthcare providers' perception of exercise for heart failure patients: a qualitative study

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**Introduction:** Although exercise is widely known to be beneficial for patients with heart failure (HF) and is recommended in the ESC guidelines, not all healthcare providers recommend exercise to these patients. It is vital to evaluate and understand the reasons why or why not healthcare providers advise exercise to be able to implement exercise in the rehabilitation for the patients with HF.

**Purpose:** To gain a deeper understanding of healthcare providers' perception of exercise for HF patients.

**Methods:** A qualitative study was performed. Interviews with 8 healthcare providers (2 nurses, 3 physicians and 3 physiotherapists) in a university hospital in Israel were conducted. Healthcare providers working with HF patients were asked to participate. The interviews were semi-structured and addressed attitudes, actions and knowledge about exercise for patients with HF. Qualitative content analysis was used to analyse the data.

**Results:** One overall theme and six categories were found. The overall theme identified was; Exercise for HF patient is important but can be hard and complex with barriers and struggles. The categories found were; 1. Exercise is important for every HF patient because of its beneficial effects; 2. Healthcare providers have several barriers in the recommendation of exercise to HF patients; 3. Exercise can be difficult for a HF patient; 4. How to overcome barriers and get the patients to exercise; 5. Patient motivation is vital and 6. Prescribing exercise in heart failure patients can be complex. The beneficial effects for patients were described as physical, psychological and emotional. The barriers to prescribe exercise included the unstable status and high symptom burden of the patients. Furthermore, participants described that not all healthcare providers are aware of the benefits of exercise and not all have resources to offer an exercise program to their patients. Patients may need different advices, the motivation to do life style changes can be low and there is a lack of clinics specialized in HF rehabilitation. Solutions described on how to overcome the barriers were related to motivating the patients, fit the exercise into daily life or arrange social support.

**Conclusion:** From the interviews it can be concluded that exercise is perceived an important part of the rehabilitation program for patients with HF because of its beneficial effects. However, the respondents who were specialized in HF identified the complexity to recommend exercise to the patients. It is therefore reasonable to assume that other healthcare providers share the same opinion and education and implementation activities are vital.

#### P1697

##### Characteristics of patients in a heart failure unit according to two admission periods: 2001-2008 vs. 2009-2015

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**Background:** Heart failure (HF) units and programmes are key in HF management. Advances in HF treatment together with the higher widespread implementation of the HF programmes in the last two decades, and a better in-hospital patient's information and education may have modified the clinical characteristics of patients referred to HF units.

**Objective:** To compare the clinical characteristics, baseline knowledge and understanding of HF, self-care behaviour and treatments of ambulatory patients referred to a HF Unit of a tertiary university hospital, according to two admission periods.

**Patients and Method:** Patients were divided in two groups based on their admission date: 2001-2008 (period 1) vs. 2009-2015 (period 2). These periods divide our cohort in two groups of similar size and are grossly related to the pre- and post-definitive implementation of a program of primary coronary intervention for AMI. Patients were evaluated with three questionnaires: an own and previously published nurse questionnaire (knowledge and self-care), the European HF Self-care Behaviour scale (EHFScBS) and the Minnesota Living with Heart Failure Questionnaire (MLWHFQ).

**Results:** Out of 1921 patients admitted to the HF Unit (960 during the first period and 961 during the second), 1901 patients (946 and 955 respectively) filled in our own nurse questionnaire. Patients of both periods had similar age (66.6 ± 12.1 vs. 66.9 ± 13.3, p=0.58) and sex (male 70.8% vs. 70.7%, p=0.95). Duration of HF tended to be higher in period 1, without reaching statistical significance (median 12 months [IQR 2-48] vs. 6 months [IQR 2-39], p=0.13). Knowledge and understanding of the disease were higher in the second period (p < 0.001), with better awareness of alarm signs (p < 0.001) and name of prescribed drugs (p < 0.001), but not better

knowledge of the action of the drugs ( $p=0.3$ ). The EHFSBS was available at first visit in 633 patients during the first period and in 916 during the second. Global score was 24.8 vs. 20.5 ( $p<0.001$ ), respectively. All items except "I take a rest during the day" and "I get a flu shot every year" were significantly better in the second period from the statistical point of view, although mean differences were always less than 1 point on the scale. Perception of quality of life was quite similar from the clinical point of view, although statistically worse in the second period (MLWHFQ 30.8 vs. 32.8,  $p=0.03$ ). Differences in treatments at first visit also differed; among others: different use in beta-blocker (61.3% vs. 79.5%,  $p<0.001$ ), ARM (25% vs. 41.5%,  $p=0.001$ ), ICD (4.2% vs. 8.8%,  $p<0.001$ ), CRT (1.4% vs. 4.6%,  $p<0.001$ ) was observed.

**Conclusion:** Although of similar age and sex, patients referred to a multidisciplinary HF Unit between the years 2001-2008 and 2009-2015 differed in multiple items at the moment of admission. Knowledge and understanding of the disease and self-care behaviour seem to be better in the second period, but perception of QOL remained similar.

### P1698

#### Supporting patient's decision making: putting patients in the driving seat

Heart Failure Association of the European Society of Cardiology

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**Background:** Developments in biomedical science and advanced heart failure treatments have resulted in patients facing complex healthcare decisions at different stages in the disease trajectory. Shared decision-making, with its emphasis on patient-centred care, has emerged as a major driver in healthcare policy. Its aim is to empower patients to enable them to be involved in decision-making. This approach requires a partnership between patients and professionals, and the sharing of information. To provide effective support, professionals need an increased understanding of the influences on how patients' make healthcare decisions.

**Purpose:** To explore patients' decision-making in their heart failure management.

**Method:**

A qualitative study using semi-structured interviews with patients recruited from a specialist hospital in the UK who were taking part in a study of gene therapy in advanced heart failure. These data were analysed using thematic analysis.

**Results:** Nine patients with a mean age of 57 years (34 to 74 years), 7 (77%) male, 3 (33%) lived alone, and 5 (55%) symptomatic on mild exertion (NYHA III). Here we report on 3 major themes: symptom relief, "burden" of treatment and information sourcing. Patients' experience of symptom relief influenced their beliefs about their heart failure management. Patients (5 (55%)) who experienced immediate symptom relief from a 'one off' invasive intervention (such as PCI) described a value to these treatments. However, they did not describe the same value to 'ongoing' treatments (such as medication) and where they did not experience an immediate improvement in their functional ability. Patients' decisions were influenced by information from friends, more than professionals and by information that validated their own views. No patient demonstrated understanding of treatment based on heart failure aetiology or LVEF. We noted no difference with age, gender and disease trajectory, but the major limitation was small numbers.

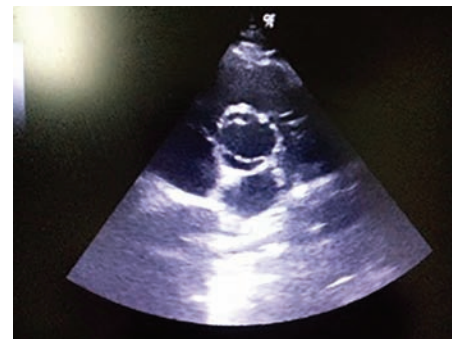
**Conclusion:** Factors that influence patients' health decisions differ according to the impact of the treatment and its ongoing monitoring on their daily life. Patients' decision-making was influenced by friends, symptom relief and treatment burden. These findings have important implications for the way in which professionals provide information about different treatment options and work with patients to support their decision-making. Further exploration in a larger sample and at different stages in the disease progression are required to confirm these provisional findings.

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%



Bicuspid aortic valve

### P1700

#### Trajectory and predominant diagnoses of readmissions after hospitalization for heart failure

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**Background:** Despite the great progress of medicine, the medical and economic problem of heart failure (HF) continue unabated. HF is associated with high mortality and rehospitalization rates. Hospital readmissions worsen patients' quality of life and generates a significant financial burden for the health care system. Aim The aim of the study was to analyze the magnitude, trajectory and cardiovascular causes of 1-year readmissions after heart failure hospitalizations.

**Methods:** The study is a retrospective analysis of all first-time HF hospitalizations reported by 310 Silesian hospitals to the Polish National Health Fund from 2006 to 2014. The HF hospitalizations were selected when any of I50 or I42 or R57 codes according to the International Classification of Diseases (ICD-10) were reported as a main disease at hospital discharge. The main ICD-10 codes of readmissions during following 1-year were obtained, as well as time since discharge to the first any-cause readmission. Results Throughout 9 years (from 2006 to 2014) the 92,348 hospitalizations due to HF were reported. The annual number of 1-year readmissions after hospitalization for heart failure varied between 47.3% and 50.2% across the years. The distribution of readmissions during the first year after hospital discharge was shown on Figure. More than 50% of 1-year readmissions were noted in the first 3 months after discharge. The most frequent causes of readmissions were presented in the Table, with HF as a leading diagnosis (26.8%). Non-cardiovascular diagnosis was found in 42.9% of readmissions. Conclusions The risk of 1-year readmission after hospitalization for heart failure remains high, with more than a half events in the first 3 months after discharge. The predominant diagnoses were heart failure and coronary artery disease.

### P1701

#### Impact of an organized regional STEMI network on heart failure patient characteristics in a heart failure clinic: pre-primary PCI (2001-2008) vs. Primary PCI (2009-2015)

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## POPULATION STUDIES / EPIDEMIOLOGY

### P1699

#### 2.34% is the prevalence of congenital heart diseases in pre-employment echocardiography studies in egyptian adults

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**Objectives:** We investigated the prevalence of congenital heart diseases in pre-employment echocardiography in Egyptian adults.

**Patients and 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 ± 7.45 years). The echocardiogram was normal in 96.2 % of the subjects. The commonest abnormality detected was mitral valve prolapse, accounting 1.5 % of

**Background:** Heart failure (HF) Clinics are key in HF management. Its implementation has become widespread in the past two decades. Advances in drug therapy, devices and coronary revascularization –mainly with the advent of primary percutaneous coronary intervention (PCI)– have become widespread.

**Objective:** To compare the clinical characteristics, treatment and baseline knowledge and self-care of ambulatory patients referred to a HF Clinic of a tertiary university hospital in two admission periods.

**Patients and Method:** Patients were divided in two groups based on their admission date: 2001-2008 (pre primary PCI period: pre-PPCI) vs. 2009-2015 (primary PCI period: PPCI). A regional STEMI network was implanted in Catalonia in the year 2009 (the "Codi IAM" network), which prioritized primary PCI in STEMI.

**Results:** 1921 patients were admitted to the HF Clinic: 960 in pre-PPCI period and 961 in PPCI period. Patients of both periods had similar age ( $66.7 \pm 12.1$  vs.  $66.9 \pm 13.3$ ,  $p = 0.73$ ) and sex (male 70.9% vs. 70.7%,  $p = 0.89$ ). HF duration tended to be higher in pre-PPCI, without reaching statistical significance (median 12 months [IQR 2-48] vs. 6 months [IQR 2-39],  $p = 0.1$ ). We found significant differences in HF aetiology: less ischemic 55.5% vs. 45.8%,  $p < 0.001$ , and more DCM 9.5% vs. 16.5%,  $p < 0.001$  in the PPCI period. Patients with a previous AMI also decreased: 49% vs. 32.3%,  $p < 0.001$ . Patients in pre-PPCI period were in worse NYHA functional class (III/IV 39.3% vs. 22.9%,  $p < 0.001$ ) and had slightly lower LVEF (32.8% vs. 34.9%,  $p = 0.001$ ). Baseline treatments also significantly differed: beta-blocker use (61.3% vs. 79.5%,  $p < 0.001$ ), ARM (25% vs. 41.5%,  $p = 0.001$ ), ICD (4.2% vs. 8.8%,  $p < 0.001$ ), CRT (1.4% vs. 4.6%,  $p < 0.001$ ) were significantly higher in the PPCI period. Self-care behaviour improved in PPCI patients according to the EHF-ScBS (24.8 vs. 20.5,  $p < 0.001$ ), while perception of quality of life did not (MLWHFQ 30.8 vs. 32.8,  $p = 0.03$ ).

**Conclusion:** Patients referred to a multidisciplinary HF Clinic between the years 2001-2008 (pre-PPCI period) and 2009-2015 (PPCI period) differed in multiple items. Lower ischemic aetiology and AMI history may reflex, at least in part, the implementation of a network for the treatment of STEMI using PPCI.

#### P1702

##### The incidence of diabetes mellitus type II in patients with acute coronary syndromes in an urban population during the last decade

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**Introduction:** Diabetes mellitus type II (DMII) has an increasing incidence worldwide, while diabetic patients emerge an increased risk for acute coronary syndromes (ACS). Coronary disease is responsible for the 70-80% of deaths in diabetic patients, while 50% of newly diagnosed diabetics already have cardiovascular disease.

**Purpose:** The purpose of the present study was to evaluate the incidence of DMII in men and women with ACS. The evaluation of this incidence bears both a scientific and social interest taking the fact that the study data were retrieved from the cardiology department of a central Hospital during the period of financial crisis (2008-2012).

**Methods:** This retrospective study included both male and female patients who were admitted in the cardiology department of a general hospital for ACS (acute myocardial infarction, unstable angina) during the last decade (2003-2012). The emergence of DMII was also evaluated in both males and females.

**Results:** A total number of 7280 patients were admitted in the cardiology department of a general hospital between 2003 and 2012 of which 3918 were men and 3362 were women. Among the total male patients 1210 were admitted due to ACS and 362 of them had already been diagnosed with DMII. Among the total female patients 724 were admitted with ACS and 298 of them were diabetic. The above results are demonstrated on Table 1.

**Conclusions:** The above results indicate a high percentage of coexistence of DMII and ACS in both male and female, but the coexistence is more prevalent in men (41%) compared to women (30%) ( $p < 0.005$ ). These observations underline the importance of DMII as a major risk factor for ACS.

A retrospective evaluation of the incidence of DMII in ACS patients in the financial crisis period compared to precrisis period was also performed and showed an increased incidence of coexistence of the two syndromes during the crisis period especially in males ( $P < 0.01$ )

TABLE 1

	ACS	ACS+DMII
MALE	1210	362
FEMALE	724	298
MALE+FEMALE	1934	660

ACS: acute coronary syndromes, DMII: diabetes mellitus type II

#### P1703

##### Effect of heart failure prevention strategy on lifestyle behaviour

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**Introduction:** The St Vincent's Screening To Prevent Heart Failure (STOP-HF) Programme has shown the clinical effectiveness of a HF prevention strategy in individuals at risk for HF. The strategy has proven to be cost effective. Reduction in the cardiovascular and HF endpoints was in part attributed to the use of RAAS modifying in the strategy. Beneficial lifestyle adjustment behaviour might add additional explanation to the success of the STOP-HF Programme. However, the impact of the strategy on lifestyle factors had not been fully examined. Thus, we aim to assess the lifestyle behaviour in the STOP-HF Programme. Method: 739 at risk individuals attending the STOP-HF Programme were included in this analysis. The demographic, characteristic, biomarkers and lifestyle behaviour were recorded. The lifestyle behaviour questionnaires were collected at two-time points, year 2004 and 2010, included smoking, alcohol intake, salt intake, 30-minute walk, and exercise habits. The exercise habit was reported as intensity of exercise by multiplying the frequency with level of exercise. Frequency is determined as times in a week of minimum 20-minute exercise. Level of exercise is graded as 1 (mild), 1.5 (moderate) and 2.5 (strenuous). Comparison within and between study arms was calculated according to appropriate statistical analysis.

**Results:** 350 (65.99 years; 44.86% male) were in control arm and 389 (63.68 years; 54.76% male) in intervention arm. The dominant co-morbidities were hypertension (71.71% vs. 69.67%), ischaemic heart disease (33.72% vs. 36.25%), diabetes mellitus (13.71% vs. 13.11%), and atrial fibrillation (10.57% vs. 12.85%). The BP (144/80mmHg vs. 143/82mmHg), BMI (27 vs. 27), and abdominal girth (38.5inch vs. 39inch) were similar at baseline. Level of BNP (21pg/ml vs. 22pg/ml), cholesterol (5mmol/L vs. 5mmol/L), LDL (2.65 mmol/L vs. 2.6mmol/L) and HDL (1.28mmol/L vs. 1.26mmol/L) were similar. The reduction of total cigarette per day within the intervention arm ( $-1.47 \pm 7.929$ ;  $p = 0.0295$ ) was significant compared to control arm ( $-0.476 \pm 5.934$ ;  $p = 0.5964$ ). Both control arm ( $1.238 \pm 7.89$ ;  $p = 0.0063$ ) and intervention arm ( $1.257 \pm 0.002$ ;  $p = 0.002$ ) showed significant increase in exercise intensity. The 30-minute walk habit did not significantly change within each study arms ( $-0.1466 \pm 3.081$  vs.  $0.0842 \pm 3.351$ ). There were non-significant reduction of total alcohol intake per week in both control arm ( $-2.041 \pm 21.19$ ) and intervention arm ( $-0.1277 \pm 11.87$ ). The change of salt habit at table and during cooking also was not significant.

**Conclusion:** These data demonstrated that despite promising significant changes of reduction in smoking habit and increase in exercise intensity within each study arm, the between study arm changes are not significant. The alcohol intake, salt intake, and 30-minute walk habits did not change significantly. These observations support the initial inference of RAAS modifying therapies role in the positive clinical outcome of STOP-HF Programme.

#### P1704

##### Chronic heart failure and medication adherence in elderly patients: results from heart failure unit, mohamed the 6th university hospital, marrakech, morocco

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**Background:** All research are focusing on the causes and treatment of heart failure, but the variables identifying factors contributing to manage medication are not routinely assessed. This study was conducted to evaluate the factors affecting medication adherence in elderly patients with chronic heart failure.

**Method:** We prospectively evaluated 100 patients, 65 years or older that had been seen with documented congestive heart failure. We included patients who had been taking heart failure medication for longer than 6 months and who were treated at our medical institution for longer than 6 months. Each patient completed a structured questionnaire and an interview survey with same examiner who asked questions and recorded the answers. Therapeutic adherence means that the patient observes the medical recommendations, taking the medication, and maintaining a lifestyle as recommended by his clinician. In our study, we focused on medication adherence.

**Results:** The frequency of medication non-adherence in elderly patients was high (75%). The results showed that daily number of drugs were associated with medication adherence. The medication adherence was significantly lower in patients whose financial state were lower and higher in cases of proper drug storage and in patients with higher self-efficacy (83%), and in case of recognition of the seriousness of heart failure complications. Both poor cognition (Using Mini Mental State) and low education were significantly associated with non-adherence. Among patients, 14% were readmitted within 90 days after discharged for recurrent heart failure. Conclusion : Medication non-adherence lowers the effectiveness of treatments and raises medical costs. Different strategies should be used to increase medication adherence in geriatric heart failure patients, depending on institutions whether they are treated.



**P1705**

**External validation of the Redin-SCORE in a contemporary cohort of outpatients with advanced heart failure**

This work was supported by Red de Investigación Cardiovascular (RD12/0042/0002), Instituto de Salud Carlos III and FEDER  
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**Background:** There are many tools to stratify the prognosis of patients with heart failure (HF), however most of them are not usually validated in other populations to prove their real clinical utility. Recently, the Redin-SCORE was proposed to predict 1-month and 1-year risk of HF-readmission of ambulatory patients.

**Purpose:** To validate the Redin-SCORE in a contemporary cohort of outpatients with advanced HF.

**Methods:** A cohort of 240 ambulatory patients with HF was prospectively followed in a tertiary HF clinic during the 2012-2014 period. The discrimination ability was validated using the C-statistics. The Redin-SCORE used six variables: left signs of HF, heart rate higher than 70 beats/min, hemoglobin less than 120/130 g/L (women/men), NT-ProBNP higher than 1000 ng/L, estimated GFR less than 60 ml/min/m<sup>2</sup> and atrial size higher than 26 mm/m<sup>2</sup>.

**Results:** Table resumes the main characteristics of both populations. Compared with the Redin-SCORE sample, patients of the validation group showed: a) less history of ischemic heart disease, b) less prevalence of diabetes, c) higher rates of atrial fibrillation, and d) better left ventricular ejection fraction. The 1-month (5.4 vs 3.1%; p=0.055) and 1-year (29.5 vs 16.9%; p<0.001) HF readmission rates were higher in the validation cohort, but only the last reached statistically significant difference. The C-statistics for 1-month and 1-year risk remained consistent after the application of homogeneity test (0.77 vs 0.72, p=0.477; 0.70 vs 0.66, p=0.417, respectively).

**Conclusions:** The Redin-SCORE is a useful tool to predict the short- and long-term risk of HF-readmission after the external validation in a more complex cohort of advanced HF outpatients.

**Clinical characteristics**

	Redin-SCORE (n = 2507)	Validation cohort (n = 240)	p-value
Age, years	66.7 (12.9)	66.6 (13.3)	0.911
Male, n (%)	1731 (69%)	165 (69%)	0.924
Ischemic heart disease, n (%)	1192 (48%)	76 (32%)	<0.001
Hypertension, n (%)	1700 (68%)	175 (73%)	0.132
Diabetes, n (%)	1058 (42%)	85 (35%)	0.037
Atrial fibrillation, n (%)	589 (24%)	91 (38%)	<0.001
Estimated GFR<60 ml/min/m <sup>2</sup> , n (%)	1127 (45%)	105 (44%)	0.704
III NYHA class, n (%)	983 (39%)	99 (41%)	0.537
LVEF, mean (SD)	35.7 (14.6)	40.6 (17.2)	<0.001
1-month HF-readmission rate, n (%)	78 (3.1%)	13 (5.4%)	0.055
1-year HF-readmission rate, n (%)	424 (16.9%)	70 (29.5%)	<0.001

**P1706**

**Clinical characteristics and outcomes of young adults hospitalised with heart failure in Asia**

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**Introduction:** Our understanding of heart failure (HF) in younger patients is limited. No previous studies have examined the demographics and outcomes of young Asian adults with HF.

**Purpose:** This study sought to compare the characteristics and outcomes of young versus old Asian adults hospitalised with HF. Methods We prospectively collected data on 1828 consecutive admissions with a primary diagnosis of HF to an urban hospital from 2010 to 2013. Diagnosis of HF was based on Framingham criteria and NTproBNP. All hospitalisations and deaths within 1 year were recorded. Patients were categorised into 4 age groups: <50, 51-65, 66-76, >75. Means were compared with a t-test and proportions with a z-test. Results The youngest patients (<50 years of age) were more likely to be male and of Malay ethnicity. Younger patients had fewer comorbidities than their older counterparts. On admission, younger patients were more likely to have paroxysmal nocturnal dyspnea and orthopnea, but less likely to have rales than older patients. Left ventricular ejection fraction and NTproBNP were lowest in the youngest group at (27% vs 42%, p<0.05) and (5272 v 6958pg/ml, p<0.05) respectively. At 1 year, HF readmission rate was similar in all age

groups. Increasing age was associated with a greater burden of non cardiovascular (CV) admissions and higher mortality.

**Conclusions:** Young Asian patients show marked differences in symptoms and signs of HF compared with their older counterparts. Despite younger patients having lower rates of 1 year mortality and non-CV readmission, all age groups had similar rates of HF hospitalisation at 1 year, this disparity warrants further investigation.

**Characteristics and outcomes**

	≤50 years (n = 168)	51-65 years (n = 547)	66-75 years (n = 430)	> 75 years (n = 683)	p-value (≤50 vs > 75)
Female (%)	26.2	22.5	41.2	58.7	< 0.05
Chinese (%)	46.4	45.7	59.3	66.2	< 0.05
Malay (%)	35.7	36.7	27.0	22.3	< 0.05
Ischemic heart disease (%)	45.8	68.6	71.5	71.9	< 0.05
Previous stroke (%)	6	12.6	15.6	21.7	< 0.05
Paroxysmal Nocturnal Dyspnea (%)	46.4	35.5	33.7	25.8	< 0.05
Orthopnea (%)	68.5	56.5	54.9	44.5	< 0.05
Rales (%)	64.9	73.7	75.6	79.6	< 0.05
All-cause death 1 year (%)	8.8	11	14.8	23.2	< 0.05
Non cardiovascular admissions 1 year (%)	13.7	18.5	22.1	24.7	< 0.05
Heart failure readmission 1 year (%)	31.0	31.3	31.6	30.9	n.s.

n.s. - not significant

**P1707**

**Trends in heart failure hospitalizations, patient characteristics, in-hospital and 1-year mortality: a population study, from 2000 to 2012.**

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**Background:** Heart failure (HF) is the main medical cause for hospital admission. This study was undertaken to evaluate trends in HF hospitalizations (HFH), in-hospital and 1-year mortality, across 13 years in the largest Italian region.

**Methods:** Hospital discharge forms recorded in the regional healthcare system database from 2000 to 2012, with HF-related diagnosis according to the Agency for Healthcare Research and Quality (AHRQ) and/or to the Center for Medicare/Medicaid Services, Hierarchical Condition Categories (CMS-HCC) criteria, were analyzed with respect to age (y,18-74; 75-84; 85+) and gender. Based on the combination of all ICD-9 CM codes, three Groups (G) were identified: in summary, G1 included most acute HF episodes with primary cardiac diagnosis; G2, included primary/secondary cardiomyopathy without acute HF codes; G3 included mixed non-cardiac conditions with HF as secondary diagnosis. Pts experiencing an HFH since 2005 without prior (2000 to 2004) admissions were analyzed as incident cases.

**Results:** 699797 HFH occurring in 370538 adults were evaluated. Regarding all HFH episodes, 70% were classified as G1, 17% as G2, and 13% as G3. Groups were different in terms of gender (F 34% in G2 vs 50% in G1 and 51% in G3, p<.0001) and age (mean age G1: F 80 ± 10, M 74 ± 11y; G2: F 73 ± 13, M 69 ± 12y; G3: F 82 ± 9, M 77 ± 10y, p<.0001 both for F and M). Annual HFH number (average 53830) and in-hospital mortality (9.4%) did not change over the years, the latter being associated with age (M: 18-74y, 5.19%; 75-84y, 10.07%; 85+y, 17.54%, p<.0001; F: 18-74y, 5.19%; 75-84y, 8.87%; 85+y: 15.18%, p<.0001) and with diagnosis Group (G1 9.1%, G2 5.6%, G3 15.9%, p<.0001). One-year mortality (28.4%) was also stable over time. New, incident cases from 2005 to 2012 were 216782 (F 51%, M 49%), with decreasing incidence (3.62 [IC 3.58-3.67] to 3.13 [IC 3.09-3.17] per 1000 adult inhabitants/y, p<.0001), and with higher proportion of 85+y pts (22.3% to 31.4%, p<.0001, Cochran-Armitage trend test) over the years. Among incident cases, distribution of diagnosis Groups and differences between Groups in terms

of gender, age, and in-hospital mortality paralleled those observed in all the hospitalizations, 2000 to 2012. However, mortality lowered over time in 18-74y incident cases, both in-hospital (5.15% to 4.36%,  $p < .0001$ ) and at 1-year (14.8% to 12.9%,  $p = .0006$ , Cochran-Armitage trend test). Inferences. While the overall burden and short to mid term mortality of HFH appear stable over the years, the analysis of incident cases, 2005 to 2012, shows favourable changes: lower incidence, higher age at first hospitalization, and higher discharge rate and 1-y survival in pts aged 18-74y, possibly reflecting improvements in heart failure prevention and management both in the acute and chronic setting.

#### P1708

##### Poor heart failure epidemiology knowledge due to incomplete clinical diagnosis at discharge. Analysis of administrative data of a nationwide population

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**Introduction:** Heart failure (HF) is a common diagnosis in hospital, whose correct encoding at discharge (primary and secondary diagnoses) is relevant to obtain accurate epidemiological information, which could improve HF knowledge and management.

**Purpose:** To evaluate the current HF encoding quality in all hospitals in Spain. **Methods:** All the discharges from Spanish hospitals corresponding to 2012-2013 with a primary diagnosis of HF, according to the ICD-9-CM classification were analyzed. HF was encoded as: systolic (HF-ref), diastolic (HF-pef), systolic and diastolic (HF-both), hypertensive disease with HF (HF-hyp) and HF unspecified (HF-uns). We also considered the departments where patients were admitted: Cardiology, Internal Medicine, Geriatrics, Emergency service and others.

**Results:** 400,861 hospital admissions were recorded, 77,652 with HF as primary diagnosis. The frequency of each diagnosis was: 59,531 HF-uns (76.7%), 11,581 HF-hyp (14.9%), 4,241 HF-ref (5.5%), 1,752 HF-pef (2.3%) and 547 HF-both (0.7%). HF admissions were mainly in Internal Medicine (60.08%), and then Cardiology (21.51%), Emergencies (7.29%), Geriatrics (3.36%) and other services (7.76%). HF accounts for 14.3% and 48.73% of all cardiovascular diagnoses at discharged in Cardiology and Internal Medicine, respectively, and up to 61.28% in Geriatrics and 61.35% in Emergencies. Surprisingly, 47.3% and 45.8% of HF-ref as primary or secondary diagnosis was established at discharged in Cardiology and Internal Medicine, respectively, which shows a homogeneous distribution of these patients in the two specialties. In contrast, only 22.9% of HF-pef diagnoses came from Cardiology vs. 65.4% from Internal Medicine.

**Conclusions:** The inaccurate HF diagnosis at discharge leads to an unacceptable high percentage of HF unspecified codification. Cardiology and Internal Medicine have almost the same proportion of total HF-ref diagnoses.

## EXERCISE TESTING & TRAINING

#### P1709

##### Motivation and daily physical activity in heart failure patients - a cross sectional pilot study

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**Background:** Patients with heart failure (HF) might find it difficult to perform physical activity. One reason for physical inactivity is different barriers that the patients need to overcome to get a more active lifestyle. One of the barriers is lack of motivation. Motivation includes advice from healthcare workers, influence from the family, physical and motoric improvement, health benefits and psychosocial reasons.

**Purpose:** The aim of this study was to investigate motivation and exercise capacity in HF patients. **Methods:** A cross-sectional explorative study was conducted in a university hospital in Israel, including 18 HF patients (mean age 60, 72% male, 56% NYHA class  $\geq$  II, mean ejection fraction 31%). To measure motivation towards physical activity, the Exercise Motivation Index Questionnaire was used which is a valid and reliable tool for investigating how the patient is influenced by different motivation to exercise, such as physical, psychological and social aspects. Scores

range from 0 to 4, where a score of 3-4 is considered as high motivation. Data on steps walked was collected using an activity monitor. **Results:** The motivation "I want to be healthier and perhaps live longer" was high rated by all patients (100%) and "I want to develop stamina and feel strong" was reported by 89% of the patients. "Working out in groups or with others is fun" had the lowest rate, rated by 39% of the patients as a high motivation. The motivations are divided in three different subscales and a total motivation. Physical motivation was the most important motivation for the patients, with a score within the range of high motivation (score 3,35). The least important motivation was the social motivation (score 2,58), with a score below the range of high motivation. There is a strong negative correlation between social motivation and total amount of steps walked ( $r = -0.91$ ,  $p = 0,03$ ).

**Conclusions:** The most important motivation for the patients to perform physical activity is to become healthier and live longer as well as to feel stronger and develop stamina. They also consider it important to have more control over their lives. These results need to be confirmed in a larger study, however they can be seen as a first step in the development of future intervention to motivate HF patients to be active.

#### P1710

##### Effects of aerobic interval training on quality of life and on exercise capacity in patients with heart failure and CRT

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To evaluate the long-term effects of aerobic interval training on quality of life and on exercise capacity in patients with ischaemic heart failure and CRT. **Methods:** 58 patients were enrolled, 30 pts- in the aerobic training group (TG) and 28 pts - in control group (GP). 30 patients with ischaemic heart failure and CRT performed 24-month individualized aerobic training program. All patients performed a symptom-limited cardiopulmonary exercise test (CPET) on a treadmill with gas exchange system "Oxycon Pro" (Germany) initially and after 24 months. We measured oxygen uptake at exercise peak (VO2peak). All patients were evaluated with the MLHFQ at baseline and in 24 months.

**Results:** At baseline VO2peak were similar in TG and CG, 13,5+/-0,9 ml/min/kg and 13,6+/-1,2 ml/min/kg, respectively ( $p_{VO2peakTG-CG} = 0,09$ ). Also at baseline MLHFQ scores in both groups not differ, 64  $\pm$  1,3 and 62  $\pm$  2,0 ml/min/kg, respectively ( $p_{VO2peakTG-CG} = 0,07$ ). Patients of TG were trained 40 minutes every day on treadmill with individualized exercise intensity, every month after control CPET exercise intensity was increased gradually. Before and after training 5 minutes morning exercises were made. After 24 months VO2peak and MLHFQ scores were better in TG than in CG. VO2peak in 24 months were 21,5+/-1,1 ml/min/kg and 14,6+/-1,2 ml/min/kg, respectively ( $p_{MLHFQTG-CG} < 0,01$ ). MLHFQ scores in 24 months were 43,2  $\pm$  2,5 and 55,6  $\pm$  2,8 respectively ( $p_{MLHFQTG-CG} < 0,01$ ).

**Conclusions:** Participation in a 24-month individualized aerobic training program resulted in significant improvements in exercise capacity and quality of life in patients with ischaemic heart failure and CRT.

#### P1711

##### Predictors of low functional capacity in moderate-severe left ventricular systolic dysfunction patients included in a cardiac rehabilitation program.

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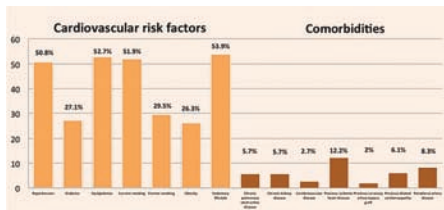
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**Introduction:** Cardiac rehabilitation programs (CRPs) in left ventricular systolic dysfunction (LVSD) patients (p.) provide optimal medical treatment (OMT), close monitoring, exercise, education and counselling. LVSD has been considered an important predictor of low functional capacity (FC). Our purpose was to describe predictors of low FC in moderate-severe LVSD p. performing a CRP.

**Methods:** We made an observational retrospective study including p. with moderate-severe LVSD admitted to a CRP between 2006 and 2015. Physical training, OMT, medical counselling, education, and smoking cessation support, were supplied for 8 to 10 weeks. Left ventricular ejection fraction (LVEF) was assessed before and after the program using TTE. FC was tested before and after the CRP in accordance with the NYHA Classification, besides a treadmill stress test (TST). Exercise capacity (EC) was reported in METs.

**Results:** A total of 298 p. were included, mean age 58.1  $\pm$  11.2 years, male 89.6%. Baseline characteristics are shown in graphic 1. In most p. (91.2%), cardiac rehabilitation was due to a recent acute coronary syndrome. No statistically significant differences depending on the previous cardiovascular risk factors (CVRF) and comorbidities among moderate (LVEF 30-40%) and severe (<30%) LVSD p. were found. Medical therapy when starting the program showed a significantly higher use of MRAs, diuretics and anticoagulants in severe than moderate LVSD p. ( $p = 0.007$ ,  $p < 0.001$ ,  $p = 0.032$ ; respectively), with no other differences among them. FC assessed by NYHA class, considering class I vs class II or III p., revealed significant differences in hypertension, diabetes and current smoking. Severe LVSD p. had a

higher NYHA class than moderate LVSD p. before(II-III: 74.1% vs 46.4%;  $p < 0.001$ ) and after the program(41.5% vs 17.3%;  $p < 0.001$ ). NYHA II or III was associated with a higher prevalence of comorbidities: chronic pulmonary obstructive disease(CPOD), cerebrovascular disease(CD) and peripheral artery disease(PAD). P. who had low EC( $< 7$  METs) had significantly more CVRF. Severe LVSD p. had a lower EC than moderate LVSD p. before( $5.7 \pm 2.8$  vs  $6.9 \pm 2.6$ ;  $p < 0.001$ ) and after the CPR( $9.4 \pm 2.8$  vs  $10.4 \pm 2.7$ ;  $p = 0.008$ ). Regarding comorbidities, a worst EC was associated with a higher prevalence of chronic kidney disease, CD and a non-significant trend of CPOD. The dropout rate was superior in p. with low EC(13.9% vs 5.6%;  $p = 0.027$ ), not depending on NYHA(8.9% vs 10.9%, NS). **Conclusions:** Severe LVSD p. included in a CRP have a lower FC and EC than moderate LVSD p.. Previous CVRF and comorbidities in moderate and severe LVSD p. associate a lower FC and EC regardless of their LVEF.



CVRFs and comorbidities prevalence

**P1712**

**Predictors of post-rehabilitation exercise capacity in heart failure patients**

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The aim of this study was to determine predictors of exercise capacity after exercise training rehabilitation in heart failure patients. Methods. We evaluated 85 hospitalized patients 41-68 years old, mean age  $53 \pm 1.8$ , 65 men, with HF NYHA class III, ejection fraction (LVEF)  $40.8 \pm 0.3\%$ . All patients performed a symptom-limited cardiopulmonary exercise test (CPET) on a treadmill with gas exchange system "Oxycon Pro" (Jaeger, Germany) initially and after 6 months. We measured oxygen uptake at lactate threshold (VO<sub>2</sub>LT), pH-threshold (VO<sub>2</sub>pH-T) and at exercise peak (VO<sub>2</sub>peak). 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 HCO<sub>3</sub>- concentration were estimated using analyzer i-STAT, cartridge CG4 (Abbot, USA). Lactate threshold (LT) and pH-threshold (pH-T) were determined by changes in pH and lactate levels in correlation with dynamics of oxygen uptake (VO<sub>2</sub>), carbon dioxide output (VCO<sub>2</sub>), minute ventilation (VE), ventilatory equivalent of carbon dioxide (VE/VCO<sub>2</sub>), respiratory exchange ratio (RER). All patients underwent physical rehabilitation program (PRP), calculated based on individualized approach of exercise physiological stages: lactate threshold and pH-threshold, that characterized the biological reserves of adaptation to physical activity. Meta-regression used to assess the association between exercise capacity and various factors.

**Results:** Variants, such: age, aetiology of heart failure, diabetes, ACE-inhibitors and  $\beta$ -blockers therapy, tachycardia, low blood pressure, low body mass index, marked elevation of BNP, creatinin, bilirubin, anemia, hyponatriemia, low left ventricular ejection fraction, restrictive mitral filling pattern had no influence on exercise capacity after physical rehabilitation. MLHFQ score at baseline ( $p < 0,01$ ), length of heart failure ( $p < 0,01$ ), exercise intensity ( $p < 0,05$ ) were found to be significantly associated with VO<sub>2</sub>max.

**Conclusion:** Lower MLHFQ score at baseline, longer duration of heart failure and higher exercise intensities were associated with a greater level of post-rehabilitation exercise capacity.

**P1713**

**Usefulness of exercised-based cardiac rehabilitation in heart failure patients after myocardial infarction**

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Chronic heart failure (CHF) is highly prevalent in myocardial infarction survivors and is a major cause of morbidity, mortality an re- hospitalizations Cardiac rehabilitation (CR) exercise training and CHF self-care counseling have each been shown to

improve clinical status and clinical outcomes in CHF. The aim of this study was to evaluate the usefulness of exercise based in house cardiac rehabilitation in patients with left ventricle dysfunction after myocardial infarction

**Patients and methods:** Out of 1854 patients who were admitted to our three weeks in- hospital rehabilitation program, we analyze a total of 189 patients who were admitted early after coronary revascularization (percutaneous coronary interventions or coronary bypass surgery) with ejection fraction below 40%. The majority of patients were males (62%). The oldest patient was 82 years of age. Ejection fraction below 25% was detected in 40%. We noted risk factors and co morbidities. Patients were selected for exercise training after six minute walking test (82%) or cardiopulmonary exercise test. After 3 weeks in hospital cardiac rehabilitation the patients were re-tested.

**Results:** The major comorbidities in our patient population were as follows: diabetes, hypertension and previous stroke. Six minutes walking test was performed and the total distance walked ranged from 180 to 380 meters and the beginning of the program. Patient had 7 -days a week training program. After the 3 weeks in hospital exercise rehabilitation the improvement in the test was ~35%. Cardiopulmonary test showed also improvement of functional capacity. We noted several rhythm disturbance complications by telemetry (VT, VES, SVES, and new on set of AF) and when needed the amiodaron or beta blockers were added. Also we noted silent ischemia in 13% after CABG with ST segment depression detected by telemetry. None had acutisation of chronic heart failure (with peripheral edema and congestion). All patients fulfilled cardiac rehabilitation program.

**Conclusions:** The study showed usefulness and safety of exercised -based in-hospital cardiac rehabilitation program. Supervised multidisciplinary cardiac rehabilitation program, including an individualized exercise component is safe and can improve functional status and exercise tolerance in patient with left ventricle dysfunction after myocardial infarction

**P1714**

**Power spectral analysis of heart rate variability during the postural change from sitting to upright position reveal sympathetic hyperactivity**

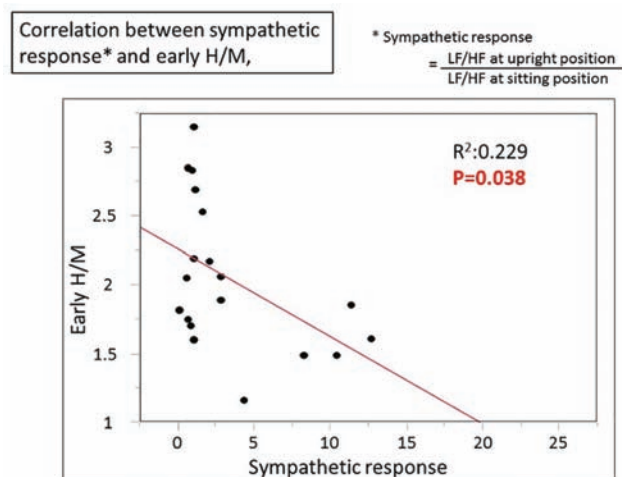
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**Background:** Power spectrum analysis (PSA) of heart rate variability (HRV) is a noninvasive technique providing a dynamic assessment of sympathetic tone.

**Methods:** We evaluated sympathetic activity with PSA of HRV of 105 CHF patients, such as coefficient of variation of RR intervals (CVRR), low-frequency (LF), high-frequency (HF) component during postural change from sitting to upright position. We compared parameters from PSA and clinical characteristics, exercise parameters from CPET, and index of MIBG scintigraphy.

**Results:** There were no significant correlation between sympathetic activity parameters and patient clinical characteristics. MIBG scintigraphy was performed in 19 patients, and early H/M was significantly correlated with sympathetic response calculated LF/HF at upright position divided by LF/HF at sitting position ( $R = 0.48$ ,  $p = 0.038$ ).

**Conclusion:** PSA of HRV during postural change might reveal sympathetic hyperactivity which is obscure at rest.





## P1715

### Chronotropic Incompetence and dynamic post-exercise autonomic dysfunction are associated with the presence and severity of erectile dysfunction

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**Introduction-Purpose:** In men with erectile dysfunction (ED), exercise stress testing (EST), while principally important to detect coronary artery disease, it is also essential to define cardiovascular (CV) risk through evaluation of maximal exercise capacity and autonomic pathologies. Aim of this study was to investigate the association between ED and EST parameters.

**Methods:** 180 ED patients and 50 men without ED underwent maximal EST. Exercise parameters including exercise capacity (metabolic equivalents, METS), peak exercise time, heart rate (HR) at 6 METS, peak exercise, HR recovery (HRR) at 1 and 2 min and chronotropic index (CI) were evaluated in all individuals. Endothelial function was evaluated with brachial flow-mediated dilatation (FMD).

**Results:** Table shows EST parameters of the two study groups. ED patients had lower peak exercise time and exercise capacity ( $P < 0.001$ ) and reduced CI ( $P < 0.01$ ) compared to men without ED. There was a significant association of ED severity with exercise duration, peak workload, HRR 2 minutes after exercise, and CI (all  $P < 0.05$ ). There also was a positive correlation of HRR and CI with FMD (all  $P < 0.05$ ).

**Conclusions:** This study shows interrelationships between exercise capacity, HRR, CI and ED. Abnormal HRR and CI are associated with systemic endothelial dysfunction. These findings elucidate pathophysiological links and may have important implications for the estimation of CV risk in ED patients.

TABLE

Exercise parameters	noED n=50	n=180	P value
Systolic BP base (mmHg)	130 ± 13	127 ± 15	0.18
Diastolic BP base (mmHg)	82 ± 10	80 ± 9	0.22
HR base (bpm)	80 ± 10	76 ± 13	0.10
Maximal Systolic BP (mmHg)	187 ± 28	180 ± 25	0.15
Maximal Diastolic BP (mmHg)	86 ± 11	85 ± 10	0.34
Maximal HR (bpm)	157 ± 18	153 ± 16	0.07
dHR (peak exercise)	73 ± 20	78 ± 18	0.03
HRR, 1 min (bpm)	29 ± 4	26 ± 5	0.55
HRR, 2 min (bpm)	49 ± 15	46 ± 15	0.32
CI	0.90 ± 0.19	0.83 ± 0.19	0.008
Exercise duration (sec)	613 ± 140	545 ± 120	< 0.001
METs	11.8 ± 2.4	10.7 ± 2.3	< 0.001

## P1716

### Reproducibility of 6-minute walk test in hemodialysed heart failure patients

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**Background:** Six minute walk test (6MWT) is one of established performance-based measures of functional capacity in heart failure (HF) patients.

**Purpose:** We wanted to evaluate reproducibility of 6MWT and its correlation to basic echocardiographic and laboratory parameters in patients with heart failure treated with chronic hemodialysis.

**Methods:** Chronic hemodialysis patients walked the 6MWT after three consecutive hemodialysis sessions. On the first test day, blood was taken for laboratory testing and echocardiographic imaging was performed. We tested reproducibility of 6MWT and its correlation with laboratory and echocardiographic parameters in both groups of patients (HD patients with chronic HF and general population of HD patients). Reproducibility of 6MWT was evaluated with interclass correlation and multivariate regression was used to establish potential correlation of walking distance in 6MWT with laboratory and echocardiographic parameters.

**Results:** We tested 29 hemodialysis patients (59% men, mean age 64.5 ± 12.6 years, 90% with arteriovenous fistula, 10% with central venous catheter, mean

NTproBNP 1403 ± 1306 pg/ml, mean 6MWT distance 355 ± 88 m), of which 22 (76%) had chronic heart failure (50% men, mean age 65.5 ± 11.7 years, mean NTproBNP 1425 ± 1226 pg/ml, 91% with arteriovenous fistula, 9% with central venous catheter, 45% had heart failure with reduced ejection fraction, mean 6MWT distance 355 ± 90 m). Reproducibility of 6MWT was high in both groups of patients (HD patients with HF: IC 0.964, 95% CI 0.913-0.985,  $p = 0.000$ ; general HD population: IC 0.964, 95% CI 0.927-0.983,  $p = 0.000$ ). None of the echocardiographic (LVEF, VTI, LVEDV, LVEDVI, LVESV, LVESVI, E/A, E/Em, Em, Sm) or basic laboratory parameters (NTproBNP, troponine T, hemoglobin) correlated with 6MWT distance.

**Conclusions:** The 6MWT has excellent reproducibility patients with heart failure treated with chronic hemodialysis. We found no significant correlation of 6MWT distance with echocardiographic or laboratory parameters.

## P1717

### The usual physical activity predicts mortality in elderly patients with advanced heart failure.

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**Objectives:** to evaluate the role of usual physical activity (PASE) on mortality in elderly patients with advanced heart failure (HF).

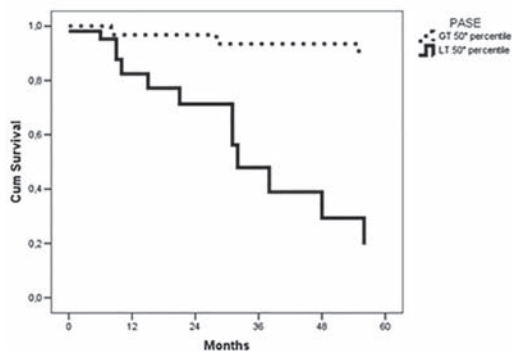
**Methods and Results:** 216 elderly patients (≥65 years) consecutively admitted to Cardiac Rehabilitation soon after HF decompensation, between January 2009 and July 2010 were enrolled. Mortality was collected in October 2015. Age, sex, NYHA class, Comorbidity by Cumulative Index Rating Scale (CIRS), Frailty by means of Fried criteria, 6-minute walk test (6-MWT), Barthel Index (BI), Geriatric Depression Scale (GDS), Mini Mental State Examination (MMSE), Physical Activity Scale for the Elderly (PASE) were measured. The mean age was 74 ± 6.1. Previous infarction and angina were present in 54.3%, 14.3% have had PTCA. The value of CIRS was 2.1 ± 0.6, BI of 69.6 ± 23.4 and PASE 53.1 ± 23.4. Cognitive impairment (MMSE < 24 was present in 32.1% while depression (GDS ≥ 5) in 48.6%. The prevalence of frailty was 61.1%, 6-MWT at entrance was 194.8 ± 104.8 meters and difference in meters between entry and discharge was 58.4 ± 60.2 96 (44%) patients died after a follow-up of 44.1 ± 21.1 months. Cox regression analysis showed that PA usually held in the week before the HF instabilization, measured with PASE, predicts mortality independently by frailty, CIRS, BI, MMSE, GDS, 6-MWT at entry and delta 6-MWT.

**Conclusions:** Advanced HF patients were characterized by high mortality, co-morbidity, disability and frailty. Low level of PA predicts mortality regardless of comorbidity, disability, cognitive function and depression.

Predictors of mortality in advanced HF

Variable	HR	95%CI	p
Age	0.910	0.822-1.008	0.072
Frailty (≥ 3)	6.692	1.293-30.608	0.023
CIRS	2.504	1.058-5.926	0.004
MMSE	1.008	0.923-1.101	0.854
GDS	1.109	0.888-1.386	0.049
PASE	0.983	0.967-0.998	0.031
6MWT	1.011	1.004-1.018	0.001
Barthel Index -at entry	0.928	0.895-0.962	0.027
Barthel Index - at dismissal	0.920	0.869-0.973	0.003
Delta 6MWT	0.999	0.993-1.006	0.852

CIRS=Cumulative Index Rating Scale, MMSE=Mini Mental State Examination, GDS=Geriatric Depression Scale, PASE=Physical Activity Scale Elderly, 6-MWT=Six minute walking test, Delta 6MWT=Difference in meters between dismissal and entry.



Pase and Mortality in advanced HF

**P1718**  
**Regional differences in exercise training implementation in heart failure: subanalyses from the ESC ExtraHF survey**

Unrestricted grant from the Heart Failure Association  
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**Introduction:** Exercise training programmes (ETPs) are crucial component in cardiac rehabilitation to help heart failure (HF) patients to recover and to stay healthy. Despite this, ETPs are not routinely implemented for HF patient. We performed a sub-analysis from the data of the ESC ExtraHF survey to investigate the presence of regional variation in use of ETPs for HF patients

**Purpose:** To investigate the presence of geographical difference in ETP availabilities, modalities, structure characteristics, and to identify the specific barriers in implementation.

**Methods:** The study was designed as a web-based survey of cardiac units in countries affiliated to the ESC. The data collected were subsequently divided in five areas, according to the UNO division of the countries involved: Northern, Southern, Eastern and Western Europe, and extra European.

Results 172 centers replied to the survey, in charge of 78,514 patients: Northern 52 centers, 15040 patients, Southern 48 centers, (27127 patients), Western Europe 34 centers, (11769 patients), Eastern Europe 24 centers, (12748 patients), ESC countries extra-Europe 14 centers, (11830 patients). Larger rate of ETP implementation was detected in the Western (76%), Northern (63%), with lower rates in Southern (58%), Eastern (50%) and ExtraEurope (36%) regions. The leading barrier reported was lack of resources in all areas but in Western region where the patients are admitted to another cardiac rehabilitation programme (Table 1) In 40 % of the cases, the non-inclusion of the ETP in the national or local guideline pathway was responsible for lack of implementation

**Discussion:** A highly recommended therapeutic tool is still poorly implemented in Europe, mainly due to lack of resources, but not in western Europe where patients had the benefit to be referred to other Centers for ETP. The fact that ETP is frequently not included in the local or national guideline pathway needs a more active role from the Scientific Organization such as HFA of the ESC

Table 1

	Northern	Southern	Western	Eastern	Extra-Europe
N° of Centers, patients	19 6677	20 13743	8 4350	12 5370	9 6870
Primary cause	Lack of resources (68%)	Lack of resources (65%)	Admission to another ETP (75%)	Lack of resources (83%)	Lack of resources (78%)
Secondary cause	Admission to another ETP (42%)	ETP not included in national/local guideline (40%)	Lack of resources (37%)	ETP not included in national/local guideline (41%)	ETP not included in national/local guideline (66%)

In Table 1 are depicted the two major causes of not implementation of ETP among the five ESC-areas. The % is over the 100% because multiple answers were admitted.

**P1719**  
**Additional criteria of urgency of heart transplantation for patients in UNOS-2 status according to spiroergometry stress testing**

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**Background:** There is significant mismatch between the demand for heart transplantation (HT) and the number of donor hearts. That's why development of additional selection criteria for patients placed in the "waiting list" in status UNOS 2 is very important now.

**Objective:** to develop the algorithm for selection of stable patients with severe heart failure (HF) for heart transplantation based on spiroergometry stress test's results.

**Methods:** We studied 32 patients with HF NYHA III-IV, 30 (94%) - male, 2 - female, average age was 46,4 ± 12,1 years. 19 (60%) of 32 patients had ischemic cardiomyopathy, 9 (28%) - dilated cardiomyopathy, two (6%) - rheumatic heart disease, 2 (6%) - congenital valve diseases. During the follow-up of 1 year, 3 (9%) of 32 patients died, HT was performed in 8 patients (25%), in others 2 mechanical assistant devices were implanted, in 2 - cardiac resynchronization devices were implanted. In other 10 (31%) pts optimization of medical therapy led to decreasing of HF symptoms and they were removed from the "waiting list". We used cardiopulmonary bicycle ergometry test (BET) to estimate not only common used predictors of mortality such as tolerance to physical loading and maximal oxygen consumption (VO2max) but also other criteria of ventilation such as carbon dioxide production relationship (VE/VCO2 slope), time of aerobic threshold destination, oxygen consumption at time of aerobic threshold destination etc. Based on al revealed in BET data we created enough accurate mathematical model of survival and death prediction during 1 year. BET was performed in vertical position of the patient using stress ergometry system 'Schiller AG' AT-104 ErgoSpiro. We started from 25 Wt with increasing in load power every 3 minutes at 25 Wt until maximal tolerated level of dyspnea appeared.

**Results:** We established additional criteria of death during 1 year based on BET results. These criteria were: the maximal oxygen consumption VO2max <30% of expected; VD/VT (ratio of physiologic dead space over tidal volume) increasing during the test; maximal tolerance to physical loading ≤50 Wt and/or <20% of expected. We used mathematical factor analysis (principal component analysis) to create predictive survival model. Sensitivity of death prediction was 100%. Based on above mentioned predictive model we created new algorithm of recipient's selection for HT using 'R' software

PROGNOSIS

**P1720**  
**Two-year follow-up of patients with acute myocardial infarction with ST elevation and new onset atrial fibrillation in relation to fibrinolytic therapy or primary PCI**

This study was supported by the program grant of the Ministry of Science of Montenegro.  
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**Purpose:** Patients with acute myocardial infarction with ST elevation (STEMI) have many complications and new-onset atrial fibrillation (AF) is one of them. The aim of the study was to evaluate the prognosis of patients with STEMI and new onset AF during the 2-year follow-up in relation to fibrinolytic therapy or primary PCI.

**Methods:** We enrolled 290 patients with STEMI 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 primary PCI (PPCI) group included patients with STEMI treated with primary PCI and fibrinolytic group included patients with STEMI treated with fibrinolytic therapy during the hospital course. The patients were followed up for two years with visits every 6 months.

**Results:** We included 290 patients with STEMI, 53 patients were treated with primary PCI (18.28%) and 209 patients (72.07%) were treated with fibrinolytic therapy, the minority of 28 patients (9.65%) were not treated either with PPCI or either with fibrinolytic therapy. There was no significant difference in mean age, male/female ratio and BMI between patients treated with PPCI and patients treated with fibrinolytic therapy. In the PPCI group there were 4 patients (7.55%) with AF and in the fibrinolytic group there were 17 patients (8.13%) with AF, p>0.05. During the hospital course died 1 patient (1.89%) in PPCI group without AF and 7 patients (3.35%) in fibrinolytic group, 1 of them with AF and 6 without AF, p>0.05. During the follow up period died 3 patients (5.66%) in PPCI group, 1 patient (1.89%) with AF and 2 patients (3.77%) without AF versus 23 patients (11.00%) in fibrinolytic group, 6 of them (2.87%) with AF and 17 patients (8.13%) without AF, p>0.05. After all, mortality was 7.55% in PPCI group vs. 14.35% in the fibrinolytic group, p>0.05.

**Conclusions:** There was no difference in incidence of new-onset AF in STEMI patients in relation to fibrinolytic therapy or PPCI. Mortality was lower in PPCI group (7.55%) then in fibrinolytic group (14.35%), but there was no difference in mortality in patients with new-onset AF and without AF.

## P1721

**Predictors of hospital mortality in a specific population of women with acute myocardial infarction and an ejection fraction lesser than 40%**C Catia Costa<sup>1</sup>; D Durao<sup>1</sup>; M Leal<sup>1</sup><sup>1</sup>Hospital of Santarem, Cardiology, Santarem, Portugal

**Introduction:** Hospital mortality in patients with acute myocardial infarction (AMI) constitutes an indicator of good health care; therefore, the knowledge of its predictors is a critical issue.

**Aims:** Assess the predictors of hospital mortality in a population of women with AMI and an ejection fraction (EF) lesser than 40% (EF < 40%).

**Methods:** Retrospective study, including 533 women with AMI and an EF < 40%. The population was divided in two groups: A, including patients with AMI who survived the event (n = 447); B, including patients with AMI who died at hospital (n = 86). Univariate and multivariate analysis were performed to find predictors of hospital death.

**Results:** Univariate analysis revealed a correlation between higher mortality with age (p < 0.001), history of stroke, peripheral arterial disease, dementia (p < 0.05), AMI with ST elevation (p < 0.001), lower blood pressure, lower EF, higher Killip class (KK) and the presence of atrial fibrillation (AF) (p < 0.001). Multivariate analysis confirmed AMI with ST segment elevation (OR 3.24, p 0.025), history of stroke (OR 3.3, p 0.013), KK (OR 2.55, p 0.018), the presence of AF (OR 2.43, p 0.021) and lower EF (OR 3.47, p 0.001) to be independent predictors of hospital mortality.

**Conclusions:** In this registry of women with EF lesser than 40%, not just common factors as the type of AMI or lower EF were predictors of hospital mortality. Other factors as history of stroke and the presence of AF were also predictors of a worst prognosis. This knowledge can lead to a better assessment of the patients and definition of therapeutic strategies.

## P1722

**Cardiac cachexia and its impact on survival in Asian patients**A Aninka Saboe<sup>1</sup>; B B Tiksnadi<sup>1</sup>; A Purnomowati<sup>1</sup>; T M Aprami<sup>1</sup><sup>1</sup>Padjajaran University, Cardiology, Bandung, Indonesia

**Background:** Cardiac cachexia (CC) is one of indicator of poor prognosis in heart failure. Unfortunately, its existence is often overlooked by many cardiologists, this is further complicated by small number of study concerning CC, and the controversial issues they encompasses. There was no previous study about cardiac cachexia in Asian population.

**Purpose:** The aim of this study is to analyze the survival in heart failure (HF) patients with cachexia complications in Asian population. **Methods:** A retrospective cohort study was conducted on the data from Hasan Sadikin General Hospital HF registry from March 2013 – August 2014. The inclusion criterias were asian population with HF patients above 18 years of age with left ventricle ejection fraction (LVEF) below 40%, time onset of HF more than 6 months and exclusion criterias were valvular diseases as primary etiology of HF and comorbid of other chronic disease (COPD, CKD, cancer). Cardiac cachexia was diagnosed in patients fulfilling the criteria from international cachexia consensus.

**Results:** There were 39 patients, most of them were female (61.5%), with mean LVEF 28.5% (+6.7). Cardiac cachexia was diagnosed in 6 (15.3%) patients. At 6 months of follow-up after initial enrollment, the cumulative rate of death from cardiovascular cause was 83% among cachectic as compared 37.5% among non-cachectic patients (p = 0.001, Adjusted HR (95%CI) = 8.05 (2.40–27.04). There were no association between mortality with sex (p = 0.268), etiology of HF (p = 0.288), LVEF (p = 0.061), comorbid condition (hypertension p = 0.237, diabetes mellitus p = 0.163).

**Conclusions:** We conclude that cardiac cachexia is an independent predictor of death in HF patients in 6 months in Asian population.

## P1723

**The heart failure marker TWEAK predicts survival in critically ill patients**M Mark Luedde<sup>1</sup>; C Roderburg<sup>2</sup>; F Benz<sup>2</sup>; A Koch<sup>2</sup>; C Trautwein<sup>2</sup>; T Luedde<sup>2</sup>; F Tacke<sup>2</sup>; N Frey<sup>1</sup><sup>1</sup>University Hospital of Schleswig-Holstein, Campus Kiel, Medical Clinic III, Kiel, Germany; <sup>2</sup>RWTH University Hospital Aachen, Internal Medicine III, Aachen, Germany

**Introduction:** TNF superfamily members, including TNF-related weak inducer of apoptosis (TWEAK) have been described as serum based biomarkers for heart failure. A novel theory proposes an important contribution of heart failure in septic disease. We therefore investigated the role of Serum TWEAK Levels and other members of the TNF superfamily in critical illness.

**Methods:** GITRL and TWEAK serum concentrations were measured in critically ill patients in comparison to healthy controls. Clinical data were recorded and correlated with GITRL and TWEAK serum levels.

**Results:** Serum levels of TWEAK and GITRL were strongly decreased in critically ill patients compared with healthy controls. Concentrations of TWEAK (and not GITRL) were further decreased when septic disease was present and was correlated with routinely used markers of inflammation and bacterial infection such as C-reactive

protein, procalcitonin and Interleukin-6. Notably, we failed to detect a correlation to other TNFR ligands such as TNF or APRIL. Finally, alterations in TWEAK levels were prognostic for patients fate during ICU treatment.

**Conclusion:** Serum levels of TWEAK and GITRL were significantly decreased in intensive care unit patients. Concentrations of TWEAK were further decreased in septic patients and alterations in TWEAK levels were associated with an unfavorable outcome. Together with recently published results on other TNFR ligands, these data for the first time highlight specific functions of the heart failure marker TWEAK in the pathophysiology of septic diseases.

## P1724

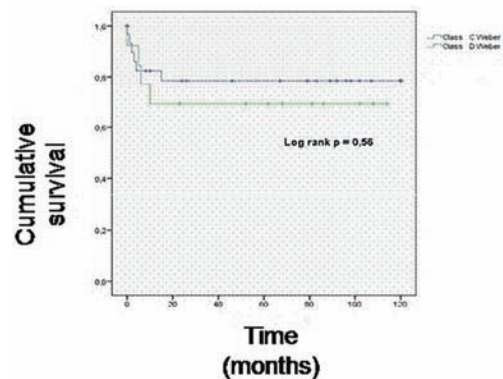
**Influence of cardiopulmonary exercise test results on mortality after cardiac transplant**CMF Christopher Strong<sup>1</sup>; P Freitas<sup>1</sup>; C Aguiar<sup>1</sup>; A Ferreira<sup>1</sup>; S Guerreiro<sup>1</sup>; G Rodrigues<sup>1</sup>; A Ventosa<sup>1</sup>; MJ Rebocho<sup>1</sup>; JP Neves<sup>2</sup>; M Mendes<sup>1</sup><sup>1</sup>Hospital de Santa Cruz, Cardiology, Lisbon, Portugal; <sup>2</sup>Hospital de Santa Cruz, Lisbon, Portugal

**Purpose:** This study aims to describe a population of patients with heart failure and the results of cardiopulmonary exercise test (CPET), and to evaluate the potential impact of these results on mortality at 6 months and 10 years after heart transplantation.

**Methods:** Retrospective single center study which included 44 patients with heart failure NYHA class III-IV who underwent CPET between 1998-2013. Clinical data of the population and follow-up at 6 months and at 10 years after cardiac transplantation were collected.

**Results:** The mean age of the population was 49 ± 11 years, with 75% of males. The most frequent causes of heart failure were idiopathic (34.1%), ischemic (29.5%), hypertrophic in dilated phase (15.9%) and valvular (11.4%). The mean left ventricle ejection fraction was 24 ± 7.8%, the average NYHA class was III, the average Meckel score was 34.1 ± 18.8. Most patients were treated with beta-adrenergic blocker (86%), ACEI / ARB (96%) and spironolactone (50%), with the maximum tolerated dose. The mean VO2 max was 12.1 ± 2.6 ml / kg / min; the average % provided for VO2 max was 39 ± 11.6%; and the average of the VE / VCO2 slope was 49.8 ± 14.3. All patients underwent cardiac transplantation, in most cases between 6 months and 1 year after CPET. It was found that 7 patients died within the first 6 months, and at 10 years post-transplant a total of 10 patients died. At 6 months, mortality was 23.1% in patients who were submitted to heart transplant in Weber class D and 12.9% in Weber class C (p 0.4); at 10 years, mortality was 30.8% in patients who performed heart transplant in Weber class D and 19.4% in Weber class C (p 0.4) - see figure. The VE / VCO slope and the predicted % for VO2max were not predictors of mortality at 6 months or at 10 years.

**Conclusion:** The mortality after heart transplantation was greater in patients with worse results on CPET carried out in recent months before transplantation.



Kaplan - Meier curve

## P1725

**Abnormal liver function and renal function impairment as an expression of multiorgan failure in acute decompensated cardiac failure**M L Talavera<sup>1</sup>; I Chillik<sup>2</sup>; A Acosta<sup>1</sup>; R Campos<sup>2</sup>; MS Trivi<sup>2</sup>; M Diez<sup>1</sup><sup>1</sup>Cardiovascular Institute of Buenos Aires (ICBA), Heart Failure, Buenos Aires, Argentina; <sup>2</sup>Cardiovascular Institute of Buenos Aires (ICBA), Cardiology, Buenos Aires, Argentina

**Background:** renal function impairment is a well known risk factor in acute decompensated cardiac failure (ADHF) and abnormal liver function tests (LFT) are related to bad outcome in this setting as well. These abnormalities are usually related with



low cardiac output and multiorgan failure.

**Objective:** to evaluate the prevalence of renal function impairment and abnormal LFT in patients (pts) with ADHF and to establish the relationship between those and death during hospitalization.

**Methods:** 223 consecutive pts admitted with ADHF between January-2013 and August-2014 were selected; Patients' basic characteristic data including sex, age, past medical history, medications, as well as blood exam results, were analyzed. Renal function impairment was defined by a > 0,3 mg/dl in creatinin value and abnormal liver function as an any upper limit increment in alanine aminotransferase, aspartyl aminotransferase, total bilirubin and/or alkaline phosphatase. The primary endpoint was death during hospitalization. Logistic regression analysis was used to evaluate factors associated to death. P < 0.05 was considered statistically significant.

**Results:** mean age was 79 years old (DS + /-11) and 60% (134 pts) were male, mean left ventricle ejection fraction was 40% (IQR25-75: 29-59) and 43% (97 pts) had an ischemic etiology; abnormal LFT was present in 62% (138 pts) at admission and previous renal failure was recorded in 37% (83 pts); during in-hospital, 68% (153 pts) and 46% (104 pts) developed any liver enzyme enchantment or renal function impairment, respectively. There were 16 deaths (7,1%) during hospitalization. Regression analysis showed that highest bilirubin levels (OR 2,04, CI95%: 1,04-3,98, p = 0,036) and renal function impairment (OR 5,41 CI95% 1,09-27, p = 0,039) were associated to death among others LFT variations and biomarkers like high sensitive troponin levels.

**Conclusions:** in ADHF, abnormal LFT and renal function impairment are easy and useful prognostic tools that help to estimate risk of death during hospitalization; they probably express multiorgan failure due to low cardiac output as a background physiopathology.

**P1726**

**Heart failure admission: does the phenotype matter?**

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**Background:** Heart failure (HF) with preserved ejection fraction (HFpEF) is a prevalent cause of hospital admission. Although left ventricle systolic dysfunction has been associated with a poor outcome, the prognosis in patients with preserved ejection fraction once the clinical syndrome of heart failure sets in is still ill defined.

**Purpose:** To compare the in-hospital and long term outcomes of patients with HFpEF and HF with reduced ejection fraction (HFrEF).

**Methods:** We included all patients admitted for acute heart failure in a single centre (cardiology ward and coronary intensive care unit). We created two groups: HFpEF - group 1 (n=34) - and HFrEF - group 2 (n=216).

**Results:** HFpEF patients were older (78 ± 9 vs 67 ± 14, P < 0.01), more often females (67.6 vs 18.7% P < 0.01) and had a shorter hospital stay (8 ± 8 vs 13 ± 11 days, P = 0.02). In-hospital mortality was similar between the two groups (14.7 vs 15.4%, P = 0.92). Concerning long term follow-up, group 1 had a better two-year event free survival (figure 1). On the contrary, there was a trend for a higher HF readmission rate in the group with HFpEF (63.0% vs 47.3%, P = 0.15).

**Conclusion:** Our data showed that HFpEF patients had a similar in-hospital prognosis, but an improved 2-year survival. Yet, this group showed a trend to a higher HF readmission rate.

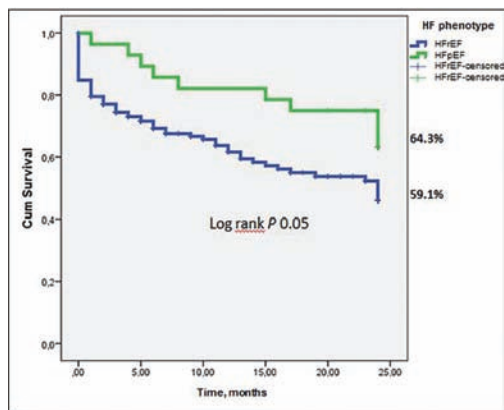


Figure 1

**P1727**

**The relationship between smoking habits and depressive symptoms in patients with systolic heart failure**

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**Background:** Depressive symptoms are common and associated with poor prognosis in chronic heart failure (CHF). Smoking is one of the most important risk factor for the development of coronary artery disease. The aims of this study were to identify the relationship between history of smoking (current smoker and ex-smoker) and depressive symptoms and to determine the effects of history smoking on Minnesota living with heart failure questionnaire (MLHFQ) and the hospitalization in CHF.

**Methods and Results:** Patient Health Questionnaire (PHQ-9) does not establish a diagnosis of depression, but screens patients who are at risk. Scores between 0 and 4 identified patients at no risk for depression, scores between 5 and 9 represented patients who screened positive for mild depressive symptoms, and patients who scored 10 were tentatively diagnosed with moderate depression. For the purposes of this study, the PHQ-9 score was dichotomized to a 'non-depressed' (PHQ-9: 0-9) and a 'depressed' cohort (PHQ-9: ≥10). Patients in this study were enlisted in the country of Georgia from a hospital-affiliated outpatient HFDMP for systolic HF located in our Central University Hospital in Georgia. 377 patients (109 female, 268 male, mean age: 64 ± 13 years, mean ejection fraction: 32% ± 6) were enrolled between in August 2007 and July 2008. 15% of patients' PHQ-9 score were ≥10. 162 (43%) patients had history of smoking in the group. While 22% of patients with smoking history were depressed 11% of patients without smoking history were depressed (p = 0.004). Depressive patients had a tendency to smoke more than patients without depression (17 ± 12 cigarettes/day vs 12 ± 13, p = 0.003). Depressive patients' MLHFQ score were higher (64 ± 14 vs 58 ± 15, p < 0.001) and hospitalization rate increased (73% vs 53%, p < 0.001) compared to non-depressive patients.

**Conclusion:** It was determined that patients with history of smoking had more depression than patients without history of smoking. Patients with history of smoking were more hospitalized and their MLHFQ scores higher than patients without smoking history in CHF.

**P1728**

**Heart failure determines survival in haemodialysis patients**

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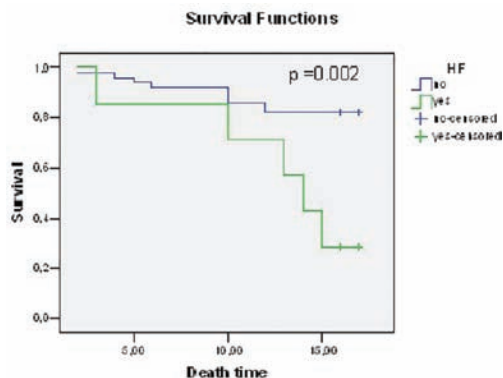
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**Objective:** Patients with end-stage renal disease on haemodialysis (HD) treatment have increased mortality and cardiovascular risk. We aimed to determine if the presence of heart failure (HF) has an additional prognostic implication in HD patients.

**Methods:** We studied 59 HD patients, 59 ± 2.4 years, 28 (47%) - female, renal disease from 10.1 ± 7 years and duration of HD 5.6 ± 5.1 years, of whom 7 patients (12%) had HF with documented left ventricular systolic dysfunction. Other clinical characteristics were as follows: arterial hypertension - 93%, diabetes - 12%, dyslipidemy - 27%, smokers/ former smokers - 53%, family history of premature coronary artery disease (CAD) - 10%, established CAD - 14%, peripheral artery disease - 5%, cerebrovascular disease - 9%.

**Results:** We followed-up our patients for 14.5 ± 3.8 months. Major adverse cardiac event (MACE), defined as cardiovascular death, acute coronary syndrome (ACS), coronary revascularization, stroke and hospitalization due to cardiovascular reasons, occurred in 17 patients (29%) during follow-up; 14 patients (24%) died [9 of them (16%) of cardiovascular death]; 26 subjects (45%) were hospitalized [15 of them (26%) had cardiovascular hospitalizations]; one patient (2%) had ACS; 6 subjects (10%) experienced stroke. Patients with HF at baseline were more likely to die during follow-up (71% vs 18%, p = 0.007), to experience cardiovascular death (57% vs 10%, p = 0.008), hospitalization (86% vs 39%, p = 0.04) and stroke (43% vs 6%, p = 0.02) and to visit emergency department (43% vs 4%, p = 0.01) compared to those without HF. Presence of HF was the strongest independent predictor for the occurrence of MACE, total and cardiovascular death during follow-up. Kaplan-Meier survival analysis demonstrated that time to death was significantly shorter in HD patients who had HF at baseline (12.7 ± 1.7 months), compared to those without HF (15.4 ± 0.5 months), p = 0.002. Time to cardiovascular death was also significantly shorter in HF patients (14.3 ± 1 months) compared to the rest of the group (15.8 ± 0.4 months), p = 0.001. Time to MACE did not differ in the groups with and without HF at baseline.

**Conclusions:** Presence of HF significantly influences prognosis in HD patients, increasing mortality and untoward cardiovascular events, and shortening the time to total and cardiovascular death.



Kaplan-Meier Survival curve

### P1729

#### Annual prognostic factors in chronic heart failure in octogenarians and nonagenarians

The study was supported by a Medical University grant.

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**Introduction:** In the elderly the most common cause of hospitalization and the leading cause of death is heart failure.

**Purpose:** The aim of this study was to determine the annual prognostic factors in chronic heart failure (CHF) in patients over 80 years old.

**Methods:** The analysis included 197 patients 80+ years old (mean age 83.6 ± 3.0 years; 46.2% of men) hospitalized in 2010-2013 in the Department of Cardiology due to CHF. Sixty two parameters were investigated: age, gender, NYHA class, body mass index, blood pressure, comorbidities, parameters of 12-lead ECG and echocardiography, results of basic laboratory tests and selected biomarkers (NT-proBNP, hs-TnT, hs-CRP). All participants remained in prospective follow-up for 12 months. We defined the primary endpoint as the cardiovascular death and the composite endpoint, which was consisted of cardiovascular death and/or hospitalization due to exacerbation of CHF. The multivariate logistic regression stepwise analysis was performed for whole population, according to left ventricular ejection fraction (LVEF < 45% and ≥ 45%) and in group with glomerular filtration rate (GFR) < 60ml/min/1.72m<sup>2</sup> to identify the prognostic factors for the mentioned endpoints.

**Results:** In one year observation 21 patients died (11%). From multivariate analysis four variables were independently associated with the primary endpoint: GFR (OR = 0.92), hypertension (OR = 0.19), lung diseases (OR = 9.36) and vascular diseases (OR = 6.07). In turn, in patients who reached the composite endpoint (n = 55), the only statistically significant was anemia (OR = 4.71). In patients with LVEF < 45% for each endpoint prognostic were vascular and lung diseases (OR range: 10 to 24). In group with LVEF ≥ 45% with composite endpoint was associated hemoglobin (OR = 0.61) and with death: white blood cell count, hs-TnT and vascular diseases (respectively OR = 1.30; OR = 1.04; OR = 3.96). And in population with GFR < 60ml/min/1.72m<sup>2</sup> the independent variables for composite endpoint were: red blood cell distribution width (OR = 1.42) and anemia (OR = 3.79), while for the primary endpoint the same two variables as for entire population: vascular (OR = 5.16) and lung diseases (OR = 4.72).

**Conclusions:** In octogenarians and nonagenarians with CHF comorbidities have important prognostic value for annual prognosis. The most aggravating factors were lung diseases.

### P1730

#### New clinical assessment scale - useful tool to analysis effect of treatment and prognosis of patients with heart failure

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**Background:** Patients with heart failure (HF) are at substantial risk of recurrent hospitalization and death. There is a need for tools to assess the success of treatment and evaluate patients' prognosis.

**Propose:** To develop a simple clinical scale [Scale for HF to Optimize Clinical Status (SHOCS)] to assess the prognosis of patients with HF in everyday practice.

**Material:** The SHOCS tool is based on patients managed in Russia by cardiology departments. Its ability to predict mortality was investigated in two single-centre studies and confirmed in two multicenter randomized trials (RT).

**Results:** The scale combines symptoms and a simple clinical assessment aligned to routine care (table1). Each NYHA class has a different SHOCS score; the correlation between NYHA and SHOCS in the study was - 0.679. This was also validated in two RT in Russia (FASON, n = 1879 and BESE, n = 1437). The prognostic value of SHOCS was investigated in two single center studies: The first study comprised 718 patients hospitalized due to decompensated HF. Patients with median SHOCS < 8.3 on admission to the hospital had a hazard ratio (HR) of 0.59 95% CL 0.49-0.71; p < 0.00012 for 5-year mortality. The second study (n 195) compared SHOCS at hospital admission and discharge and followed patients for seven years. Median SHOCS on admission and discharge was 5 IQR [3;7] and 2 IQR [1;2]. Patients with SHOCS < 5 on admission had better survival. (HR=0.540, 95%CL 0.359-0.812). HR of highest versus lowest quartile was 2.46 95% CL [1.44 to 4.21]. Moreover, patients who remained symptomatic at discharge (SHOCS ≥ 2) had a greater risk of death. (HR 1.59 95% CL 1.06 to 2.37). Multivariable analysis showed that SHOCS is an independent predictor of mortality.

**Conclusion:** SHOCS is a simple and powerful tool to investigate the prognosis of patients admitted with decompensated HF and the effect of treatment.

#### Clinical assessment scale

1. Breathlessness	0 - no; 1 - during exercise; 2 - at rest
2. Increase in weight over the last week	0 - no; 1 - yes
3. Palpitations	0 - no; 1 - yes
4. Orthopnoea	0 - no; 1 - yes (2+ pillows); 2 - yes (2+ pillows) + woken up due to breathlessness; 3 - Yes + and can only sleep sitting up
5. Jugular vein distension	0 - no; 1 - yes when patient lying flat; 2 - yes when patient standing up
6. Rales	0 - No; 1 - lung bases (1/3 of lungs area); 2 - up to scapula's angle (2/3 of lungs area); 3 - throughout the lungs
7. Third heart sound	0 - no; 1 - yes
8. liver	0 - normal; 1 - enlargement up to 5cm below subcostal border 2 - enlargement greater than 5cm below subcostal border
9. Peripheral edema	0 - no; 1 - minimal ankle oedema; 2 - moderate ankle edema; 3 - ascites/anasarca/generalised oedema
10. Systolic Blood pressure	0 - > 120 mmHg; 1 - 100-120 mmHg; 2 - < 100 mmHg

### P1731

#### Differential prognostic impact of atrial fibrillation in non-obese vs. obese patients with heart failure with preserved ejection fraction

Grant-in-Aid for Scientific Research (#20174906)

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**Background:** The presence of atrial fibrillation (AF) is associated with adverse clinical outcomes in patients with heart failure (HF). On the other hand, obesity is associated with left ventricular hypertrophy, diastolic dysfunction and the occurrence of AF. Nevertheless, it has been reported that in HF population, obese patients have more favorable clinical outcomes, often referred to as "obesity paradox". In this context, the clinical impact of AF in obese/non-obese patients has not been characterized.

**Purpose:** We sought to determine the prognostic impact of AF in HF patients with different body mass index (BMI).

**Methods:** West Tokyo Heart Failure Registry (WET-HF) is the multi-center registry enrolling acute decompensated HF (ADHF) patients who were hospitalized at the 4 major teaching hospitals in western Tokyo area. We analyzed 1,681 patients who were enrolled from 2005 to 2013. We categorized them into 3 groups of low/medium/high BMI (low, BMI < 20, L; medium, 20 ≤ BMI ≤ 24, M; high, BMI > 24, H; n = 344/621/539). Furthermore, we categorized them into HF with preserved ejection fraction (HFpEF) group which was defined as EF of 40% or more (n = 681) and HF with reduced EF (HFrEF) group which was defined as EF of less than 40%

(n=633). The clinical endpoint was defined as all cause death or readmission for ADHF.

**Results:** The median follow-up was 411 days in overall population. In the Kaplan-Meier analysis, the occurrence of clinical endpoint was more common in patients with AF than those without AF ( $P=0.007$ , Log rank test). Patients who had AF on admission was associated with higher probability of endpoint in HFpEF group ( $P=0.006$ , Log rank test), but not in HFrEF group. On the other hand, endpoint was more common in lower BMI groups ( $P<0.0001$ , Log rank test) in overall population. AF was associated with higher rate of endpoint in L ( $P=0.02$ ) and H ( $P=0.04$ ), but not in M. When study subjects were further divided into HFpEF and HFrEF groups, AF was associated with higher rate of endpoint in HFpEF, but not in HFrEF for L and M ( $P=0.006$  and  $0.02$ , respectively). Conversely, AF was associated with higher rate of endpoint in HFrEF instead of HFpEF for H ( $P=0.02$ ). **Conclusions:** Presence of AF had a significant impact on clinical outcomes in L and M with HFpEF. Further investigation will be warranted to identify its underlying mechanisms.

### P1732

#### Validation of the MAGGIC heart failure risk score in Korean heart failure registry

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**Background:** There exist previous risk models for patients with HF. But, each uses a single cohort of patients and hence their generalizability to other populations is questionable. The aim of this study was to evaluate the performance of a recently developed risk score from the meta-analysis for mortality in heart failure by external validation in a national heart failure registry. **Method:** We included 5265 patients from the Korean acute heart failure registry (KorAHF) and excluded patients with in-hospital death. From 13 routinely available patient characteristics (Age, gender, diabetes, COPD, HF diagnosed within the last 18 months, current smokers, NYHA class, use of beta blocker, ACEI or ARB, BMI, systolic BP, Cr and EF), the Meta-analysis Global Group in Chronic Heart Failure (MAGGIC) constructed a risk score for prediction of mortality in heart failure. The risk score was calculated for each patient by summing the individual contribution from all 13 risk factors as described in the MAGGIC project heart failure risk score publication. The outcome measure was 1-year mortality. The predicted probability of death obtained from the calculated risk score was compared with the observed 1- and 2-year mortality, and model discrimination and calibration were assessed by formal tests.

**Results:** Among total 5625 patients, we included 4783 patients without in-hospital death and missing value of 13 routinely available clinical characteristics. Of 13 variables, sex, systolic BP, smoking and ejection fraction were not significant independent risk variables. The overall 1-year and 2-year mortality in the study population was 17.58% and 30.64% respectively. The risk score were significantly different between alive and died group ( $30.19 \pm 6.12$  vs.  $25.24 \pm 6.88$ ,  $p<0.001$  at 1 year,  $30.76 \pm 6.24$  vs.  $25.96 \pm 6.91$ ,  $p<0.001$  at 2 year) which means risk score revealed good discrimination. To test calibration of model, we used a Hosmer-Lemeshow goodness-of-fit test. There was not a significant differences between observed and model-predicted 1-year and 2-year mortality ( $p=0.5463$  and  $0.6905$ , respectively).

**Conclusion:** In the Korean heart failure registry, the MAGGIC project heart failure risk score performed good in a large nationwide contemporary external validation cohort.

### P1733

#### Impact on late clinical outcomes of permanent pacemaker implantation after transcatheter aortic valve implantation.

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Very few data exist on the clinical impact of permanent pacemaker implantation (PPI) after transcatheter aortic valve implantation. The aim of this study was to assess the impact of PPI after transcatheter aortic valve implantation on late outcomes

**Methods and Results:** A total of 456 consecutive patients without prior PPI undergoing transcatheter aortic valve implantation were included. Of them, 112 patients (24.2%) required a PPI within the first 30 days after transcatheter aortic valve implantation, mean time  $53.7 \pm 38$  hours. At a mean follow-up of  $30.4 \pm 20$  months, there was more mortality in patients with PPI 32.7% vs. 22.3%, OR = 1.69 (95% CI

1.04-2.75),  $p=0.0024$ , but no association was observed between the need for PPI and all-cause mortality (hazard ratio, 1.39; 95% confidence interval, 0.918-2.411;  $P=0.120$ ), cardiovascular mortality (hazard ratio, 0.74; 95% confidence interval, 0.311-1.795;  $P=0.515$ ), and rehospitalisation for heart failure (hazard ratio, 1.67; 95% confidence interval, 0.738-3.76;  $P=0.219$ ). There were 5 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  $60.7 \pm 14$  mmHg to  $63.2 \pm 15$  mmHg after TAVI and decreased to  $61.2 \pm 10$  mmHg at 1 years and  $45.8 \pm 20$  mmHg at 2 years ( $p$  for post-TAVI trend 0.102).

**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. However, new PPI did have a negative effect on left ventricular function over time.

### P1734

#### Prognostic value of diuretic dose in ambulatory patients with chronic heart failure

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**Background:** diuretics, such as furosemide, are deemed essential for the treatment of patients with chronic heart failure (HF), but it is not well known whether increasing doses of furosemide are associated with increased mortality or hospitalization in this population of patients.

**Purpose:** evaluate of the prognostic impact of diuretic dose in ambulatory patients with chronic HF and to evaluate whether this relationship remains significant after considering the state of congestion.

**Methods:** we conducted a retrospective analysis of patients with chronic HF and reduced left ventricular ejection fraction (LVEF  $\leq 45\%$ ) in follow-up at our HF Center. Inclusion criteria were optimized therapy and clinical stability (neither events nor therapeutic changes) in the previous three months. Daily diuretic dose was considered as continue variable and as a categorical variables ( $\leq 50$  mg/die vs  $>50$  mg/die; 50 mg was the median diuretic daily dose). Volemia status (congestion or hypervolemia vs euvolemia) was defined according to the Sodium Retention Score, calculated by assigning a score of 1 for each of the following signs or symptoms: weight gain, hepatomegaly, gallop rhythm, and increased jugular venous pressure; a score of 1 to 3 in presence of rales; a score of 1 to 4 in presence of peripheral edema; a score  $\geq 3$  indicates a state of hypervolemia. The median follow-up was 43 months; the end-point was a composite of all cause death and hospitalizations for HF or cardiovascular causes.

**Results:** a total of 570 patients were enrolled (mean age  $67 \pm 12$  years, 83% male); during the follow-up; the composite end-point occurred in 294 patients (52%). Diuretic dose was a predictor of events in the overall population in both univariable ( $p$ -value  $< 0.001$ ) and multivariable analysis ( $p$ -value = 0.026), together with age ( $p$ -value = 0.001), LVEF ( $p$ -value = 0.005) and congestion state ( $p$ -value  $< 0.001$ ). In the sub-group of euvolemic patients, in a multivariable model (including NYHA classes, sex, serum creatinine, hemoglobin, mitral regurgitation and heart rate) age ( $p=0.017$ ), LVEF ( $p=0.006$ ) and high diuretic dose ( $p$  value = 0.043) were independent markers of worse prognosis. In hypervolemic patients only age ( $p=0.039$ ) and LVEF ( $p=0.047$ ) were independently associated with adverse events.

**Conclusion:** increasing doses of furosemide are associated with adverse outcomes, after adjustment for other predictors of poor prognosis, only in patients without clinical congestion. In hypervolemic patients higher diuretic dose remains an indirect measure of the severity of the disease.

### P1735

#### Effect of left ventricular systolic dysfunction on clinical outcome after transcatheter aortic valve implantation

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**Background:** Patients with severe aortic stenosis and reduced left ventricular ejection fraction (LVEF) have a poor prognosis with conservative therapy but a high operative mortality when treated surgically. Recently, transcatheter aortic valve implantation (TAVI) has emerged as an alternative to surgical aortic valve replacement for patients considered at high or prohibitive operative risk. The objective of this study was to analyze the impact the TAVI in patients with severe aortic stenosis with reduced left ventricular ejection fraction.

**Methods and results:** Between April 2008 and December 2015, 500 patients with symptomatic aortic valve stenosis who were considered high risk or non surgical



candidates underwent implantation with the CoreValve prosthesis. Echocardiographic data were collected before and after the procedure. Impaired LV function was defined by a left ventricular ejection fraction (LVEF < 40%). In 85 patients (17%) had reduced left ventricular ejection function (LVEF < 40%).

**Results:** The patients with reduced LVEF had more comorbidities compared with normal function: Charlson index  $4 \pm 1.8$  vs.  $3.2 \pm 1.7$ ,  $P = 0.001$ ; Karnofsky index  $49 \pm 18$  vs.  $63.8 \pm 17.6$ ,  $P = 0.001$ ; Frailty 29.4% vs. 15.4%,  $P = 0.002$ , worse Logistic EuroSCORE  $26.9 \pm 16$  vs.  $15.4 \pm 9.7$ ,  $P < 0.001$ , were more often males (58.8% vs. 37.2%,  $P = 0.01$ , more symptomatic (NYHA class IV 58.8% vs. 24.3%,  $p < 0.001$ , were younger ( $75.7 \pm 7.4$  vs.  $79.8 \pm 5$ ,  $P = 0.001$ ) and had a higher prevalence of prior coronary artery disease (62.4% vs. 39%,  $p = 0.001$ ). Patients with reduced LVEF showed a good evolution of left ventricular ejection fraction over time (pre, post-procedure and 1 years):  $33.9 \pm 5$  vs.  $44.2 \pm 11$  vs.  $51.7 \pm 12\%$ , respectively  $p = 0.001$  No difference was observed between the 2 groups in in-hospital mortality (4.7% vs. 3.4%,  $P = 0.548$ ). At a mean follow-up of  $34.3 \pm 23$  months, there was a trend to lower mortality in patients with reduced LVEF (12.2% vs. 21.4%,  $p = 0.057$ ).

**Conclusions:** In patients with severe aortic stenosis and depressed LV systolic function, TAVI is associated with better LVEF recovery and the immediate and long-term outcome after TAVI did not differ between patients with an impaired and preserved LVEF.

### P1736

#### Mortality risk of chronic heart failure patients according to non-invasive lung impedance and New York heart association class in the impedance-HF trial

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**Background:** stratification of Chronic Heart Failure (CHF) patients by their risk of death is important. The most common predictor used for this purpose is the New York Heart Association (NYHA) class. Such an analysis was performed on data from the IMPEDANCE-HF trial where CHF patients were randomly (1:1) treated in the outpatient clinic with or without measuring lung impedance (LI) to evaluate its impact on recurrent hospitalizations for heart failure (HF).

**Methods:** Hazard Ratio (HR) was calculated (by Cox regression analyses) for all-cause and HF-related death according to NYHA and LI values. Study population was 256 CHF patients with LVEF  $\leq 35\%$  in NYHA class I-IV. NYHA and LI were evaluated during monthly visits in outpatient clinics for average a follow-up of 4 years. Average NYHA and LI values throughout follow up by quartiles were used for analysis. NYHA quartiles were defined as follow: I: 0-1.4 (usual NYHA class), II: 1.41-2.19, III: 2.2-3, and IV: 3-4. Measured LI was presented as deviation from normal baseline in percent with quartiles defined as follows: I: 0 to -17.4%, II: -17.5 to -25%, III: -25.1 to -33.6% and IV: <-33.7%. Quartiles for NYHA and LI were normalized by 1st quartile for the calculation of HR.

**Results:** HR for all-cause mortality according to NYHA class were found: 1.1 (95% CI: 0.7-1.9,  $p = 0.6$ ) for 2nd quartile, 4.6 (95% CI: 2.7-8.0,  $p < 0.0001$ ) for 3rd quartile and 22.2 (95% CI: 7.7-66.7,  $p < 0.0001$ ) for 4th quartile. HR for HF-related death based by NYHA class were: 1.6 (95% CI: 0.8-3.2,  $p = 0.15$ ) for 2nd quartile, 9.5 (95% CI: 4.2-22.2,  $p < 0.0001$ ) for 3rd quartile and 34.2 (95% CI: 7.7-87,  $p < 0.0001$ ) for the 4th quartile. The HR for all-cause death based on LI quartiles were: 2.7 (95% CI: 1.6-4.6,  $p < 0.001$ ) for the 2nd quartile, 4.4 (95% CI: 2.5-7.7,  $p < 0.0001$ ) for the 3rd quartile and 10.0 (95% CI: 5.3-18.9,  $p < 0.0001$ ) for the 4th quartile. HR for HF-related death according to LI were: 4.9 (95% CI: 2.4-10.2,  $p < 0.0001$ ) for the 2nd quartile, 12.7 (95% CI: 5.1-31.3,  $p < 0.0001$ ) for the 3rd quartile and 31.3 (95% CI: 10.0-90.9,  $p < 0.0001$ ) for the 4th quartile.

**Conclusion:** Results demonstrate that both NYHA class and LI strongly predict all-cause and HF-related mortality but LI is more strong and specific predictor.

### P1737

#### Prognostic impact of acute heart failure on long-term mortality in patients with ST-elevation myocardial infarction

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**Purpose:** Acute heart failure (AHF) has an adverse impact on outcome in patients with ST-elevation myocardial infarction (STEMI). AHF at admission and AHF which developed during hospitalization have different prognostic impact on short-term mortality in STEMI patients treated with primary percutaneous coronary intervention (pPCI). The aim of this study is to evaluate the prognostic impact of AHF on long-term mortality in patients with STEMI treated with pPCI.

**Method:** We analysed 1719 consecutive STEMI patients treated with pPCI included in Clinical Center of Serbia STEMI Register. Patients presenting with cardiogenic shock were excluded. The follow-up period was 5 years.

**Results:** AHF was registered in 396 (23%) patients. Among patients with AHF

288 (72.7%) presented with HF and 108 (27.2%) developed HF during hospitalization. In comparison with patients without HF, patients with AHF were more likely to be older and to be female; they were more likely to have previous myocardial infarction, longer pain duration (before first medical contact), diabetes, lower creatinine clearance, anterior myocardial infarction, lower left ventricular ejection fraction (EF), 3-vessel coronary disease (on initial angiogram), significant left main stenosis, pre-procedural flow TIMI=0 and post-procedural flow TIMI <3. Five year mortality rates in patients with AHF at admission, in patients who developed HF during hospitalization and in patients without HF were 31.7%, 15.8% and 3.8% ( $p < 0.001$ ) respectively (Figure 1). In Cox regression model AHF (at any time) was a strong independent predictor of 5-year mortality -HR 2.92, (95%CI 1.21-3.39),  $p < 0.001$ . The risk of 5-year mortality differed in patients with AHF at admission and in those who developed HF during hospitalization: AHF at admission- HR 3.45 (95%CI 2.02-6.03),  $p < 0.001$ ; AHF during hospitalization- HR 1.96 (95%CI 1.13-3.04),  $p = 0.039$ . Other independent predictors of 5-year mortality were: (older) age HR 1.04 (95%CI 1.03-1.06),  $p < 0.001$ ; EF < 40% HR 2.91 (95%CI 1.72-4.92)  $p < 0.001$  and post-procedural flow TIMI < 3 HR 1.79 (95%CI 1.12-2.87),  $p = 0.015$ .

**Conclusion:** AHF in patients with STEMI treated with pPCI was a strong independent predictor of 5-year mortality. The risk of 5-year mortality was higher in patients who presented with AHF than in patients who developed HF during hospitalization. AHF at admission was the strongest independent predictor of long-term outcome in analysed patients.

Figure 1. Kaplan-Meier curves estimating the probability of 5-year mortality according to AHF

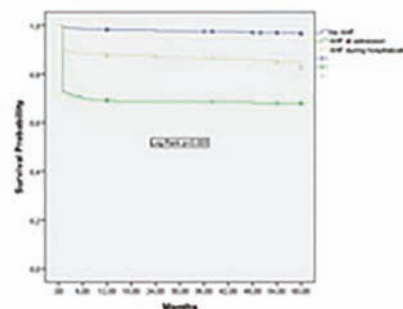


Figure 1.

### P1738

#### Differential prognostic value of post-exercise heart rate recovery in patients with chronic heart failure according to etiology

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**Background:** Heart rate recovery (HRR) after exercise is an index of parasympathetic function associated with clinical outcomes in patients with chronic heart failure (CHF). However, its differential prognostic value according to the etiology of cardiomyopathy (CMP) is not well investigated.

**Purpose:** We aimed to evaluate the differential clinical impact of HRR according to etiologies of CHF in consecutively enrolled cohort.

**Methods:** We measured HRR (calculated as the difference between heart rate at peak exercise and after 2 minute of recovery) in 318 consecutively enrolled CHF patients (255 male, 114 idiopathic dilated CMP, 134 ischemic CMP,  $55 \pm 13$  years, mean ejection fraction  $34.1 \pm 9.9\%$ ). Primary endpoint was cardiovascular (CV) events defined as CV mortality, cardiac transplantation or rehospitalization due to HF aggravation.

**Results:** The CV events occurred in 37 (11.6%) patients (6 cardiovascular deaths and 6 cardiac transplantations) during follow up period (median 567 days). When the overall patients were divided by HRR according to Contal and O'Quigley's method, low HRR was associated with poor clinical outcome ( $P = 0.021$ ). Multivariate Cox regression analysis revealed that HRR was found to be an independent predictor of CV events in overall CHF patients ( $P = 0.043$ ) and also in idiopathic dilated CMP ( $P = 0.01$ ) but not in ischemic CMP ( $P = 0.118$ ) or in CHF of other etiologies ( $P = 0.057$ ) when controlled for age, body mass index, renal function and beta-blocker use.

**Conclusion:** HRR is an independent prognostic marker in patients with CHF and its prognostic value is more prominent in patients with idiopathic dilated CMP but not in

ischemic CMP or CHF of other etiologies. These findings may explain the differential relationship between autonomic dysfunction and clinical outcome in these patients.

10.7% PAH-connective tissue and 17.9% type 3/4 of ISHLT classification. Total mortality was 14.3%; 0% for RVSRI  $\leq$  -0.6%cm<sup>2</sup> and 26.7% for RVSRI  $>$  -0.6%cm<sup>2</sup>

Multivariate analysis	Overall CHF patients		Idiopathic dilated CMP		Ischemic CMP		CHF of other etiologies	
	HR(95%CI)	P-value	HR(95%CI)	P-value	HR(95%CI)	P-value	HR(95%CI)	P-value
Low HRR	2.157(1.021-4.556)		0.043		4.112(1.399-12.087)		0.010	
Age	0.991(0.967-1.016)		0.491		0.996(0.964-1.029)		0.817	
BMI	0.956(0.867-1.054)		0.367		0.993(0.872-1.132)		0.922	
eGFR <60	1.832(0.843-3.979)		0.126		2.002(0.664-6.031)		0.217	
B-blocker use	0.358(0.18-0.079)		0.003		0.309(0.123-0.780)		0.012	

PULMONARY HYPERTENSION

P1739

**Angiotensin-converting enzyme inhibitors, angiotensin-II receptor antagonists, beta-blockers and ivabradine as supportive therapy in pulmonary hypertension: drug safety and tolerability**

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**Background:** In the 2015 ESC/ERS Guidelines for diagnosis and treatment of pulmonary hypertension (PH), the use of angiotensin-converting enzyme inhibitors (ACEi), angiotensin-II receptor blockers (ARBs), beta-blockers (BBs) and ivabradine (Iva) is not recommended in patients with PAH unless required by co-morbidities, because no convincing data are available on the efficacy and safety of such drugs in patients with PAH. Aim of the study was to therefore evaluate safety and tolerability of these drugs in patients with PH enrolled in the Daunia Heart Failure registry.

**Materials and Methods:** the study retrospectively analyzed a total of 55 consecutive outpatients with PH. Medical history, heart rate, systolic blood pressure, Body Mass Index, NYHA class, and medications were recorded. Clinical follow up was performed every 4 months. Clinical follow up was anticipated in case of worsening decompensated right heart failure. Drug withdrawal was reported when occurred.

**Results:** after a mean 2133 ± 289 days of follow-up, only three patients stopped treatment with Iva (15% withdrawal rate), while nine patients stopped treatment with ACEi/ARBs (42%) and nine BBs (40% tolerability). Considering the occurrence of death and hospitalization for heart failure, non-significant rates were found comparing ivabradine group vs non-ivabradine group (46% and 50% vs 24% and 41%, p: ns), ACEi/ARBs group vs non-ACEi/ARBs group (p: ns) and BB group vs non-BB group (p: ns). When considering the combined use of Iva and BBs, different rates of hospitalization for heart failure and mortality were observed (4 groups according to the use of ivabradine and beta-blockers (Iva-/BBs-10% and 0% respectively; Iva-/BBs+64% and 21%; Iva+/BBs- 69% and 54%; Iva+/BBs+31% and 38%).

**Conclusions:** non-significant differences in terms of safety and survival were found in PH patients with supportive therapies based on ACEi, ARBs, BBs and ivabradine in PH patients.

P1740

**Right ventricle systolic remodeling index is a new echocardiography parameter that predicts long time survival in patients with pulmonary hypertension**

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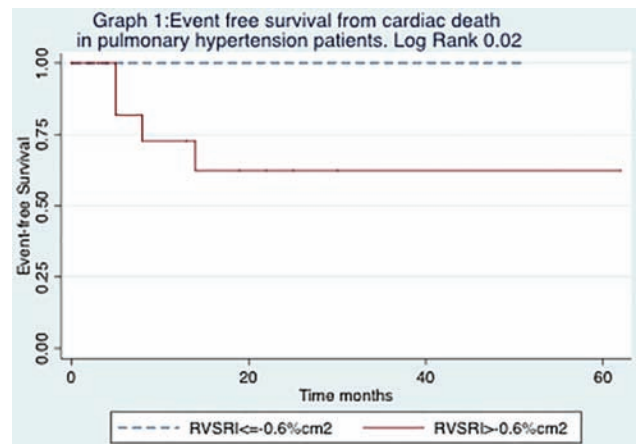
**Purpose:** Pulmonary hypertension (PH) is a progressive multifactorial disease. PH mortality is related to right ventricle (RV) ability to adapt in a high afterload environment. We purposed to evaluate a novel parameter defined: "RV systolic remodelling index (RVSRI) (%/cm<sup>2</sup>)" for long time survival prediction in PH patients.

**Method:** No left ventricle related PH patients were enrolled. 2D trans thoracic (TTE) speckle tracking echocardiography (Vivid 7500 GE) was performed by two expert operators in RV 4C modified view. RVSRI was defined as a ratio: RV free wall longitudinal strain (RVFWL)%/ RV area (RVA)cm<sup>2</sup>; that ratio represents myocardium systolic function by cm<sup>2</sup> of RV. Cardiac death was the final point. Baseline evaluation included complete RV TTE, clinical evaluation and hemodynamic PH confirmation. The study adhered to Helsinki and Istanbul declaration.

**Results:** We followed 28 patients, main follow 19.1 months, main age 43.3 ± 13.4; 25% were idiopathic pulmonary artery hypertension (PAH); 46.4% PAH-congenital;

(Log Rank p 0.02). RV heart failure was the final cause of death in all. No differences were found in : TAPSE, RV S', main PA pressure, maximal tricuspid regurgitation velocity or RV tei index between groups according to RVSRI. RVSRI correlated with cardiac index (CI) Pearson 0.49, p 0.013. RVSRI showed a no significant deterioration according to Post tricuspid PAH, Eisenmenger, idiopathic PAH or PAH-connective tissue.

**Conclusion:** RVSRI is an ETT parameter that describes two types of RV remodelling and predicts long time survival in different aetiologies of PH patients.



P1741

**Exercise-induced oxygen desaturation in patients with idiopathic pulmonary arterial hypertension**

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Exercise-induced oxygen desaturation (EID) is associated with increased risk of mortality in idiopathic pulmonary arterial hypertension (IPAH). The aim of this study was to investigate the characteristics of patients who had EID during six minute walking test (6 MWT). Fifty-seven patients were included in the study. Rest and post-exercise SpO<sub>2</sub> were measured using a pulse oximeter with a nger probe. Borg scale was used to measure the levels of dyspnea and fatigue. Pulmonary functions were assessed with spirometry. Twenty-one (36.8%) patients (group I) had EID (14F/7M; mean age 41.8) and 36 were non-desaturated (22F/14M; mean age 44.1). Groups had similar 6MWT distances. Group I had significantly higher post-exercise dyspnea, fatigue and had higher change in post exercise dyspnea and fatigue scores. FEV1/FVC was significantly lower in group I. Resting SpO<sub>2</sub> values showed significantly negative correlation with the resting fatigue, post-exercise dyspnea and fatigue, and positive correlation with FVC%, FEV1%, FEV1/FVC. Change in SpO<sub>2</sub> values showed significantly negative correlation with resting fatigue, post-exercise dyspnea and fatigue, and post-exercise change in dyspnea and fatigue. FEV1/FVC was positively correlated with change in SpO<sub>2</sub>. In conclusion, IPAH patients with EID despite walking similar distances perceived more dyspnea, fatigue and they had worse pulmonary function as assessed by FEV1/FVC ratio.

## P1742

**Accuracy and precision of systolic pulmonary pressure assessed by echocardiography among patients with pulmonary hypertension**

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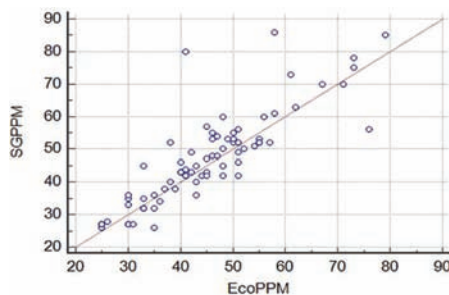
**Background:** Non-invasive estimation of pulmonary pressures by Doppler echocardiography (DE) is an important tool for the management of pulmonary hypertension (PH) patients. Previous reports suggested the use of the velocity-time integral of the tricuspid reflux (VTI-TR) for estimating the mean pulmonary pressure (MPP). However, there is limited information regarding precision and accuracy of the VTI-TR.

**Objective:** Estimate the correlation between mean pulmonary pressures assessed by DE using the tricuspid VTI and right heart catheterization (RHC).

**Material and methods:** Patients with confirmed PH diagnosis (MPP  $\geq$  25 mm Hg) that underwent RHC between March 2012 and May 2015 from three heart failure centers were included in the analysis. The echocardiographic studies were performed using two ultrasound systems (Vivid 5s and Esaote 30 Gold). The MPP was obtained by adding the VTI-TR to the estimated right atrial pressure (RAP), determined by the variation in the size of the inferior vena cava with inspiration. Hemodynamic confirmation of pulmonary pressures was obtained by a RHC using a Swan-Ganz catheter. RHC and DE were performed with less than 24 hours of difference between them and the physicians were blind to echocardiography results. The MPP obtained by the two methods were compared using Lin's concordance correlation coefficient and Bland Altman plot. MPP was categorized in 11 groups per 10 mmHg increase and quadratic weighted kappa ( $\kappa$ ) was performed for qualitative agreement measures.

**Results:** A total of 80 patients with diagnosis of PH were included. Mean age was 57.5 years (SD 19) and 73% were women. PH group (G) distribution was G1 64%; GII 16%; GIII 8%; GIV 6% and GV 6%. 79% had heart failure, 26% syncope and 23% chest pain; mean distance in the 6 minute walk test was 326 meters (SD 137). Mean RHC pressures (mm Hg) were: MPP 48 (SD 15), systolic pulmonary pressure (SPP) 76 (SD20), diastolic pulmonary pressure (DPP) 34 (SD12), RAP 10 (SD 5,1). The transpulmonary gradient was 35 and mean cardiac index 2,7 liters/min/mts<sup>2</sup>. Analysis of DE data shown: mean TAPSE 18 mm (SD 4), SPP 73 mm Hg (SD 16) and MPP 45,6 mm Hg (SD 12,1). The concordance correlation coefficient resulted in 0.83 (95% CI 0.74-0.88), with a Pearson r of 0.84 (precision) and a Cb correction factor of 0.97 (accuracy) (figure 1). The Bland Altman plot shows a mean difference of 2 mmHg (SD 7,6). The  $\kappa$  coefficient was 0.80 (95% CI 0.70-0.90). Although related to a small number of observations, DE underestimated MPP above 70 mmHg.

**Conclusion:** A moderate to high correlation in MPP assessment between a non-invasive technique (VTI-TR) and right heart catheterization was observed among patients with PH. These results supports the use of DE as a reliable diagnosis measure of MPP among patients with PH. Further research may be needed to assess accuracy in very high PH patients (MPP above 70 mmHg).



Correlation of Mean Pulmonary Pressure

## P1743

**Prevalence of adverse prognostic factors at diagnosis of pulmonary hypertension**

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**Background:** Pulmonary hypertension (PH) is a multifactorial condition associated with high morbidity and mortality. Multidisciplinary approach is required for its diagnosis and treatment. In the past decades there have been many advances in the epidemiological, pathophysiological and therapeutic knowledge of the disease. However, there is little information available regarding clinical and prognostic factors in patients diagnosed with PH in Latin America.

**Aims:** Determine the prevalence and clinical characteristics of adverse prognostic factors in a population with initial diagnosis of PH.

**Methods:** Patients with initial diagnosis of PH (<7 days) confirmed by right heart catheterization (RHC)(mean pulmonary-artery pressure (MPP)  $\geq$  25 mm Hg) from three heart failure and pulmonary hypertension services were analyzed between March 2012 and May 2015. Data recorded included: Personal data, PH group (G), clinical features, direct hemodynamic parameters by RHC, 6 minute walk (6MW) test distance and echocardiographic variables. We defined as adverse prognosis factors: history of heart failure (HF), syncope, advance functional class (FC) (NYHA III-IV), performance in the 6MW test  $\leq$  350 meters (m), presence of pericardial effusion (PE), tricuspid annular plane systolic excursion (TAPSE)  $\leq$  15 mm right atrial pressure (RAP)  $\geq$  12 mm Hg and cardiac index (CI)  $\leq$  2,2 litros/min/mts<sup>2</sup>. Data obtained were analyzed with BioEstat 5.3 program.

**Results:** Multicenter, consecutive and prospective study. A total of 80 patients were included, 73% women. Mean age was 57,5 years (SD 19), 33%  $\geq$  70 years. The mean delay in diagnosis was 26 months after the first sign or symptom recorded. PH group distribution: G1 64%, GII 16%, GIII 8%, GIV 6% and GV6%. FC of presentation: I 4%, II 41%, III 34% and IV 21%. 6MW test mean distance was 315 m (SD 145). RHC: MPP 51 mm Hg (SD 15), systolic pulmonary pressure (SPP) 78 mm Hg (SD 20), diastolic pulmonary pressure 34 mm Hg (SD 12), RAP 10 mm Hg ( $\pm$  5,1), CI 2,7 litres/min/mts<sup>2</sup>. Ecocardiographic data: right ventricle systolic function impaired in 85% (slight 45%, moderate 25% and severe 15%). Mean TAPSE 18 mm (SD 4), SPP 73 mm Hg (SD 16). Adverse prognostic factors prevalence was: HF: 75%, syncope: 26%, advance FC: 55%, 6 MW test  $\leq$  350 m: 32%, TAPSE  $\leq$  15 mm: 22%, PE: 31%, RAP  $\geq$  12 mm Hg: 27%, CI  $\leq$  2,2 litros/min/mts<sup>2</sup>: 18%

**Conclusions:** In this population with initial diagnosis of pulmonary hypertension an elevated proportion of men and patients over 70 years old was observed. At diagnosis time a high number of patients present adverse prognosis factors. This findings remark the need to use early diagnosis and therapeutic strategies.

## P1744

**Right ventricle characterization in patients with severe pulmonary hypertension due to post tricuspid shunts in contrast with other etiologies.**

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**Purpose:** Pulmonary artery hypertension (PAH) due to post tricuspid (PTS) shunt defects have better prognosis compared with other etiologies. Right ventricle (RV) seems to be the key for better survival. The main of the study was determinate differences in RV characteristics of PTS vs other etiologies in PAH.

**Methods:** Trans thoracic echo was done by two operators. We evaluated: Longitudinal strain (LS) 2D speckle tracking, TAPSE, RV fractional shortening (RVFS); RV tissular systolic peak (RVSP); TEI RV index (TEIRV); RV diastolic area (RVdA); RV systolic area (RVSA); RV basal diameter(d) (RVBd); RV outflow tract d (RVOTD), RVOT fractional shortening (RVOTFS); main PA pressure (mPAP); tricuspid regurgitation velocity (TRV); left ventricle ejection fraction (LVEF); RV global LS (RVGLS); free wall RV LS (FWRVLS); RV basal segment LS (BRVLS); inter ventricular septum LS (IVSLS); posteroseptal medial segment LS (PSmLS) and cardiac index(CI). RV remodeling was defined as RVR =FWRVLS/RVdA(%/cm2). Groups were: groupA(gA): PTS PAH and groupB(gB): pre tricuspid shunts, idiopathic PAH and type 3/ 4 PAH according ISHLT.

**Results:** We followed 46 patients only in sildenafil. The 15.2% were in gA; in gB: 30.4% idiopathic; 45.7% congenital; 23.9% type 3/4 ISHLT. Mortality: gA 28.5% vs gB 14.38%. Age 41.9  $\pm$  14.4 years. As expected gA vs gB showed longer RV: (RVSA p 0.02; RVdA p 0.003; RVBd p 0.003); higher mPAP: 68.8  $\pm$  2.9 vs 46.2  $\pm$  10 mmHg (p 0.0002) and TRV 7.5  $\pm$  4.9 vs 4.2  $\pm$  0.6m/s(p 0.0001). No differences in TAPSE (17.5mm); TEIRV (0.8); RVSP(10.3cm/s); RVGLS (-14.9%) or RVFS (33.8  $\pm$  11.3 %). Between gA and gB there was a trend in less dilated RVOTD $\geq$ 35mm(0 vs 27%), better RVOTFS $\leq$ 30%(33.3 vs 71.4%),worse PSmL%(-9.5  $\pm$  9 vs -14.4  $\pm$  5.4) and IVSLS%(-10.0  $\pm$  6 vs -14.5  $\pm$  6). Segmental RV asses showed gA vs gB: FWRVLS %(-20  $\pm$  3.4 vs -14  $\pm$  6.9 p 0.05), BRVLS %(-22  $\pm$  9 vs -13  $\pm$  9 p 0.03) and CI (4.2  $\pm$  1.1 vs 2.8  $\pm$  0.9 ml/min/m2). RVR showed inverse correlation with CI pw -0.5 (p 0.01); and it was twice in gA than gB 2: -1  $\pm$  0.4 vs -0.5  $\pm$  0.4 (p 0.02 IC -0.8 - -0.08).

**Conclusion:** PTS PAH patients show longer RV. Despite higher mPAP and RTV, PTS patients have better LS of RV free wall; better RV remodeling and CI than gB. RVR described as FWRVLS/RVdA relation is a parameter that should be more studied as possible good marker of RV remodeling by echo.

## P1745

**Right ventricular vascularization in patients with pulmonary arterial hypertension.**

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**Introduction:** Chronic pressure overload of the right ventricle (RV) leads to increased oxygen and metabolic demand which are important triggers of angiogenesis. Aim



To determine vascularization of RV in patients with pulmonary arterial hypertension (PAH) and its impact on survival.

**Methods:** We enrolled consecutive patients with PAH diagnosed in single pulmonary hypertension centre between 2011 and 2015, who underwent routine coronary angiography. Control group comprised of age- and sex-matched subjects without PAH who were diagnosed for ischemic heart disease but had normal coronary vessels. Artery branches from segments I-III of the right coronary artery (right ventricular branches, RVB) and branches of the left coronary artery (LVB) were assessed by investigator blinded to diagnosis. The mean diameter of RVBs calculated as a sum of diameters of all RVBs divided by the number of all RVBs was used as a marker of right ventricle vascularisation. For survival analysis we used univariate Cox proportional hazard model. Results We recruited 37 PAH patients (idiopathic, n = 25; associated with connective tissue disease, n = 12) and 37 controls of similar age ( $56 \pm 18$  vs  $56 \pm 13$  years,  $p = 0.99$ ) and sex (73% vs 73% of women,  $p = 0.99$ ). PAH patients were in World Health Organization class: II (n = 10), III (n = 24), and IV (n = 3), mean distance in 6-minute walking test was  $302 \pm 110$ m, median pulmonary artery pressure:  $45 [35-57]$ mmHg, median pulmonary vascular resistance:  $10.8 [7.3-16.0]$ WU, and median cardiac index:  $1.88 [1.45-2.45]$ L/m<sup>2</sup>/min. PAH patients as compared to control group had more RVBs ( $7.2 \pm 1.6$  vs  $6.2 \pm 1.3$ ,  $p = 0.01$ ) and mean diameter of RVBs ( $1.35 \pm 0.20$ mm vs  $1.22 \pm 0.14$ mm,  $p = 0.001$ ). We did not find any difference in the number of the branches of left coronary artery ( $4.5 \pm 1.0$  vs  $4.1 \pm 0.9$ ,  $p = 0.14$ ). In univariate Cox model mean RVB diameter predicted survival of PAH patients (HR = 0.01 [0.001-0.35],  $p = 0.03$ ). Conclusion Vascularization of the right ventricle is increased in patients with PAH than in controls without pulmonary hypertension. Increased mean diameter of RVBs is associated with better survival.

## RIGHT VENTRICULAR FUNCTION

### P1746

#### Assessment of right ventricular to pulmonary circulation uncoupling at peak exercise in heart failure by the relationship between pulmonary systolic pressure vs free-wall right ventricular strain

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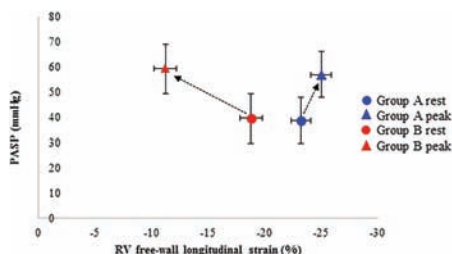
**Background:** Speckle tracking analysis is an emerging technique that can be useful to assess abnormalities in cardiac contractility before traditional echo parameters, with particular interest to right ventricle (RV) performance.

**Purpose:** To investigate whether RV 2D speckle tracking analysis at peak exercise could stratify a heart failure reduced ejection fraction (HFrEF) population in different functional phenotypes, with particular emphasis on RV to pulmonary circulation relationship.

**Methods:** 36 HFrEF patients (mean age  $69 \pm 12$ ; male 69%; NYHA I-II-III-IV 19-17-25-5 %) underwent a maximal cardiopulmonary exercise testing evaluation (bike, incremental ramp protocol) combined with Echo-Doppler and off-line speckle tracking analysis. Study population was divided in two groups according to median value of 2D right ventricle free-wall longitudinal strain at peak exercise (Group A RVLS at peak  $< -19$ , 17 patients vs Group B  $\geq -19$ , 19 patients). In all patients we performed traditional echo and 2D longitudinal speckle tracking analysis at rest and peak exercise.

**Results:** Despite similar left ventricle ejection fraction (Group A  $36 \pm 9\%$  vs Group B  $32 \pm 9\%$ ,  $p = ns$ ) and right ventricle longitudinal strain (RVLS) at rest (Group A  $-23.2 \pm 7\%$  vs Group B  $-18.8 \pm 9.1\%$ ,  $p = ns$ ), Group B patients showed a similar exercise performance (Peak VO<sub>2</sub> Group A  $31.6 \pm 7.4$  vs Group B  $11.6 \pm 3.4$  mlO<sub>2</sub>/Kg/min,  $p = ns$ ) but more impaired ventilation (VE/VCO<sub>2</sub> slope Group A  $31.6 \pm 7.4$  vs Group B  $37.4 \pm 8.8$ ,  $p < 0.05$ ), and a clear RV to PC uncoupling at peak exercise as assessed by the relationship between pulmonary systolic pressure vs free-wall RVLS (see figure below). Strain data were according to traditional echo parameters.

**Conclusions:** In HFrEF RV speckle tracking analysis at peak exercise seems a useful technique for unmasking RV to PC uncoupling and the unfavorable gas exchange and ventilatory phenotypes.



### P1747

#### Pediatric heart transplantation recipients: echocardiographic evaluation of right heart structure and function

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**Introduction:** Although in adult cardiac transplant recipient patients the right heart is a major determinant of prognosis, its impact in pediatric age has not been adequately investigated.

**Purpose:** To investigate right ventricular (RV) morphology and function in pediatric cardiac transplant recipient patients using both standard transthoracic echocardiography and new echocardiographic techniques (2D-strain).

**Methods:** 20 relatively stable pediatric cardiac transplant recipient patients (M/F: 11/9; mean age  $14.5 \pm 4.5$  years; length of follow-up:  $3.8 \pm 3$  years) (Group A) and 40 healthy age and sex matched controls (Group B) underwent standard echocardiography, tissue Doppler imaging (TDI), and 2D-strain, focused on RV analysis. Along with left ventricular (LV) heart parameters, RV measurements included end-diastolic diameters at basal and mid-cavity level; base-to-apex length; tricuspid annulus plane systolic excursion (TAPSE); TDI RV systolic peak velocity (Sm); and global 2D-strain. Finally pulmonary artery systolic pressure (PASP) was calculated using the peak systolic tricuspid regurgitation velocity (TRV).

**Results:** LV diameters and ejection fraction did not significantly differ between two groups. On the other hand, in Group A patients mass index was increased and RV diameters were significantly increased ( $p < 0.001$ ), whereas TAPSE and RV Sm were significantly lower ( $p < 0.05$ ). Furthermore, in Group A patients, 2D RV strain was significantly reduced ( $p < 0.001$ ) regardless PASP. By multivariable analysis, in Group A patients age at transplantation was the only independent determinant of RV diameters and 2D-strain ( $p < 0.01$ ).

**Conclusions:** Pediatric population heart transplant recipient patients show a reduction of RV performance function assessed by TAPSE, right ventricular Sm and global 2D-strain. Of interest, there is a significant correlation between RV dysfunction and length of follow-up. However, further studies with larger populations are needed to confirm these data to define the role of new echocardiographic technologies in their clinical management.

### P1748

#### Echocardiography predicts right ventricular size and function in patients with dilated cardiomyopathy: a comparison with magnetic resonance imaging

Supported by unrestricted grants to the Dept of Cardiology, Oslo University Hospital from Inger and John Fredriksen and an anonymous donor K Kaspar Broch<sup>1</sup>; E Hopp<sup>2</sup>; L Gullestad<sup>3</sup>; S Aakhus<sup>3</sup>

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**Introduction:** Right ventricular (RV) size and function can be difficult to estimate by echocardiography due to the complex geometric shape of the right ventricle. Magnetic resonance imaging (MRI) is the gold standard when assessing RV size and function, but is costly and resource demanding.

**Purpose:** We aimed to assess echocardiographic indices of RV size and function in a prospectively recruited population of patients with dilated cardiomyopathy (DCM). We compared results with those obtained by MRI.

**Methods:** In 44 patients with idiopathic DCM and an LV ejection fraction (EF)  $< 40\%$ , we performed echocardiography and cardiac MRI. Image analysis was performed blinded to patient characteristics and to the results of the other image modality. The echocardiograms were analysed off-line according to current recommendations with particular focus on RV function. For the MRI measurements, RV endocardial borders were traced manually, and volumes and ejection fractions were calculated by short axis slice summation.

**Results:** RV end diastolic and end systolic volumes were  $198 \pm 76$  ml and  $124 \pm 74$  ml, and RV ejection fraction (EF) was  $40 \pm 14\%$  as measured by MRI. Left ventricular EF was  $28 \pm 12\%$ . End diastolic and end systolic RV area were firmly associated with corresponding RV volumes as measured by MRI ( $r = 0.79$ ;  $p < 0.001$  and  $r = 0.86$ ;  $p < 0.001$ , respectively). All pre-specified measures of RV function: fractional area change; tricuspid annulus plane systolic excursion (TAPSE); and RV peak strain were associated with RV EF as measured by MRI. (Table). The association was somewhat weaker for TAPSE, even after adjusting for right ventricular long axis dimension by echocardiography. The relatively low association between TAPSE and RV EF might be due to translational movement of the right ventricle in these patients with severely dilated and dysfunctional left ventricles.

**Conclusions:** Indices of RV function obtained by echocardiography, in particular RV strain, correlates strongly with RV EF as measured by MRI in patients with dilated cardiomyopathy. TAPSE may be less reliable in this population.

Indices of right ventricular function			
Echo parameter	Value	Association with RV EF by MRI	
r	p		
RV fractional area change	19 ± 6	0.69	< 0.001
RV global strain	-13.5 ± 4.2	-0.76	< 0.001
RV free wall strain	-17.8 ± 5.2	-0.77	< 0.001
TAPSE (mm)	19 ± 6	0.46	0.002
Adjusted TAPSE (mm/cm)	2.2 ± 0.7	0.53	< 0.001

### P1749

#### Right ventricular improvement parallels left ventricular improvement after introduction of therapy for dilated cardiomyopathy

Supported by unrestricted grants to the Dept of Cardiology, Oslo University Hospital from Inger and John Fredriksen and an anonymous donor K Kaspar Broch<sup>1</sup>; E Hopp<sup>2</sup>; AK Andreassen<sup>3</sup>; S Aakhus<sup>3</sup>; L Gullestad<sup>3</sup>

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**Introduction:** Dilated cardiomyopathy (DCM) is characterised by left ventricular (LV) dilation and functional impairment, but also affects right ventricular (RV) function. Magnetic resonance imaging (MRI) is considered the gold standard when assessing RV size and function. RV function has not been well characterised in patients with DCM.

**Purpose:** We aimed to assess RV function in patients with recent-onset DCM, and to determine whether RV functional improvement occurred with the introduction of pharmacological treatment for heart failure.

**Methods:** We prospectively recruited 88 patients aged 52 ± 13 years, 30 % females, with idiopathic DCM and an LV ejection fraction (EF) < 40 %. Baseline work-up included cardiac MRI, echocardiography, and right sided heart catheterisation. MRI was repeated in 59 patients after one year. Predictors of baseline RV EF were analysed by regression analyses. Changes from baseline to one year were assessed by paired t-tests.

**Results:** At baseline, RV end diastolic and end systolic volumes were 206 ± 75 ml and 131 ± 71 ml. RV EF was 39 ± 13%, and 71 patients (81%) had an RV EF < 50%. LV and RV EFs were strongly associated ( $r = 0.73$ ;  $p < 0.001$ ). LV EF by MRI, pulmonary capillary wedge pressure, and E/e', representing LV diastolic function, were all independently associated with RV EF (Table). After one year on drug therapy for heart failure, LV and RV EFs improved by 14 ± 13 and 8 ± 12 percentage points, respectively. The improvement in RV EF closely paralleled the improvement in LV EF ( $r = 0.76$ ;  $p < 0.001$ ), and was more pronounced in patients with a poor RV EF at baseline ( $r = 0.68$ ;  $p < 0.001$ ).

**Conclusions:** In DCM, RV function is reduced, but improves in parallel with LV functional improvement after the initiation of therapy for heart failure. LV systolic and diastolic function and filling pressure are determinants of RV function in these patients.

Predictors of RV ejection fraction			
Variable	Baseline value	Univariate analysis	Multivariate analysis
r	p	Beta	p
Age (years)	52 ± 13	0.17	0.11
Gender (M/F)	62/26		0.03
Duration of symptoms (months)	7 (3 - 16)	0.06	0.60
Left ventricular ejection fraction (%)	28 ± 11	0.73	0.69 < 0.001
Pulmonary wedge pressure (mmHg)	14 ± 8	0.57	< 0.001
E/e'	12 (9 - 17)	0.24	0.03

Predictors of right ventricular (RV) ejection fraction and their association with RV ejection fraction.

### P1750

#### Value of global longitudinal strain in right ventricle myocardial infarction diagnosis

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**Background:** Right ventricular (RV) dysfunction after inferior acute myocardial infarction (AMI) is frequent and associated with a poor prognosis. Quantification of RV deformation by speckle-tracking echocardiography is a widely available and reproducible technique that readily provides an integrated analysis of all segments of the right ventricle. The aim of this study was to investigate the accuracy of conventional echocardiographic parameters and speckle-tracking echocardiographic strain parameters in assessing RV function after inferior AMI.

**Methods:** Thirty one patients admitted for inferior AMI were prospectively studied. Right ventricular function was assessed by echocardiography within 2 to 4 days of hospital admission. Right ventricular infarction was defined by ST elevation in rights leads (V3R and V4R). Right ventricular global peak longitudinal systolic strain (GLPSS) was calculated by averaging the strain values of the apex, base, and mid cavity.

**Results:** In patients with inferior myocardial infarction, right ventricular dysfunction was documented in 10 patients. There was significant difference between group 1 (n = 10) and group 2 (n = 21) in TAPSE (13.20 ± 1.3 vs 20.59 ± 5.5,  $p < 0.001$ ), MPI by tissue Doppler (0. ± 0.65 vs 0.39 ± 0.1,  $p < 0.001$ ) and in tissue Doppler systolic velocity from RV free wall (S' 8.80 ± 1.1 vs 13.29 ± 2.5,  $p = 0.01$ ). Right ventricular fractional area change (RVFAC) (0.29 ± 0.9 vs 0.39 ± 0.9,  $p = 0.02$ ). Right ventricular GLPSS was the best echographic parameter correlate with RVFAC ( $r = -0.48$ ,  $P = 0.006$ ) and possessed good diagnostic value for RV dysfunction, which was comparable with tricuspid annular plane systolic excursion (TAPSE) ( $r = -0.47$ ,  $P = 0.007$ ) and doppler systolic velocity from RV free wall ( $r = -0.66$ ,  $P < 0.001$ ).

**Conclusions:** In patients with inferior AMIs, RV GLPSS displays higher diagnostic value than conventional echocardiographic parameters.

### P1751

#### Correlation of ST-2 blood levels and the condition of the right heart departments in patients with severe heart failure

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**Aim:** To investigate a relationship of biomarkers ST-2 and right heart hemodynamic, laboratory indices (NT-proBNP, C-reactive protein (CRP)) in patients with end stage of heart failure (HF).

**Methods:** ST2 blood assessment and hemodynamic of right heart (tricuspid regurgitation (TR), systolic pressure of pulmonary artery (SP PA, mm Hg), right ventricular end-systolic (ESS RV, mm2) and end-diastolic square (EDS RV, mm2)) were assessed. This study involved pts 18 - 65 years old, with end-stage chronic heart failure (III-IV functional class), with a poor prognosis, no remaining alternative treatment options, accepted in the transplant waiting list.

**Results:** In vivo ST2 blood level and hemodynamic parameters that characterize right heart function in patients with severe HF showed significant and strong correlation: with ESS RV ( $r = 0.72$ ,  $=0.008$ ), EDS RV ( $r = 0.64$ ,  $=0.009$ ), TR ( $r = 0.70$ ,  $=0.011$ ). The correlative connection of medium strength was revealed with the indices of SP PA ( $r = 0.42$ ,  $=0.008$ ). And was performed the comparative analysis of echocardiography parameters in groups of patients with HF formed on the basis of the primary levels of ST2 (tabl. 1). Our results demonstrate that in patients with ST2 ≥ 30 ng/ml all crucial echocardiography parameters were significantly higher: SP PA - by 25,0% ( $=0.009$ ), ESS RV - by 50,0% ( $=0.007$ ), EDS RV - by 32,0% ( $=0.011$ ), TR - by 20,0% ( $p = 0.031$ ).

But was founded weak significant correlation between group of laboratory markers of the severity of heart failure: NTproBNP and CRP blood levels ( $r = 0.29$ ,  $=0.049$ ) with ST2.

**Conclusions:** Serum levels of the interleukin-1 receptor family member ST2 is independent of traditional factors, such as age and body mass index and hemodynamic of the left part of heart in the end stage of heart failure before transplantation, which usually affect levels of CRP, NTproBNP. Soluble ST2 could reflect the state of right ventricular and can be used for diagnose of chronic heart failure that depending of insufficiency of the right heart.

Hemodynamic parameters of right heart			
Parameter	ST-2 < 30 ng/ml (Me (LQ-UQ))	ST-2 ≥ 30 ng/ml (Me (LQ-UQ))	
SP PA, mm Hg	44,0 (38,0-52,0)	55,0 (51,0-57,5)	0,009
TR, degree	2,5 (1,0-3,0)	3,0 (2,5-4,0)	0,031
EDS RV, cm <sup>2</sup>	76,0 (45,0-96,0)	114,0 (75,0-159,0)	0,011
ESS RV, cm <sup>2</sup>	50,0 (27,0-77,0)	66,0 (50,0-113,0)	0,007

## P1752

**Clinical scores for right ventricular failure prediction after left ventricular assist device implantation: should we trust them?**

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**Background:** In the era of continuous flow left ventricular assist devices (LVAD), the decision of whether a patient will tolerate isolated LVAD support or will need biventricular support (BIVAD) can be challenging. Incorrect decision making with delayed right ventricular (RV) assist device implantation results in increased morbidity and mortality. Several risk stratification tools have been recently developed to predict the need of right assist device (RVAD) implant concomitant to continuous flow LVAD implantation, but none seems to outperform the others. We reviewed our experience to validate the most recent strategies that should be able to identify patients who are at risk of post LVAD right ventricular failure (RVF).

**Methods:** We retrospectively collected demographic, hemodynamic, and echocardiographic variables for 34 consecutive patients who underwent VAD implant from 2010 through June 2015 (LVAD=32, BIVAD=2). We defined pre-operative RVF based upon echocardiographic parameters, taking into account RV contractility, tricuspid regurgitation, and tricuspid annular motion (TAPSE). Post-operative RV failure was defined according to INTERMACS Protocol 3 definition (CVP>18mmHg, CI < 2 l/min/m<sup>2</sup>, need for nitric oxide or inotrope therapy > 7 days after LVAD implant). For each patient, we calculated the CRITT score (CVP > 15 mmHg, RV Dysfunction, Intubation preoperatively, Tricuspid regurgitation, Tachycardia > 100 and each variables is assigned a score of 0 or 1) and applied the Pittsburgh Decision Tree (PDT) specifically designed for continuous flow circulatory support devices. We assessed the performance of the score by entering it in a logistic regression model with RV failure as the outcome. The PDT was entered as a single binary predictor.

**Results:** The mean age was 52 ± 12; 70.5% were men. The indication was bridge to transplant in 100%. Etiology was ischemic in 42%; 14.7% required additional mechanical circulatory support after LVAD implant (BVAD=2, ECMO=3). All patients received continuous flow LVADs (Heartmate II=13, HeartWare=21). By 30 days, 22 patients (64.7%) developed RVF defined as the need for RVAD (n=2); pulmonary vasodilator use > 48h (n=18); inotropes for > 14 days post LVAD (n=22). According to CRITT score the RVF expected rate was 29% (10 patients had 4 or 5 corresponding to 80% risk of RVF). According to PDT, 8 patients needed BVAD. CRITT score achieved best performances (C statistics = 0.60; CI 95%; sensitivity = 90%; specificity 8.3%; accuracy 61.8%).

**Conclusions:** These data indicate that even clinical RVF risk prediction models developed in the era of continuous flow pumps have rather limited clinical applicability. We definitely need new clinical test based on quantitative pre-operative imaging data, able to quantify the functional reserve of RV to drive our clinical decision about using an isolated LVAD versus BIVAD, especially in the destination therapy perspective.

## LEFT VENTRICULAR FUNCTION

## P1753

**Inducible myocardial ischemia due to obstructive coronary artery disease is associated with subclinical LV dysfunction in patients with stable angina**

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**Background:** Repetitive myocardial ischemia might impair LV function in patients with stable coronary artery macrovascular and/or microvascular disease (CAD).

**Purpose:** To assess the relationship between inducible myocardial ischemia, presence of obstructive CAD and LV function in patients with stable angina.

**Methods:** Clinical, functional and imaging data were collected in 362 patients (212 males, 150 females, mean age 60 ± 9 years) with stable angina and suspected CAD enrolled in the Evaluation of INtegrated Cardiac Imaging (EVINCI) study. All patients underwent echocardiography and circulating NT-proBNP measurements to assess LV function, stress imaging to detect myocardial ischemia and coronary computed tomography angiography (CCTA) to assess the presence of obstructive CAD (>50% stenosis of a major coronary vessel). Only patients with LVEF ≥ 50% were included in this substudy.

**Results:** LVEF was 60 [55-66] %, median [25-75 percentiles], and NT-proBNP was 60.7 [30.7-128.0] ng/L in the whole population. Patients were subdivided in 4 groups according to the presence/absence of myocardial ischemia and obstructive CAD.

LVEF and NT-proBNP values are compared among groups in Figure 1. Patients with obstructive CAD+Ischemia had significantly lower LVEF and significantly higher NT-proBNP values than the other groups. At multivariate analysis including age, sex, cardiovascular risk factors, drugs, CTA and stress imaging results, presence of obstructive CAD+Ischemia was the only coronary pattern predicting both LVEF (Coefficient: - 0.119 ± 0.03 (SE), p < 0.0001) and NT-proBNP (0.512 ± 0.15, p = 0.0009) values.

**Conclusions:** In patients with stable angina, inducible myocardial ischemia caused by macrovascular obstructive CAD is associated with early impairment of LV function.

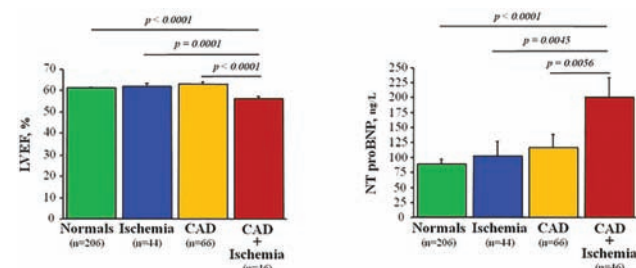


Figure 1

## P1754

**Correlates of reduced left ventricle ejection fraction in young patients with acute myocardial infarction**

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**Background:** Acute myocardial infarction (AMI) is an important cause of left ventricular systolic dysfunction in young patients.

**Purposes:** To identify the clinical, biological, electrocardiographic and angiographic factors associated with reduced left ventricle ejection fraction (LVEF) after AMI in patients younger than 45 years and to evaluate its impact on long-term outcome.

**Methods:** The studied population consisted of 168 consecutive young adults (mean age 39 ± 5 years) admitted for AMI in two acute cardiac care units between January 2009 and December 2011. The baseline characteristics, procedures and treatment were collected at the time of the index event and analyzed for the two groups: patients with LVEF ≥ 50% and those with LVEF < 50%. The patients were followed-up for up to 4 years (mean 3 ± 1 years); the main outcome was a composite of major adverse cardiac events (MACE): cardiovascular death, new myocardial infarction, further revascularization and emergency cardiac readmissions.

**Results:** Reduced LVEF was found in 64 patients (38%) with no significant difference between men and women (40% vs 28.6%, p = 0.2). There was a strong negative correlation between LVEF and admission glycemia (r = -0.2247, p = 0.003), white blood cells number (r = -0.3290, p < 0.001) and hs C-reactive protein (r = -0.5095, p = 0.006). Mean heart rate was significantly higher in the reduced LVEF group on both initial (89 ± 20 vs. 82 ± 18 bpm, p = 0.02) and at 24 hours after admission measurements (81 ± 17 vs. 72 ± 13 bpm, p < 0.001). In the STEMI patients, the median "symptom onset - reperfusion" time (LVEF < 50%: 307 (217-465) min vs LVEF ≥ 50%: 250 (180-420) min, p = 0.2) and TIMI 3 flow in the culprit artery (84% vs. 79%, p = 0.4) were similar between the two groups but the persistence of ST elevation > 50% post-reperfusion correlated with LVEF < 50% even in patients with TIMI 3 flow (OR 0.19, IC 95% 0.06-0.57). Regardless of the AMI type, factors independently associated with reduced LVEF were left anterior descendant artery significant stenosis (OR 5.00, IC 95%, 1.81-13.80), tri-vessel disease (OR 40.6, IC 95%, 4.70-350.08), admission leucocyte number (OR 1.002, IC 95%, 1.00-1.003), 24 hours heart rate (OR 1.04, IC 95%, 1.00-1.08), pathological Q waves (OR 6.24, IC 95%, 1.32-29.46) while positive history of premature CVD was still associated with LVEF > 50% (0.05, IC 95%, 0.00-0.48).

In survival analysis, 3 years MACE rate was higher in the LVEF < 50% group of young patients (40.7% vs 23.1%, logrank 8.28, p = 0.004).

**Conclusions:** 1) The mechanisms for reduced EF after AMI in young are likely to be multifactorial. Beside established factors like severe and extensive atherosclerotic coronary disease, admission leucocyte count and some early electrocardiogram signs may predict LV systolic dysfunction after AMI in young patients.

2) LVEF < 50% is correlated with poor outcome after AMI in patients younger than 45 years of age.



**P1755****Recovery of left ventricular systolic function: implications for the implantation of icd and crt-d?**

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**Introduction:** Implantation of cardioverter-defibrillator (ICD) is a well established therapy for primary prevention of sudden death in patients with left ventricular (LV) systolic dysfunction. Nevertheless, questions remain about the indication for maintaining this therapy at the time of generator replacement, in patients with LV function improvement and no dysrhythmic events.

**Purpose:** To evaluate the prevalence of LV function recovery in patients with ICD for primary prevention of sudden death, and the associated variables.

**Methods:** Retrospective analysis including patients with ischemic cardiomyopathy or non-ischemic dilated cardiomyopathy and LV ejection fraction (EF)  $\leq 35\%$  submitted to implantation of ICD, with or without associated cardiac resynchronization therapy (CRT), for primary prevention of sudden death, between 2011 and 2014.

**Results:** Fifty-nine patients, with mean age  $61 \pm 10$  years and male predominance (68%) were included. There was a higher prevalence of ischemic cardiomyopathy (66%), 71% were submitted to implantation of an ICD and 29% of a CRT-D. The baseline mean EF was  $28 \pm 6\%$  and the median NT-proBNP was 1565 pg/ml (interquartile range 315-3456 pg/ml). During a mean follow-up of  $825 \pm 412$  days, 34.9% of the 43 patients with available data had LV function recovery (defined as final EF  $> 35\%$ , with improvement  $\geq 5\%$ ). The incidence of appropriate therapies was 17% and the mortality rate 15%. LV function recovery was more common in patients with associated CRT, although this difference did not reach statistical significance (54% vs. 27%,  $p=0.086$ ). The variables associated with LV function recovery were non-ischemic etiology (53% vs. 23%,  $p=0.045$ ; OR 3.8, 95% CI 1.0-14.0), absence of late enhancement on cardiac MRI (100% vs. 0%,  $p=0.025$ ) and NT-proBNP  $< 1500$  pg/ml (73% vs. 17%,  $p=0.007$ ; OR 13.3 95% CI 1.78-100.0). ROC curve analysis showed that baseline NT-proBNP had a good discriminative capacity for LV function recovery (AUC = 0.74,  $p=0.033$ ); the best cut-off was 1320 pg/ml (sensitivity 77%, specificity 71%). LV function recovery was also associated with a lower risk of death during follow-up (0% vs. 25%,  $p=0.034$ ; OR 1.33 95% CI 1.1-1.7).

**Conclusions:** In this study of patients submitted to implantation of ICD or CRT-D for primary prevention of sudden death, LV function recovery was common, and associated with a lower long-term mortality. We found that LV systolic function recovery was associated with non-ischemic etiology, absence of late enhancement on cardiac MRI and baseline NT-proBNP. These data may contribute for a better identification of patients who will benefit the most from this therapy.

**P1756****Three-dimensional and speckle tracking echocardiography application for early identification of left ventricular remodelling after myocardial infarction**

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**Introduction:** Cardiac remodelling is generally accepted as a determinant of the clinical course of heart failure. The usefulness of 3D echocardiography (3DE) has been demonstrated in the evaluation of cardiac chamber volumes and mass, which avoids geometric assumptions. Speckle-tracking echocardiography (STE) has emerged also as a novel technique for left ventricular (LV) functional assessment, but both techniques have a lack of information about its prognostic value for LV remodelling after acute myocardial infarction (AMI).

**Purpose:** To determine the prognostic value of 3DE and STE parameters for LV remodelling after AMI.

**Methods:** This was a prospective study where 75 AMI patients were included and underwent 3DE and STE examination within 3 days of AMI and at 6-month follow-up. LV remodelling was defined as a  $\geq 15\%$  increase in the LV end-diastolic volume (EDV) at follow-up compared with the baseline. Statistical analysis was performed using Kruskal-Wallis analysis (median (min-max)), ROC curves and logistic regression.

**Results:** At follow-up, 22 patients (27%) were classified as having LV remodelling. Morphometric parameters of LV measured by 3DE were significant between LV remodeling group and non-remodeling group patients: EDV-140.9 ml (66.3-255.95) vs. 115.2 ml (53.3-156.9) ( $p=0.006$ ), end-systolic volume (ESV) - 89 ml (25.9-139.2) vs. 66.9 ml (35.28-111.63) ( $p=0.003$ ), sphericity index (SI) - 0.43 (0.23-0.66) vs. 0.31 (0.14-0.74) ( $p=0.001$ ) and systolic dyssynchrony index (SDI) - 4.75% (2-11.1) vs. 3.6% (0.5-8.1) ( $p=0.034$ ), respectively). Echocardiographic parameters measured by STE were the same in both groups, except for LV torsion ( $1.53^\circ/\text{cm}$  (0.56-1.98) and  $2.02^\circ/\text{cm}$  (0.72-2.93),  $p=0.008$ ). Logistic regression and ROC analysis revealed that some 3DE parameters and LV torsion had significant predictive value for occurrence of LV remodeling (Table 1).

**Conclusions:** 3DE parameters had a high prognostic value for prediction of LV remodelling after AMI where sphericity index is superior. LV torsion as STE parameter could also be a useful parameter of LV remodelling prediction when 3DE is not applicable.

Table 1

Parameters	Cut- off value	Sensitivity (%)	Specificity (%)	AUC	p-value
3D EDV (ml)	> 115.3	71	79	0.74	0.028
3D ESV (ml)	> 69.8	69	78	0.73	0.042
3D SDI (%)	> 4.6	73	77	0.78	<0.001
3D SI	> 0.50	90	91	0.96	<0.001
LV torsion ( $^\circ/\text{cm}$ )	< 1.34	62	74	0.70	0.038

Predictive value of echocardiographic parameters measured by 3DE and STE for LV remodelling development

**P1757****Left ventricular remodeling in women with surgical and natural menopause**

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**Purpose:** To assess structural and functional changes of left ventricle in postmenopausal women in dependence on menopause type and arterial hypertension characteristics.

**Methods:** 203 postmenopausal women were included in the investigation: the 1st group - 61 women with natural menopause (average age  $46.2 \pm 4.7$  years, menopause duration  $4.3 \pm 2.1$  years); and the 2nd group - 142 women with surgical menopause (average age  $44.3 \pm 5.4$  years, menopause duration  $3.8 \pm 2.4$  years). All patients underwent general clinical examination, menopausal index evaluation, ambulatory blood pressure (BP) monitoring (Cardiotens-01, Meditech, Hungary), echocardiographic examination with systolic and diastolic left ventricular (LV) function assessment. Statistical methods such as Cruskal-Wallis criteria and  $\chi^2$  test were used.

**Results:** The frequency of arterial hypertension in women with natural and surgical menopause was the same: 42,3% (60 pts) in the 1st group and 45,9% (28 pts) in the 2nd group, respectively ( $p>0,05$ ). Only 39 postmenopausal women (19,2%) had normal LV geometry; 57 pts (28,1%) demonstrated concentric remodeling, 89 pts (43,8%) - LV concentric hypertrophy, and 18 women (8,9%) - eccentric hypertrophy. The frequency of LV concentric hypertrophy in the 2nd group was wider than in the 1st group (47,9% (68 pts) vs 24,4% (21 pts),  $p=0,049$ ); while women of the 1st group more often had LV eccentric hypertrophy (19,7% (12 pts) vs 4,9% (7 pts),  $p=0,0002$ ) and normal geometry (26,2% (16 pts) vs 15,5% (22 pts),  $p=0,0017$ ). Hypertensive postmenopausal women more often had LV concentric hypertrophy (60,2% (53 pts) vs 31,3% (36 pts) in normotensive women,  $p=0,005$ ), while normotensive postmenopausal women more often demonstrated LV concentric remodeling (33,9% (39 pts) vs 20,5% (18 pts),  $p=0,042$ ) and LV normal geometry (23,5% (27 pts) vs 12,5% (11 pts),  $p=0,034$ ).

Nobody of included postmenopausal women had LV reduced ejection fraction. Presence of LV diastolic function disturbance was the same in the 1st and in the 2nd groups (59,2 (84 pts) and 56,8% (50 pts), respectively,  $p=0,231$ ) and did not depend on BP level: 56,8% (50 pts) in hypertensive and 59,1% (68 pts) in normotensive women,  $p=0,118$ . Patients with LV concentric hypertrophy had LV diastolic dysfunction in 84,3% cases (75 pts); with LV concentric remodeling - in 52,6% cases (30 pts) - with LV eccentric hypertrophy - in 31,6% cases (6 pts), this difference was statistically significant.

**Conclusions:** Patterns of LV remodeling development in postmenopausal women depend on menopause type and BP level. LV diastolic function evolution for the most part depends on LV remodeling type, but not on menopause type or arterial hypertension presence.

**P1758****ST-elevation myocardial infarction with reduced left ventricular ejection fraction: insights into persisting left ventricular dysfunction. A pPCI-Registry analysis.**

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**Background:** Primary percutaneous coronary intervention (pPCI) largely reduced the rate of left ventricular (LV) dysfunction after ST-segment elevation acute myocardial infarction (STEMI). Though LV recovery begins early following revascularization, the optimal timing for re-assessment of LV function is still unclear.

**Purpose:** To assess the proportion and timing of LV recovery in STEMI patients presenting with LV dysfunction treated by pPCI and to identify possible early predictors of adverse LV remodeling.

**Methods and Results:** STEMI patients with LV ejection fraction (LVEF<40%) at presentation treated by pPCI from 2007 to 2013 were included whether they had an available 3-step LVEF assessment (<24 hours post-pPCI, discharge and follow-up). Primary endpoint was LVEF≤35% at follow-up. At a median time of 3 months, 43 out of 154 patients (28%) had LVEF≤35%. In patients with persistent LV dysfunction, LVEF was lower at admission and increased less during hospitalization (from 31 ± 6 to 35 ± 4% Vs 35 ± 5 to 43 ± 8% for patients with 3-months LVEF>35%, p < 0.001). Independent predictors of 3-months LVEF≤35% were creatinine at admission, peak troponin I and LVEF. Of note, LVEF re-assessment at discharge (median time 6 days, IQR 4-9) showed an increased accuracy to predict 3-months LV dysfunction compared to LVEF at admission (AUC 0.80, 95%CI 0.72-0.88 Vs AUC 0.69, 95%CI 0.58-0.79 respectively, p = 0.03).

**Conclusions:** In most of patients presenting with STEMI and LV dysfunction, a significant LV recovery can be observed early following pPCI. LVEF measurement at discharge indeed emerged as the best indicator of late persistence of severe LV dysfunction.

**P1759**

**Systolic performance of the left ventricle after myocardial infarction. The absence of ST elevation costs myocardium**

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Treatment of acute coronary syndromes (ACS) depend upon their clinical and electrocardiographic (ECG) presentation. However, both acute myocardial infarctions with (STEMI) and without (NSTEMI) ST elevation affect left ventricular (LV) function, which may be assessed by conventional echocardiography but also lately using 2D speckle tracking (2D STE). The aim of this study was to compare the effect of STEMIs and NSTEMIs on global longitudinal deformation of the LV (LVGLS).

We studied 28 consecutive patients (pts) with inferior STEMI, as well as 31 pts with NSTEMI. All had echocardiographic evidence of hypokinesia/akinesia of the inferior wall. All pts with STEMI underwent primary percutaneous coronary angioplasty of the culprit lesion, while pts with NSTEMI underwent a coronary angiogram with subsequent angioplasty within 72 hours from the onset of pain. In both STEMI and NSTEMI pts, PTCA was performed at the right or the circumflex coronary artery, depending on the dominance. In all pts the echocardiographic study (TTE) was carried out the day after revascularization.. The findings of the TTE are presented on the Table. While there was no difference in LVEDD between pts with STEMI and NSTEMI (p = 0.836), EF and LVGLS differ significantly (p = 0.015 and p = 0.043, respectively). Surprisingly, although in STEMIs, ischemia was likely affecting a greater proportion of myocardium, LVGLS and LVEF were worse in patients with NSTEMIs. This may be due to delayed revascularization in NSTEMIs, that provides the necessary ischemic time for greater myocardial damage to occur. The time at which revascularization takes place in ACS, may have a direct effect in systolic performance of the LV. It is possible that the worst prognosis of NSTEMIs compared to STEMIs in the medium term, may be related to this difference.

Table 1

	STEMI	NSTEMI	p value
LVEDD (mm)	49.64 ± 3.93	49.87 ± 4.87	0.836
EF (%)	54.07 ± 5.42	50.23 ± 6.31	0.015
LVGLS (%)	-15.03 ± 3.75	-12.93 ± 4.06	0.043

**HFpEF - HEART FAILURE WITH PRESERVED EJECTION FRACTION**

**P1760**

**The role of diastolic heart failure in the development of atrial fibrillation paroxysms in patients with hypertension**

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**Background:** in patients with AH and paroxysmal AF myocardial hypertrophy, high LV myocardial stiffness is in some cases associated with increased LV filing pressure. In turn, the high LV filing pressure may result in development of occult diastolic HF and AF paroxysms. EchoCG detection of this condition involves certain challenges.

**Purpose:** to increase the diagnostic efficiency of diastolic heart failure and to estimate its role in the development of atrial fibrillation in patients with hypertension based on laboratory, electrophysiological, structural data and stress induced changes.

**Methods:** clinical, instrumental (stress echocardiography, transesophageal electro-physiological study), laboratory and statistical.

**Results:** it was established that patients with HTN and AF paroxysms with clinical signs of low functional HF classes (NYHA I-II) are predominantly female (65%). In this group of patients heart remodeling includes LV concentric hypertrophy and diastolic dysfunction with HF development. Diastolic functional reserve index cut-off value (DFRI=14) for identifying HF patients was calculated. The relationship between DFRI, clinical signs, heart remodeling, NT-proBNP and characteristics of AF was defined. During the electrical remodeling parameter assessment it was also proved the relationship of atrial conduction disorders, with clinical, laboratory and echocardiographic data, reflecting the development of diastolic HF, which confirms its impact on myocardial electrophysiological properties and AF development.

**Conclusion:** stress echocardiography can be used for early detection of diastolic heart failure in patients with AF paroxysms, AH and LV diastolic dysfunction; values of DFRI <14 conv. units indicate development of HF induced by low LV diastolic reserve.

**P1761**

**Features of very elderly heart failure patients between heart failure with preserved ejection fraction and heart failure with reduced ejection fraction.**

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**Background:** Heart failure (HF) is principally a disorder of older adults with prevalence and incidence rates that increase progressively with age. Although heart failure (HF) affects all segments of populations, older patients have been markedly underrepresented in most major HF trial. Incident heart failure in older adult patients is predominantly characterized by the phenotype of HF with normal or preserved left ventricular (LV) systolic function (HFpEF). Patients with HFpEF have lower risk of in-hospital mortality, and a similar post-discharge mortality risk and equally rehospitalization as patients with HF and LV systolic dysfunction. We investigate the features of very high aged heart failure patients between HFpEF and HF with reduced EF (HFrEF).

**Methods:** We examined 73 patients who were 90 years old and more, and were admitted in our hospital for acute decompensated heart failure from April 1, 2010 through March 31, 2014. The patients were divided into three groups: those with an ejection fraction of less than 40 percent (HFrEF), those with an ejection fraction of 40 to 50 percent (heart failure with borderline ejection fraction), and those with an ejection fraction of more than 50 percent (HFpEF). Two groups were studied in detail: those with an ejection fraction of less than 40 percent and those with an ejection fraction of more than 50 percent. The main outcome measures were death within one year and readmission to the hospital for heart failure.

**Results:** There were 48 (65.8%) HFpEF patients and 25 (34.2%) HFrEF patients. The length of hospital stay was similar in both groups (40.2 ± 30.7 days vs. 38.4 ± 33.1 days; p = 0.654). Patients with HFpEF had similar risk of in-hospital mortality (12.5% vs. 16.0%; p = 0.680). During 1 year follow-up, patients with HFpEF had a similar mortality risk (14.6% vs. 16.0%; p = 0.872) and rehospitalization rates (33.3% vs. 36.0%; p = 0.820) compared with patients in HFrEF.

**Conclusion:** 90 years old or more heart failure patients has similar prognosis in both HFpEF and HFrEF.

**P1762**

**Heart failure with preserved ejection fraction: is the role of arterial stiffness established?**

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**Background:** heart failure with preserved ejection fraction (HFpEF) amounts the 50% of cases of heart failure. Diagnosis and prognosis of this disease are still uncertain. The diagnosis of HFpEF 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 identified by Doppler report of increased LV filling pressure. We aimed at correlating LV diastolic parameters with central haemodynamics ones.

**Methods:** we prospectively enrolled 25 outpatients affected by HFpEF followed by our Heart Failure Center. They underwent transthoracic echocardiography and applanation tonometry. We focused on echocardiographic parameters meeting the criteria previously established to diagnose HFpEF: LVEF, E/E', E/A and DT, Ard and Ad, left atrial volume index (LAVI), LV mass index (LVMI). Applanation tonometry was carried on the right radial artery to calculate aortic blood pressure, augmentation pressure (AP) and augmentation index (Aix@75).

**Results:** 15 (60%) were male; mean age was 75 ± 8 years. 89% were hypertensive, 44% diabetic, 33% obese, 20% in atrial fibrillation. Mean LVEF was 64 ± 7%; all patients had E/E' between 8 and 15; none had E/A < 0.5 and DT > 280 ms; 93% had Ard-Ad > 30; 50% had LAVI > 40 mL/m<sup>2</sup>; 50% had LVMI > 122g/m<sup>2</sup> for women

and  $>149\text{g/m}^2$  for men. Aortic pressures were:  $124 \pm 16 / 77 \pm 9$  mmHg (mean  $96 \pm 10$ , pulse  $47 \pm 15$  mmHg); AP was  $15 \pm 8$  mmHg and  $\text{Alx@75}$   $26 \pm 7\%$ . We found no correlation between the echocardiographic and the tonometric parameters considered.

**Conclusion:** HFpEF is a frequent condition which still remains without a specific therapy. Its aetiopathology is heterogeneous. A recent meta-analysis strongly linked arterial stiffness with LV diastolic function in patients with HFpEF. Our data seem to suggest that this relationship exists in hypertensive patients, but different subgroups of subjects affected by HFpEF (e.g., diabetes mellitus, atrial fibrillation, obesity) may share different pathogenic pathways.

### P1763

#### Timing of left ventricular deformation and dyssynchrony in HFpEF and treated arterial hypertension

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**Purpose:** Hypertension (HTN) is a relevant precursor of heart failure, especially with preserved ejection fraction (HFpEF), and treatment of HTN has been shown to reduce this risk.

**Methods:** We studied 215 HFpEF patients enrolled in the PARAMOUNT HFpEF trial, 179 patients with uncontrolled HTN, preserved EF and without heart failure from the EXCEED trial, and 45 healthy controls. Hypertensive patients were treated with blood pressure lowering for 24 weeks. We assessed LV synchrony and time to peak contraction (longitudinal strain), indexed to RR interval, in 6 LV segments.

**Results:** Time to peak contraction was greatest in the hypertensive group and directly related to systolic blood pressure. LV dyssynchrony was highest in patients with HFpEF, followed by hypertensives, and significantly different from normal in both groups (Table). After anti-HTN therapy for 24 weeks, SBP in HTN was reduced to values similar to HFpEF, with overall improvement in both measures of synchrony and time to peak strain. Despite similar achieved SBP, patients with HFpEF remained significantly more dyssynchronous than those with HTN.

**Conclusion:** Intensive therapy in HTN without heart failure significantly reduces time to peak strain and mildly abnormal ventricular synchrony. Prolonged antihypertensive treatment might attenuate the progression from hypertension to HFpEF by improving these measures of cardiac mechanics in vulnerable patients.

Table

	Controls	HFPEF	HTN baseline	HTN following treatment	P-value
SBP (mmHg)	128.97 ± 15.18	136.52 ± 15.18	164.32 ± 15.73	133.62 ± 13.02	< 0.0001
Dyssynchrony (ms)	49.05 ± 40.54	86.97 ± 57.33	71.14 ± 55.80	66.32 ± 49.25	< 0.0001
T_PLS/RR (ms)	0.44 ± 0.07	0.46 ± 0.10	0.48 ± 0.10	0.45 ± 0.08	< 0.003

T\_PLS/RR = time to peak longitudinal strain indexed by RR interval. Values are given as mean ± standard deviation. P values for group.

### P1764

#### Reporting quality of randomised controlled trials investigating efficacy of pharmacological therapies for heart failure with preserved ejection fraction

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**Introduction:** Randomised controlled trials (RCT) provide the highest level of evidence on healthcare interventions. Accurate interpretation of results and inclusion in meta-analysis require clear and adequate reporting, particularly of the methods and results. The CONSORT statement, first published in 1996 and later revised in 2001 and 2010, aims to improve reporting quality of RCTs. It includes 37 points covering 25 areas of trial reporting. Heart failure with preserved ejection fraction (HFpEF) is a major cause of morbidity and mortality, comparable to heart failure with reduced ejection fraction. While many studies have investigated the efficacy of various pharmacological agents, scarcity of consensus guidelines reflects the conflicting results generated from RCTs.

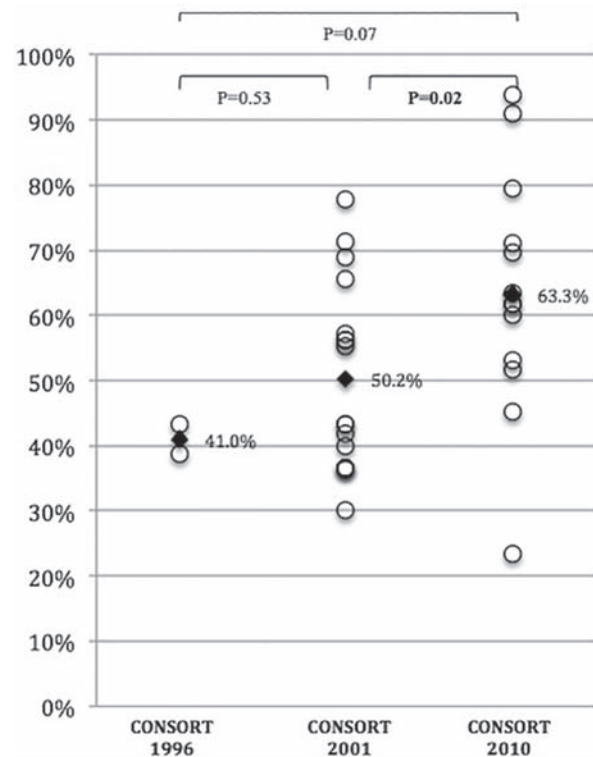
**Purpose:** We aim to systematically identify RCTs of pharmacological interventions

in HFPEF, assess reporting quality using the CONSORT 2010 statement, and identify trends and areas for improvement.

**Methods:** Medline, EMBASE and CENTRAL databases were systematically searched from 1 January 1996 to 1 September 2015 and assessed for inclusion using pre-specified inclusion-exclusion criteria. Reporting quality was assessed by two authors using the CONSORT 2010 score. Each item was scored and weighted equally. An overall reporting quality score was calculated for each study. Statistical analysis was performed with SPSS.

**Results:** Initial search identified 3426 studies, with 32 included in the final analysis. There was inter-observer agreement for 91% of marks (1078/1184); Cohen's kappa score 0.85. The mean overall score was 55.3% (range 23.3-93.8%, SD 17.3%). The mean score for methods and results were 51.0% (15.4-92.9%, 19.4%) and 51.9% (12.5-100.0%, 23.4%) respectively. The best reported criteria, where applicable, were protocol referencing (100%), interim statistical analysis (100%), changes to methods (100%), statistical methods (97%), result interpretation (97%) and eligibility criteria (97%). The worst reported were reporting of binary outcomes (0%, 0/7), abstract (9%), allocation concealment mechanism (12%), trial ending (12%), settings and locations (21%) and implementation of randomization (21%). The reporting scores showed significant correlation with journal impact factor ( $r=0.54$ ,  $P<0.01$ ), 5-year impact factor ( $r=0.49$ ,  $P<0.01$ ) and publication year ( $r=0.49$ ,  $P<0.01$ ). Mean scores increased after publication of each updated CONSORT statement: from 41.0% (range 38.7-43.3%, SD 3.3) to 48.6% (30.0-77.8%, SD 14.5) after CONSORT 2001 ( $p=0.53$ ), and from 48.6% to 63.3% (23.3-93.8% SD 17.6) after CONSORT 2010 ( $P=0.02$ ) (Figure).

**Conclusion:** This study identified all RCTs of pharmacological interventions in HFPEF. We demonstrate that while reporting standards have improved with time, the majority of HFPEF studies did not meet the CONSORT standards. Better compliance with reporting standards is needed in future HFPEF trials.



Individual study CONSORT 2010 scores

### P1765

#### Diagnosis, clinical course and one-year outcome in patients hospitalized for heart failure with preserved ejection fraction - results from the polish cohort of the ESC-HF long-term registry

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**Background:** Compared to heart failure with reduced ejection fraction (HF-REF), far less is known about clinical course of heart failure with preserved ejection fraction (HF-PEF) and the diagnosis of HF-PEF is more challenging.

**Purpose:** To assess the prevalence of HF-PEF among Polish patients hospitalized for HF, to evaluate the pertinence of HF-PEF diagnosis and to compare HF-PEF and HF-REF patients with respect to clinical course and one-year outcomes.

**Methods:** The analysis included 661 Polish patients hospitalized for HF, selected from the ESC-HF Long-Term Registry. Patients with an ejection fraction (EF) of  $\geq 50\%$  were included in the HF-PEF group and patients with an EF of  $< 50\%$  - in the HF-REF group. The primary endpoint was all-cause death at one year. The secondary endpoint was a composite of all-cause death and rehospitalization for HF at one year.

**Results:** HF-PEF was present in 187 (28%) patients. Out of those 187 patients, mitral inflow pattern (E/A ratio) was echocardiographically assessed in 116 (62%) patients and classified as restrictive/pseudonormal in 37 (20%) patients. Compared to HF-REF subjects, patients with HF-PEF were characterized by older age, higher prevalence of female gender, hypertension, atrial fibrillation and sleep apnea, lower prevalence of coronary artery disease and smoking, lower hemoglobin and creatinine concentrations and higher serum sodium level. Despite lower B-type natriuretic peptide concentrations and lower prevalence of moderate-to-severe mitral regurgitation in HF-PEF patients, congestive symptoms at admission were as severe as in patients with HF-REF. There were no significant differences in in-hospital mortality between the two groups. One-year mortality was high in both groups (16.5% in HF-PEF vs 21.0% in HF-REF,  $P = 0.22$ ). There was a trend towards a lower frequency of the secondary endpoint in the HF-PEF group (31.9% in HF-PEF vs 40.0% in HF-REF,  $P = 0.07$ ). Independent risk factors of unfavorable one-year outcome in HF-PEF patients included older age, worse clinical status at hospital admission, the presence of moderate-to-severe aortic stenosis and lower serum sodium concentration.

**Conclusions:** In clinical practice, even easily obtainable echocardiographic indices of diastolic dysfunction are relatively rarely acquired. One-year survival of HF-PEF patients is not significantly better than that of HF-REF patients.

#### P1766

##### Myocardial contraction fraction stratifies prognosis in HFpEF caused by AL of m-ATTR cardiac amyloidosis

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**Background:** In cardiac amyloidosis ejection fraction (EF) is often preserved until the late stage of the disease in the vast majority of patients, who therefore fulfil the definition of heart failure with preserved ejection fraction (HFpEF). However, many indices of systolic function – such as midwall fractional shortening (MWFS), mitral annulus longitudinal systolic excursion (MAPSE), and tissue Doppler systolic peak (TDI-S2) – are depressed, showing evidence of systolic impairment despite preserved ejection fraction. A relatively new index of chamber systolic function is the myocardial contraction fraction (MCF), a volumetric measure of myocardial shortening that is defined as the ratio between stroke volume (SV) and myocardial volume (MV, i.e. left ventricular mass divided by the 1.05 g/ml, the mean density of myocardium).

**Objective and Methods:** To compare MCF with other indices of systolic function, i.e. EF, MWFS, MAPSE, and TDI-S2 in different aetiologies of cardiac amyloidosis, 173 cardiac light-chain (AL) and 102 mutated transthyretin (m-ATTR) amyloidosis patients underwent two-dimensional echocardiography at diagnosis. Cox proportional hazard modeling was used to determine the association of the different systolic indices with survival, over a median follow-up of 38.9 months (range, 19-75 months).

**Results:** When comparing m-TTR with AL cardiac amyloidosis, no difference was observed in EF ( $57 \pm 9$  vs.  $58 \pm 10$  %;  $p = \text{ns}$ ), MAPSE ( $9.3 \pm 3.4$  vs.  $8.6 \pm 3.4$  mm,  $p = \text{ns}$ ), and TDI-S2 ( $9.0 \pm 3.6$  vs.  $8.6 \pm 3.5$  mm,  $p = \text{ns}$ ). In contrast, both MWFS ( $10.3 \pm 1.4$  vs.  $11.2 \pm 1.5$ ;  $p < 0.05$ ) and MCF ( $21.9 \pm 9.8$  vs.  $28.5 \pm 11.1$ ;  $p < 0.001$ ) were lower in cardiac m-ATTR, indicating a higher degree of systolic impairment in the mutated transthyretin-related when compared with the light-chain cardiac amyloidosis aetiologies. In cardiac AL, MWFS% and MCF – but not EF – resulted independent predictors of overall survival. In contrast, in cardiac m-ATTR amyloidosis the only independent prognostic factor was MCF, whereas the other indices of systolic function did not enter the model.

**Conclusions:** Myocardial contraction fraction is superior to ejection fraction in predicting overall survival among HFpEF patients caused by either AL of m-ATTR cardiac amyloidosis.

#### P1767

##### Additional value of Galectin-3 respect to BNP in acute heart failure patients with preserved ejection fraction

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**Background:** Almost half of patients with acute heart failure (AHF) experienced a Heart failure with preserved ejection fraction (HFpEF). HFpEF diagnosis is difficult using traditional diagnostic tools; specific laboratory markers able to recognize this setting are lacking. Galectin-3 (Gal-3) is an emerging biomarker useful in individuals at risk for HF, in both acute and chronic HF.

**Purpose:** The aim of our study is to analyse the relation and prognostic value of Gal-3, BNP and renal dysfunction in patients with HFpEF compared to patients with Heart Failure and reduced ejection fraction (HFrEF). We also evaluated the association between Gal-3 and the degree of diastolic dysfunction, LV geometry and stiffness.

**Methods:** We enrolled 98 patients with AHF and we measured Gal-3, BNP, C-reactive protein (CRP) and estimated glomerular filtration rate (eGFR) within 12 hours since hospital admission. On the basis of echocardiographic findings we divided our sample into two groups: patients with HFrEF (ejection fraction  $< 50\%$ ) or HFpEF (ejection fraction  $> 50\%$ ).

**Results:** No differences in Gal-3 levels were found in the two subgroups (HFrEF;  $19.5 \pm 5.1$  ng/mL; HFpEF;  $20.5 \pm 8.7$   $p = 0.56$ ). Gal-3 was inversely related to renal dysfunction (Gal-3 vs eGFR  $r = -0.30$ ,  $p = 0.01$ ) but did not correlate with BNP levels ( $r = 0.22$ ,  $p = 0.06$ ). Higher levels of Gal-3 were associated with more advanced diastolic dysfunction only in HFpEF (Impaired relaxation pattern: Gal-3 =  $15.2 \pm 4.3$  ng/mL; pseudo-normal filling pattern: Gal-3 =  $18.7 \pm 7.1$  ng/mL and restrictive filling pattern: Gal-3 =  $27.5 \pm 10.1$  ng/mL  $p = 0.009$ ). In addition Gal-3 was related to diastolic LV stiffness (all patients;  $r = 0.4$ ,  $p = 0.01$  HFpEF  $r = 0.58$   $p < 0.001$ ). Cox regression analysis showed that Gal-3 was related to poor outcome independently from renal dysfunction and other risk factors in HFpEF patients. (2,59 [HR] 1,27-5,26;  $p < 0.008$ ). Oppositely in HFrEF patients, Gal-3 was related to poor outcome only when associated to renal dysfunction. (1,45 [HR] 1,12-1,88;  $p < 0.01$ )

**Conclusions:** Gal-3 is not able to discern HFrEF respect to HFpEF patients. Unlike BNP, it is related to diastolic dysfunction severity and LV stiffness in HFpEF. Gal-3 has a prognostic role independently from renal dysfunction in subjects with HFpEF but not in HFrEF.

## BASIC SCIENCE: DRUG THERAPY, OTHER

#### P1769

##### Complex effects of the myosin activator omecamtiv mecarbil on cardiac contractility

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**Background:** Omecamtiv mecarbil (OM) is a novel inotrope in evaluation for heart failure treatment. Currently, the effects of OM upon contractile function of intact cardiac tissue are relatively unknown.

**Objective:** The objective of the study was to characterize the contractile effects of OM.

**Methods:** Contractility and kinetics of the contraction-relaxation cycle (CRC) were measured in rat left ventricular strips. Sarcomere shortening and CRC were measured in isolated rat ventricular cardiomyocytes.

**Results:** In ventricular strips, OM ( $1 \mu\text{M}$ ) increased contractile force (Fmax), reaching a maximum of  $8 \pm 1\%$  above control. In cardiomyocytes, OM increased sarcomere shortening by  $48 \pm 16\%$  above baseline. OM increased time to peak force (TPF) in ventricular strips, time to peak shortening (TPS) in unloaded cardiomyocytes and relaxation time (RT) in both preparations, with RT being substantially increased compared to TPF in ventricular strips. OM slowed the diastolic relengthening rate in cardiomyocytes and increased diastolic tension at stimulation frequencies greater than 2 Hz in ventricular strips at  $31^\circ\text{C}$ . Higher concentrations of OM were required to increase diastolic tension when temperature was increased to  $37^\circ\text{C}$ . OM sensitized the concentration-response relationship to  $\text{Ca}^{2+}$  in the lower range of  $[\text{Ca}^{2+}]_i$ , but reduced the maximum inotropic response (IR) to  $\text{Ca}^{2+}$ . OM reduced the maximum IR to  $\beta$ -AR stimulation without altering the EC50 of  $\beta$ - or  $\alpha$ 1-adrenoceptors.

**Conclusion:** This study demonstrates that in addition to increasing Fmax and sarcomere shortening and sensitizing the myocardium to  $\text{Ca}^{2+}$ , OM also substantially slowed the kinetics of relaxation in rat myocardium, resulting in increased diastolic tension at higher heart rates, more at lower temperature. Finally, OM reduced maximal  $\beta$ -AR-evoked IR. Further evaluation of the potential clinical utility of OM should take its complex effects on cardiac contractility into account.

## P1770

**Comparative bioenergetic effects of levosimendan and omecamtiv mecarbil in guinea-pig cardiac myocytes**D Puetz<sup>1</sup>; M Michael Kohlhaas<sup>1</sup>; C Maack<sup>1</sup><sup>1</sup>Saarland University Hospital, Department of Internal Medicine III, Homburg, Germany

**Background:** Cardiogenic shock is an unmet clinical need since current inotropic drugs (in particular, catecholamines) increase mortality in patients with acute heart failure. As underlying reasons, pro-arrhythmic effects and elevated oxygen consumption of catecholamines have been put forward. Levosimendan (Levo) was originally considered as a calcium-sensitizer that elevates contractile force without increasing intracellular calcium, while other reports suggested that Levo is an inhibitor of phosphodiesterases (PDEs), a property deemed adverse in heart failure. In contrast, omecamtiv mecarbil (OM) is a myosin activator that prolongs cardiac contraction without elevating oxygen consumption in dogs with heart failure. In humans, OM improves cardiac output and tended to improve symptoms in patients with acute heart failure. We have recently discovered that increasing calcium affinity of myofilaments with the pure calcium-sensitizer EMD-57033 increased systolic force development, but this was associated with oxidation of mitochondrial redox state of NAD(P)H/FAD, which was associated with pronounced mitochondrial emission of reactive oxygen species (ROS). Here, we evaluated the bioenergetic (redox) properties of Levo in comparison with OM in guinea-pig cardiac myocytes.

**Methods and Results:** Here, cardiac myocytes were isolated from guinea pig hearts and field-stimulated at 1 Hz and 37°C. OM substantially prolonged the time to peak of cell shortening in a concentration-dependent manner (0.01–30 µM). This was associated with an increase in diastolic tension but only minor increases in systolic sarcomere shortening (optimum at 3 µM). Despite the substantial increase in diastolic tension, the redox states of NAD(P)H/FAD remained stable, in agreement with the previously reported unchanged oxygen consumption. Levo (up to 10 µM) had overall minimal effects on sarcomere shortening, diastolic tension and NAD(P)H/FAD redox states. However, the concentration-dependent increase of sarcomere shortening was shifted to the left (increased potency) and its maximal effect became potentiated (increased efficacy) by pre-incubation of cardiac myocytes with a sub-threshold concentration of isoproterenol (1 nM). Under all conditions, the redox states of NAD(P)H and FAD remained stable in response to Levo (with or without isoproterenol).

**Conclusions:** Levosimendan does not behave as a calcium-sensitizer, but rather as a PDE-inhibitor, since its stimulating effect on sarcomere shortening becomes apparent only after beta-adrenergic prestimulation. In contrast, OM induces diastolic dysfunction rather than increasing sarcomere shortening, however, the prolongation of systolic sarcomere shortening came at no elevated oxygen demand. Together, while the PDE-inhibiting effects of Levo may predispose to arrhythmias, OM may induce diastolic dysfunction at concentrations that reasonably affect systolic sarcomere shortening.

## P1771

**Circulating blood levels of growth differentiation factor 11 are decreased in dogs with heart failure and restored after long-term therapy with elamipretide (Bendavia, MTP-131)**HN Hani Sabbah<sup>1</sup>; RC Gupta<sup>1</sup>; V Sing-Gupta<sup>1</sup><sup>1</sup>Henry Ford Hospital, Detroit, United States of America

**Introduction:** Growth differentiation factor 11 (GDF11), a member of the transforming growth factor beta superfamily, has been shown to decrease with advanced age. GDF11 is implicated as having a role in the stem cell differentiation into cardiomyocytes, in reducing brain natriuretic peptide (BNP) and increasing expression of SERCA-2a, an enzyme necessary for myocardial contraction and relaxation. Supplementation of GDF11 protein in mice has been shown to ameliorate age-related dysfunction of skeletal muscle (SM). Many of the abnormalities seen with advanced age also manifest in heart failure (HF) including cardiomyocyte dysfunction and loss, SM dysfunction and reduced SERCA-2a activity and expression. We previously showed that these abnormalities can be reversed in dogs with HF following long-term therapy with elamipretide (Bendavia, MTP-131), a novel mitochondria targeting peptide.

**Purpose/Hypothesis:** In the present study, we tested the hypothesis that plasma level of GDF11 is reduced in dogs with chronic HF and are restored following long-term therapy with elamipretide.

**Methods:** Venous blood samples were obtained from 14 dogs at baseline (normal state) prior to induction of HF, after the induction of HF by intracoronary microembolizations but prior to any therapy and again at 3 months after initiating therapy with either subcutaneous elamipretide (0.5 mg/kg/day, n = 7) or saline v/v (Control, n = 7). Plasma levels of GDF11 were measured using a dog specific commercially available (MyBiosource, San Diego, CA) enzyme-linked immunosorbent assay (ELISA) kit.

**Results:** In control dogs, plasma level of GDF11 was 61.3 ± 3.8 pg/ml at baseline and decreased to 36.2 ± 0.9 pg/ml (p < 0.05) when dogs were in HF and remained lower at 3 months after initiating therapy with saline (36.1 ± 0.7 pg/ml). In dogs treated with elamipretide, plasma level of GDF11 was 62.9 ± 5.6 pg/ml at baseline,

decreased to 37.4 ± 1.0 pg/ml (p < 0.05) when dogs were in HF and increased to near normal levels (59.3 ± 4.0 pg/ml) at 3 months after initiating therapy with elamipretide.

**Conclusions:** As in aging, circulating plasma levels of GDF11 are decreased in HF dogs. Long-term treatment with elamipretide reverses this decline. These findings are consistent with previous observations of improved cardiomyocyte function, increased SERCA-2a activity, decreased circulating levels of BNP and improved SM structure in dogs with HF treated with elamipretide.

## P1772

**Trimetazidine effects on the quality of life of women with chronic heart failure**NA Koriagina<sup>1</sup>; AV Petrischeva<sup>1</sup>; AA Shadrin<sup>1</sup>; LM Vasilts<sup>1</sup>; VV Schekotov<sup>1</sup><sup>1</sup>Medical Academy, Perm, Russian Federation

**Objective:** To evaluate the effect of trimetazidine on the quality of life of women with chronic heart failure (CHF) of ischemic etiology.

**Methods:** 100 patients ischemic CHF, II-IV (NYHA) at the age of 65.7 ± 8.7 years, were divided into two groups. 1 group (n = 50) in addition to standard CHF therapy received trimetazidine 35 mg 2 times a day for 6 months. Patients 2 groups (n = 50) were in the basic therapy. Determination of the quality of life was carried out using the Minnesota questionnaire for heart failure at baseline and after 6 months of continuous administration of trimetazidine, and Hospital Anxiety and Depression Scale. 0 points consistent with the best quality of life, 105 points - the worst.

**Results:** against addition of trimetazidine to standard therapy of CHF mean score in group 1 decreased by 28.7 ± 20.1%, while in the 2nd - on 5.7 ± 3.5% (p < 0.01), as well as reducing symptoms of anxiety in Group 1 with 10 points to 7 points, and depression with 11 ballvol to 6 points, 2 group level of anxiety and depression remained unchanged.

**Conclusions:** The addition of trimetazidine to standard heart failure therapy has a positive effect on quality of life and manifestations of anxiety and depressive syndrome in patients with chronic heart failure.

**BASIC SCIENCE: RENIN-ANGIOTENSIN-ALDOSTERONE ANTAGONISTS**

## P1773

**Finerenone inhibits mechanisms of cardiac fibrosis in vitro**

Bayer Pharma AG

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**Purpose:** Aldosterone induces cardiac fibrosis via activation of the mineralocorticoid receptor (MR) that predisposes to arrhythmias and heart failure. We studied the role finerenone, a selective non-steroidal MR antagonist, for the molecular mechanisms of fibrotic remodeling in cultured cardiac fibroblasts.

**Methods and Results:** Aldosterone exposure in cardiac fibroblasts induced a nuclear translocation of MR (nuclear to cytoplasm MR localization, control 2.3 ± 4.0 vs. aldosterone 6.8 ± 5.7, p < 0.001) that was prevented by finerenone (2.1 ± 2.5, p < 0.0001 vs. control). Finerenone dose-dependently decreased the protein expression of connective tissue growth factor (CTGF). This effect of finerenone 500nM was comparable to that of spironolactone 500nM (74 ± 15% and 70 ± 19%, respectively; both p < 0.01 vs. control). Finerenone prevented the aldosterone induced CTGF overexpression (187 ± 42%, p < 0.01 vs. control, and 89 ± 34%, p < 0.01 vs. aldosterone, respectively). Co-treatment with angiotensin II in addition to aldosterone enhanced CTGF upregulation (210 ± 69%, p < 0.0001 vs. control) that was completely prevented by finerenone (100 ± 10%, p < 0.001 vs. aldosterone+angiotensin II). Aldosterone did not alter the transforming growth factor β (TGF-β) expression whereas angiotensin II (172 ± 34%, p < 0.0001 vs. control) did. Conclusively, the TGF-β expression was unaffected by finerenone but the angiotensin II induced TGF-β overexpression was prevented with telmisartan (117 ± 29%, p < 0.01 vs. angiotensin II). Finerenone inhibited the aldosterone-induced upregulation of microRNA-21 expression (354 ± 229%, p < 0.01 vs. control, and 130 ± 46%, p < 0.05 vs. aldosterone, respectively). The increase in fibronectin expression induced by the co-treatment aldosterone and angiotensin II (187 ± 45%, p < 0.0001 vs. control) was prevented with finerenone pre-treatment (116 ± 28%, p < 0.001 vs. aldosterone+angiotensin II) as well as the aldosterone-induced upregulation of the lysyl oxidase (149 ± 19%, p < 0.001 vs. control, and 85 ± 29%, p < 0.0001 vs. aldosterone, respectively).

**Conclusion:** Finerenone prevents nuclear translocation of the mineralocorticoid receptor and is a potent inhibitor of the pro-fibrotic factors CTGF, microRNA-21,

fibronectin and lysyl oxidase. Therefore, finerenone may represent a novel substance to prevent maladaptive cardiac structural remodelling.

## BASIC SCIENCE: HFpEF - HEART FAILURE WITH PRESERVED EJECTION FRACTION

### P1774

#### Effect of neuregulin-1 on angiotensin II-induced ventricular inflammation, fibrosis and stiffening

FWO (Application number, G0C5214), a grant from the European Commission (FP7-HEALTH-F2-2010-261409), IOF POC of the University of Antwerp Z Zarha Vermeulen<sup>1</sup>; L Vandekerckhove<sup>1</sup>; VFS Segers<sup>1</sup>; AS Hervent<sup>1</sup>; GW De Keulenaer<sup>1</sup>

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**Purpose:** Heart failure mitigating effects of the endothelium-derived growth factor Neuregulin-1 (NRG-1) are currently tested in clinical trials. Surprisingly, however, NRG-1's underlying mechanisms of cardiac protection remain poorly understood. Here, we hypothesized that NRG-1/ErbB4 signaling attenuates left ventricular (LV) fibrosis and stiffening, and regulates cardiac fibroblast function.

**Methods:** LV fibrosis and stiffening were induced by treatment of mice with Angiotensin II (Ang II, osmotic mini-pumps, 1000 ng.kg<sup>-1</sup>.day<sup>-1</sup>, 4 weeks). NRG-1/ErbB4 signaling was either activated by co-treatment with rhNRG-1 (20 µg.kg<sup>-1</sup>.day<sup>-1</sup>, i.p. injection 5 days/week), or inhibited by fibroblast-specific deletion of ErbB4 (by crossing C57BL/6-ErbB4F/F mice and BALB/c-S100a4-Cre+ mice). The effect of rhNRG-1 on fibroblast gene expression was studied in cultured primary fibroblasts by cDNA MicroArray analysis with the Illumina MouseRef-8 v2.0 Expression BeadChip. Results In wild type mice, rhNRG-1 treatment significantly attenuated Ang II-induced LV fibrosis (quantified by histology and molecular analysis) and prevented Ang II-induced LV passive stiffening (quantified by invasive hemodynamic recordings). Blood pressure was not affected. Consistently, in ErbB4+/-;Cre+ mice, LV fibrotic response to Ang II-treatment was robustly enhanced. cDNA MicroArray comparison of PBS- and rhNRG-1-treated primary fibroblasts showed 960 differentially expressed genes of which 450 were down-regulated and 510 were up-regulated. Network and pathway analysis using the Ingenuity Pathway Analysis (IPA) software confirmed that rhNRG-1 significantly inhibited the pathway of connective tissue development, but also unmasked that rhNRG-1 significantly downregulated several inflammatory pathways. Upstream regulator analysis identified the downregulation of several cytokines (mostly from the interleukin family), cytokine receptors and transcription factors of cytokine signaling (mostly from the IRF and STAT family) hence generating the hypothesis that rhNRG-1 also mediates anti-inflammatory effects. To further test this hypothesis, wild type mice were exposed to Ang II for 3 days to induce a myocardial inflammatory response. As expected, co-treatment with rhNRG-1 significantly abrogated myocardial infiltration of both neutrophils and macrophages. Conclusion This study shows a prominent role for NRG-1/ErbB4 signaling in the control of LV fibrosis during Ang II-induced LV remodeling. Both direct anti-fibrotic effects and indirect anti-inflammatory effects seem to underlie this effect. These data contribute to the understanding of the therapeutic effects of rhNRG-1 in heart failure.

## BASIC SCIENCE: ANIMAL MODELS AND EXPERIMENTATION

### P1775

#### Distinct myocardial expression of mitochondrial regulators is associated with characteristic differences of in vivo hemodynamics in physiological and pathological left ventricular hypertrophy

Hungarian Scientific Research Fund (OTKA 105555) to Bela Merkely A Olah<sup>1</sup>; BT Nemeth<sup>1</sup>; C Matyas<sup>1</sup>; A Lux<sup>1</sup>; M Ruppert<sup>1</sup>; D Kellermayer<sup>1</sup>; AA Sayour<sup>1</sup>; L Szabo<sup>1</sup>; B Merkely<sup>1</sup>; T Radovits<sup>1</sup>

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**Purpose:** Left ventricular (LV) hypertrophy is a physiological or pathological response of LV myocardium to increased cardiac load and is associated with characteristic molecular changes. Currently, a direct comparison of functional consequences of physiological (PhyH) and pathological hypertrophy (PaH) is missing. We aimed at comparing hemodynamic alterations in well established rat models of physiological and pathological hypertrophy by using LV pressure-volume (P-V) analysis and investigating possible underlying molecular mechanisms.

**Methods:** PhyH and PaH were induced in rats by swim training and by abdominal aortic banding, respectively. Morphology of the heart was investigated by echocardiography. Detailed characterization of cardiac function was completed by LV P-V analysis. In addition histological and molecular biological measurements were performed. All data were normalized to the corresponding control group.

**Results:** Echocardiography revealed myocardial hypertrophy of similar degree in both models (LV mass index: +21.7±2.1% PhyH vs. +27.3±3.3% PaH, n.s.), which was confirmed by post-mortem heart weight data. In aortic-banded rats we detected only subendocardial fibrosis. Reactivation of fetal gene program could be observed only in PaH model. PhyH was associated with increased stroke volume, whereas unaltered stroke volume were detected in PaH along with markedly elevated end-systolic pressure values. Sensitive indices of LV contractility were increased in both models, in parallel with the degree of hypertrophy. Active relaxation was ameliorated in athlete's heart, while it showed marked impairment in PaH (time constant of LV pressure decay (τ): -7.7±2.6% PhyH vs. +37.0±11.1% PaH, p<0.01). LV mechanical efficiency and ventriculo-arterial coupling were improved in PhyH, whereas remained unchanged in PaH. Myocardial gene expression of mitochondrial regulators showed marked differences between PaH and PhyH (peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1α): +19.1±10.3% PhyH vs. -37.8±7.2% PaH, p<0.01), while markers of oxidative stress and inflammation did not differ between the groups.

**Conclusions:** We provided the first comparative hemodynamic characterization of PhyH and compensated PaH in relevant rodent models. Increased LV contractility could be observed in both types of LV hypertrophy, characteristic distinction was detected in energy-dependent diastolic function (active relaxation) and mechanoenergetics (mechanical efficiency), which might be explained by mitochondrial differences.

### P1776

#### An allogeneic bioengineered myocardial graft limits infarct size and improves cardiac function: pre-clinical study in the porcine myocardial infarction model

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**Background:** Cardiac tissue engineering combines scaffolds and cells, aiming to renew myocardium and restore cardiac function after myocardial infarction (MI).

**Purpose:** Herein, we developed a scalable engineered myocardial graft (EMG) and evaluated its impact on cardiac function and scar dynamics in the swine MI model.

**Methods:** EMG, comprising a decellularized porcine myocardial scaffold repopulated with GFP-labeled porcine adipose tissue-derived progenitor cells (pATDPCs), was engrafted to the myocardial surface of allogeneic swine after MI induction. Cardiac function was assessed using magnetic resonance imaging. Infarct size, scar healing, and vascularization were evaluated using quantitative morphometry and histopathology. Animals were sacrificed one month post-MI.

**Results:** Compared to control-MI animals, EMG-treated animals exhibited significantly higher left ventricular ejection fraction relative to baseline (3.26±2.85 vs. -7.97±4.29; P=0.047) and post-MI (61.30±3.07% vs. 50.76±2.62%; P=0.001). Relative to control-MI animals, EMG-treated animals had a 68% smaller infarct size (2.46±0.60% vs. 7.63±2.26%; P=0.048) and significantly lower type I/III collagen ratio (2.26±0.72 vs. 13.01±6.85; P=0.032). GFP+ pATDPCs migrated to underlying ischemic myocardium and expressed cardiac lineage markers (GATA4, MEF2, SERCA2, connexin43, and cTnI) and endothelial makers (IsoB4 and CD31). Newly-formed blood vessels were connected to host myocardium. EMG promoted increased infarct myocardium vascularization, with blood vessel densities of 3.64±0.50% for EMG-treated animals and 1.72±0.12% for control-MI animals (P=0.011).

**Conclusions:** In the pre-clinical swine MI model, the newly developed EMG improved cardiac function and injured myocardium neovascularization, reduced infarct size, and limited fibrosis progression. This scalable allogeneic EMG is ready for clinical translation.

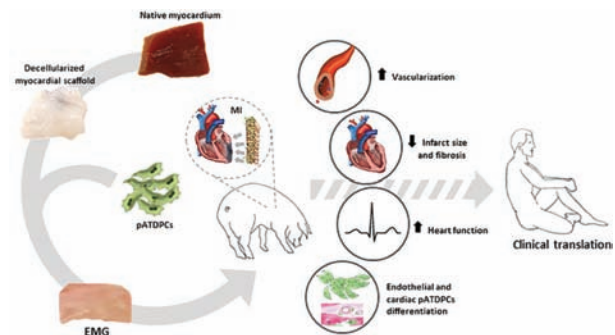


Figure 1. Effects promoted by the EMG



## P1777

**Chronic phosphodiesterase-5 inhibition prevents the development of diabetic cardiomyopathy in a rat model of type-2 diabetes mellitus**

Hungarian Scientific Research Fund (OTKA PD 100245)

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**Purpose:** Diabetes mellitus (DM) is associated with characteristic structural and functional changes of the heart, termed diabetic cardiomyopathy. The pathophysiological role of cGMP signaling has been intensively investigated in DM. Elevated levels of the second messenger cGMP have been shown to exert cardioprotective effects in various heart diseases. We investigated the effect of chronic inhibition of the cGMP-degrading enzyme phosphodiesterase-5 (PDE5) by vardenafil in type-2 DM related cardiomyopathy.

**Methods:** For type-2 DM Zucker Diabetic Fatty (ZDF) rats were used. ZDF Lean (ZDFL) rats served as controls. Animals received either vehicle (ZDFL, ZDF) or 10mg/kg BW vardenafil per os (ZDFLvard, ZDFvard) from 7 to 32 weeks of age. Cardiac morphology was followed by echocardiography. Left ventricular (LV) function was assessed by pressure-volume (P-V) analysis. Gene expression measurements of atrial natriuretic factor (ANF; qRT-PCR), cardiomyocyte diameter/tibia length (CD/TL) and Masson's staining (fibrosis score (FS)) were used to prove pathological myocardium hypertrophy.

**Results:** Cardiac hypertrophy (echocardiography: LV anterior wall thickness in systole (LVAWs):  $2.81 \pm 0.1$ mm; relative wall thickness (RWT):  $0.49 \pm 0.02$ ; LVmass/TL:  $0.30 \pm 0.01$ g/cm; CD/TL:  $3.53 \pm 0.02$  $\mu$ m/cm; ANF:  $3.04 \pm 0.26$  vs ZDFL (LVAWs:  $2.53 \pm 0.04$ mm; RWT:  $0.43 \pm 0.02$ ; LVmass/TL:  $0.23 \pm 0.004$ g/cm; CD/TL:  $3.09 \pm 0.02$  $\mu$ m/cm; ANF:  $0.92 \pm 0.17$ );  $p < 0.05$ ) and fibrotic remodelling (FS:  $1.05 \pm 0.09$  vs ZDFL ( $0.57 \pm 0.13$ );  $p < 0.05$ ) have been observed in ZDF. Drug treatment significantly decreased myocardial hypertrophy and fibrosis (LVAWs:  $2.47 \pm 0.05$ mm; CD/TL:  $3.15 \pm 0.02$ ; ANF:  $1.39 \pm 0.21$ ; FS:  $0.59 \pm 0.08$  vs ZDF;  $p < 0.05$ ) in DM. PV analysis showed impaired diastolic function and increased cardiac stiffness (time constant of LV pressure decay ( $\tau$ ):  $9.17 \pm 0.25$ ms; slope of end-diastolic P-V relationship (EDPVR):  $0.078 \pm 0.002$ mmHg/ $\mu$ l vs ZDFL ( $\tau$ :  $8.18 \pm 0.13$ ms; EDPVR:  $0.045 \pm 0.003$ mmHg/ $\mu$ l);  $p < 0.05$ ) while contractility parameters and blood pressure remained unchanged in ZDF. Vardenafil improved diastolic parameters ( $\tau$ :  $8.62 \pm 0.34$ ms, EDPVR:  $0.062 \pm 0.006$ mmHg/ $\mu$ l vs ZDF;  $p < 0.05$ ). Vardenafil did not have any effects in ZDFL.

**Conclusions:** We reported that chronic administration of vardenafil prevents DM associated myocardial complications. PDE5 inhibition might be an important target to improve cardiovascular outcome in diabetic patients in the future.

## P1778

**Bicoronary infusion of nitroglycerin and atrial natriuretic peptide improves diastolic distensibility in healthy pigs.**A Alogna<sup>1</sup>; M Manning<sup>2</sup>; B Zirngast<sup>3</sup>; M Schwarzl<sup>4</sup>; P Steendijk<sup>5</sup>; B Pieske<sup>1</sup>; H Post<sup>1</sup>

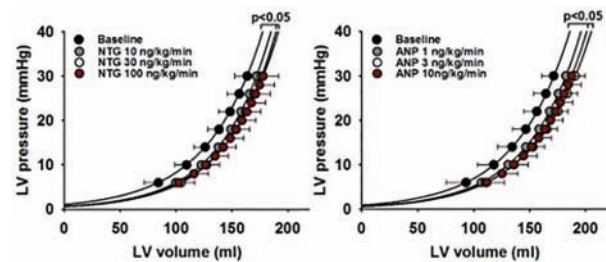
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**Background:** Experimental data indicate that the acute post-translational modification of the myofibrillar titin spring by cGMP-activated protein kinase G can increase left ventricular (LV) end-diastolic distensibility (LVed-Dist). Intracellular cGMP production can be stimulated either by nitric oxide via the soluble guanylate cyclase (sGC), or by the natriuretic peptides via the particulate guanylate cyclase (pGC). We tested the hypothesis that acute intracoronary infusion of nitroglycerin (NTG) or atrial natriuretic peptide (ANP) would exert direct myocardial effects and improve LVed-Dist in healthy myocardium.

**Methods:** 5 anaesthetized, closed-chest pigs (59  $\pm$  2kg) were acutely instrumented with a left ventricular (LV) pressure-volume catheter, a Swan-Ganz catheter and an aortic balloon catheter. Two 5F coronary catheters were positioned in the right and left coronary ostia via femoral access. Pressure-volume relationships were derived from short aortic occlusions. Following baseline measurements, NTG was infused bicoronarily at 10, 30 and 100 ng/kg/min over 20 min, respectively. After 30 min wash-out, the same protocol was repeated with ANP at 1, 3 and 10 ng/kg/min. \*:  $p < 0.05$  vs baseline

**Results:** LV peak pressure slightly decreased at the highest dose compared to baseline (NTG:  $87 \pm 3^*$  vs  $94 \pm 4$ , ANP:  $85 \pm 4^*$  vs  $96 \pm 6$ ) while systemic vascular resistance was not altered during NTG infusion and to a minor extent during the highest dose of ANP ( $11.1 \pm 0.6^*$  vs  $12.7 \pm 0.7$  mmHg/l/min). The maximum rate of positive LV pressure change, LV dP/dtmax, decreased and the calculated end-systolic volume at 100 mmHg end-systolic pressure increased dose-dependently, indicating a negative inotropic effect. The end-diastolic pressure volume relationships (EDPVR, graph) before and during infusion of NTG and ANP were shifted rightwards compared to the respective baseline (see graphs).

**Conclusion:** The acute pharmacological stimulation of cGMP-dependent signalling improves LV end-diastolic distensibility in healthy pigs in vivo. The molecular mechanisms mediating such acute modulation of LV distensibility may represent pharmacological targets to treat a pathological loss of LV distensibility as, for instance, heart failure with preserved ejection fraction (HFpEF).



EDPVRs baseline vs NTG-ANP

## P1779

**Intravenous administration of CoQ10 evokes increase in NO-mediated blood vessels relaxation**

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**Introduction:** The presence of endothelial dysfunction is associated with an increased mortality risk in patients with chronic heart failure. Coenzyme Q10 (CoQ10) is recommended for treatment of patients with congestive heart failure, but due to its low bioavailability it is necessary long term administration in order to reach therapeutic effect. One of the proposed mechanisms of beneficial effects of Coq10 is improvement in the vasodilating NO-mediated function of endothelium.

**Purpose:** Investigation of the fast effects of CoQ10, administered intravenously, on the NO-mediated vasorelaxation, evoked by acetylcholine. Methods. Male Wistar rats (300-350g) were anaesthetized with chloralhydrate (400 mg/kg, ip) and placed on a heated surgical pad at constant body temperature  $37 \pm 0.5$  °C. 3% water-based solution of CoQ10 (30 mg/kg) or saline (0.9% NaCl, 1 mL/kg) were administered intravenously via the femoral vein. 2 h after drugs administration the animals were anaesthetized by chloralhydrate over dose (600 mg kg<sup>-1</sup>, ip) and decapitated. The descending thoracic aorta was carefully excised and cut into ring segments 3 mm in length and then transferred into 10-ml organ baths containing Krebs solution bubbled with a mixture of 95% O<sub>2</sub> and 5% CO<sub>2</sub>. The rings were precontracted with 0.3  $\mu$ M Phenylephrine (PE), and after a steady-state tension had been reached, increasing concentrations of ACh (0.001  $\mu$ M - 30  $\mu$ M) were cumulatively added to the organ bath.

**Results:** ACh elicited a concentration-dependent relaxation of rat aortic rings. The maximum relaxation (E max, %) was obtained at a ACh concentration of 30  $\mu$ M. In the CoQ10-treated group the relaxant responses to ACh were markedly potentiated when compared with the control (saline) group ( $94.2 \pm 2.0\%$  vs  $68.1 \pm 4.4\%$ , respectively,  $p < 0.01$ ). It was significant difference in pD<sub>2</sub> (-lg EC<sub>50</sub>,) values of the control and treatment groups ( $5.79 \pm 0.29$  vs  $8.14 \pm 0.65$ ,  $p < 0.05$ ).

**Conclusion:** 2h duration of CoQ10 (30 mg/kg) action is enough for improving the vasodilating NO-mediated function of endothelium. This mechanism could be partially responsible for positive effects of CoQ10 in congestive heart failure.

## P1780

**Prolonged dipyridamole use is associated to amelioration of myocardial perfusion disturbance in experimental chronic Chagas cardiomyopathy**

Fundação de Amparo à Pesquisa do Estado de São Paulo - FAPESP

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**Background:** Microvascular ischemia is a conspicuous finding in chronic chagasic cardiomyopathy (CCC) that may be involved in the development of left ventricular systolic dysfunction (LVSD).

**Purpose:** We aimed at assessing the effect of the prolonged use of dipyridamole (DIPY) on myocardial perfusion and left ventricle systolic function in a model of CCC.

**Methods:** We investigated 3 groups of female hamsters: animals infected with T. cruzi and treated with DIPY (CH+DIPY, n=15), infected and treated with saline (CH+Saline, n=15), non-infected and treated with DIPY (CO+DIPY, n=12) or treated with saline (CO+Saline, n=11). After 6 months of infection (baseline condition), the animals were submitted to echocardiography and to Sestamibi-Tc99m SPECT

myocardial perfusion scintigraphy (MPS). The animals were then treated with DIPY (4 mg/kg ip) twice a day or saline for 4 weeks and then reevaluated using the same imaging methods. The area of resting myocardial perfusion defects (PD) were calculated by computing the pixels exhibiting radiotracer uptake <50% compared to the maximum pixel value.

**Results:** The baseline and post-treatment results of PD and LVEF are summarized in the table. In the baseline condition, the chagasic animals showed larger area of PD than controls (p=0.0005), but similar LVEF (p=0.3). After treatment there was a significant reduction of the PD only in the CH+DIPY group (p=0.004), but not in the CH+placebo group or the controls (p > 0.05). After treatment, CH+DIPY animals exhibited a PD area similar to that of treated control animals (p > 0.05). Both chagasic groups, treated with DIPY and placebo, showed a reduction of LVEF in the post-treatment when compared to baseline. (p < 0.001). No significant change of the LVEF was observed in controls.

**Conclusions:** The prolonged use of DIPY in animals with CCC was associated with a significant reduction of PD. However, the resolution of microvascular ischemia using DIPY has not prevented the progression of left ventricular dysfunction. These results suggest that microvascular ischemia may not be a central mechanism of myocardial damage in the physiopathogenic complex of CCC.

Baseline and post-treatment results

Groups	Perfusion Defect		LVEF	
	baseline (%)	post (%)	baseline (%)	post (%)
CH+DIPY	20.87 ± 4.25	6.6 ± 1.83*	66.3 ± 2.47	54.64 ± 1.72*
CH+Placebo	12.92 ± 3.53	11.15 ± 2.74	69.3 ± 1.44	54.36 ± 2.48*
CO+DIPY	4.83 ± 0.94	2.75 ± 0.88	61.21 ± 1.85	56.03 ± 3.46
CO+Placebo	3.54 ± 0.76	5.54 ± 0.91	65.1 ± 3.10	59.96 ± 2.78

\*p < 0.05 compared to baseline

**P1781**

**The Wilms tumour 1 gene as a molecular discriminator between ischemic and non-ischemic end-stage heart failure**

BFU2014-52299-P, Ministerio de Economía y Competitividad, Spain  
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**Purpose:** There is evidence suggesting that reactivation of a key embryonic epicardial gene, Wilm's tumour 1 (Wt1) in the adult may lead to better outcomes after cardiac injury. The aim was to study cardiac Wt1 expression across different heart failure (HF) scenarios in patients with end-stage systolic HF with reduced ejection fraction (HFrEF) as well as in the porcine model of HF with preserved EF (HFpEF).

**Methods:** Levels of Wt1 transcript (by RT-PCR) and protein (by Western blot) variants were determined in left ventricular (LV) samples taken at the time of heart transplantation in patients with end-stage HFrEF (LVEF=18.2 ± 6%) due to idiopathic (n = 10) and ischemic (n = 10) dilated cardiomyopathy (DCM) as well as in LV-samples derived from neonatal piglets (n = 12) with doxorubicin (Dox)-induced HFpEF and pulmonary congestion. The human non-transplantable hearts (n = 11) and cardiac samples from non-failing piglets (n = 8) were used as controls, respectively. Wt1 variants were cloned, expressed in model cell lines and used to verify the specificity of the antibodies to be used in Western blot assays.

**Results:** Splicing of exon 5 (E5) and of a stretch of nine nucleotides in the 3' end of exon 9 (abbreviated as KTS) give rise to four major WT1 variants. These WT1 splicing variants are expressed in non-failing human heart with a relative abundance ranking of Wt1D [+E5/+KTS] > Wt1B [+E5/-KTS] ~ Wt1C [-E5/+KTS] >> Wt1A [-E5/-KTS]. The Wt1D [+E5/+KTS] variant represents nearly 50% of total WT1 expression being the predominant or the only protein isoform detected by Western blot, mainly as a 60 kDa band, in non-failing human hearts. The same splicing variants are also revealed in non-failing porcine hearts. The expression of the Wt1D [+E5/+KTS] variant is significantly (~3 fold) downregulated (at both transcript and protein levels) in failing LV ventricles from patients with ischemic DCM. However, and in contrast, there were no significant differences in expression of the Wt1D [+E5/+KTS] variant in patients with idiopathic DCM compared to non-failing donor hearts. Other Wt1 splicing variants were expressed at a lower level in ischemic DCM hearts compared to that in non-failing or idiopathic DCM human hearts. Cardiac Wt1 expression was not altered in Dox-induced porcine model of HFpEF.

**Conclusions:** We demonstrate selective downregulation of cardiac Wt1 expression in patients with ischemic but not idiopathic DCM that is in contrast with the concept of common final pathways in end-stage HF.

**P1782**

**Protective effect of doxycycline against the development of isoproterenol induced heart failure**

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**Introduction:** It has already been proved that doxycycline is able to lessen left ventricular (LV) hypertrophy. In our recent study we examined whether this agent has poly(ADPribose) polymerase (PARP) inhibitor activity and beneficially affects the development of postinfarction heart failure.

**Methods:** Male, 16weekoldrats were divided into four groups: Group 1: control rats (C); Group 2: doxycycline treated group (DOX); Group 3: isoproterenol stressed group (ISO); Group 4: isoproterenol and doxycycline treated group (ISO+DOX). Heart failure was induced with subcutaneous injection of 80mg/kg isoproterenol on two consecutive days. Afterwards doxycycline treatment was administered for 8 weeks with an oral dosage of 50mg/kg/day. Plasma Btype natriuretic peptide level was measured and echocardiography was performed before and at the end of the treated period. To determine the extent of interstitial fibrosis, Masson's trichrome staining was used. The changes of the activation level of Akt1, GSK3β, NFκB, NFATc2,GATA4 and the level of PARylation were quantified by Western blot.

**Results:** By the end of the study period LV endsystolic volume (LVESV) and systolic leftventricular inner diameter were increased (LVIDs), ejection fraction (EF) significantly decreased in the ISO group. An elevated ventricular weight to tibia length (VW/TL) ratio and plasma BNP level was found in the ISO group (p < 0.05 vs. Control). Histological analysis revealed increased myocardial fibrosis in ISO groups (p < 0.05 vs. Control). Isoproterenol induced increased level of PARylation and increased activation of NFκB and NFATc2. These alterations were significantly attenuated by doxycycline treatment (p < 0.05 vs. ISO). Phosphorylation of Akt1, GSK3β and activity of GATA4 were enhanced. Discussion: Doxycycline significantly moderated the development of heart failure after isoproterenol treatment besides the already known MMP2 inhibition viaits PARP inhibitory effect.

Echocardiographic parameters

	Baseline	C	DOX	ISO	ISO+DOX
EF (%)	75.62*	71.16*	71.82*	58.68	70.44*
Septum (mm)	1.68	1.67	1.66	1.86	1.59
Post. wall (mm)	1.57	1.53	1.64	1.78	1.64
LVIDs (mm)	4.42*	4.82*	4.87*	6.65	5.02*
LVESV (ul)	88.83*	108.72*	110.57*	158.16	119.31*

\*P < 0.05 vs. ISO

**P1783**

**Expression of IL-33/ST2 system in non-cardiac tissues after myocardial infarction.**

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 MJ Fernandez-Del Palacio<sup>2</sup>; MT Perez-Martinez<sup>1</sup>; M Navarro<sup>1</sup>; I Garrido-Bravo<sup>1</sup>;  
 FJ Pastor-Perez<sup>1</sup>; DA Pascual-Figal<sup>1</sup>

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**Introduction:** Interleukin-33 (IL-33) is a cytokine that binds to the membrane receptor (ST2L) and activates downstream signaling that confers cardioprotection after acute myocardial infarction (MI), whereas the soluble isoform (sST2) acts as a decoy receptor by sequestering IL-33 and blocking the cardioprotective effect of IL-33/ST2L system. In MI patients, plasma sST2 rises early and is associated with adverse remodeling, increased risk of heart failure and death. sST2 can be produced by both cardiac fibroblasts and cardiomyocytes after MI. However, the expression of sST2 could not be exclusive of the heart and other tissues may be a source of sST2 after MI, which is relevant to establish therapeutic strategies that decrease their expression.

**Purpose:** To assess the kinetics of IL-33, sST2 and ST2L expression in non-cardiac tissues after MI. **Methods:** 50 Wistar rats were subjected to MI by permanent ligation of the left anterior descending coronary artery and were randomized to be sacrificed 1, 2, 4, 12 or 24 weeks after MI (10 animals per group). In addition, 8 animals underwent surgery without ligation (control group). The mRNA expression of IL-33, sST2 and ST2L was measured by quantitative RT-PCR in lung, liver and kidney. ST2 protein expression was also assessed by immunohistochemical staining. Each value is expressed as fold of control ± standard error.

**Results:** Compared to control group, infarcted animals showed an increase in weight of lungs and liver from the first week after MI. The sST2 mRNA level significantly increased in the lungs from the first week after MI (4.3 ± 0.9, p = 0.004). This increase remained high until 24 weeks after MI (5.2 ± 1.2, p = 0.02). This kinetic

was confirmed by immunohistochemistry. In contrast, expression levels of IL-33 and its receptor (ST2L) decreased acutely after MI, while were normalized after 4 weeks post-MI. No significant changes were observed in the mRNA expression level of sST2, ST2L or IL-33 in liver or kidney compared to control group.

**Conclusions:** Following MI, early increased expression of sST2 in the lung occurs, which may increase circulating sST2. This increase is long term maintained and could contribute to block the cardioprotective signaling mediated by IL33/ST2L and thus to a worse evolution after MI.

#### P1784

##### Fimasartan protects cardiac myocyte damage in ischemic heart diseases

National Research Foundation of Korea (NRF-2014R1A1A1002824)

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The progressive cardiac dysfunction after myocardial infarction (MI) related with left ventricular fibrosis and remodeling. In previous study, angiotensin receptor blocker (ARB) treatment before the onset or during the acute stage of MI was effectively inhibited the progression of post-MI heart failure. This study investigated whether new ARB 'Fimasartan' is able to protect in the post-MI progression of left ventricular (LV) dysfunction and unknown under lining mechanism. MI was induced in SD rats by permanent ligation of the left anterior descending artery (LAD). Treatment with Fimasartan (10mg/kg) was initiated 24 hours post-MI and continued for 7 weeks through oral administration. All animals performed baseline echocardiography and then randomly assigned into 3 groups; surgery control (Sham group, n = 8), MI without fimasartan treatment (MI group, n = 11), and MI with fimasartan treatment (MI+Fima group, n = 14), respectively. In histologic finding, infarct size and fibrosis were significantly decreased in MI+Fima compare to MI. Echocardiography was performed in 1 week and 7 weeks post-MI and before MI surgery as baseline. LV end-systolic and diastolic dimension, and LV function was dramatically preserved in MI+Fima after 7 weeks compare with MI group (FS, 71.65 ± 1.49% VS 51.77 ± 5.14%). Hemodynamic measurement was observed 3 days after final echocardiography. Results showed great positive (+4526 ± 240 mmHg/sec) and negative dP/dt (-4187 ± 303) in MI+Fima compare with MI group (+3670 ± 239, -3301 ± 280 mmHg/sec, p < 0.05 respectively). From microarray, fimasartan treatment dramatically decreased inflammatory signal and increased lipid metabolic relate genes. In addition, mitochondria membrane ion transport and damage response genes were increased. A new ARB, fimasartan, strongly inhibit LV remodeling and development of cardiac dysfunction in myocardial infarction thorough preserve mitochondria survival. It shows possibility of fimasartan as a clinical treatment option to prevent progression of heart failure after MI.

#### P1785

##### TBX1 in cardiac remodeling induced after myocardial infarction.

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**Introduction:** The T-box protein 1 (TBX1) is a key fetal transcription factor in the embryonic heart development. After myocardial infarction (MI), adult heart returns to the fetal gene program, which activates mechanisms such as hypertrophy or fibrosis in order to maintain the contractile capacity of the infarcted heart.

**Purpose:** To assess the involvement of TBX1 in myocardial remodeling after MI, and if it is modulated by a therapy with proven benefit as mineralocorticoid receptor with eplerenone. **Methods:** 60 rats were subjected to MI by permanent ligation of the left anterior descending coronary artery: 50 animals were randomized to be sacrificed 1, 2, 4, 12 or 24 weeks after MI: 10 animals were treated with eplerenone (100 mg/kg/day) seven days before the MI and sacrificed 4 weeks post-MI. 8 animals underwent surgery without ligation (control group). Cardiac expression of TBX1, fetal genes (ANP, BNP,  $\beta$ -MHC and  $\alpha$ -actin-1) and fibrosis markers (collagen-I, collagen-III, TGF- $\beta$ , galectin-3 and  $\alpha$ -SMA) was assessed by quantitative RT-PCR or Western blotting. Left ventricular function variables were assessed before the sacrifice using a transthoracic echocardiographic examination.

**Results:** Gene and protein expression of TBX1 increased in the infarcted myocardium with a peak of expression after 1-week post-MI (p < 0.01), but did not change in the non-infarcted myocardium. The mRNA expression of fetal genes and fibrosis markers also increased, with a maximum of expression after 4-weeks post-MI (p < 0.01) and 1-week post-MI (p < 0.001), respectively. TBX1 expression correlated to the expression of fibrosis markers (p < 0.01), but not fetal genes. Eplerenone reduced the increase of TBX1 and fibrosis induced after MI, which was associated with an improvement of cardiac function analyzed by echocardiography.

**Conclusions:** The results show the post-MI reactivation of TBX1 expression and

suggest their involvement as pro-fibrotic molecule in the adverse remodeling, it may be involved in the benefit of mineralocorticoid blockade.

#### P1786

##### Three engineered allogeneic porcine iPSCs scaffolds after myocardial infarction in swine

SAF2014-59892, La MARATÓ de TV3 (201502-30, 201516-10), TerCel (RD12/0019/0029), RIC (RD12/0042/0047) and Fondo Europeo de Desarrollo Regional (FEDER)

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**Introduction:** Engineered constructs using induced pluripotent stem (iPS) cells to regenerate a myocardial scar may become true regenerative alternatives. 1

**Purpose:** This work evaluates safety and efficacy of undifferentiated porcine allogeneic GFP+iPS cells in three settings: embedded within an adipose pericardial graft (APG), an acellular pericardial scaffold (Scaffold), or both (APG-Scaffold) after acute myocardial infarction (MI) in swine.

**Methods:** Porcine iPSCs (p-iPS) were derived by transient expression of a single non-viral polycistronic vector in porcine skin fibroblasts. 2 Fifty seven swine underwent MI by coronary artery ligation, and distributed into three groups with biomatrices but p-iPS-free (APG n = 6; Scaffold n = 13; APG-Scaffold, n = 7), and three groups with p-iPS-enriched constructs (p-iPS-APG n = 9; p-iPS-Scaffold, n = 11; and p-iPS-APG-Scaffold, n = 11). Histopathology and cardiac magnetic resonance imaging (MRI) were used.

**Results:** Histopathology confirmed: first, absence of teratogenesis at multi-organ level after 3 months of follow-up; second, no evidence of p-iPS by immunohistochemistry nor real time-PCR neither within the myocardial scar or biomatrices; third, similar infarct size in all studied groups. Pre-sacrifice cardiac MRI revealed no significant benefit in left ventricular ejection fraction, cardiac output, end diastolic volume, and end systolic volume.

**Conclusions:** Undifferentiated allogeneic p-iPS delivery within three different engineering approaches is safe. Nevertheless, p-iPS could not be identified upon sacrifice and do not seem to support functional benefit after MI in swine.

#### P1787

##### Effect of exercise training on cardiac FNDC5 and BDNF post myocardial infarction

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**Introduction:** After myocardial infarction (MI), cardiomyocyte apoptosis and fibrosis contribute to the progressive left ventricle (LV) remodeling and dysfunction. Early initiation of exercise training post MI attenuates these cardiac changes. Exercise increases brain-derived neurotrophic factor (BDNF) in the hippocampus, which appears to be initiated by up-regulation of the myokine, fibronectin type III domain-containing protein 5 (FNDC5). In the heart, activation of BDNF may play a cardioprotective role post MI by inhibiting cardiomyocyte apoptosis and causing angiogenesis. Whether increases in FNDC5 and BDNF also occur in the heart by exercise post MI has not yet been studied.

**Purpose:** To determine changes in cardiac FNDC5 and BDNF and LV function post MI by exercise training.

**Methods:** After sham surgery (n = 7) or ligation of left descending coronary artery, MI rats were divided into sedentary (Sed-MI, n = 10) or exercise group (ExT-MI, n = 9) for a 4-week exercise program 5 days per week on a motor-driven treadmill. At the end, LV function was assessed by echocardiography and Millar catheter. FNDC5 and BDNF mRNA and protein was measured in non-infarct, peri-infarct and infarct areas of the LV by real-time PCR and western blot.

**Results:** MI size tended to be lower in ExT-MI compared to Sed-MI (P = 0.31). Exercise attenuated the decrease in EF and the increase in LVEDP. In Sed-MI, FNDC5 mRNA was decreased in all areas, the most in infarct area. BDNF mRNA was not different in all areas, but mature BDNF (mBDNF) protein decreased significantly in infarct area. Exercise attenuated the reduction in FNDC5 mRNA, and increased BDNF mRNA in peri-infarct area and mBDNF protein in non- and peri-infarct areas. EF correlated with mBDNF protein expression in non-infarct area.

**Conclusion:** Exercise training post MI attenuates reduction in FNDC5 and increases mBDNF protein in non- and peri-infarct areas of the LV. This may be contribute to improved cardiac function.



	Sham	Sed-MI	ExT-MI
MI size (%)		30 ± 2	25 ± 1
EF (%)	84 ± 1	54 ± 3*	65 ± 2*#
LVEDP (mmHg)	3 ± 1	21 ± 3*	9 ± 1*#
FNDC5 mRNA/5 µg of total RNA (x10 <sup>-1</sup> ) (Non-/Peri-/Infarct areas)	11 ± 0	7 ± 1*/5 ± 0*/2 ± 0*†	8 ± 1*/7 ± 1*/3 ± 0
BDNF mRNA/5 µg of total RNA (x10 <sup>-2</sup> ) (Non-/Peri-/Infarct areas)	10 ± 1	9 ± 1/9 ± 0/8 ± 1	10 ± 2/16 ± 2#/11 ± 1
mBDNF protein/GAPDH (Non-/Peri-/Infarct areas)	0.7 ± 0.1	0.5 ± 0.1/0.5 ± 0.1/0.3 ± 0*1.0 ± 0.2#/0.8 ± 0.1#/0.3 ± 0.1	

Values are means ± SE. \*P < 0.05 vs. Sham. #P < 0.05 vs. Sed-MI. †P < 0.01 vs. other areas of Sed-MI.

### P1788

#### Dietary-induced obesity causes cardiomyopathy in Lee-Sung minipigs model – role of mitochondrial dynamics and oxidative stress

MOST 104-2313-B-002-038-MY3 (from Ministry of Science and Technology) and NTU-CRESRP-104R7615-3 (from National Taiwan University)  
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**Background & Aims:** Mitochondrial dynamics, a process of biogenesis, fusion, fission and mitophagy, determine its morphology, quality, and functions; and is essential for maintaining a healthy mitochondrial network. As a highly oxidative tissue, mitochondria play a major role in maintaining the optimal cardiac function. Recently, many studies focus on the link between mitochondrial dysfunctions and cardiovascular diseases. In our previous study, we establish a dietary-induced obese (DIO) minipig model via Western diet feeding. This DIO minipigs have heavier body weight, accumulate more ectopic fat, and exhibit the metabolic syndrome, including hyperglycemia, hyperlipidemia, hypertension and fatty liver. The aim of this study was to elucidate the role of mitochondrial dynamic and oxidative stress in the heart of DIO minipigs.

**Methods:** Four-month-old Lee-Sung minipigs (LS) (initial body weight: 26.6 ± 1.3 kg) were randomly divided into two groups and fed the control diet (C) or a Western diet (W) for 6 months.

**Results:** The W pigs displayed a greater heart weight and more collagen accumulation in the heart, demonstrating a DIO-related cardiomyopathy. The W pigs exhibited a lower antioxidant capacity and higher oxidative stress in the left ventricle (LV). A decrease of ATP production was found in the LV of W pigs. Western diet caused a downregulation in the protein expression of PGC-1 $\alpha$  (marker of mitochondrial biogenesis) and OPA1 (marker of mitochondrial fusion), and an upregulation in FIS1 (marker of mitochondrial fission) and LC3II (marker of mitophagy) in the LV of W pigs.

**Conclusions:** The results suggest that mitochondrial dynamics and oxidative stress are involved in the progression of DIO-related cardiac injury. In addition, we provide a novel heart disease minipigs model with characteristic more like human heart diseases which had impaired mitochondrial dynamics and increased oxidative stress.

### P1789

#### Zebrafish model to study heart failure progression

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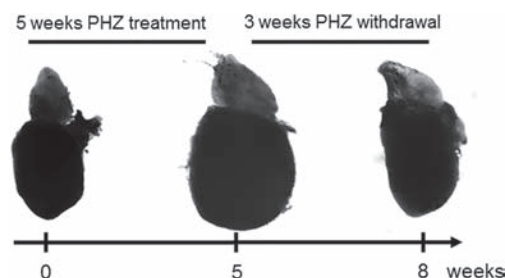
**Introduction:** Current medications used to treat heart failure patients can reverse left ventricular hypertrophy to some extent but are still ineffective against the escalating epidemic of heart failure. Thus, new therapeutic approaches are needed to suppress or ideally reverse heart failure development. Unlike mammals, zebrafish possess the incredible ability to regenerate cardiac tissue. The aim of this study was to evaluate whether zebrafish model can be used to study heart failure progression.

**Methods:** Eight to ten month old wild-type AB male zebrafish were treated with phenylhydrazine hydrochloride (PHZ) to generate heart failure (n = 86). After 5 weeks of treatment, PHZ was withdrawn and fish were followed up for 3 weeks. Hearts were imaged in living fish by ultrasound to assess ventricle size and function.

Functional capacity was evaluated in a dedicated swim tunnel. After sacrifice, hearts were collected for tissue staining or gene expression analysis.

**Results:** 5 weeks of PHZ-treatment led to a significant increase of 33% in ventricle size, and a decrease in heart rate (11%), fractional shortening (24%) and swim capacity (29%) (all p < 0.05). Ventricular wall thickness increased by 229%, ANP and BNP expression also increased significantly (p < 0.05). A higher number of apoptotic and proliferative cells were found in the myocardium of treated zebrafish. Two weeks after PHZ withdrawal, the ventricle regained its basal size. The swimming performance normalized after 1 week. ANP and BNP expression returned to basal levels after 2 weeks, and tissue morphology was normal at the end of the 3-week regeneration period. The picture shows photographs of representative hearts at baseline, after 5 weeks of PHZ treatment, and after 3 weeks of drug withdrawal

**Conclusion:** We showed that zebrafish constitutes an ideal experimental model to study heart failure development and regression. This model represents a unique opportunity to study the mechanisms of heart failure and test novel drugs



Heart Failure Progression in Zebrafish

### P1790

#### Non-invasive evaluation of an engineered bioactive graft using impedance spectroscopy after myocardial infarction in swine

SAF2014-59892, La MARATÓ de TV3 (201502-30, 201516-10), TerCel (RD12/0019/0029), RIC (RD12/0042/0047) and Fondo Europeo de Desarrollo Regional (FEDER)

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**Introduction:** Cardiac tissue engineering, which combines cells and biomaterials, is promising for limiting the sequelae of myocardial infarction (MI). In this context, decellularized tissues offer a natural microenvironment, driving cellular attachment, survival, migration, proliferation, and differentiation.<sup>2,3</sup>

**Purpose:** We assessed myocardial function and scar evolution after implantation of an Engineered Bioactive Impedance Graft (EBIG) in a swine MI model.

**Methods:** The EBIG was made of a scaffold of decellularized human pericardium, GFP-labelled porcine adipose tissue-derived progenitor cells (pATPCs), and a customized-design Electrical Impedance Spectroscopy (EIS) monitoring system (Figure 1). In a non-invasive manner, cardiac function was evaluated by magnetic resonance imaging (MRI), and scar healing by a customized-design EIS system incorporated within the implanted graft. In addition, infarct size, fibrosis, vascular density, and inflammation were also assessed.

**Results:** Upon sacrifice one month after the intervention, MRI detected a significant improvement in left ventricular ejection fraction (7.5 ± 4.9% vs. 1.4 ± 3.7%; P = 0.038) and stroke volume (11.5 ± 5.9 mL vs. 3 ± 4.5 mL; P = 0.019) in EBIG-treated animals. Non-invasive EIS data analysis showed differences in both impedance magnitude ratio (-0.02 ± 0.04/day vs. -0.48 ± 0.07/day; P = 0.002) and phase angle slope (-0.18 ± 0.24°/day vs. -3.52 ± 0.84°/day; P = 0.004) in EBIG compared to control animals. Moreover, in EBIG-treated animals, the infarct size was 48% smaller (3.4 ± 0.6% vs. 6.5 ± 1%; P = 0.015), less inflammation was found by means of CD25+ lymphocytes (0.65 ± 0.12 vs. 1.26 ± 0.2; P = 0.006), and a lower collagen I/III ratio was detected (0.49 ± 0.06 vs. 1.66 ± 0.5; P = 0.019).

**Conclusions:** An EBIG composed of acellular pericardium with adipose progenitors reduced infarct size and improved cardiac function in a pre-clinical model of MI. Non-invasive EIS monitoring tracked differential scar healing in EBIG treated animals confirmed by less inflammation and altered collagen deposit.

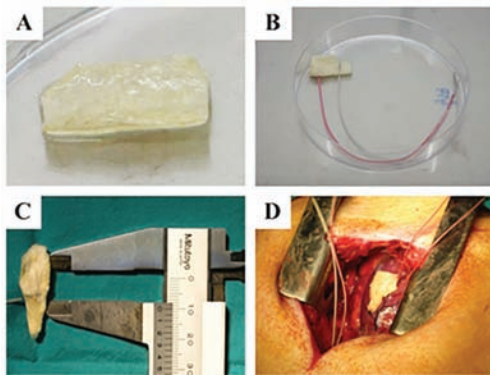


Figure 1

**P1791****Pulmonary artery banding-induced adaptive and maladaptive remodelling of the right ventricle in the rat**

Portuguese Foundation for Science and Technology (FCT-PTDC/SAU-FCT/100442/2008 and PTDC/DTP-FTO/0130/2012)

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Pulmonary arterial hypertension (PAH), the most serious chronic disorder of the pulmonary circulation, is characterized by pulmonary vasoconstriction and remodelling, resulting in increased afterload on the right ventricle (RV). In fact, RV function is the main determinant of prognosis in PAH. Most frequently used experimental models of PAH include the monocrotaline- and chronic hypoxia induced-PAH, which primarily affect the pulmonary circulation. Alternatively, pulmonary artery banding (PAB) can be performed to achieve RV overload without affecting the pulmonary vasculature, allowing researchers to determine the RV-specific effects of their drugs/interventions.

In this work we characterize in full detail, PAB-induced adaptive and maladaptive remodelling of the RV, 3 weeks after PAB surgery, using two different degrees of pulmonary artery constriction. Our results show that by applying a mild constriction, the RV develops adaptive hypertrophy, with preserved systolic and diastolic function, while application of a severe constriction resulted in maladaptive hypertrophy, with chamber dilation, and systolic and diastolic dysfunction, up to the isolated cardiomyocyte level.

Alternatively to previous works, we describe for the first time a reliable and short-time PAB model, in which RV adaptation can be distinguished 3 weeks after surgery, by applying two different degrees of constriction, allowing researchers to better study RV physiology and transition to dysfunction and failure, as well as to determine the effects of new therapies.

**P1792****Kv4.x ion channels expression reorganized on cardiomyocytes with altered mechanical and physiological parameters influenced by ophiobolins**

TAMOP-4.2.2.A-11/1/KONV-2012-0035 and

TAMOP-4.2.2.D-15/1/KONV-2015-0024

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The transient outward (I<sub>to</sub>) currents are determined by Kv4.2 and kv4.3 ion channels where the activity of I<sub>to,fast</sub> and I<sub>to,slow</sub> currents is not obligately dependent upon the expressed level of Kv4.x transcript. Ophiobolins are major members of the ophiobolin complex of phytotoxic metabolites, and they possess antitumor, antibacterial, antifungal activities. Increasing evidence points to a role of MGB1 as underlying factors and Sap97 related to inflammation. The Sap97 associates with Kv4-type channels in complex modulating their kinetic properties. Our hypothesis was that the Sap97 mainly localizes 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 I<sub>to</sub> current. The aim was to use purified ophiobolins as an effective molecular tool in

the study of inflammation. In this swot we have investigated the mechanical factors by atomic force microscope technique (AFM) and the surface expression of Kv4 ion channels on cardiomyocytes using electron microscope and immunofluorescence methods. AFM study showed that the elasticity of the cell surface, the Young modulus is moderately changed as well as cell volume and the highest of the cells in the presence of ophiobolin with low concentration. However after treatment with ophiobolin the binding of Sap97 to Kv4.x channels and distribution of their complexes are altered in the membrane and physiological behaviour of myocytes as compared to control cells. A growing body of research use 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 suggest that Sap97 deactivation or reduction can lead (directly or indirectly) to changes in the functional cell surface expression of Kv4.x channels with mechanical parameters, with biophysical and biochemical properties of cardiac I<sub>to</sub> current.

**P1793****The induction of mild hypothermia increases pulmonary vascular resistance in healthy pigs**

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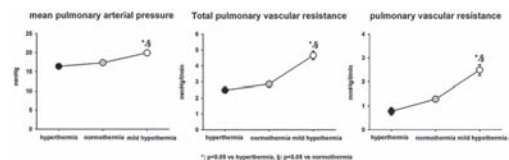
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**Introduction:** The induction of mild hypothermia increases systemic vascular resistance and reduces the need for vasopressors in resuscitated patients. However, much less is known about the effect of temperature on pulmonary vascular resistance. We therefore retrospectively analysed hemodynamic data obtained in anaesthetized healthy pigs subjected to hyperthermia (40.5°C, HT), normothermia (38.0°C, NT) and mild hypothermia (33.0°C, MH).

**Methods:** 9 anaesthetized healthy pigs (67 ± 2 kg) were acutely instrumented with a Swan-Ganz and a left ventricular (LV) pressure-volume catheter in a closed-chest setting. Temperature was controlled by an intravascular device. After baseline measurements at HT, pigs were cooled to NT and further down to MH. Total pulmonary vascular resistance (TPVR) was calculated as mean pulmonary arterial pressure (mPAP)/cardiac output (CO), and PVR was estimated as (mPAP minus LV end-diastolic pressure) divided by CO.

**Results:** CO (6.7 ± 0.3 vs 6.1 ± 0.3 vs 4.4 ± 0.2 l/min) decreased with cooling from HT to MH, while mPAP increased slightly (graph). TPVR and PVR (graph) increased substantially with cooling. Whole body oxygen consumption (WB-VO<sub>2</sub>) (395 ± 19 vs 314 ± 24 vs 199 ± 16 ml kg<sup>-1</sup> min<sup>-1</sup>, all p < 0.05) decreased by 50% from HT to MH, while mixed venous oxygen saturation increased (53 ± 2 vs 60 ± 2 vs 66 ± 2 mmHg, all p < 0.05), indicating a preserved systemic oxygen supply-demand balance during cooling.

**Conclusion:** Cooling from HT to MH increases pulmonary vascular resistance more than twofold. This increase does not result in overt pulmonary hypertension due to the physiologic decrease of cardiac output during hypothermia. However, caution may be advised when MH is induced in resuscitated patients with increased pulmonary vascular resistance (i.e. pulmonary embolism or chronic pulmonary hypertension).

**P1794****Value of amino acids for cardioprotection**

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The main obstacle for the creation of reliable methods of long-term heart preservation is pathological changes in cardiomyocytes (CM) under conditions of ischemia. A key mechanism of CM damage is oxidative stress. The most important components of living cells maintaining homeostasis and exhibiting antioxidant properties are amino acids. However the role of amino acids in maintaining the myocardium antioxidant protection during its preservation is not clear. The aim of our study was to assess antioxidant capacity of myocardium during heart preservation in solutions with different amino acids composition. Methods. The study is based

on experimental studies on 88 adult male Wistar rats weighing 250-300 g were kept under standard vivarium conditions and in compliance with the rules for the humane treatment of laboratory animals. Hearts were excised from anesthetized with 10% sodium thiopental sodium rats and immersed at 4°C for 3 hours in preservation solutions: Krebs-Henseleit solution (control), Custodiol and the Krebs-Henseleit solution with the L-amino acids (AA) or its different combinations. Antioxidant activity (AOA) was determined by the ability of the isolated using bovine serum albumin and collagenase type IV CM to inhibit the radical 2,2'-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS•+) at the 10th minute incubation and expressed as median (25th percentile – 75th percentile)% compared with control probe of reagent kit (Oxistat, Belarus).

**Results:** AOA of control CM and CM stored with histidine-valine were dramatically decreased to 30.0(20.0;33.3)% and 21.7(16.7;26.7)%, resp. AOA of CM after immersing in solutions with different AA didn't differ from control. At the same time CM stored in Custodiol or the Krebs-Henseleit solution with the another combinations of L-amino acids (tryptophan (2 mM)-arginine (10mM), tryptophan (2mM) - asparagine (4 mM) and tryptophan (2 mM) - glutamine (4 mM)) exhibited more preserved antioxidant activity ( $p < 0.001$  compared with control).

**Conclusion:** For maintaining myocardium AOA heart preservation solution should contain amino acids with different mechanisms of antioxidant action.

### P1795

#### Multiparametric MRI-based characterization of atrial and ventricle function in relationship to changes in ACE/ACE-2 angiotensin profile in mice with dilated cardiomyopathy

This work was supported by European Regional Development Fund from European Union (grant coordinated by JCET-UJ, No WND-POIG.01.01.02-00-069/09-00) U Tyrankiewicz<sup>1</sup>; M Olkowicz<sup>2</sup>; M Jablonska<sup>1</sup>; A Orzyłowska<sup>1</sup>; A Bar<sup>3</sup>; K Jezkova<sup>4</sup>; M Bartus<sup>5</sup>; RT Smolenski<sup>2</sup>; T Skorka<sup>1</sup>; S Chlopicki<sup>5</sup>  
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We comprehensively characterized alteration in cardiac function in vivo using MRI, and in isolated working heart in relation to capillarization and ACE/ACE-2 angiotensin profile (by LC-MS) in 2,4,6,8,10,12 month-old Tgαq<sup>44</sup> and FVB mice. In 6 month-old mice Tgαq<sup>44</sup> mice despite full preservation of cardiac function atrial volumes, ventricle strains, and coronary flow response to increased preload were altered. In 8-9-months-old Tgαq<sup>44</sup> mice a decreased cardiac performance, with preserved cardiac reserve to dobutamine were observed, while the final stage of HF (12-14-months-old Tgαq<sup>44</sup> mice) was characterized by decreased global cardiac performance, lack of cardiac reserve, with diminished cardiac capillarization. ACE-2 was progressively activated in 6-8-months old Tgαq<sup>44</sup> mice as evidenced by increased plasma concentration of angiotensin (1-7), angiotensin (1-9), alamandine, while ACE was progressively activated starting from 8-month old Tgαq<sup>44</sup> mice as evidenced by increased plasma angiotensin II, III, IV and Ang A. Profile of angiotensins in the heart supported ACE/ACE-2 alterations with Ang (1-12) playing a prominent role. In conclusion, despite cardiomyocytes-specific trigger of the HF pathology in Tgαq<sup>44</sup> mice the progression of decompensated HF is associated with both systemic and local RAC-ACE activation that is counterbalanced by prominent ACE-2 activation in the adaptive phase of HF.

### P1796

#### Mouse cardiac LXRα overexpression as a model to modulate cardiac metabolism and trigger specific fetal gene expression to ameliorate pathological hypertrophy

NWO VIDI  
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**Purpose:** Liver X receptors (LXRs) are key regulators of glucose and lipid metabolism in cardiac hypertrophic pathogenesis. These metabolic processes are altered in heart failure and in the diabetic heart. Here we explored a mouse model with cardiac LXRα overexpression and subjected these mice either to cardiac pressure overload or to a high fat diet inducing type 2 diabetes.

**Methods:** Murine Lxrα was cloned behind the α-myosin heavy chain (αMhc) promoter to create transgenic (LXRα-Tg) mice and transgene-negative littermates (WT). Cardiac pressure overload in these mice was generated by transverse aortic constriction (TAC) for 5 weeks. Type 2 diabetes was induced by high fat diet (HFD, 60

kcal% fat) over 16 weeks and compared to low fat diet (LFD, 10 kcal% fat). In vitro studies were performed in isolated primary neonatal rat ventricle myocytes.

**Results:** Overexpression of LXRα protects the heart against hypertrophy in both the TAC pressure overload model and in type 2 diabetic mice. Overexpression markedly enhanced the capacity for myocardial glucose uptake at baseline and further enhanced this under hypertrophic stress conditions. In the HF-diet mice, increased cardiac glucose uptake was mediated in part through AMPK phosphorylation and restoration of GLUT4 expression. Most fetal gene program genes were less induced in LXRα overexpressing mice, which correlates with the diminished hypertrophic response. Expression of natriuretic peptides, ANP and BNP, was, however, elevated in the LXRα-Tg mice and could mediate the observed anti-hypertrophic effect. LXRα promoted energy independent utilization of glucose via the hexosamine biosynthesis pathway, resulting in O-GlcNAc modification of transcription factors GATA4 and Mef2c, which control the induction of natriuretic peptide expression. Moreover, in silico analysis of the ANP/BNP region using algorithms specific for the identification of LXR binding sites (LXREs), revealed the presence of several conserved LXREs. Cardiac LXRα chromatin immunoprecipitation assays confirmed binding of LXRα to two conserved LXREs in the ANP/BNP promoter region, indicating that these are direct targets of LXRα.

**Conclusions:** LXRα helps to orchestrate an adaptive metabolic response to chronic cardiac stress, and modulating LXRα may provide a unique opportunity for intervening in myocyte metabolism. We speculate that LXRα controls the expression of ANP and BNP directly via binding to LXRE elements in the promoter regions and indirectly via O-GlcNAc modification of GATA4 and Mef2c transcription factors.

## BASIC SCIENCE: CELLULAR BIOLOGY

### P1797

#### Hypertrophy induced KIF5B controls mitochondrial localization and function in neonatal rat cardiomyocytes

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**Purpose:** Cardiac hypertrophy is associated with growth and functional changes of cardiomyocytes, including mitochondrial alterations, but the latter is still poorly understood. Here we investigated mitochondrial function and dynamics in primary neonatal rat ventricular myocytes (NRVMs) stimulated with insulin growth factor-1 (IGF-1) or phenylephrine (PE), mimicking physiological and pathological hypertrophic responses, respectively.

**Methods:** Mitochondrial oxidative phosphorylation (OXPHOS) activities were investigated in cultured primary NRVMs treated with PE or IGF-1. Mitochondrial oxygen consumption rates (OCR) were determined with a Seahorse flux analyzer in intact and permeabilized NRVMs. Mitochondrial biogenesis, localization and gene expression profiling was performed and KIF5B function was investigated.

**Results:** A decreased activity of the mitochondrial electron transport chain (ETC) (state 3) was observed in permeabilized NRVMs stimulated with PE, whereas this was improved in IGF-1 stimulated NRVMs. In intact NRVMs, mitochondrial oxidation capacity rate (OCR) was, increased in PE stimulated NRVMs, but remained constant in IGF-1 stimulated NRVMs. After stimulation with PE, mitochondria localized to the periphery of the cell. To study the differences in more detail, we performed gene array studies. IGF-1 and PE stimulated NRVMs did not reveal major differences in gene expression of mitochondrial encoding proteins, but we identified a motor protein implicated in mitochondrial localization, kinesin5B (KIF5B), which was clearly elevated in PE stimulated NRVMs but not in IGF-1 stimulated NRVMs. We confirmed that KIF5B expression was elevated in animal models with pathological cardiac hypertrophy. Silencing of KIF5B reverted the peripheral mitochondrial localization in PE stimulated NRVMs and diminished PE induced increases in mitochondrial OCR, indicating that KIF5B dependent localization affects mitochondrial respiration in PE stimulated NRVMs.

**Conclusions:** These results indicate that KIF5B contributes to mitochondrial dynamics and function in cardiomyocytes and may play a role in pathological hypertrophic responses in vivo

### P1798

#### Hyperinsulinemia and overweight in obese Zucker rats effectively suppressed by exercise training with hypoxia recovery

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It is currently unknown whether hypoxia training can effectively suppress overweight and hyperinsulinemia in genetically obese animals. In this study, both lean and obese Zucker rats were randomly assigned into the following groups: control (CON, n = 7), exercise training (EX, n = 7), hypoxia (HYP, n = 7) and exercise training with hypoxia recovery (EX+HYP, n = 7). During a 6-week training period, rats performed swimming exercise progressively from 30 to 180 min.day<sup>-1</sup>, and recovered under hypoxia (14%



oxygen for 8 h.day<sup>-1</sup>). Obese Zucker rats exhibited substantially greater fasting insulin levels, and exaggerated glucose and insulin responses following an oral glucose challenge compared with lean rats. At the beginning of week 6, body weight, fasting glucose, fasting insulin, area under curve of glucose (GAUC) and insulin (IAC) in the EX+HYP group were significantly lower than CON group among the obese rats. Meanwhile, only GAUC was significantly lower in the EX group compared to the CON group. At the end of week 6, capillaries to fibre ratio (C/F), capillary density (CD) and type IIa fibre proportion of the plantaris muscle in the EX group were significantly greater than the CON group (PB0.05), but no additive effect of hypoxia on exercise training was observed. Our data demonstrate that exercise training with prolonged hypoxia recovery offers better metabolic benefits than exercise training alone for the obese Zucker rats. This advantage was closely associated with effective weight reduction.

#### P1799

##### ERK1/2 mediates lipopolysaccharide-upregulated FGF-2, uPA, MMP-2, MMP-9 and cellular migration in primary cardiac fibroblasts

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Upregulation of fibroblast growth factor (FGF), urokinase plasminogen activator (uPA), tissue plasminogen activator (tPA) and matrix metalloproteinases (MMPs) is associated with the development of myocardial infarction (MI), dilated cardiomyopathy, cardiac fibrosis and heart failure (HF). Evidences suggest that lipopolysaccharide (LPS) participates in the inflammatory response in the cardiovascular system; however, it is unknown if LPS is sufficient to upregulate expressions and/or activity of FGF-2, uPA, tPA, MMP-2 and MMP-9 in cardiac fibroblasts. In the present study, we treated primary cardiac fibroblasts with LPS to explore whether LPS upregulates FGF-2, uPA, tPA, MMP-2, MMP-9 and cellular migration, and further to identify the precise molecular and cellular mechanisms behind these upregulatory responses. Here we show that LPS challenge increased the protein levels of FGF-2, uPA, MMP-2 and MMP-9, and induced the activity of MMP-2 and MMP-9 in cardiac fibroblasts. After administration of inhibitors including U0126 (ERK1/2 inhibitor), SB203580 (p38 MAPK inhibitor), SP600125 (JNK1/2 inhibitor), CsA (calcineurin inhibitor) and QNZ (NFκB inhibitor), the LPS-upregulated expression and/or activity of FGF-2, uPA, MMP-2 and MMP-9 in cardiac fibroblasts is markedly inhibited only by ERK1/2 inhibitors, U0126. Collectively, these results suggest that LPS upregulates the expression and/or activity of FGF-2, uPA, MMP-2 and MMP-9, and the subsequent cell migration through ERK1/2 signaling pathway in primary cardiac fibroblasts. Our findings further provide a link between the LPS-induced cardiac dysfunction and the ERK1/2 signaling pathway that mediates the upregulation of FGF-2, uPA, MMP-2, MMP-9 and cellular migration in primary cardiac fibroblasts

#### P1800

##### PKA/PKC mediated changes in phosphorylation of inhibitor-1 at residues thr35 and ser67 contribute to elevated intracellular sodium in failing hearts

BHF and Wellcome Trust

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**Purpose:** Inhibitor-1 (I-1) is an endogenous regulator of type-1 protein phosphatase (PP1). I-1 integrates the effects of two major signalling pathways in the heart, β-adrenergic/PKA and calcium/PKC. PKA phosphorylates I-1 at Thr35 thereby reducing PP1 activity, whereas, PKCα phosphorylates I-1 at Ser67 and thus activates PP1. Here we examined the effects of I-1 phosphorylation on intracellular Na concentrations (via Na/K ATPase and its accessory protein phospholemman, PLM) in isolated mouse and rat cardiomyocytes. Furthermore, we examined I-1 phosphorylation status in failing human hearts and donor controls. METHODS AND

**Results:** Rat and mouse ventricular myocytes were infected with adenoviruses encoding WT I-1 (I-1WT), Ser67A mutant (I-1S67A) or GFP-control. Changes in protein expression and phosphorylation, Na/K ATPase current and intracellular Na were investigated using western blot, patch clamp and sodium-sensitive dye, respectively. Expression of I-1WT significantly increased PLM phosphorylation at its PKA site Ser68, increased Na/K ATPase current and reduced intracellular Na concentrations in cardiomyocytes under basal and β-receptor activated conditions (1 nM of isoprenaline) of GFP controls. In cells expressing I-1S67A mutant (where PKC cannot phosphorylate I-1 Ser67 residue) further increases in phosphorylation of PLM-Ser68 where observed of I-1WT, under basal conditions (46%) and β-receptor activated conditions (110%). Furthermore, I-1S67A induced a significant decrease in intracellular Na concentration (8.47 ± 0.73 mM), cf I-1WT (10.94 ± 0.87 mM). This decrease in Na was absent in myocytes isolated from mice where all three PLM phospho-residues were mutated to alanines, indicating that the I-1 effects are mediated via PLM. In left ventricular myocardium from patients with heart failure, I-1 expression and phosphorylation at Thr35 residue was reduced and Ser67 increased, indicating upregulated PP-1 activity in failing hearts. Indeed, phosphorylation of major PP1 targets, phospholemman Ser68 and phospholamban Ser16 were both

significantly reduced in failing hearts (n=8). No significant changes were detected in expression of Na/K ATPase, Serca2a, total PLM or in phosphorylation at PLM Ser63 and Thr69 residues.

**Conclusions:** We provide evidence that in cardiomyocytes intracellular Na is regulated by the phosphorylation status of I-1 and that this mechanism is modulated by the PKA-PKC crosstalk. This novel mechanism, is disrupted in failing hearts favoring reduced Na/K ATPase and SERCA activity and thus may be a major contributor to maladaptive hypertrophy and arrhythmogenesis.

#### P1801

##### A new potential strategy for targeting pathological cardiac hypertrophy: the dimer interface of ERK1/2

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**Background:** The extracellular signal-regulated kinases 1 and 2 (ERK1/2) have a central role in cardiac hypertrophy and cell survival. Hypertrophic stimuli trigger ERK1/2 activation, ERK dimerization and subsequently ERKThr188-autophosphorylation, a prerequisite for ERK1/2-mediated pathological cardiac hypertrophy. Here, we investigated interference with ERK dimerization as a therapeutic strategy to prevent pathological cardiac hypertrophy. Methods. To evaluate the impact of monomeric ERK, we used monomeric ERK2Δ174-177 and a peptide that interferes with ERK dimerization. The effects of ERK2Δ174-177 and the peptide were analyzed with regard to cardiomyocyte size, [3H]-isoleucine incorporation, ERK1/2 target phosphorylation, TUNEL positive cells and confocal ERK localization assays. Transgenic mice with cardiac overexpression of ERK2Δ174-177 were generated to assess cardiac hypertrophy and apoptosis in response to transverse aortic constriction (TAC) or exercise.

**Results:** Overexpression of monomeric ERK2Δ174-177 in neonatal rat cardiomyocytes (NRCM) resulted in an attenuated hypertrophic response to phenylephrine stimulation. In contrast to ERK1/2 inhibition by PD98059, ERK2Δ174-177 did not induce cardiomyocyte apoptosis. In line with these results, ERK2Δ174-177 expression reduced TAC induced cardiac hypertrophy without exacerbation of cardiomyocyte apoptosis and preserved cardiac function. In addition, mRNA expression levels of collagen and brain natriuretic peptide (BNP) were significantly reduced in ERK2Δ174-177 transgenic mice upon TAC compared to control mice. As cardiac hypertrophy is important under certain physiological conditions, we also analyzed the outcome of ERK2Δ174-177 overexpression in response to a physiological stimulus, i.e. running exercise, which revealed no impairment by monomeric ERK2 on cardiac growth or function. Further, interference with the dimerization of endogenous ERK using the ERK binding peptide significantly reduced ERKThr188 phosphorylation. Subsequently, NRCM expressing the peptide showed less hypertrophy upon phenylephrine stimulation compared to control cells – most likely via prevention of nuclear translocation of ERK2 and nuclear ERK target phosphorylation. Interestingly, the peptide neither impaired overall ERK1/2 activation nor cardiomyocyte survival.

**Conclusion:** These data indicate that inhibition of ERK dimerization selectively attenuates pathological cardiac growth without cardiac adverse effects. Interference with the ERK dimer interface might therefore be a valuable and promising approach to prevent pathological hypertrophy.

#### P1802

##### A central role for Hippo pathway and actin filament dynamics in microRNA-induced cardiomyocyte proliferation

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**Background:** Loss of cardiac function after myocardial infarction (MI) remains a main cause of heart failure, which might be overcome by innovative, pro-regenerative treatments. By performing a genome-wide microRNA (miRNA) screening, we identified a series of human miRNAs capable of promoting cardiomyocyte proliferation and cardiac regeneration after MI. RNA-seq analysis of the effects induced by these miRNA uncovered a potential link between the Hippo pathway, which is known to regulate cell proliferation in the embryo, and actin filament dynamics.

**Hypothesis:** We hypothesized that our pro-proliferative miRNAs act by inactivating the Hippo pathway and set out to discover the link between their effect and the regulation of actin filament dynamics.

**Methods:** We analyzed involvement of the Hippo pathway in mediating the effects of the identified miRNAs by studying activation of Yap (the final effector in the pathway) by transcription reporter, RNAi and gene expression studies. Acting dynamics was investigated by immunofluorescence and specific drug treatment of cardiomyocytes. Final endpoints was cardiomyocyte proliferation by Edu staining (S-phase), phosphoH3 positivity (G2/M) and Aurora B localization in midbodies (kariokinesis).

**Results:** We discovered that 9 out of the 10 most effective miRNAs in driving cardiomyocytes proliferation also activated Yap-mediated transcription, as concluded by TEAD reporter gene analyses, increased transcription of the endogenous Yap reporter genes *Ctgf*, *Cyr61*, *Birc5* and *Ankd1* and nuclear import of active, unphosphorylated Yap after nuclear-cytoplasmic fractionation. In particular, miR-199a-3p was found to act through the direct downregulation of at least three mRNA targets impinging on the Hippo pathway, namely the upstream inhibitory kinase *Tak1*, the E3 ubiquitin ligase destroying Yap *bTrCP* and the regulator of actin cytoskeleton dynamics *Cofilin 2* (*Cfl2*). We discovered that both miR-199a-3p and *Cfl2* siRNA treatments induced actin polymerization, which was inhibited by the F-actin inhibitor cytochalasin D; treatment with this drug also strongly decreased activation and nuclear localization of Yap.

**Conclusion:** Induction of cardiomyocyte proliferation by miRNAs involves regulation of the Hippo pathway and modulation of the actin cytoskeleton. These results implicate novel molecular mechanisms able to boost cardiac muscle regeneration after myocardial injury.

### P1803

#### Cardiac specific overexpression of phosphodiesterase 4b in mice limits beta-adrenergic response and associated pro-arrhythmic Ca(2+) events

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**Purpose:** In the heart, phosphodiesterase type 4 (PDE4) plays a major role in the hydrolysis of cAMP generated by  $\beta$ -adrenergic receptors ( $\beta$ -AR). We have previously shown that inactivation of the PDE4B isoform in mice leads to an increase of the L-type Ca(2+) current (I(Ca,L)) and cardiac arrhythmias upon  $\beta$ -AR stimulation. Here, we characterized the effects of cardiac-specific PDE4B overexpression ( $\alpha$ -MHC promoter) on cardiac function and  $\beta$ -AR signaling in male transgenic (TG) mice and WT littermates at 10-16 weeks of age.

**Methods and Results:** TG mice had 7-fold increase in ventricular cAMP-PDE activity evaluated by radioenzymatic assay, associated with a small (18%) but significant increase in heart weight to body weight ratio as compared to WT. In vivo, telemetry showed similar heart rate and echocardiography revealed a lower ejection fraction in TG vs. WT (64  $\pm$  5% vs. 79  $\pm$  5%, n=6, p<0.05). Nonetheless, TG showed a better performance than WT when subjected to incremental treadmill test to exhaustion (n=10-11, p<0.05). In Langendorff-perfused hearts, the potency of isoprenaline (Iso) was decreased in TG (EC50=3.8 nM vs. 1.4 nM, n=4, p<0.05), whereas basal cardiac function was unchanged suggesting that the decreased cardiac function observed in vivo was due to decreased responsiveness to catecholamines. Accordingly, basal sarcomere shortening and Ca(2+) transient amplitude recorded with an Ionoptix<sup>®</sup> system in isolated ventricular myocytes loaded with Fura-2 AM (3  $\mu$ M) were unchanged at baseline but their potentiation by Iso (0.3-100nM) was decreased in TG. PDE4 inhibition by Ro 20-1724 (Ro, 10  $\mu$ M) restored a normal  $\beta$ -AR response. Interestingly, the proportion of cells exhibiting spontaneous Ca(2+) events and contractions upon Iso was significantly smaller in TG compared to WT (18% vs. 48% at 10 nM and 46% vs. 77% at 100 nM, n=3, n=7-11, p<0.05).  $\beta$ -AR stimulation of I(Ca,L) recorded with the patch-clamp technique was decreased by 60% in TG (n=4, n=16-31). Similarly,  $\beta$ -AR stimulation of intracellular cAMP levels and PKA activity measured with FRET biosensors were blunted by 75% in TG (n=3, n=7-11, p<0.001) and these differences were abolished by Ro. PLB and TnI levels were unchanged, but their phosphorylation at Ser16 and Thr17 (PLB) and Ser23/24 (TnI) was strongly reduced.

**Conclusion:** Cardiac PDE4B overexpression decreases  $\beta$ -AR response but preserves exercise capacity and prevents pro-arrhythmic Ca(2+) events. Thus, PDE4B overexpression could be protective in pathological situations where  $\beta$ -AR stimulation is chronically augmented.

### P1804

#### Evidence and role of neuronal sodium channel Nav1.8 in human failing cardiomyocytes

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**Purpose:** In heart failure, persistent current through Na channel (INaL) is augmented that may lead to arrhythmias. We sought to examine the existence of Nav1.8, its contribution to augmented INaL thereby to arrhythmias in the human heart and its role for cardiac pathology. Furthermore, we were interested whether CaMKII $\delta$  colocalises with Nav1.8 under pathophysiological condition thereby regulating its function.

**Methods:** For this study, we utilised human myocardium (n=52) with different pathophysiological conditions from atrium and ventricle while non-failing myocardium served as control. To investigate Nav1.8 regulation, myocardium homogenates were prepared and performed Western blot. Association and colocalisation of CaMKII $\delta$  with Nav1.8 was studied by coimmunoprecipitation and double immunofluorescence staining. Furthermore, to investigate contribution of Nav1.8 on cellular electrophysiology, whole-cell patch-clamp and confocal microscopy was performed in the presence/absence of a novel specific Nav1.8 blocker A-803467 (30nM/L).

**Results:** We show for the first time that Nav1.8 was significantly upregulated in hypertrophy and heart failure compared to non-failing myocardium. Most importantly, parallel to Nav1.8 upregulation Nav1.5 was downregulated. However, no significant difference in Nav1.8 was observed between sinus rhythm and atrial fibrillation. There was also a significant increase in association and colocalisation of Nav1.8 with CaMKII $\delta$  in failing hearts compared to non-failing, further confirmed by immunofluorescence staining. Interestingly, Nav1.8 showed overlapping with CaMKII $\delta$  at both the intercalated-disc and T-tubules. Whole-cell patch-clamp showed a significant reduction in INaL and abbreviation of APD after addition of a novel specific Nav1.8 blocker in both atrial and ventricular failing cardiomyocytes. Moreover, SR-Ca2+ sparks measurement revealed reduction in Ca2+ leaks by addition of Nav1.8 blocker suggesting a significant role of Nav1.8 for cellular electrophysiology.

**Conclusion:** We showed for the first time that neuronal sodium channel Nav1.8 is overexpressed and colocalises with CaMKII $\delta$  in the human failing heart. Furthermore, blocking of Nav1.8 by a specific novel blocker reduces the, in heart failure augmented proarrhythmic INaL, causes abbreviation of APD and also reduces SR-Ca2+ leaks in human failing cardiomyocytes. The association of Nav1.8 with CaMKII $\delta$  might result in increased INaL and Ca2+ mishandling under condition of enhanced CaMKII $\delta$  activity as in heart failure and may serve as an arrhythmic trigger which would be of clinical relevance.

### P1805

#### Impact of GMP-PKG pathway modulation on titin phosphorylation and titin-based myocardial passive stiffness

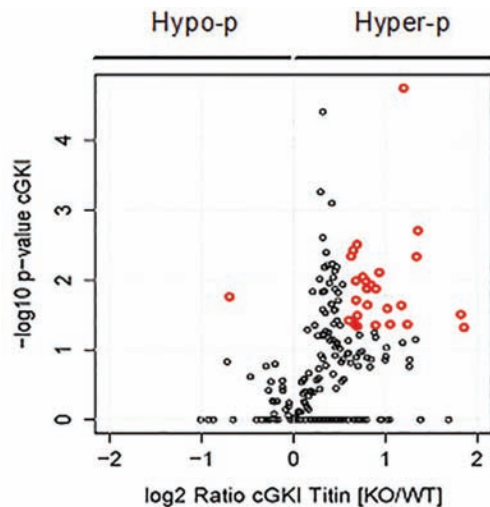
DFG  
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**Rationale:** The crucial contribution of the giant myofibrillar protein titin to diastolic stiffness and cardiomyocyte passive force (F<sub>passive</sub>) is dependent, in part, on titin isoform composition and phosphorylation. Phosphorylation of titin by cyclic guanosine monophosphate (cGMP)-dependent protein kinase G (PKG) lowers titin-based stiffness, thus mediating a mechanical signaling process that is disturbed in heart failure.

**Objective:** To elucidate which elements of the nitric oxide (NO) cGMP-PKG signaling network are critical for titin phosphorylation and stiffness in vivo.

**Methods and Results:** We employed genetic knockout (KO) mouse models deficient for enzymes of the cGMP-PKG pathway, including cardiomyocyte-specific deletion of the guanylyl cyclase (GC)-A receptor and cGMP-dependent PKG (cGKI), as well as global deletion of soluble GC (sGC). We assessed titin phosphorylation by immunoblotting using phosphoserine-specific titin antibodies and by mass spectrometry quantification using stable isotope labeling of amino acids in mixed cultures of heart tissue from either wild-type (WT) or KO mice. The F<sub>passive</sub> of single permeabilized cardiomyocytes was recorded before and after administration of PKG. In all three genetic models, all-titin phosphorylation was reduced compared to WT hearts. The important PKG-dependent phospho-S4080 site within the N2-Bus region of mouse titin was hypophosphorylated in all three KO models. Unexpectedly, mass spectrometry analysis revealed that most class 1 titin phospho-sites within the molecular spring segment, including the Ig-domain regions, were hyperphosphorylated. Only a few sites showed a phosphorylation deficit or remaining unchanged. Particularly in the cGKI model many class 1 phospho-sites were hyperphosphorylated compared to WT hearts (see figure), indicative of the presence of compensatory processes following loss of PKG; indeed, this was associated with upregulation of several kinases that phosphorylate titin and a clear rise in F<sub>passive</sub> in KO vs. WT cardiomyocytes. While administration of PKG lowered F<sub>passive</sub> of WT and KO cardiomyocytes in all models, this effect was more pronounced in the cGKI KO.

**Conclusions:** Multiple in vivo phosphorylated class I titin phospho-sites were identified within the molecular spring segment, some of which depended on the cGMP-PKG pathway. While cGMP-activated PKG remains an important titin-targeting kinase, many titin phospho-sites may be regulated through a network of protein kinases/phosphatases.



Volcano plot

## BASIC SCIENCE: GENE AND CELL THERAPY

## P1806

**c-kit+ resident cardiac stem cells improve left ventricular fibrosis in pressure overload**

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**Aims:** The role of c-kit (CD117)+ resident cardiac stem cells (RCSC) in cardiac fibrogenesis is not completely understood.

**Methods & Results:** To investigate the effect of RCSC on myocardial remodeling, c-kit+ RCSC were isolated from hearts of C57/Bl6-Tg (ACTb-EGFP)10sb/J mice expressing green fluorescent protein (GFP) and expanded in vitro. All cells were c-kit+Sca-1-CD45-CD31-CD34-tryptase- and 80% expressed Oct3/4 and Klf4 in the nucleus. c-kit+RCSC cultivated in the Ham's F-12 stem cell medium until the third passage spontaneously differentiated and expressed markers of main cardiac lineages, podocalyxin, CD31, von Willebrand factor, troponin T-C,  $\alpha$ -smooth muscle actin, DDR2 and SDF-1 receptor CXCR4. The most pronounced increase was observed for podocalyxin and von Willebrand factor (20 to 30-fold). Cultivation for 5 weeks in differentiation medium induced differentiation of c-kit+GFP+RCSC mainly towards a smooth muscle phenotype. C57/Bl6N wildtype mice were subjected to transverse aortic constriction (TAC, 360  $\mu$ m) or sham-operation. 5x10<sup>5</sup> c-kit+RCSC or c-kit- cardiac cells or cell buffer were infused intravenously 24h post surgery (n = 11-24 per group). The mRNA-expression level of Oct3/4 and hypoxia-inducible factor-1 $\alpha$  in the left ventricles (LV) of TAC mice was enhanced 24h after transplantation. 35 days post TAC, the density of GFP+ cells in the myocardium was increased by two-fold. Infusion of c-kit+RCSC post TAC markedly reduced myocardial fibrosis, the number of cardiac fibroblasts identified by immunostaining for intracellular fibronectin and DDR2 and the expression of collagen I $\alpha$ 2 and connective tissue growth factor. Infusion of c-kit- cardiac cells did not ameliorate cardiac fibrosis. In parallel, expression of pro-angiogenic mediators (FGFb, IL-4, IL-6, TGF $\beta$ , leptin) and the density of CD31+ and CD31+GFP+ endothelial cells were increased. Transplantation reduced brain- and atrial natriuretic peptides and the cardiomyocyte cross-sectional area. Infusion of c-kit+RCSC reduced rate of apoptosis and oxidative stress in cardiomyocytes and in non-cardiomyocyte cells. Transplantation of c-kit+RCSC increased the percentage of cycling Ki67+ cardiomyocytes in the SHAM group, the percentage of cycling Ki67+ non-cardiomyocytes in both experimental groups, the number of nestin+GFP- cardiomyocytes and the percentage of nestin+Ki67+ non-cardiomyocytes in pressure-overloaded LV.

**Conclusions:** Transplantation of c-kit+ resident cardiac stem cells ameliorates cardiac fibrosis in pressure overload in mice.

## P1807

**An in vivo selection strategy for the identification of novel cytokines inducing cardiac retention of murine mesenchymal stromal cells after myocardial infarction**

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**Purpose:** Numerous studies have shown that transplantation of mesenchymal stromal cells (MSCs) in the infarcted heart improves cardiac function through paracrine mechanisms. However, the injected cells are gradually lost at the site of injury, thus limiting the window of therapeutic efficacy. To identify novel factors able to improve engraftment and long-term survival of MSCs, we developed an innovative Functional Selection (FunSel) procedure aimed at the in vivo identification of effective molecules.

**Methods:** A collection of 80 murine cytokines cloned into AAV2 vectors was used for the batch transduction of MSCs ex vivo, followed by intracardiac administration of the cells in non-ischemic or ischemic conditions. Three weeks after injection, when most cells were normally lost, viral genomes were recovered from the few persisting cells and their relative abundance was analyzed by next generation sequencing. We expected that protective factors mediating cell retention would be enriched over the others. The identified cytokines were tested individually in tracking experiments in the myocardium and the efficacy of top hit was assessed in a model of myocardial infarction by echocardiography, histology and molecular analysis. The molecular mechanisms were investigated by immunofluorescence, apoptosis and adhesion assays.

**Results:** Among the in vivo selected cytokines, we found factor already associated with MSC homing and survival, such as Ccl2 and Ccl7. Unexpectedly, the most effective factor in mediating cardiac MSC retention was Cardiotrophin1 (Ctf1), a pro-hypertrophic cytokine never associated with this property before. We found that the effect of Ctf1 was the consequence of the induction of MSC survival through STAT3 activation and, most notably, the promotion of MSC adhesive properties by the dynamic activation of Focal Adhesion Kinase (FAK). In vivo, AAV2-Ctf1-transduced MSCs preserved cardiac function and reduced infarct size after myocardial infarction. These effects strictly correlated with the persistence of Ctf1-expressing cells in the healing hearts for at least two months and with the consequent prolonged release of soluble molecules by MSCs.

**Conclusions:** These results support the feasibility of the in vivo FunSel approach and identify Ctf1 as a powerful cytokine supporting MSC adhesion and retention in the ischemic myocardium, thus providing benefit after cardiac damage.

## P1808

**The H19 long non-coding RNA regulates pathological cardiac hypertrophy**

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**Objective:** It has been shown in the past that small regulatory RNAs, called microRNAs, are key players in the development of cardiovascular diseases. Notably, long-non coding RNAs are an emerging entity under investigation. Since heart failure is the most deadly, yet still not curatively treatable ailment, it makes sense to look for new means to tackle this issue. The H19 gene has been well described as an orchestrator of several genetic disorders and other maladies, for example gastric cancer. Nevertheless its function in the heart remains unidentified. Consequently, we investigate the role and functional implications of H19 in cardiac hypertrophy as a hallmark of heart failure.

**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 induces 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 rodents, pig and humans, we assessed its role in failing human hearts. In accordance with our findings in the mouse model, hypertrophic heart tissue from aortic stenosis patients demonstrates a strong downregulation of H19, suggesting an analogy in cardiac disease between different mammals.

**Conclusion:** In this report we identified the lncRNA H19 as a key player in cardiac hypertrophy. A decrease in H19 expression level in pressure-overloaded murine hearts and in hypertrophic human hearts is related to an increase in cardiomyocyte



cell size. To put it in a nutshell, H19 is a prospective therapeutic target in order to halt the genesis of heart failure.

### P1809

#### Safety and efficacy of transcatheter injection of induced-pluripotent stem cells-derived mesenchymal cells in a swine subacute model of myocardial ischemia.

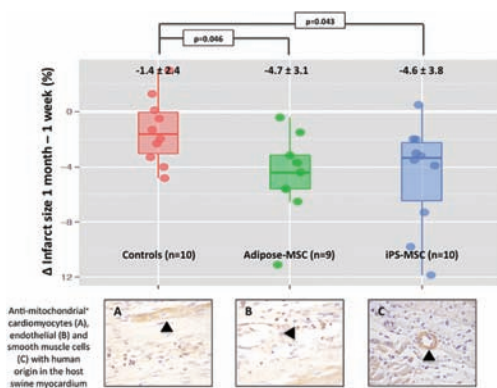
National Program for Internationalization of R&D (PLE2009-0147, Regenerative Therapies with Stem Cells for Heart Failure), Spanish Ministry of Economy R Ricardo Sanz Ruiz<sup>1</sup>; V Crisostomo Ayala<sup>2</sup>; A Casado Plasencia<sup>1</sup>; ME Fernandez Santos<sup>1</sup>; N Montserrat Pulido<sup>3</sup>; S Suarez Sancho<sup>1</sup>; AM Climent<sup>1</sup>; F Aienza Fernandez<sup>1</sup>; FM Sanchez Margallo<sup>2</sup>; F Fernandez-Aviles<sup>1</sup>  
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**Purpose** Mesenchymal stem cells (MSC) are the most promising cells for ischemic myocardial repair. Nowadays we can obtain them from induced pluripotent stem cells (iPS). Our objective is to compare the safety and efficacy of "conventional" MSC and iPS-derived MSC in a large animal model of myocardial ischemia.

**Methods:** Phase I/II preclinical randomized, placebo-controlled trial, with 30 large white pigs included. Acute myocardial infarction (AMI) was created after 90-min occlusion of the LAD. The 3 groups were: injection of 20x10<sup>6</sup> MSC from human adipose tissue (n=10); injection of 20x10<sup>6</sup> MSC from human iPS (n=10); injection of saline (n=10). Injections were performed in the scar border with the NOGA XP platform, 7 days after AMI. Safety endpoints include MACE, malignant arrhythmias and lab parameters (intraoperative and for 5 weeks). Efficacy endpoints include scar size and LV parameters (MRI) and myocardial repair by histology (fibrosis and capillary density, staining with human mitochondrial antibodies) at 5 weeks.

**Results:** Thirty pigs were included, weight 37.4 ± 6.2 kg. Troponin I values (mg/L) raised from 0.24 ± 0.35 to 0.32 ± 0.23 postinjection (p=0.02). Cell injection was successful in all cases, with 1 episode of ventricular fibrillation successfully cardioverted and 1 case of non-cardiac death (vascular complication). Both types of MSC reduced infarct size compared to controls to a similar extent (fig). Development of cardiomyocytic and vascular structures from human origin were identified in pathological studies (preliminary results, fig).

**Conclusions:** MSC NOGA-guided injections 7 days after AMI were safe. Cardiac repair potentiality was similar between adipose and iPS-derived MSC.



Scar size and pathological studies

### P1810

#### Safety and efficacy of first in-human use of muscle-derived stem cells transfected with connexin-43 gene for chronic heart failure

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**Background:** Patients with advanced heart failure (HF) have still poor prognosis despite number of available treatments, including implantable and assist devices. Therefore, the use of stem cells is still a promising approach to treatment of this clinical entity. Among various cell types, skeletal myoblasts (SkMb) were first studied. Although there were some encouraging results, significant amount of malignant

ventricular arrhythmias (VA) decreased the volume of clinical research involving those cells. However, the latest studies showed that overexpression of connexin-43 (Cx43) led to improvement of electromechanical coupling and engraftment of SkMb into the myocardium in animal models and in vitro human cardiomyocytes.

**Objectives:** To evaluate the safety and efficacy of transcatheter delivery of muscle-derived stem/progenitor cells (MDS/PC) with connexin-43 overexpression in patients with advanced HF.

**Methods:** Thirteen subjects with advanced HF, NYHA class II-III, with implanted cardioverter-defibrillator, ineligible/disagreeing to other interventions, including transplantation ("no option group") were enrolled. For safety and efficacy assessment patients were followed-up for at least 6 months (physical exam, cardiopulmonary exercise test, rhythm monitoring, ECHO/SPECT imaging, electroanatomical mapping [12/13 patients]).

**Results:** The mean total number of cultured MDS/PCs was 552.3 ± 282.6x10<sup>6</sup> and the mean number of injected Cx-43 MDS/PC was 161 ± 115x10<sup>6</sup> per patient. Cx43 overexpression (Cx43+) was significantly higher in all but one subject (Cx43-: due to transfection error).

**Efficacy analysis:** Injection of MDS/PC was associated with a significant improvement of exercise capacity: NYHA (3 ± 0 vs. 1.8 ± 0.7, p=0.003), exercise duration (388.69 ± 141.83 vs. 462.08 ± 176.69 s, p=0.025), peak oxygen consumption (14.38 ± 3.97 vs. 15.83 ± 3.74 ml/kg/min, p=0.022) and oxygen pulse (10.58 ± 2.89 vs. 18.88 ± 22.63, p=0.012). BNP levels, LV ejection fraction and end-diastolic volumes tended to improve, however no significant differences were documented. There was a significant decrease in scar size expressed by increase in mean total unipolar voltages (8.83 ± 2.80 vs. 10.22 ± 3.41 mV, p=0.041).

**Safety analysis:** No deaths were documented. Cx43+ patients (n=12) had no VA. Cx43-neg (n=1) subject suffered from recurrent VT (2xICD interventions 2 and 3 months of implantation, IV/PO. amiodarone, good effect).

**Conclusions:** Our pilot study demonstrated for the first time that injection of Cx-43+ MDS/PCs in patients with severe HF led to significant improvement of exercise capacity and myocardial viability while inducing no significant ventricular arrhythmia. It may be due to improved electrical coupling of the injected cells and injured myocardium and thus better in-situ mechanical cooperation of both cell types. Therefore, further clinical studies with Cx43+ MDS/PCs are warranted.

### P1811

#### A combined and surgical ventricular reconstruction therapeutic approach produces attenuation of remodeling in infarcted rats

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**Background:** Left ventricular reconstruction surgery (LVR) has been shown to provide transient improvement in LV function in infarcted hearts; however long-term results have been disappointing, as LVR-induced benefits are typically not sustained. We hypothesized that administration of cardiomyocyte-derived cells (CDCs), which have been shown to promote myocardial repair and regeneration of infarcted hearts, may result in long-term preservation of the beneficial effects of LVR in ischemic cardiomyopathy.

**Purpose:** To investigate the effects of a combined biological and surgical therapeutic approach comprising cell therapy with CDCs and LVR on LV remodeling in infarcted rats

**Methods:** In female Wistar Kyoto rats myocardial infarction (MI) was induced by permanent ligation of the left descending coronary artery after left thoracotomy. Two weeks later, after a second thoracotomy, animals were randomly allocated to 3 groups: in Group 1 (n=9) the infarcted apex was plicated and 3\*10<sup>6</sup> CDCs were injected in the border zone of the LV plication, while Group 2 animals (n=9) received vehicle solution in the border zone of the plication. Group 3 animals (n=10) received intramyocardial injections of vehicle solution in the infarct border zone, without plication of the apex. Echocardiograms (conventional and 2D speckle-tracking) were performed at baseline (prior to the second thoracotomy), 4 days post-apex plication, and 3 months post-MI. LV ejection fraction (EF), LV volumes, LV circumferential strain (CS) and peak systolic LV torsion were assessed.

**Results:** At baseline, all animal groups had comparable LVEF, LV end-diastolic volume (EDV) and LV end-systolic volume (ESV). Four days post-LV apex plication, Group 1 and Group 2 animals exhibited comparable significant improvement in EF and comparable significant reduction in LVEDV. Three months post-MI, Group 1 animals had decreased LVEDV (274 ± 9 uL vs 357 ± 29 uL vs 369 ± 19 uL, p=0.003, in Groups 1, 2 and 3 respectively, p < 0.003), decreased LVESV (149 ± 8 uL vs 216 ± 26 uL vs 232 ± 13 uL, p=0.002), less impaired CS (-14.2 ± 0.4% vs -10.9 ± 0.6% vs -10.9 ± 0.7%, p=0.001), increased peak systolic torsion (7.8 ± 0.6 °/cm vs 4.7 ± 0.7 °/cm vs 4.4 ± 0.8 °/cm, p=0.006) and increased EF (48 ± 4% vs 36 ± 4% vs 35 ± 3%, p=0.005) compared to animals in Groups 2 and 3.

**Conclusion:** In infarcted rat hearts, intramyocardial delivery of CDCs in conjunction with LVR resulted in significant and sustained amelioration of LV remodeling and improvement in global and regional LV function, compared to LVR alone.

**P1812****First evidence of cardiac stem cells from the left ventricular apical tip in patients undergone LVAD implant**

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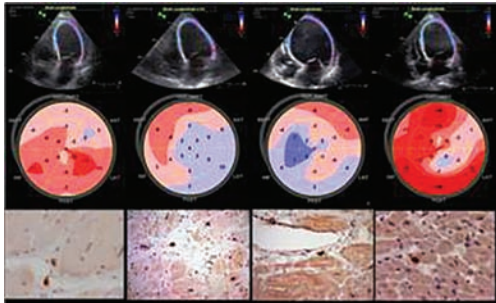
<sup>3</sup>Pathology Unit, Siena, Italy

**Background:** Recent studies have challenged the dogma that the adult heart is a postmitotic organ and raise the possibility of the existence of resident cardiac stem cells (CSCs). Our study aimed at exploring if the isolation of colonies of CSCs from "ventricular tip" obtained from patients with end-stage heart failure (HF) undergoing left ventricular assist device (LVAD) implantation was possible and how it correlated with LV dysfunctional area extent.

**Methods:** Four consecutive patients with ischemic cardiomyopathy and end-stage HF submitted to LVAD implantation were studied. The explanted "ventricular tip" was used as a sample of apical myocardial tissue for the pathological exam. Patients underwent clinical and echocardiographic examination, both standard transthoracic echocardiography (TTE) and speckle tracking echocardiography (STE) before LVAD implantation.

**Results:** All patients presented severe apical dysfunction, with apical akinesis/diskinesis and very low levels of apical longitudinal strain ( $-3.5 \pm 2.9\%$ ). Despite this, it was demonstrated the presence of CSCs in pathological myocardial samples of "ventricular tip" in all the 4 patients. It was found 6 c-kit cells in 10 fields magnification 40x.

**Conclusions:** Multipotent cells can be isolated in the LV apical segment of patients undergone LVAD implantation despite LV apical fibrosis.



Stem cells from LV apical tip

**P1813****Candesartan cilexetil and extract of Polygonum sp. influence on the number of stem cells in vitro**

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**Purpose:** To conduct analysis of the influence of candesartan cilexetil (angiotensin II type 1 receptor blocker) and extract of Polygonum sp. in different dosages on variations in the number of endothelial progenitor cells CD117+ in vitro.

**Methods:** Bone marrow cells of C57Bl/6 mice were sampled for further experiments. The cells were grown in flasks containing DMEM supplemented with 10% of fetal bovine serum with addition of 0.1 % antibiotics in CO<sub>2</sub>-incubator (5% CO<sub>2</sub>, 37°C). Candesartan cilexetil and extract of Polygonum sp. were supplied to the cell culture. Flow cytometric method was applied for the analysis.

**Results:** Nowadays cardiovascular diseases are one of the most widespread scourges in economically developed countries and the majority of the population all over the world suffers from these pathologies. Stem cell technologies are used for treatment of various diseases, including cardiovascular diseases. It is shown that mobilized stem cells and endothelial progenitor cells have the capacity to migrate into the heart muscle and endothelium with the subsequent positive therapeutic effect.

It was found during this study that candesartan cilexetil at 1.5 µg/ml dose and 3 µg/ml dose decreased the number of CD117+ stem cells in vitro in comparison with the control. Extract of Polygonum sp. at low doses (under 30 µg/ml) didn't cause statistically significant changes. High doses of Polygonum sp. extract (over 30 µg/ml) increased the amount of CD117+ stem cells in vitro ( $p < 0.05$ ).

Combination of candesartan cilexetil at 1.5 µg/ml dose and extract of Polygonum sp. at 10 µg/ml dose didn't raise the number of CD117+ cells in vitro in comparison with the control. Mixed application of candesartan cilexetil at 1.5 µg/ml dose and extract of Polygonum sp. at 30 µg/ml dose and 50 µg/ml dose increased the ratio of CD117+ stem cells ( $p < 0.05$ ). This substances didn't influence cell cycle and change the number of apoptotic cells.

**Conclusions:** It was found that candesartan cilexetil alone didn't increase the number of CD117+ stem cells in vitro, whereas the first evidence was recorded that concerted use of candesartan cilexetil and extract of Polygonum sp. in different dosages stimulated formation of examined stem cells. The obtained results may lay the basis for further studies aimed at elaboration of novel complex drug for treatment of cardiovascular diseases capable to mobilize endothelial progenitor cells.

**P1814****Epigenetically reprogrammed mesenchymal stem cells improve myocardial remodeling and cardiac function after myocardial infarction by modulating post-infarct inflammation and neoangiogenesis**

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**Background:** The efficacy of transplantation of default mesenchymal stem cells (MSCs) is controversial because of their limited plasticity and decreased function in elderly patients with myocardial infarction (MI). We investigated whether epigenetically reprogrammed-MSCs ameliorate myocardial remodeling in a mouse model of MI.

**Methods:** Bone marrow-derived MSCs were sequentially treated with 5 mM/L of valproic acid and 100 nM/L of 5-azacytidine for 24 hours, respectively. Quantitative RT-PCR was performed to evaluate the effect of epigenetic modifiers on the gene expression of MSCs. 2 x 10<sup>5</sup> default MSCs, 2 x 10<sup>5</sup> epigenetically reprogrammed-MSCs, or phosphate-buffered saline were injected into peri-infarct zone immediately after ligating proximal portion of left anterior descending artery. On days 28 after MI, in vivo cardiac magnetic resonance (CMR) and harvest of heart tissue was sequentially performed.

**Results:** Epigenetic modification of MSCs significantly induced gene expression of anti-inflammatory markers such as transforming growth factor- $\beta$ , indoleamine 2,3-dioxygenase. Basic fibroblast growth factor increased 1.6 fold and GATA4 increased 1.7 fold at the mRNA level. Transplantation of modified-MSCs showed improved ejection fraction on CMR. In histopathologic analysis, infarct size was significantly decreased in modified-MSCs transplanted mice ( $p = 0.002$ ). When assessing capillary density of peri-infarct zone, larger number of CD31+ staining vascular structures was observed in modified-MSCs transplanted mice. Immunofluorescence stain showed marked increase of CD4+CD25+Foxp3+ regulatory T cells as well as CD68+MR+ M2 macrophage and decrease of CD68+iNOS+ M1 macrophage in modified-MSCs transplanted mice.

**Conclusions:** Transplantation of epigenetically reprogrammed-MSCs significantly improves cardiac function by modulating post-infarct inflammation and neoangiogenesis in a preclinical model of AMI.

	Histopathology		Cardiac MR	
	H&E	Masson Trichrome	End-diastole	End-systole
Control				
Default MSCs				
Pretreated MSCs				

**P1815****Understanding the metabolism of cardiac progenitor cells: a first step towards controlling their proliferation and differentiation?**

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Cardiac regenerative approaches using progenitor cells (CPC) may be limited by their low survival and differentiation when injected at the border zone of an infarct. We investigated the bioenergetic transition underlying CPC differentiation in order to identify key metabolic regulators that could be modulated to promote their repair capacity.

Sca1+ CPC were isolated from adult mouse hearts by MACS separation. Under normoxic conditions, glucose consumption and lactate release were significantly higher in CPC than in neonatal rat cardiac myocytes (NRCM) with a ratio of 2 moles of lactate released per mole of glucose supporting a high glycolytic metabolism. Glucose consumption and lactate release were increased in hypoxia (1%O<sub>2</sub>), together with increased abundance of the monocarboxylic transporter MCT4 (lactate efflux mediator), of Glut-1 and of PFKFB3 (key regulator of glycolytic rate). BrdU incorporation in CPC was critically dependent on pyruvate, glucose and glutamine availability (but not lactate) under normoxia and hypoxia. Oxygen consumption analysis indicated that CPC and NRCM display active mitochondrial ATP production. Notably, basal and maximal respiration were higher in NRCM compared to CPC. Consistently, mitochondrial populations were differentially active in both cell types, as reflected by a 40% decrease in tetramethylrhodamine methyl ester staining intensity (flow cytometry) in CPC compared to NRCM. Moreover, the expression of TOM20 (translocase of outer mitochondrial membrane) was also 50% lower in CPC compared to NRCM and MitoTracker Green reveals by imaging small sphere-shaped mitochondria in CPC whereas they form a branched network in NRCM, reflecting differential dynamic organelles in both cell types. This CPC phenotype dramatically changed upon differentiation (azacytidine/TGFβ/ascorbic acid; 4 weeks in normoxia), with a reduction by third of glucose consumption and lactate release compared to proliferative cells. In conclusion, despite active mitochondrial ATP production, undifferentiated CPC exhibit lower respiratory reserve than CM, which correlates with a less mature mitochondrial network. However, they exhibit aerobic glycolysis and lactate production, which further increased under hypoxia together with (HIF-1α dependent) PFKFB3, Glut-1 and MCT4. Such glycolytic activity, together with glutamine metabolism supports their proliferation but is dramatically downregulated upon differentiation. This may open the way for pharmacological modulation of the survival/differentiation of CPC for cell therapeutic repair through their mitochondrial fusion and biogenesis.

#### P1816

##### Enhancement of the paracrine potential of human adipose derived stem cells when cultured as spheroid bodies

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**Background:** Ischemic heart disease remains a leading cause of mortality and morbidity worldwide. Cardiac cell therapy (CCT) is a promising therapeutic strategy to help in cardiac repair. Adipose tissue constitutes an important reservoir for the stem cells. Both preclinical and clinical data have shown that adipose derived stem cells (ASCs) could improve cardiac function and volumes, mostly through a paracrine mechanism.

**Study Aim:** The objective of our in vitro study is to characterize and compare the secretion profile of ASCs, when cultured under standard conditions (i.e. as a monolayer (ML)) versus in a three-dimension (3-D) structure (i.e. as a spheroid body (SB)).

**Methods:** Human ASCs (hASCs) were expanded in standard culture conditions in a monolayer form. ASCs were characterized according to both surface markers expression (assessed by immunofluorescence) and their ability to maintain multi-lineage differentiation. Alternatively, ASCs were also cultured as 3-D structure as spheroid bodies (SBs), by using the hanging drop technique. Luminex and ELISA assays were conducted to quantify key anti-inflammatory and angiogenic mediators to compare the two study groups.

**Results:** hASCs expressed similar surface markers as those documented for bone marrow MSCs including CD44, CD105 and CD90. Their ability to differentiate into adipogenic, chondrogenic and osteogenic lineage were unaltered. Paracrine activity of hASCs was enhanced when cultured as hASC-SBs. SBs secreted higher levels of anti-inflammatory cytokines such as MCP-1, IL-6 and IL-10, in a time dependent manner (Figure). Similarly, hASC-SBs exhibited greater pro-angiogenic potential as VEGF levels were increased also compared to hASC-MLs.

**Conclusion:** hASC represent a promising cell source for CCT and cardiac repair. Their paracrine, therapeutic potential can be optimized. Our findings clearly showed that hASCs cultured as 3D structures (i.e. as SBs) exhibit an improvement in both anti-inflammatory and angiogenic properties. Spheroid body formation thus represents an effective alternative to enhance the therapeutic potential of hASCs.

#### P1817

##### Bone marrow cell transplantation in acute myocardial infarction and left ventricular dysfunction: lack of long term beneficial effects

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**Purpose:** Bone marrow progenitor cells may improve cardiac function and outcome in patients after acute myocardial infarction (AMI). In a single-centre randomised controlled trial we observed a beneficial effect of intracoronary transfer of autologous bone-marrow cells on global left ventricular (LV) function, autonomic control, and exercise tolerance at 12 months' follow-up. In a mean 37 ± 5 month follow-up we aimed to assess the persistence of the beneficial effect on cardiac parameters

(Echocardiography) Methods- After successful percutaneous coronary intervention (PCI) for acute ST-segment elevation myocardial infarction and residual LV dysfunction, 41 patients were randomly assigned to either a control group (CTR, n = 20, on optimum postinfarction treatment) or a bone-marrow-cell group (BMC, n = 21, optimum treatment plus intracoronary transfer of autologous bone-marrow cells 5 ± 1 days after successful PCI). Test analyses were done by two investigators blinded for treatment assignment. Results- No differences in clinical characteristics or therapy between the two groups. Global LVEF at baseline (determined 4 ± 1 days after PCI) was 38.4 ± 1.5 in BMC, and 38.9 ± 1.4 in the CTR group (P=NS). After 12 months, mean global LVEF increased by 14.4 ± 3.8 % in the BMC group vs. 6.8 ± 3.4 % in the CTR group (P0.05) with an anti-remodeling effect in the former: LVEDV was -14.3 ± 1.5 % in BMC vs. 3.9 ± 3.5 % in CTR, while LVESV was -14.7 ± 5.9 % in BMC vs. 4.0 ± 4.2 % in CTR (P < 0.05). After an average 37 ± 5 month follow-up, no significant difference between the two groups in any of the evaluated parameters including LVEF (+2.0 ± 9.4% vs. +5.0 ± 10.2%, p = NS), LVESV (+2.6 ± 33.9 ml vs. +4.0 ± 55.8 ml, p = NS) and LVEDV (+2.6 ± 52.6 ml vs. 20.2 ± 58.9 ml, p = NS). Furthermore, no differences were observed in any relevant clinical parameters such as adverse clinical events, in-stent stenosis or pro-arrhythmic events between treated and control groups.

**Conclusions:** A potential beneficial effect of intracoronary transfer of autologous bone-marrow-cells on haemodynamic indices in post AMI patients with depressed left ventricular function present on the short but not long term analysis is consistent with other larger studies where intra- coronary application of BMCs did not promote a sustained improvement of LV

## BASIC SCIENCE: ISCHEMIA / REPERFUSION / PRECONDITIONING / POSTCONDITIONING

#### P1818

##### Comparative assessment of left ventricular remodeling in patients after coronary artery bypass grafting, depending on the method of operation

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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. Methods of research. 105 patients suffering from ischemic heart disease (IHD) were examined (45 women and 60 men), aged from 39 to 76 years, who have two (5 people), three (30 people) and more than four (70 people) coronary arteries (CA) damaged. Hemodynamically significant artery stenosis were diagnosed at all patients, at that 95 patients had vascular occlusion of different localization, 10 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 (5 people), three (55 people) and more than four (45 people) shunts. In the 1-st group of patients (70 people) CABG was done in the conditions of cardiopulmonary bypass (CPB) and pharmaco-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 times, 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.

#### P1819

##### Pre-hospital delay in patients with ST-elevation-myocardial infarction: clinical characteristics and outcomes

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**Introduction:** Pre-hospital delay results in impaired outcome after ST-Elevation-Myocardial Infarction (STEMI). The time between the onset of pain to first medical contact (FMC) depends on the recognition of symptoms by the patient and the celerity to seek medical help.



**Purpose:** Identify the factors associated with late diagnosis of STEMI.

**Methods:** Pain-to-FMC and long-term outcomes were documented in 534 individuals presenting with STEMI from 2010 to 2014. The baseline parameters of patients with pain-to-FMC $\leq$ 60 minutes ("early presenters" (EP)) were compared to patients with pain-to-FMC $>$ 60 minutes ("late presenters" (LP)). Groups were also compared regarding mortality rate and a primary composite endpoint (re-MI, stroke, and cardiovascular mortality) at one year follow-up.

**Results:** Late presenters were older (EP=59.89  $\pm$  1.33 vs LP=63.98  $\pm$  0.66 years;  $p < 0.05$ ), had a higher prevalence of arterial hypertension (EP=48% vs. LP=56.4%,  $p < 0.05$ ) and Diabetes Mellitus (EP=13.3% vs. LP=25.9%,  $p < 0.01$ ) in the univariate analysis. No differences were found regarding prior dyslipidemia, angina, acute myocardial infarction, peripheral artery disease or family history. EP were more submitted to primary percutaneous coronary intervention (EP=92.7% vs LP = 77.9%,  $p < 0.01$ ).

LP had more Killip Class $>$ 1 at admission (EP=9.6% vs LP=22.0%,  $p < 0.01$ ) and at 72h (EP=20.2% vs LP = 31.5%,  $p < 0.02$ ) and higher levels of BNP (EP=373.6  $\pm$  69.5 vs LP=559.9  $\pm$  38.5,  $p < 0.01$ ). They were more medicated with loop diuretics (EP=23.5% vs LP = 32.6%,  $p < 0.05$ ) and aldosterone receptor antagonists (EP=5.1% vs LP=12.6%  $p < 0.05$ ).

At 1-year follow-up there were no significant statistical differences regarding mortality (EP=8.3% vs LP=14.5,  $p = 0.098$ ) and primary composite endpoint (EP = 11.5% vs LP = 17.7%,  $p = 0.121$ ).

After multivariable adjustment, Diabetes Mellitus (OR 2.221; CI 1.277–3.861) was independently associated with delayed FMC.

**Conclusion:** In this real world cohort, Diabetes Mellitus was associated with later diagnostic of ST-Elevation-Myocardial Infarction. Patients presenting to first medical contact after 60 minutes of pain onset showed a trend towards higher mortality. Special attention should be paid to avoid diagnostic delays in these patients.

#### P1820

##### The association between percutaneous coronary intervention and abdominal or thoracic drainage of congestive heart failure with reduced ejection fraction patients

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**Background/Introduction:** The correlation between percutaneous coronary intervention (PCI) and abdominal ascites or pleural effusion drainage of heart failure with reduced ejection fraction (HFrEF) patients, is not well studied.

**Purpose:** We aimed to identify the association between PCI and abdominal ascites or thoracic drainage incidence of HFrEF patients enrolled in a Middle Eastern single centre heart failure registry.

**Methods:** We performed subgroup analysis of prospectively collected data of 174 consecutive HFrEF patients hospitalized over 12-month period.

**Results:** Ultrasound guided drainage was performed more frequently in ischemic compared to non-ischemic cardiomyopathy patients (8% vs. 0.9%;  $P = 0.024$ ). Among the 23 (13%) PCI patients, there was no need for abdominal or thoracic drainage, compared to 151 (67%) non-PCI patients ( $P = < 0.0001$ ). Females had higher statistically insignificant drainage incidence compared to males (10% vs. 4%;  $P = 0.261$ ).

**Conclusion:** PCI is associated with significant reduction of drainage requirement of HFrEF patients. Ischemic cardiomyopathy, female gender and non-PCI feasible subgroups were at high risk for abdominal or thoracic drainage requirement.

Subgroup characteristics				
Gender characteristics	Males (n = 135)	Females (n = 39)	P value	CI
Age	58.1 (13.50)	64.8 (9.04)	< 0.001	(-10.40, -3.03)
EF	23 (9.15)	28.2 (12.85)	0.023	(-9.61, -0.75)
Drainage procedure (n = 10)	4% (n = 6)	10% (n = 4)	0.261	(-0.15, 0.043)
Ischemic etiology				
Age	54.8 (14.9)	62.6 (10.5)	0.01	(-11.97, -3.70)
EF	21.5 (9.93)	25.9 (10.2)	0.006	(-7.42, -1.24)
Drainage procedure (n = 10)	0.9% (n = 1)	8% (n = 9)	0.024	(-0.12, -0.009)
PCI				
Age	59.3 (13.3)	61.7 (9.71)	0.292	(-7.11, 2.20)
EF	23.4 (10.3)	29.2 (9.11)	0.008	(-10.08, -1.62)
Drainage procedure (n = 10)	6.60%	0%	0.001	(0.026, 0.105)

EF, ejection fraction; PCI, percutaneous coronary intervention. Data are mean (SD) unless noted otherwise.

#### P1821

##### The influence of remodeling of left ventricle on results of surgical treatment of ischemic heart disease

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**Aim:** 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 105 patients (45 women and 60 men) with coronary artery disease from 39 to 76 years, with obstruction of two (5 patients), three (25 patients), more than four (75 patients) coronary arteries (CA). All patients had hemodynamically significant CA obstruction; 77 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 (5 patients), three (25 patients) and more than 4 grafts (75 patients). We performed a 4 months observation of 105 patients with (CAD) who underwent (CABG). Patients were divided into two groups: group 1 included 45 people with CAD without a history (MI) and the 2-nd group consisted of 60 patients with postinfarction cardiosclerosis (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, leded 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.

#### P1822

##### Serum uric acid levels and heart failure in acute myocardial infarction

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**Background:** Serum uric acid (SUA) levels are associated with poor outcomes in patients with stable and unstable coronary heart disease.

**Purpose:** We investigated the relationship between SUA and heart failure (HF) in subjects with acute myocardial infarction (AMI) and the impact of hyperuricemia on prognosis of AMI patients.

**Methods:** A total of 184 patients (aged 63.7  $\pm$  12.4 years, 64.1% men) diagnosed with AMI (56.5% with ST elevation AMI (STEMI) and 43.5% with non ST elevation AMI (NSTEMI)) were evaluated. Uric acid levels were assessed at the admission and all patients have undergone coronary arteriography. The composite of major adverse cardiac events (MACE) including cardiovascular death, HF, revascularization (percutaneous coronary intervention or CABG), new AMI, stroke or transient ischemic attack has been evaluated for a 30 days and 6 months follow up period.

**Results:** There were 27.2% AMI patients with acute HF. Average value of ejection fraction of LV was 41.7  $\pm$  9.3%. Average value of SUA in STEMI was 348.33  $\pm$  101.5 mmol/l and 377.5  $\pm$  116.5 mmol/l in NSTEMI. There was significant difference between SUA levels regarding HF presence ( $p = 0.041$ ), and negative correlation between LVEF and SUA (Pearson -0.205,  $p = 0.05$ ). Hyperuricemia in AMI patients was related to extent of coronary artery disease in the means of number of coronary arteries with significant lesions detected ( $p = 0.034$ ). SUA level was independent predictor of 6 months MACE, including HF occurrence, in AMI patients (OR 4.766, CI 95% 0.988-0.999,  $p = 0.029$ ), predominantly in STEMI patients (OR 4.962, CI 95% 0.976-0.999,  $p = 0.026$ ).

**Conclusion:** Elevated SUA is associated with HF in AMI and has prognostic impact on outcome. This low-cost routinely available biomarker, could improve risk stratification of patients with AMI, especially in patients with STEMI.

#### P1823

##### Favorable effect of remote ischemic preconditioning on postischemic-reperfusion function of the myocardium

VEGA 2/0133/15, 2/0201/15; APVV-0102-11

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**Background:** Remote ischemic preconditioning (RIP) represent a suitable model for investigation of adaptive mechanisms leading to reduction of extent of ischemia-reperfusion injury in the myocardium. RIP represented the impulse, which was not induced directly in rat myocardium, but in distant place by short-term occlusion of the artery supplying the lower limb.

**Purpose:** We studied the role of mitochondria in mechanisms of increasing ischemic tolerance by RIP induction.

**Methods:** The protocol of RIP consisted of 3 cycles of 5 minute ischemia and 5 minute reperfusion. Subsequently, the hearts were perfused in the Langendorff mode. Heart mitochondria were isolated and forwarded to biochemical and biophysical investigation performed after 15 minute stabilised perfusion, 30 minute global ischemia and 40 minute post-ischemic reperfusion. Levels of interleukin 10 (IL-10) were determined using the elisa kit (RAT IL-10 Platinum ELISA). Fluidity of mitochondrial membrane were assessed by estimating fluorescence anisotropy of 1,6-diphenyl-1,3,5-hexatriene (DPH). Content of oxidised isoforms of coenzyme Q (CoQ9ox a CoQ10ox) was measured in isolated mitochondria by HPLC method.

**Results:** We noticed the significant ( $p < 0.05$ ) decrease in anisotropy reflecting the increase in mitochondrial membrane fluidity of RIP group in comparison with the control group after reperfusion. The nonsignificant increase in oxidised isoforms of coenzyme Q (CoQ9ox, CoQ10ox) during stabilisation induced by RIP reflects the moderate increase of free radicals having just a signal character and initiates the protective mechanisms. Downward trend of the coenzyme Q concentrations (CoQ9ox, CoQ10ox) in RIP group after ischemic-reperfusion injury confirmed the positive role of RIP to huge formation of free radicals. In RIP group after ischemic-reperfusion load, the content of oxidized isoforms CoQ9ox was nonsignificantly reduced by 5.62% compared to control group after reperfusion phase of myocardium.

**Conclusions:** The observed trend of increased concentration of IL-10 after IR injury in the group subjected RIP suggests the involvement of inflammatory processes in the mechanisms of endogenous myocardial protection. RIP induced endogenous protective mechanisms by increasing the membrane fluidity, thereby improved the energy demand during ischemia. The process of short-term adaptation, such as the RIP induced positive signal is sufficient enough to start the process of myocardial protection against ischemia-reperfusion injury.

#### P1824

##### Glutathione as possible mediator of the paradoxical synergy between inhibition and stimulation of H<sub>2</sub>S synthesis in terms of cardioprotection

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Glutathione is an essential molecule for antioxidant defense. It is synthesized by glutamate-cysteine ligase enzyme (GCL) from L-cysteine which alternatively might be used for production of hydrogen sulfide (H<sub>2</sub>S) by cystathionine-gamma-lyase (CSE). In this work we used CSE and GCL inhibitors (D,L-propargylglycine (PAG) and D,L-buthionine-(S,R)-sulfoximine (BSO) correspondingly) in order to modulate the metabolic pathways of L-cysteine in cardiac ischemia/reperfusion model.

Wistar rats were divided into five groups of 6-8 animals each (control, PAG (11.3 mg/kg), L-cysteine (121 mg/kg), PAG+L-cysteine, BSO(22.2 mg/kg)+PAG+L-cysteine). The aorta was cannulated, and then the heart was mounted on a Langendorff apparatus. Next, a balloon was inserted into the left ventricle and the left ventricular developed pressure (LVDP), the first derivative (dp/dt) were registered by Global Lab software. Coronary flow (CF), heart rate and oxygen cost of myocardial work (OCMW) in pre-ischemia and reperfusion period were calculated. All groups underwent a 20-minute global ischemia followed by a 40-minute reperfusion. Mitochondrial membrane permeability in situ was evaluated by UV-spectra absorbance of effluent probes collected from the pulmonary catheter during first minute of reperfusion and tested at 230-260 nm. The heart tissue was examined for superoxide radical, hydroxyl radical, and diene conjugates content by spectrophotometrical method.

PAG as well as L-cysteine slightly improved heart function recovery during reperfusion. Simultaneous application of both, PAG+L-cysteine, manifested in strong cardioprotective effect in terms of 95% recovery of the LVDP and the dp/dt throughout the whole period of reperfusion. PAG+L-cysteine significantly decreased reactive oxygen species production and diene conjugates due to I/R, thus, preventing oxidative stress and non-effective oxygen utilization by ischemized myocardium. The OCMW was increased only by 34% at 10th min of reperfusion in PAG+L-cysteine group. In control group, the OCMW was increased by 139% ( $p < 0.05$ ). Notably, there was no ischemic contracture in PAG+L-cysteine group comparing to 45 mmHg in control hearts. In addition, coronary effluents demonstrated lower UV-absorbance spectra than in control indicating lesser damaging effect of I/R on cardiomyocytes membranes. Pre-treatment of rats with BSO completely abolished cardioprotective effect of PAG+L-cysteine suggesting the role of glutathione as a main trigger in PAG+L-cysteine induced cardioprotection. Thus, PAG and L-cysteine might be promising as the cardioprotective combination for endogenous glutathione stimulation.

## MODERATED POSTER SESSION 6 – COMORBIDITIES

Tuesday 24 May 2016 10:00–11:00

Location: Poster Area

1843

### 3-month survival of the improvement of functional capacity after in-hospital short courses of leg neuromuscular electric stimulation in patients with decompensated chronic heart failure

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**Background:** In stable chronic heart failure (CHF) long-term neuromuscular electric stimulation (NMES) of leg muscles is beneficial for aerobic capacity and muscle force.

**Aim of the study:** To evaluate the impact of short-term NMES on functional capacity, well-being and quality of life in patients hospitalized with decompensated CHF and the survival of the effect after discharge in the randomized sham-controlled trial.

**Methods:** 45 patients with decompensated CHF (58,2% male, mean age 66,4 ± 10,2 years) were randomized for NMES (n = 22) or sham NMES (n = 23) starting from the 2-3d day after admission to the hospital in addition to standard medical treatment. Anterior and posterior thigh and calf muscles were stimulated simultaneously, using symmetric biphasic rectangular electric impulses with pulse duration = 1 ± 0,5 ms, current frequency = 25 ± 1 Hz and the duty cycle 1 ± 0,1 s - on and 2 ± 0,1 s - off. In the group of effective NMES the amplitude of stimulation was adjusted up to maximally tolerated muscle contraction, in the group of sham stimulation the amplitude was minimal and caused only skin sensation. Mean session time in two groups was 58,7 ± 18,6 and 54,54 ± 10,4 min (=0,003), number of sessions - 8,8 ± 2,9 in effective and 8,0 ± 2,0 in the sham group (ns). General well-being by visual-analogue scale (VAS), 6-minute walk test (6-mwt), Duke Activity Status Index (DASI) and Minnesota Living with Heart Failure Questionnaire (MLHFQ) were assessed at baseline, at discharge from the hospital, after 1 and 3 months after discharge.

**Results:** At discharge MLHFQ score improved from 55,6 ± 8,5 to 34,2 ± 9,0 (p < 0,05) in effective NMES and from 56,5 ± 7,1 to 48,7 ± 8,1 (p < 0,05) in the sham group, DASI from 12,1 ± 5,6 to 18,3 ± 7,2 (p=0,017) and from 11,6 ± 3,8 to 13,4 ± 4,3 (ns), 6mwt from 206,1 ± 61,3 to 299,5 ± 91,1 m (p=0,005) and from 211,4 ± 51,6 to 236,8 ± 54,7 m (p = 0.056) respectively. All measures at discharge were significantly better in the effective NMES group than in the sham group. Well-being improved equally in both groups: from 3,0 ± 0,6 to 7,0 ± 0,8 in effective NMES and from 3,4 ± 0,8 to 7,0 ± 0,7 points in the sham group. 3 months after discharge there were no changes of MLHFQ (37,8 ± 5,8 in NMES vs 47,6 ± 6,4 in sham, p < 0,05) and 6mwt (282,1 ± 83,2 vs 220,4 ± 46,1 m, p < 0,05), DASI further improved (21,0 ± 7,8 vs 15,4 ± 3,9, p=0,01), and VAS improved only in NMES group (8,1 ± 1,0 vs 6,3 ± 1,1, < 0,05).

**Conclusion:** In patients hospitalized with decompensated CHF short-term leg neuromuscular electric stimulation in addition to usual treatment improves exercise capacity, activity and quality of life. The effect survives at least 3 months and facilitates further increase of daily activity after discharge. NMES can be used as initial rehabilitation modality for patients unable to exercise.

1844

### Prognostic value of right ventricular systolic function in cardiac amyloidosis AREMCAR

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**Background:** Right ventricular (RV) dysfunction is a strong predictor of poor outcomes in heart failure. Its prognosis meaning in cardiac amyloidosis (CA) is unclear.

**Purpose:** To assess RV structure and function in CA using standard echocardiography, strain imaging, MRI, and pathological studies; to evaluate the prognostic value of RV parameters, as well as of left ventricular (LV), clinical and biological parameters.

**Methods:** 129 patients with suspected CA and an interventricular septum thickness (IVST) >= 12 mm underwent echocardiography with measurement of LV and RV longitudinal strain (LS), late gadolinium enhancement (LGE) cardiac MRI, and standard evaluation.

**Results:** Among 82 confirmed CA, types were immunoglobulin light chain (AL, n = 26), hereditary transthyretin (m-TTR, n = 37) and senile (WT-TTR, n = 19). Compared to those without, CA patients had significantly lower RV fractional shortening (RV-FS), tricuspid annular plane systolic excursion (TAPSE), tissue Doppler systolic velocity, and global RV-LS, without difference between CA types. RV-LGE, observed in 62% of CA patients, was associated with lower global and basal RV-FS. Median follow-up was 8(2;16) months. Using multivariate analysis, NYHA-class and low TAPSE independently predicted major adverse cardiac events defined as death, heart transplantation, and acute heart failure. Independent determinants of TAPSE < 14 mm, the best identified cut-off value, were LV ejection fraction, estimated filling pressure (E/e'), and pulmonary artery pressure, but not RV-LGE.

**Conclusions:** RV dysfunction is common in CA, and might be linked to LV involvement rather than RV amyloid burden. Its routine evaluation by a simple TAPSE may be an aid in assessing the prognosis of CA patients.

1845

### Estimated glomerular filtration rate formulas and acute heart failure: does it worth to complicate?

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**Purpose:** Chronic kidney disease has an undisputable prognostic influence in acute decompensated heart failure (ADHF) patients. Classically, glomerular filtration rate (GFR) is estimated with the Modification of Diet in Renal Disease (MDRD) formula. Three new glomerular filtration rate (GFR) estimating equations recently emerged, based on serum creatinine (CKD-EPI Cr), serum cystatin C (CKD-EPI Cyst) or a combination of both (CKD-EPI Cr/Cyst). These formulas are validated in kidney disease screening, however, the clinical impact in ADHF is unknown. Our aim was to evaluate the prognostic value of these new estimated GFR (eGFR) formulas and to compare its discriminatory capacity regarding mortality after an episode of ADHF.

**Methods:** Observational and longitudinal study of 112 consecutive patients (69 ± 14 years old, 79% male gender) with ADHF, admitted along 5 years. Serum creatinine and cystatin C were evaluated at admission and a clinical follow-up of 13 ± 13 months was performed targeting all cause mortality. The variables with independent predictive value for mortality in our sample were determined through a logistic binary regression (stepwise).

**Results:** The mean eGFR according to the different formulas were: MDRD: 57 ± 32, CKD-EPI Cr: 53 ± 28, CKD-EPI Cyst: 51 ± 30, CKD-EPI Cr/Cyst: 51 ± 27 ml/min/m<sup>2</sup>; and the percentage of patients with a eGFR < 30 ml/min/m<sup>2</sup> according to the 4 formulas were: MDRD - 22%, CKD-EPI Cr - 27%, CKD-EPI Cyst - 33% e CKD-EPI Cr/Cyst - 27%. Mortality during follow-up after an episode of ADHF was 38%. All formulas were significantly associated with mortality during follow-up (MDRD: area under the curve [AUC] 0.61, P = 0.046; CKD-EPI Cr: AUC 0.62, P = 0.03; CKD-EPI Cyst: AUC 0.65, P < 0.01; CKD-EPI Cr/Cyst: AUC 0.66; P < 0.01). There was no difference in the discriminatory power of the four formulas to predict, in an isolate way, mortality during follow-up (P > 0.05 for the comparison of the AUC). The age plus serum levels of sodium and alkaline phosphatases were considered independent predictors of mortality, with a good calibration and discriminatory capacity (AUC 0.80, P < 0.01, Hosmer-Lemeshow 0.72). The introduction of the above mentioned



formulas to the previous model, did not significantly improve the accuracy of the model (figure 1).

**Conclusion:** The four eGFR formulas had the same accuracy to predict mortality after an admission for ADHF, either on an individual basis or when adjusted for other variables. Thereby, in ADHF clinical setting the new eGFR did not add an additional clinical or prognostic value.

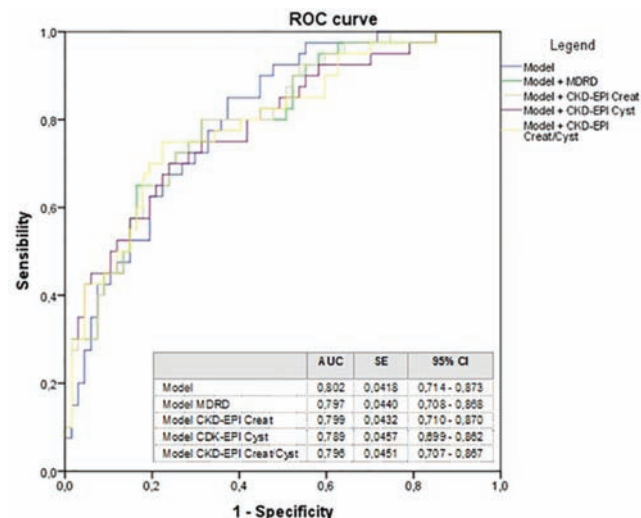


Figure 1

#### 1846

##### Ergoreflex overactivity in mitochondrial disease: linking skeletal myopathy to exercise intolerance, dysautonomia, and cardiac damage

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**Background:** Mitochondrial disease (MD) is a neuromuscular disorder. MD patients often complain of exercise limitation because of dyspnoea and muscle fatigue; autonomic imbalance with sympathetic predominance is a recurrent finding in these patients.

**Purpose:** We aimed to clarify the mechanisms through which muscle depletion leads to intolerance to effort and dysautonomia in MD.

**Methods:** Twenty-five adult patients with MD and previously demonstrated skeletal myopathy, aged 48 ± 3 years, underwent a cardiorespiratory screening composed of cardiac magnetic resonance (CMR), cardiopulmonary exercise testing (CPET), Holter monitoring, norepinephrine (NE) dosage, ergoreflex and baroreflex assessment. Thirteen patients were matched with respect to age and sex to healthy, sedentary controls.

**Results:** Two patients had cardiac hypertrophy, and eight had myocardial fibrosis. At CPET, maximal workload and peak oxygen consumption/kg were significantly lower in patients than controls (both  $P < 0.001$ ). The ergoreflex is a neural mechanism regulating ventilation and autonomic function during muscle activation. Its sensitivity, measured through post-exercise circulatory occlusion, is increased in chronic heart failure-related skeletal myopathy, promoting dyspnoea and muscle fatigue on exertion. In our MD patients ergoreflex sensitivity was markedly higher than controls ( $P < 0.001$ ). It correlated with the fat-to-water ratio at proton muscle spectroscopy (Spearman's  $Rho = 0.779$ ,  $P = 0.042$ ), suggesting a link between muscle damage and ergoreflex overactivity. Ergoreflex sensitivity displayed an inverse correlation with peak workload ( $Rho = 0.711$ ,  $P < 0.001$ ) and peak oxygen consumption/kg ( $Rho = 0.648$ ,  $P < 0.001$ ); increased ergoreflex sensitivity might then contribute to reduced exercise tolerance. Ergoreflex overactivity could also account for adrenergic activation and vagal withdrawal, demonstrated by lower baroreflex sensitivity and higher NE levels (both  $P < 0.001$ ), and reduced heart rate variability. Indeed, ergoreflex sensitivity correlated directly with NE ( $Rho = 0.322$ ,  $P = 0.020$ ), and inversely with the standard deviation of RR intervals ( $Rho = 0.530$ ,  $P = 0.013$ ). At univariate analysis, NE levels were the only predictors of myocardial fibrosis at CMR. NE levels were higher in patients with fibrosis than those without ( $P = 0.034$ ); a 692 ng/L cut-off was selected (area under the curve 0.800, sensitivity 90%, specificity 75%).

**Conclusion:** In MD, skeletal myopathy can increase ergoreflex sensitivity, causing exercise intolerance and sympatho-vagal imbalance. Sustained sympathetic overactivity may contribute to cardiac damage.

#### 1847

##### Efficacy and safety of dipeptidyl peptidase 4 inhibitors in patients with type 2 diabetes mellitus: a meta-analysis of 116 trials

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**Background:** Dipeptidyl Peptidase 4 Inhibitors (DPP4-I) are widely used to improve glycemic control in type 2 diabetes mellitus (DM) patients. However, although cardiovascular (CV) outcome studies conducted to assess the safety of these drugs demonstrated no effects on major CV events and mortality, concerns were raised on the association between DPP4-I use and increased incidence of heart failure (HF) hospitalization reported in one phase III trial.

**Purpose:** To evaluate the effects of DPP4-I on HF hospitalization, major CV events and mortality in type 2 DM patients by a meta-analysis.

**Methods:** Randomized trials enrolling more than 200 patients, comparing DPP4-I versus placebo or active treatments in patients with DM and reporting at least one event among all-cause and CV mortality, stroke, myocardial infarction (MI) and HF hospitalization, were searched. Meta-analysis was performed to assess the influence of treatment on pre-specified end points. The assumption of homogeneity between the treatment effects in different trials was tested by Q statistic and further quantified by I<sup>2</sup> statistic.

**Results:** 116 randomized clinical trials enrolling 108,405 patients (60,077 on DPP4-I and 48,328 on control/placebo), with a follow-up ranging from 4 to 209 weeks, were included in the analysis. Compared to control, treatment with DPP4-I did not affect all-cause (RR: 1.011; 95% CI 0.936 to 1.092;  $p = 0.784$ ;  $pQ = 0.995$ ;  $i^2 = 0\%$ ) and CV (RR: 0.975; 95% CI: 0.887 to 1.072;  $p = 0.603$ ;  $pQ = 0.979$ ;  $i^2 = 0\%$ ) mortality, as well as risk of MI (RR: 0.919; 95% CI: 0.839 to 1.007;  $p = 0.070$ ;  $pQ = 0.968$ ;  $i^2 = 0\%$ ), stroke (RR: 0.935; 95% CI: 0.821 to 1.064;  $p = 0.307$ ;  $pQ = 0.994$ ;  $i^2 = 0\%$ ) and HF (RR: 1.84; 95% CI: 0.975 to 1.207;  $p = 0.137$ ;  $pQ = 0.956$ ;  $i^2 = 0\%$ ). Analyses were then repeated according the different control arm used (placebo or active treatments). Compared to active treatments, DPP4-I significantly reduced the risk of MI (RR: 0.524; 95% CI: 0.356 to 0.771;  $p = 0.001$ ;  $pQ = 0.962$ ;  $i^2 = 0\%$ ) and stroke (RR: 0.604; 95% CI: 0.382 to 0.954;  $p = 0.031$ ;  $pQ = 0.905$ ;  $i^2 = 0\%$ ), without any effect on all-cause (RR: 0.761; 95% CI: 0.517 to 1.121;  $p = 0.166$ ;  $pQ = 0.964$ ;  $i^2 = 0\%$ ) and CV (RR: 0.669; 95% CI: 0.363 to 1.233;  $p = 0.197$ ;  $pQ = 0.921$ ;  $i^2 = 0\%$ ) mortality and risk of HF (RR: 0.665; 95% CI: 0.394 to 1.123;  $p = 0.127$ ;  $pQ = 0.747$ ;  $i^2 = 0\%$ ). Compared to placebo, DPP4-I did not affect all-cause (RR: 1.027; 95% CI: 0.949 to 1.111;  $p = 0.511$ ;  $pQ = 0.975$ ;  $i^2 = 0\%$ ) and CV (RR: 0.989; 95% CI: 0.898 to 1.090;  $p = 0.828$ ;  $pQ = 0.955$ ;  $i^2 = 0\%$ ) mortality, as well as the risk of MI (RR: 0.954; 95% CI: 0.868 to 1.049;  $p = 0.334$ ;  $pQ = 0.956$ ;  $i^2 = 0\%$ ), stroke (RR: 0.977; 95% CI: 0.851 to 1.121;  $p = 0.739$ ;  $pQ = 0.968$ ;  $i^2 = 0\%$ ) and HF (RR: 1.112; 95% CI: 0.996 to 1.242;  $p = 0.059$ ;  $pQ = 0.948$ ;  $i^2 = 0\%$ ).

**Conclusions:** Use of DPP4-I in type 2 diabetic patients is safe and is not associated with unfavorable effects on incidence of new HF, major CV end points or mortality.

#### 1848

##### Cardiovascular prognosis in hypertrophic cardiomyopathy: insights from cardiopulmonary exercise testing.

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**Background:** Major advances have been made in pharmacological and non-pharmacological approaches in patients with hypertrophic cardiomyopathy (HCM). The challenge is now to identify early those patients at high risk of cardiovascular (CV) events and of heart failure (HF) development/progression.

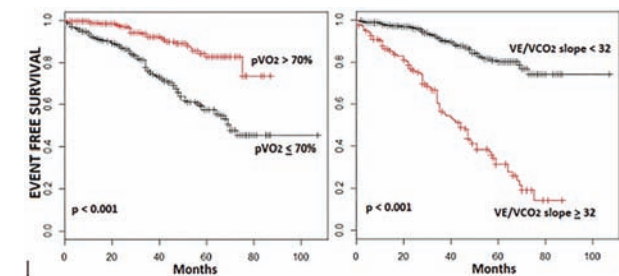
**Methods:** A total of 620 consecutive stable HCM outpatients were enrolled and prospectively followed in five tertiary HCM Italian centers between September 2007 and October 2015. Each HCM patient underwent a de-novo full clinical assessment, including a maximal CPET with a personalized ramp exercise protocol. All patients had planned clinical reviews every 6–12 months or earlier. The primary end-point was represented by: death to HF or stroke, cardiac transplantation, progression to a stable NYHA class III or IV, hospitalization due to HF worsening, cerebro-vascular non-fatal events and new onset of atrial fibrillation.

**Results:** Median follow-up was 3.9 years with a total of 2,755 patient-year. During the follow-up period, 138 (22%) reached at least one of the events considered. Multivariate analysis showed that left atrial diameter (LAd), abnormal blood pressure response at exercise (ABPRE), ventilatory efficiency (VE/CO<sub>2</sub> slope) and peak oxygen uptake (pVO<sub>2</sub>) were independently associated to the study end-point. The ROC analysis showed a pVO<sub>2</sub> < 70% of maximum predicted as well as a VE/CO<sub>2</sub>

slope>32 as the cut-off values with the best accuracy in predicting the study end-point (AUCs: 80% and 85%, respectively). Conclusion. The present study provides evidence of the CPET prognostic role in patients with HCM, particularly with respect to CV events.

Characteristics of overall population			
	Overall Sample [n: 620]	Primary End-Point	
General data		Yes [n: 138]	No [n: 482]
Age, years	49 ± 16	50.7 ± 16.8	48.5 ± 15.7
Male, n (%)	425 (69%)	82 (60%)	343 (71%)†
NYHA III, n (%)	35 (5.7%)	20 (14.5%)	15 (3.1%)
LVOTO, n (%)	200 (32%)	53 (38%)	147 (30%)†
ABPRE, n (%)	112 (18.1%)	47 (34%)	65 (13%)§
LAd, mm	42 ± 7	46 ± 7	41 ± 7§
LVEF, %	62 ± 7	59 ± 8	63 ± 6*
Peak VO <sub>2</sub> , %	71 ± 19	58 ± 17	75 ± 19§
VE/VO <sub>2</sub> slope	28.7 ± 5.8	33.4 ± 6.5	27.3 ± 4.8§

Data expressed as mean ± SD, as absolute number of patients (% on total sample). NYHA: New York Heart Association; LVEF: LV ejection fraction. §p < 0.001; \*p < 0.01; †p < 0.05.



Kaplan-Meier estimator of events

1849

Heart failure following myocardial infarction: a cohort study of incidence and prognostic factors in 24 745 patients using linked electronic records

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**Background/Introduction:** Linked electronic health records (EHR) from primary and secondary care offer the opportunity to investigate the contemporary incidence of and risk factors for heart failure (HF) after a first myocardial infarction (MI).

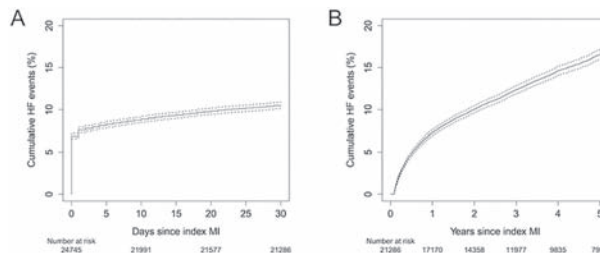
**Purpose:** To investigate the incidence of and risk factors for HF after a first MI.

**Methods:** The UK based CALIBER (CArdiovascular research using Linked Bespoke studies and Electronic health Records) programme, linking primary care data to hospital admissions and national MI and mortality registries was used to identify all patients aged 18 years or older who experienced a first MI between 1 January 1998 and 25 March 2010 and had no prior HF history. Time to HF was modeled using Cox proportional hazard models, with HF defined as the first recorded HF diagnosis in any of the CALIBER sources.

**Results:** 24,745 patients without a prior history of HF experienced a first MI. During a median follow-up of 3.7 years, 6005 (24.3%) patients developed HF, crude incidence rate of 66.1 cases (95% CI: 64.4–67.8) per 1000 person-years. During the first 30 days from index MI, 2581 (10.4%) patients developed HF (Fig. 1A). Among event free patients during the first 30 days, 2779/21286 (13.1%) subsequently developed HF over the following 5 years (Fig. 1B). Of the patients with an index MI between 1998-2001 938/5229 (17.9%) developed HF during a 3-year follow-up compared with 1496/6939 (21.6%) patients with a first MI between 2004-2007. Baseline characteristics independently associated with HF development were:

age [HR per 10 years increase: 1.45 (95%CI 1.41–1.49)], greater socioeconomic deprivation (5th [HR 1.27 (95%CI 1.13–1.42)] vs. 1st quintile), a history of hypertension [HR 1.16 (95%CI 1.09–1.23)], diabetes [HR 1.44 (95%CI 1.34–1.55)], atrial fibrillation [HR 1.63 (95%CI 1.51–1.75)], peripheral arterial disease [HR 1.38 (95%CI 1.26–1.51)], COPD [HR 1.28 (95%CI 1.17–1.40)] and ST-elevation MI [HR 1.21 (95%CI 1.11–1.32)]. Results did not change after imputing missing covariate data, or accounting for competing risks.

**Conclusion:** One in 4 people developed HF within 4 years of experiencing a first MI. Key clinical characteristics identify patients at greater risk of HF following MI, some of which are modifiable.



Crude incidence of HF after index MI

1850

The role of conventional mitral surgery in patients with functional regurgitation and left ventricular dysfunction: a three-centers experience

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**Background:** Percutaneous trans-catheter approaches are being investigated as potential alternatives to conventional open interventions for the management of functional mitral regurgitation (FMR). The optimal strategy in patients with FMR and moderate-severe left ventricular dysfunction is still debated. Purpose We retrospectively evaluated the outcomes of patients with FMR and left ventricular dysfunction at three different hospitals to assess the current role of conventional open surgery and predictors of poor results.

**Methods:** From 2001 to 2015, 202 patients (136 males, mean age 69 years) with ischemic (139 pts) and non-ischemic (63 pts) FMR and an ejection fraction (EF) less than or equal to 45% underwent conventional mitral valve surgery. Mean preoperative EF was 35.3 ± 6.5%. Mean PASP was 47 ± 15 mmHg. Fifty-two patients had diabetes, 31 peripheral vasculopathy and 27 cerebro-vascular accidents. Variables with a P value < 0,10 at univariate analysis entered the multivariate logistic regression to determine predictors of deaths. Kaplan–Meier estimates were calculated and compared using a log-rank. Results Mitral valve repair was performed in 83 pts (41%). A biological or mechanical prosthesis was implanted in 85 and 34 patients respectively. CABG was performed in 109 pts. Cardiopulmonary-bypass and cross-clamp times were 164 ± 57 and 115 ± 40 minutes. Perioperative IABP was necessary in 26% of patients. In-hospital mortality was 7.4%. Postoperative low cardiac output occurred in 46 patients while neurological complications in 17. Twelve patients required a continuous veno-venous hemofiltration or dialysis. Overall survival rates were 87, 82, and 75% at 1, 5 and 10 years. Mortality was significantly higher in patients with diabetes (log rank 0,03) and renal failure (log rank 0,006). No differences were observed when considering etiology of FMR (ischemic vs. non-ischemic), type of surgery (replacement vs. repair), lower EF (<30% vs. > 30%). At multivariate analysis, diabetes (P=0,05; HR 4,4; C.I. 1-21), peripheral vasculopathy (P=0,01; HR 6,3; C.I. 1,35-29,7) and CPB time (P=0,01; HR 1,012; C.I. 1,002-1,022) were independent predictors of 30-days mortality.

**Conclusions:** Conventional mitral surgery still represents a satisfactory option in very complex patients with FMR and moderate/severe myocardial dysfunction. Diabetes, peripheral vasculopathy, and cardiopulmonary bypass time are independent predictors of in-hospital deaths. Patients with a combined cardio-renal impairment, diabetes, and peripheral vasculopathy can probably better benefit from alternative/trans-catheter therapies.

1851

Prevalence and prognostic impact of chronic obstructive pulmonary disease in patients with chronic heart failure. Data from the GISSI-Heart Failure trial.

AstraZeneca, Pfizer, Sigma-Tau, Società Prodotti Antibiotici Spa  
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 L Staszewsky<sup>6</sup>; R Marchioli<sup>7</sup>; AP Maggioni<sup>4</sup>; L Tavazzi<sup>8</sup>

<sup>1</sup>University of Genoa, Genoa, Italy; <sup>2</sup>Fondazione Maugeri, Veruno, Italy; <sup>3</sup>University of Verona, Verona, Italy; <sup>4</sup>Associazione Nazionale Medici Cardiologi Ospedalieri Research Center, Florence, Italy; <sup>5</sup>Santa Maria degli Angeli Hospital, Pordenone, Italy; <sup>6</sup>IRCCS - Istituto di Ricerche Farmacologiche Mario Negri, Milan, Italy; <sup>7</sup>Quintiles, Milan, Italy; <sup>8</sup>Maria Cecilia Hospital, Cotignola, Italy

**Background and aims:** Chronic obstructive pulmonary disease (COPD) is a common comorbidity in patients with heart failure (HF), yet its prevalence, characterization and long-term prognostic impact remain controversial. Herein we aimed to assess the clinical characteristics and outcomes of COPD patients enrolled in the GISSI-HF trial.

**Methods:** The study randomized 6975 ambulatory patients with chronic HF to either n-3 polyunsaturated fatty acids or placebo and followed them up for a median of 3.9 years. We performed a retrospective analysis of clinical characteristics and outcomes of the 1533 patients diagnosed with COPD at study enrollment (22%).

**Results:** COPD was associated with a worse clinical presentation and an increased burden of comorbidities, including diabetes, hypertension, history of atrial fibrillation and peripheral vascular disease (all  $p < 0.0001$ ). At unadjusted and at adjusted Cox proportional hazard analysis, COPD was found to be an independent predictor of both predefined primary study endpoints, including all-cause mortality (adjusted HR 1.28, 95%CI 1.15-1.43,  $p < 0.0001$ ) and all-cause mortality or hospitalization for cardiovascular reasons (adjusted HR 1.19, 95%CI 1.10-1.30,  $p < 0.0001$ ). Both cardiovascular (adjusted HR 1.20, 95%CI 1.05-1.36,  $p = 0.007$ ) and non-cardiovascular mortality (adjusted HR 1.56, 95%CI 1.26-1.94,  $p < 0.0001$ ) were significantly increased in COPD HF patients, as well as hospitalizations for any reason (adjusted HR 1.23, 95%CI 1.14-1.34,  $p < 0.0001$ ), for cardiovascular reasons (adjusted HR 1.16, 95%CI 1.06-1.27,  $p = 0.002$ ) and for HF (adjusted HR 1.27, 95%CI 1.14-1.43,  $p < 0.0001$ ). Figure 1.A and figure 1.B show the Kaplan Meier survival curves for the two co-primary endpoints mentioned above, in patients with COPD and without COPD.

**Conclusions:** COPD is an independent predictor of mortality and hospitalizations in ambulatory HF patients evaluated over a 4-year period. Increased awareness and improved management of COPD may reduce the burden of this morbidity to patients with HF.

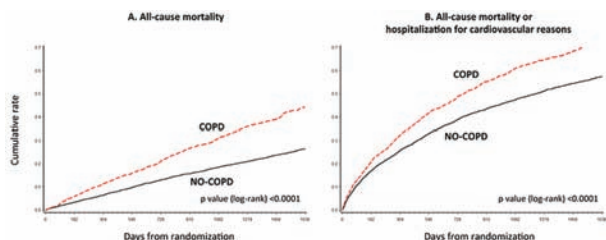


Figure 1

1852

**Is serum cortisol a predictor of left ventricular remodelling after an event of cardiac decompensation?**

M Christa<sup>1</sup>; S Brenner<sup>1</sup>; C Malsch<sup>1</sup>; G Gueder<sup>1</sup>; D Berliner<sup>1</sup>; C Morbach<sup>1</sup>; C Angermann<sup>1</sup>; S Stoerk<sup>1</sup>

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**Background and Purpose:** Stress hormones like cortisol and aldosterone are associated with higher mortality risk in heart failure (HF). Cardiac decompensation

exerts stress on the failing heart and may influence cardiac recovery by altered cortisol levels. We investigated whether levels of corticosteroid hormones after an event of cardiac decompensation predict left ventricular (LV) remodelling after 6 months.

**Methods:** The Interdisciplinary Network for Heart Failure (INH) trial recruited 1022 patients hospitalized for cardiac decompensation with LVEF (echo)  $\leq 40\%$  at discharge. Serum levels of cortisol and aldosterone were measured prior to discharge.  $n = 533$  subjects with complete data incl. echocardiography 6 months after discharge were analysed in this post-hoc analysis. Specifically, use of mineralocorticoid receptor antagonists (MRA) was considered in analyses. Linear regression analyses were run considering the specific nature of skewed data (Tobit regression).

**Results:** The median age of the study cohort was 68 years (quartiles: 59;75), 76% of the patients were male and 46% took MRA. At baseline, median values of serum cortisol, aldosterone and LV end-diastolic diameter (LVEDD) were 14.7 (11.4;18.3)  $\mu\text{g/dl}$ , 56 (10;98)  $\text{pg/ml}$  and 62 (57;66) mm, respectively. After six months, a median change of LVEDD  $-1(-8;+4)\text{mm}$  was observed. Baseline levels of serum cortisol but not aldosterone were related to the change in LVEDD: T-value for log cortisol 1.99;  $p = 0.05$ ; T-Value for log aldosterone  $-1.55$ ;  $p = 0.12$ . By contrast, change in LVEF was not predicted by any corticosteroid. After adjustment for potential confounders (selected from anthropometrics, echocardiography and laboratory) the predictive utility of cortisol was slightly attenuated (Table 1). Of note, not taking a MRA remained a decisive modulating factor in multivariable analyses.

**Conclusion:** In this post-hoc analysis, based on a modest sample size, we observed that higher levels of cortisol predict a larger increase in LVEDD 6 months after an event of acute cardiac decompensation. This association was particularly pronounced in subjects not taking MRA, but was abolished in subjects on MRA. Our findings indicate that cortisol is indeed involved in the mediation of remodelling after an event of acute cardiac decompensation. However, further contributing factors still need to be identified.

**Table 1: Independent prediction of 6-month changes in LVEDD by serum cortisol (multivariable stepwise regression)**

	Change LVEDD in mm	
	T	P value
<b>Step 0:</b> Log serum cortisol at baseline	1.99	0.047
<b>Step 1:</b> Baseline LVEDD	1.73	0.085
<b>Step 2:</b> Age, sex, NYHA class, baseline LVEDD	1.54	0.125
MRA yes	0.41	0.683
MRA no	1.61	0.108
<b>Step 3:</b> Age, sex, NYHA class, baseline LVEDD, Log GFR, Log hs-CRP, Log NT-proBNP	1.87	0.062
MRA yes	0.52	0.604
MRA no	1.88	0.062

Stepwise increasing levels of adjustment (linear regression). For step 3, independent predictors for cortisol were forced into the analysis, and repeated for patients with or without MRA intake.



# CLINICAL CASE CORNER 6: FRIENDLY FIRE: THE HEART DEALS WITH CANCER

Tuesday 24 May 2016 10:00–11:00

Location: Poster Area

1853

## Major cardiovascular events in long-term survivor of childhood cancer

FJ Francisco Javier Irazusta Cordoba<sup>1</sup>; J Caro Codon<sup>1</sup>; O Gonzalez Fernandez<sup>1</sup>; P Meras Colunga<sup>1</sup>; V Rial Baston<sup>1</sup>; SO Rosillo Rodriguez<sup>1</sup>; E Refoyo Salicio<sup>1</sup>; M Moreno Yanguela<sup>1</sup>; JL Lopez-Sendon<sup>1</sup>; T Lopez Fernandez<sup>1</sup>  
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**Introduction:** Anticancer therapies have led to a long life expectancy for many patients; however, treatment-related comorbidities, and mainly cardiac toxicity, have become an issue for long-term cancer survivors.

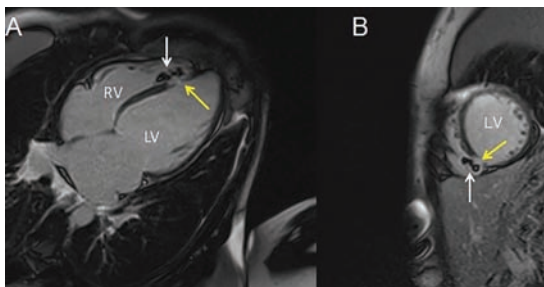
**Clinical case:** A 38-year-old woman presented to the emergency department of our hospital after one week of low respiratory tract infection symptoms and a 20-minute episode of acute oppressive chest pain.

Her medical history was remarkable for a diagnosis of Wilms tumor at 12 years old. She was treated with surgery and anthracycline-based chemotherapy (ABCT). Ten years later she received a diagnosis of femur osteosarcoma, being treated with surgery and adjuvant ABCT. Subsequently, at 34 years old, she developed chemotherapy-related left ventricular dysfunction (CRLVD) and, therefore, was receiving regular follow-up in the cardiology outpatient clinic.

On physical examination stood out a systolic murmur with no other remarkable findings. A 12-lead ECG was performed, without encountering signs suggestive of myocardial ischemia. Laboratory tests revealed mild elevation of C-reactive and significant elevation of Troponin I (23.55 ng/mL, normal range < 0.04 ng/mL) and NT-proBNP (3750 pg/mL, normal range < 125 pg/mL). The patient underwent transthoracic echocardiography, which revealed moderate-to-severe left ventricular dysfunction, inferior and posterior wall akinesia, and severe mitral regurgitation. Given the history of CRLVD, the presence of cold symptoms and an increase in troponin level, a differential diagnosis of myocarditis was raised. Subsequent coronary computed tomography angiography (CCTA) revealed normal coronary arteries. The patient remained asymptomatic during the hospitalization and a cardiac magnetic resonance (CMR) was scheduled to continue the diagnostic process. CMR showed an image suggestive of mural thrombus in the right side of the interventricular septum, adjacent to an akinetic region with transmural late gadolinium enhancement. Finally, a diagnosis of septal acute myocardial infarction (AMI) with normal coronary arteries, presumably embolic, was performed in a young woman with CRLVD.

**Discussion:** Cardiac toxicity is one of most feared side-effects of anticancer agents so that the gain in life expectancy due to anticancer therapy might be countered by increased mortality due to cardiac problems. In our patient CRLVD diagnosis was performed belatedly, and even with focused treatment for heart failure, left ventricular ejection fraction did not improve. Later she suffered an AMI regarding an embolic event, but differential diagnosis with viral myocarditis was really difficult. Final diagnosis was performed by the CMR.

**Conclusion:** This particular case illustrates the importance of the development of programs directed towards the early diagnosis and treatment of CRLV. Cardiac imaging evaluation is the cornerstone in the diagnosis and decision-making process of these patients.



Embolic AMI diagnosed by CMR

1854

## Beyond heart failure in an oncological patient

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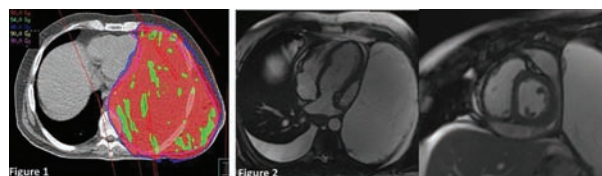
We present the case of a 43-year-old man with a previous history of dyslipidemia and hyperuricemia. In April 2015, he consulted for progressive dyspnea and left pleural effusion. Three months later he referred worsening of symptoms and a 25 cm pleural mass were seen in July 2015. Left pleuropneumectomy was performed, with anatomopathological result of synovial sarcoma. The surgery got complicated with massive intrasurgical haemorrhage that required massive transfusion. After adjuvant chemotherapy with adriamycin and ifosfamide, a reevaluation with PET was done, showing no residual disease. Then, adjuvant radiotherapy to the left chest wall with concurrent gemcitabine was administered (Fig1).

He was referred to our department in December 2015 because of shortness of breath (NYHA III) and edema in lower extremities. On examination, hypotension and elevated jugular venous pressure was noted. EKG showed sinus tachycardia and QRS low voltages. An echocardiogram demonstrated moderate pericardial effusion that conditioned collapse of the right atrium and right ventricle with inferior vena cava plethora and normal systolic function.

Because of cardiac tamponade, a pericardial window draining into right pleural space was made. The pericardial fluid cytology was negative for malignancy. However, no clinical improvement was noted and he was readmitted 10 days later with right heart failure (HF). The echocardiogram dismissed cardiac tamponade, and showed dilated inferior cava with no other complains. Intravenous diuretic treatment was started, with slight improvement.

A week later he developed symptomatic atrial fibrillation with rapid ventricular rate and hypotension, so intravenous amiodarone was given restoring sinus rhythm. Posterior evolution was torpid and the patient developed a low cardiac output syndrome. The echocardiogram showed signs of heart constriction, but the acoustic window was suboptimal so a cardiac magnetic resonance (CMR) was performed. The CMR showed pericardial thickening (5 mm maximum) with lobulated pericardial effusion (29 mm of maximum thickness) (Fig2) and paradoxical movement of the septum with limitation of left ventricular relaxation. No collapse was observed. All these data suggested constrictive pericarditis, probably induced by radiation. After hemodynamic stabilization, pericardiectomy was performed. Pathological diagnosis was fibrous pericardium with no signs of malignancy. Right HF remained even after the procedure, and he is still on treatment for HF, being NYHA II now.

Radiation-induced pericardial disease should be a differential diagnosis in oncological patients suffering from symptoms related to chronic HF and pericardial thickening or effusion. Examination should be done with appropriate noninvasive (echocardiography, CMR) and invasive technics (cardiac catheterization). Early pericardiectomy has been advocated immediately after confirming the diagnosis. Otherwise, surgical outcome is not always favorable.



Radiation map and CMR

1855

**Right ventricle heart failure in pulmonary embolism caused by neoplastic infiltration of the vena cava superior and the right atrium**M Zechowicz<sup>1</sup>; M Rucinska<sup>1</sup><sup>1</sup>University of Warmia and Mazury, Department of Oncology, Olsztyn, Poland

**Introduction:** The risk of venous thromboembolism (VTE) is significantly higher in cancer patients than in the general population and its diagnosis deteriorates the overall prognosis. It can present as the first manifestation of a neoplasm, its progression or recurrence. It appears usually as a deep vein thrombosis (DVT), rarely it manifests as an isolated pulmonary embolism (PE).

**Case study:** A 53-year-old female patient, who was treated with chemotherapy (ChTH) and radiotherapy (RTH) due to metastatic mediastinal cancer of unknown primary location (FPI) in the past, was admitted due to increasing dyspnoea, tachycardia and cervical veins distension. Transthoracic echocardiography (TTE) showed indirect signs of pulmonary hypertension and a movable structure in the right atrium (RA) suggesting a thrombotic process. Computed Tomography (CT) confirmed the presence of PE and revealed cancer recurrence in the mediastinum. No DVT was present in ultrasonography of the lower limbs. As there was no clinical improvement after unfractionated heparin treatment, another cause of PE was suspected. Further CT scans reconstructions with magnetic resonance (MRI) revealed neoplastic infiltration of vena cava superior, penetrating to its lumen and to the atrial cavity. The PE material in segmental arteries seemed to be both thrombotic and of neoplastic origin. The patient was qualified for oncological treatment with palliative RTH followed by ChTH, and dalteparin (200 UI/kg/day) was recommended as anticoagulant treatment. In the follow-up, the right ventricle heart failure signs diminished and the patient covered a greater distance (444 and 420 meters respectively) in 6-minutes walking test. Decrease in size of the structure in RA was observed in TTE and 3D-Echocardiography and the right ventricle systolic pressure normalized.

**Discussion:** Risk of VTE coexisting with neoplasm is the highest (4–13 times) in patients suffering from metastatic pancreas, stomach and lung cancer. Such patients have also a higher risk of VTE recurrence as well as a higher risk of bleeding during anticoagulation. With the anticancer treatment the risk of VTE increases additionally about 7-fold. The presented case showed the occurrence of PE as the first manifestation of the neoplastic disease progression, which can also represent its higher aggressiveness. Additionally, the co-occurrence of VTE and the structure in the RA pretending a thrombus resulted in delay of the right diagnosis, as the symptoms of right ventricle heart failure fitted the primary diagnosis of PE and simultaneously masked the neoplastic infiltration of responsible vessels. It was found necessary to combine TTE, CT and MRI for the final accurate diagnosis and the simultaneous cardio-oncological treatment was implemented.

**Conclusions:** A symptomatic right ventricle heart failure in patients with a history of cancer needs diagnosing towards PE. An isolated PE in metastatic cancer can be both thrombotic and of neoplastic origin.

1856

**Rapidly progressive aortic and tricuspid regurgitation after radiotherapy for breast cancer**Al Ana Isabel Azevedo<sup>1</sup>; A Dias<sup>1</sup>; J Ribeiro<sup>1</sup>; M Fonseca<sup>1</sup>; N Ferreira<sup>1</sup>; L Vouga<sup>1</sup>; V Gama Ribeiro<sup>1</sup><sup>1</sup>Hospital Center Vila Nova Gaia, Porto, Portugal

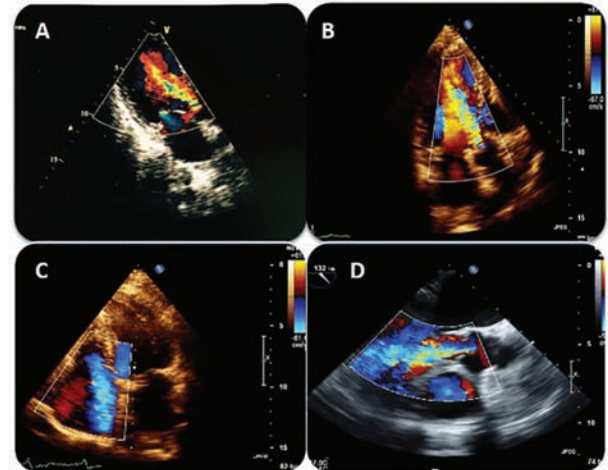
**Introduction** Radiation therapy has improved survival in early stage breast cancer. However, heart irradiation can damage virtually any cardiac structure. Clinical manifestations of cardiotoxicity can appear after a long follow-up and there is not a minimum radiation dose considered to be entirely safe.

**Case report:** A 66-year-old woman presented with syncope and atypical chest pain. She had history of left breast cancer at 42 years-old, submitted to left mastectomy and adjunctive chemotherapy and radiotherapy (RT). Physical examination was unremarkable. Electrocardiogram revealed second degree atrioventricular (AV) block (Mobitz II), left anterior fascicular block and right bundle branch block. Transthoracic echocardiography (TTE) showed mild aortic valve regurgitation (AVR) and normal left ventricle systolic function (LVSF). Cardiac magnetic resonance confirmed mild AVR and no signs of ischemia or fibrosis. A dual chamber pacemaker was implanted. One-year later, atypical chest pain persisted and progressive worsening fatigue, facial and lower limb oedema developed. TTE showed moderate AVR (A), mild mitral regurgitation and mild to moderate tricuspid regurgitation (TR), with normal pulmonary artery systolic pressure (PASP) and LVSF. Optimal medical therapy was adopted. Four months later, TTE showed moderate to severe AVR (B) and moderate TR (C), with normal PASP and LVSF. Cardiac catheterization showed no coronary artery disease and severe AVR. Two months later, on transoesophageal echocardiography, AVR was quantitative assessed as moderate (D) and severe TR with pulmonary hypertension and signs of right ventricle pressure overload were seen. Pulmonary angioCT excluded embolism or parenchymal abnormalities. The patient underwent surgical replacement of the aortic valve with a mechanical prosthesis and tricuspid annuloplasty. On TTE one-month after surgery, severe TR

persisted and mild right ventricle dysfunction was present. The patient remained clinically stable.

**Discussion:** Incidental radiation of the heart is associated with cardiovascular disease. There is a dose-dependent relation and cardiotoxicity is greater for RT of left-sided breast cancer. Conduction abnormalities include left or right bundle branch block and different degrees of AV block. Syncope is the most common symptom. Aortic valve regurgitation is the most common valvular abnormality and patients can develop symptoms of heart failure several years after RT. Valve replacement is the mainstay of treatment for severe valvulopathy and echocardiographic screening for valvular heart disease is advisable 10 years after RT.

**Conclusion:** RT-induced cardiotoxicity affects any heart structure in a dose-dependent relation. AVR is the most common valvulopathy and can manifest several years after RT. Multidisciplinary involvement (cardio-oncology) in the planning of thoracic RT and long term follow-up are essential for preventing and/or early detecting radiation-induced cardiotoxicity.



1857

**Phantom tumor of the lung in a patient with mitral valve infective endocarditis**S Matic<sup>1</sup>; K Kristina Andjelkovic<sup>1</sup>; D Kalimanovska Ostric<sup>1</sup>; V Karadzic<sup>1</sup>; B Orbovic<sup>1</sup><sup>1</sup>School of Medicine, University of Belgrade, Cardiology Clinic, CCS, Belgrade, Serbia

Infective endocarditis is still a deadly disease, despite management improvement achieved. Heart failure is common complication and frequently the reason for early surgery.

We present a 58-yr-old female patient was admitted on orthopedic department of the local hospital with symptom of severe back pain. There was no evidence of vertebral lesion, but inflammation markers were increased. Few days later she became 39,9 C febrile and felt poor. Antibiotics were administered and she became afebrile. One week after she was admitted to the hospital, she felt short breath and pulmonary embolism was suspected. At the same time echocardiography finding was severe mitral regurgitation (MR) in enlarged left atrium and 2,5 x 1,7 cm large mitral valve vegetation. Hence, mitral valve endocarditis was diagnosed. She was transferred to cardiology clinic. Laboratory and microbiology tests were performed. BNP and inflammatory parameters levels were increased. Three blood cultures were negative. Chest radiography was unremarkable. Echocardiography finding was the same as the first done. Antibiotics were given empirically. All the time the patient was hypotensive, in sinus rhythm but tachycardic, with hypoproteinemic leg edema and small bilateral pleural effusion. Suddenly, she got hemoptysis. At the same time we have noticed inguinal lymphadenopathy. D-dimer was not significantly increased. The control chest radiography showed in her right pulmonary hilum tumor-like phenomena. She was observed by pulmonologist. Chest CT-scan showed suspected tumorous process. Bronchoscopy and biopsy were performed. Neither malignant process, nor pulmonary embolism was diagnosed. The histopathological finding of biopsied enlarged lymphoid nodus showed inflammatory reaction. After the high doses of furosemide administered, our patient has stabilized. Hemoptysis and tumor-like phenomena disappeared. They were just uncommon acute heart failure manifestations. BNP level was lower, too. The control five samples of blood cultures were sterile. Surgical treatment has been indicated. The latest echocardiographic finding before the operation showed enlarged diastolic dimension of left ventricle, rupture of degenerative changed posterior mitral cusp and severe MR in enlarged left atrium. It was

three months of intensive conservative treatment since the first manifestation of her illness occurred, needed to be adequately prepared for surgery. Artificial mitral valve was implanted. One month after the operation, she was completely healed and went home. The control echocardiography showed normal sized left ventricle with good ejection fraction (54%).

Heart failure with atypical manifestation, such as phantom tumor of the lung, can delay surgery treatment that is necessary in patients with infective endocarditis, due to unnecessary additional diagnostic. Therefore, practitioners should be cautious in such clinical pitfalls.

### 1858

#### Acute heart failure due to reversible cardiomyopathy in patient under b-raf inhibitor for metastatic melanoma.

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Vemurafenib is an orally administered drug that inhibits BRAF kinase and blocks tumor growth by hindering cellular proliferation. It is indicated for the treatment of BRAF-mutated unresectable and metastatic melanoma. The most commonly reported adverse events includes joint pain, rash, alopecia, photosensitivity and fatigue. The main cardiac side effect is a QT prolongation which may cause life threatening cardiac arrhythmias such as torsades de pointes. For this reason a close monitoring with electrocardiogram for the entire duration of the treatment is necessary. We report a severe acute heart failure due to a reversible cardiomyopathy in a patient treated with Vemurafenib. A 40 years old woman with a metastatic melanoma was sent to cardiologic evaluation for shortness of breath (NYHA III), ankle swelling and heart murmur developed after the ninth administration course. No previous history of cardiovascular disease was reported except for a border line not treated hypertension and smoking history. Electrocardiogram showed non-specific ST alteration with T-wave inversion in chest leads (V4-V5-V6) meanwhile the echocardiographic assessment revealed a severe left ventricular function impairment (LVEF 35%). There was a left ventricle (LVED 62mm) and atrium enlargement, mild to severe mitral regurgitation and pulmonary hypertension (PAPs 55mmHg). In the effort to treat the cardiomyopathy, we started a therapy with ACE inhibitors, beta blockers, diuretics and digoxin. The first diagnosis was a multi-factorial disease due to hypertension and valvular insufficiency. However in the hypothesis of a iatrogenic damage, Vemurafenib has been suspended. The symptoms and ECG alterations improved in 2 months. The left ventricular function totally recovered in the latter 4 months as well as the pulmonary pressure. Little information is known about the cardio toxicity of the tyrosine kinase inhibitor, however, in these case, the fast recovery after Vemurafenib holding seems to exclude an immune-mediated mechanism. The reversible nature of Vemurafenib-induced cardio toxicity suggests a cellular mechanism of the dysfunction. The interaction of BRAF inhibitors with ionic channels and kinase (ATP or calcium related), may induce the loss of capacity to produce energy. This mechanism can explain the association with QT-alteration and myocardial dysfunction. In Vemurafenib administer protocol, time depending ECG controls are mandatory to detect early QT-elongation. In our case not specific ECG alteration anticipated myocardial dysfunction despite not clinical related. We suggest that all patients under B-RAF inhibitor therapy should receive a particular attention for ECG little modifications, that can show early signs of myocardial toxicity which are to be confirmed by echocardiographic assessment (LVEF).

### 1859

#### Cardiogenic shock during first infusion of chemotherapy in a patient with Hodgkin's lymphoma: an unusual evenience

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Hodgkin's lymphoma (HL) is a common type of cancer of the lymphatic system. The outcomes of HL have improved due to advances in treatment (Tx). However, survivors have an increased risk for cardiovascular morbidity and mortality related to cardiotoxicity (CTX) of Tx, also because of use of anthracycline (AXA). Typically, CTX happens in mid- or long-term follow-up, but it can rarely occur also in an acute phase.

A classical HL was diagnosed in a 60 years-old male, ex smoker and with a previous cerebral TIA. The haematological scheduled plan consisted in 2 cycles of ABVD (Adriamycin; Bleomycin; Vinblastine; Dacarbazine) followed by a new staging. The pre-Tx cardiac evaluation was normal, showing no clinical, ECG and echocardiographic alterations. Near the end of the first ABVD-cycle, during the infusion of dacarbazine, the patient presented a cardiogenic shock characterized by pulmonary oedema, treated with infusion of inotropes (dobutamine followed by epinephrine) and diuretics. Transferred to our Cardiac Care Unit, the ECG showed no ST-abnormalities and echocardiography (TTE) revealed a severe left ventricular

dysfunction (EF 25%). In the following days, the patient was also treated with levosimendan with an improvement of haemodynamic and clinical status. In order to realize the cause of myocardial dysfunction, a coronary CT scan was performed, showing a coronary artery disease (CAD). Thus, an angiography was planned revealing a not significant two-vessel disease. The cardiac MRI, executed in the same days, demonstrated the recovery of systolic function, no oedema and no early or late gadolinium-enhancement. After 15 days the patient was discharged with a normal EF (56%) at the TTE. In the following weeks, he underwent a different haematological Tx with bendamustine, without any cardiac complication and with a discrete haematological response. Unfortunately, some months later, he was re-hospitalized because of a septic shock in absence of cardiac involvement, with a lethal outcome. In this case the acute and reversible ventricular dysfunction was probably due to the AXA-infusion, as other possible concomitant causes, such as significant CAD or myocarditis, have been excluded. The risk to develop a heart failure (HF) after AXA-containing Tx is well known. However, the CTX leading to HF, usually, develops after some weeks or months from the start of Tx, because of it is dose-dependent and produced by an oxidative stress. Indeed, a hyper-acute CTX, responsible for the critical scenario observed in our case, is very rare. Moreover, we attended to a full recovery of cardiac function, sign of a non-irreversible injury. To our knowledge, in literature there is only another similar case, describing an acute HF developed, however, 30 hours after an AXA-Tx, with a total recovery in some days. In these rare cases, the pathophysiology is still unknown. Further in-vitro and clinical studies are needed to understand and prevent the events of hyper-acute AXA-CT.

### 1860

#### Acute heart failure in patient with giant left atrial mass

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1. A 49-year-old man was evaluated for hacking cough and exertional dyspnea for a few months and palpitations and orthopnoea for two weeks especially at night, in supine position. A recent chest x-ray showed an enlarged cardiac shadow.

2. The outpatient evaluation revealed a blood pressure of 105/70 mmHg, irregular heartbeats and an elevated heart rate. The electrocardiogram showed an high heart rate atrial fibrillation (150 bpm) and widespread alterations of ventricular repolarization.

The transthoracic echocardiogram revealed a large atrial mass inhabiting the majority of the left atrium volume. The mass had round shape, irregular profile, inhomogeneous echogenicity and large planting base on the atrial septum. Its low mobility during cardiac cycle was due to its dimensions: longitudinal diameter was of 82 mm and a transverse diameter of 62 mm, resulting in almost complete occlusion of the left atrium, that was severely dilated. The Doppler analysis of mitral valve function revealed a moderate mitral functional regurgitation. Left ventricle dimensions were normal, but ejection fraction, estimated according the Simpsons' rule, was severely reduced (20%), due to diffuse hypokinesia.

3. The echocardiographic characteristics of the mass (localization in left atrium, planting base on the atrial septum, round shape, irregular profile, inhomogeneous echogenicity), lead the diagnosis of myxoma. On the other hand it could not be excluded the diagnosis of a thrombotic mass (the patient's rhythm was atrial fibrillation) or another tumoral mass.

4. After an initial treatment with low doses of beta-blockers and digoxin to obtain the rate control, heparin sc and diuretics, the patient was referred to the Cardiac Surgery Unit. A chest TAC-PET examination excluded an extracardiac diffusion of the mass. After the surgical removal of the mass, the post-operative histological examination confirmed the diagnosis of myxoma. The post-operative period ran without complications. Two months after the surgical intervention the echocardiographic control showed an improvement of left ventricle function (ejection fraction of 40%).

5. This case is particularly interesting for the unusually dimensions of the mass and the clinical presentation with increasing symptoms of heart failure.

Left atrial myxomas, are the most common benign primary heart tumors. Because of nonspecific symptoms, early diagnosis can be difficult. Symptoms may occur at any time, but often they occur according to changes of body position and may include shortness of breath, palpitations, syncope and chest pain. The echocardiographic diagnosis should be integrated by a transesophageal examination to better define the characteristic of the mass and to exclude multiple masses. The surgical treatment is indicated for the high risk of embolization related with the mass.

### 1861

#### Early manifestation of restrictive cardiomyopathy in young patient with light chain deposition disease

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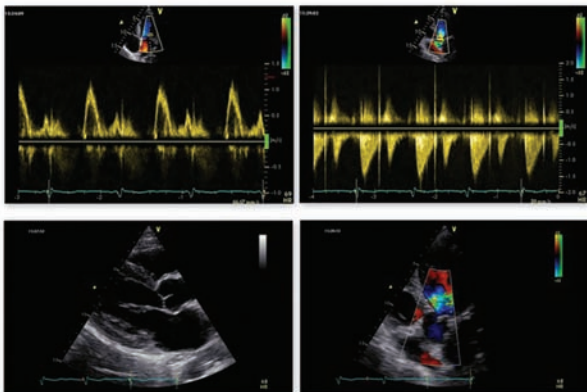
A 30 years old male presented with exertional shortness of breath and general fatigue which extremely progressed over the past 2 weeks in February 2016. In September 2015 he was diagnosed with light chain deposition disease (LCDD), identified as paraproteinemia with pathological kappa/lambda ratio and renal



dysfunction. There were no significant clinical changes of respiratory and cardiovascular systems, except arterial hypertension, at first occurred in March 2015. Physical exam: BMI- 23.5, BP 155/90 mm Hg, HR 72, paleness of skin, no other changes. Light chain's diagnostics: free kappa light chain – 164 mg/l, lambda – 10.9 mg/dl, kappa/lambda ratio 15.05. Bone marrow biopsies suggested an underlying plasmocytoma: presence of 18 % of pathological plasma cells. ECG – regular sinus rhythm with HR 75, no significant changes. Thoracic echo: moderate enlargement of left atrium (46 mm), minimal mitral insufficiency, normal large left ventricle (LVEDD 47 mm), PW -14 mm, IVS -15 mm, EF - 65 %. Restrictive diastolic dysfunction. Pulmonary hypertension – 46 mm Hg. These echocardiographic findings suggested development of restrictive cardiomyopathy in patient with LCDD, primarily manifested with nephropathy. During last 5 months renal disorder has been progressively increased: eGFR falls down from 60 to 30 ml/min/1.73m<sup>2</sup>.

LCDD is a monoclonal proliferative plasma cell disorder characterized by tissue deposition of light chain immunoglobulins, predominately in the tubular basement membranes of the kidneys. This case shows that cardiac involvement can present early in the course of disease as a pattern of restrictive cardiomyopathy. The differential diagnosis includes idiopathic hypertrophic cardiomyopathy, amyloid heart disease, Fabry's disease, Loeffler's endomyocardial fibrosis etc. Endomyocardial biopsy is the gold standard to differentiate between specific histopathologic entities in all cardiomyopathies. In myocardial LCDD light chain fragments mostly kappa chains do not organize into amyloid fibrils, but form granular deposits. In contrast in primary AL amyloidosis mostly lambda chains organize into fibrillar structure that are deposited predominantly perimycytic in patchy pattern. Light chain deposits are amorphous, Congo red negative, but positive to light chains on immunofluorescence examination on snap frozen biopsies. Our patient had renal biopsy, which approved LCDD. There is no specific treatment of cardiac involvement of LCDD, in particular conventional chemotherapy regimens for multiply myeloma, combined with classic heart failure therapy. Our patient has finished course of chemotherapy, now he receives Privigen, Valsartan 160 mg, Concor 2,5 mg.

LCDD of the myocardium is a rare cause of restrictive cardiomyopathy, associated with impaired renal function and underlying plasma cell dyscrasia. In the majority of cases cardiac involvement is very detrimental, reducing therapeutic options and survival.



Echo image

1862

#### Cardiogenic shock developed 24 hours after initiation of capecitabine therapy

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Capecitabine is a chemotherapeutic agent widely used to treat gastrointestinal and breast malignancies. It is the oral pro-drug of 5-fluorouracil, with similar cardiac toxicity. We present the case of a patient who developed cardiogenic shock shortly

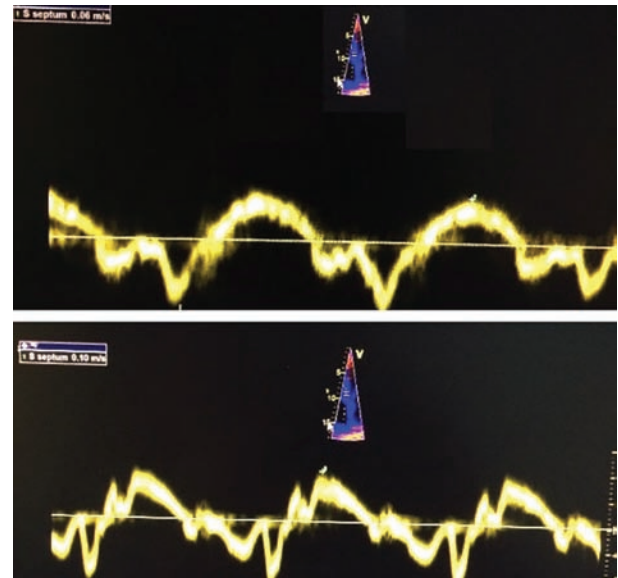
after capecitabine administration, with rapid resolution and complete normalization of left ventricular function.

A 48 year-old patient was admitted to our unit with signs and symptoms of acute heart failure and hemodynamic instability, 24 hours after the initiation of capecitabine therapy, which had been prescribed for gastrointestinal cancer. He had no history of heart disease and he had a normal echocardiogram during a routine check-up before starting chemotherapy. The physical examination revealed signs of shock with a blood pressure of 70/40 mm Hg. The initial evaluation showed nonspecific ST-T wave changes on his ECG and normal levels of cardiac biomarkers. His transthoracic echocardiogram revealed a dilated, globally hypokinetic left ventricle (LV), with a severely impaired systolic function (EF=23%). Over the course of 7 days of treatment, inotropic support included, his clinical status came back to normal, with complete normalization of his LV systolic function.

The spectrum of cardiac toxic effects of capecitabine varies from coronary thrombosis and coronary vasospasm to toxic myocarditis, arrhythmias, cardiogenic shock and sudden cardiac death. The cardinal symptom associated with capecitabine administration is chest pain, while acute heart failure and cardiac arrest are less frequently reported. Several mechanisms have been proposed for capecitabine cardiotoxicity, including direct myocardial injury, autoimmune phenomena and coronary vasospasm. Predisposing factors for the risk of cardiac toxicity are not clear.

Our patient presented with cardiogenic shock, requiring ICU admission and inotropic support. He had no clinical or electrocardiographic evidence of coronary vasospasm, while his cardiac biomarkers' dynamic wasn't consistent with acute myocarditis. We think that the underlying mechanism was mainly direct toxicity to the myocardium. His follow-up echocardiogram performed 7 days after admission revealed normal systolic function (EF=56%) without evidence of wall motion abnormalities.

Capecitabine-induced cardiotoxicity is a rare but potentially fatal complication; all patients should undergo echocardiographic evaluation before starting chemotherapy and close follow-up is needed in order to avoid severe complications. Oncologists as well as cardiologists should be highly aware of this phenomenon and collaborate closely in order to ensure patients' safety.



Tissue Doppler (admission, discharge)

## POSTER SESSION 4

Tuesday 24 May 2016 08:30–12:30

Location: Poster Area

### ACUTE HEART FAILURE

#### P1869

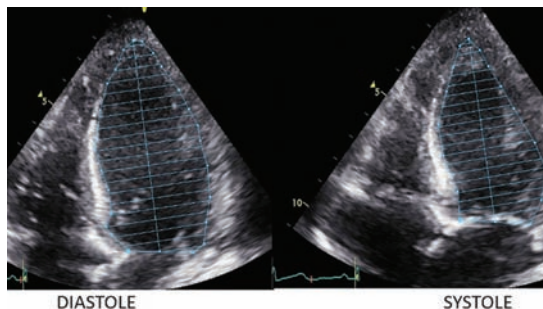
##### Reverse takotsubo cardiomyopathy and cardiogenic shock with polyuria

NIL

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A middle aged Malay gentleman who is a known case of COPD (Chronic obstructive pulmonary disease), presented with worsening shortness of breath for 2 days and chest tightness. He presented late to the emergency. On admission he was in severe Respiratory acidosis with pCO<sub>2</sub> (partial pressure of Co<sub>2</sub>) of 109.8 mmHg and pH of 7.010. He was hypotensive with blood pressure of 75/47 mm Hg, and polyuria (> 3.5 litres/day). High sensitivity troponin T was elevated at 843 ng/L (normal value is <15ng/L). NTproBNP is 4125 pg/mL. (Cutoff levels 900 pg/mL for ages 50-75 yrs with Positive prediction of 83%). His inflammatory markers were normal. His Electrocardiogram showed sinus rhythm with anterior q waves in leads V2 and V3 and ST segment elevation in anterior precordial leads. Other blood tests are within normal parameters. Transthoracic echocardiogram revealed multiple regional wall motion abnormalities corresponding to multiple territories, basal, mid LV hypokinesis with apical hyperkinesis and LV ejection fraction of 45% (image). He was treated for the acute exacerbation of COPD. His hypotension is supported by a single vasopressor which was weaned off. Coronary angiogram showed minor coronary artery disease without any significant obstruction. He was diagnosed to have inverse (Reverse) variant Takotsubo cardiomyopathy based on the proposed Mayo clinic criteria. His polyuria in this setting of cardiogenic shock which could be secondary and attributed to the release of natriuretic peptides from stress cardiomyopathy which could be higher in basal variant since the myocardium involved is larger. The patient significantly improved with vasopressors and was discharged home in 3 days. This acute episode of heart failure is likely precipitated by COPD exacerbation for which he was given education and preventive measures. This case highlights the importance of recognition of basal variant of stress cardiomyopathy and its clinical implications. Many patients often require supportive measures till the acute stressor is dealt with.



Echo features

#### P1870

##### Feasibility of a fast-track pathway of care of the patients with acute dyspnea using handheld echocardiography

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**Purpose:** to evaluate the feasibility and diagnostic accuracy of a "fast-track" pathway of care of the patients with acute dyspnea requiring urgent cardiac evaluation with a handheld echocardiography (HHE) device compared to classic echocardiographic evaluation.

**Methods:** a prospective study was performed on 65 patients (41 females, mean age 68 ± 12 years) with acute dyspnea referred for urgent cardiac evaluation in a multidisciplinary hospital, in whom bedside ECG and HHE were performed, followed by classic echocardiographic evaluation.

**Results:** The mean waiting time till ultrasound examination was performed was 16 ± 6 minutes when using HHE compared with 45 ± 19 (p < 0.01) minutes by using classic ultrasound machine and the duration of the examination was shorter when using HHE: 15 ± 2 minutes vs. 21 ± 13 minutes (p < 0,1). The degree of correlation of the results was excellent in the case of left ventricular dilatation (kappa coefficient of agreement=0,85) and LV dysfunction (k=0,82) and good when valvular abnormalities were found (k=0,67)

**Conclusion:** handheld echocardiography can speed up the diagnostic pathway in patients with acute dyspnea and to provide reliable data to assess the severity of the underlying mechanism of acute dyspnea.

#### P1871

##### Heart failure in women and men during acute coronary syndrome: interaction for long-term cardiovascular mortality (The ABC-4 Study on Heart Disease)

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**Background:** Natural history studies have suggested important differences in survival between men and women in a broad spectrum of heart failure (HF) severity. Nonetheless, the relationship between gender and HF for adverse prognosis after acute coronary syndrome (ACS) has not been thoroughly examined, especially in the long term. We investigated the gender-based differences in the association between HF during ACS and post-discharge, long-term cardiovascular (CV) mortality.

**Methods:** The present study included 557 patients enrolled in three intensive coronary care units and discharged alive. HF during ACS was evaluated by Killip class and left ventricular ejection fraction (LVEF). Interaction between gender and HF after 15 years of follow up was studied using Cox models including a formal interaction term.

**Results:** Median age was 67 (interquartile range [IQR], (59–75) years, 29% were females, 37% had non-ST elevation myocardial infarction and 32% Killip class>1, and median LVEF was 53% (IQR 46–61). All but five patients were followed up to 15 years, representing 5332 person-years. Of these, 40.2% died of CV-related causes. Crude CV mortality rate was higher among women (52.2%) than men (35.3%; P < 0.0001). At a univariable level, a negative interaction between female gender and Killip class for CV mortality was found [hazard ratio (HR) = 0.51 (0.34–0.77), P = 0.002]. In five multivariable models after controlling for age, main CV risk factors, clinical features, post-discharge medical treatment, and mechanical coronary reperfusion, the interaction was significant across all models [HR = 0.63 (0.42–0.95), P = 0.02 in the fully adjusted model]. LVEF showed no significant hazard associated with female gender on univariable analysis [HR=1.4 (0.9–2.0), P = 0.11] but did so in all adjusted models [HR=1.7 (1.2–2.5), P = 0.005 in the fully adjusted model].

**Conclusions:** Gender is a consistent, independent effect modifier in the association between HF and long-term CV mortality after ACS.

#### P1872

##### Prognostic value of plasma renin concentration (PRC) in patients with acute heart failure (AHF)

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**Purpose:** PRC is an independent prognostic factor and superior to plasma renin activity in predicting outcome in patients with chronic heart failure. The prognostic significance of PRC in patients with AHF is unknown. We examined the prognostic utility of PRC, in conjunction with other prognostic factors, in patients with AHF.

**Methods:** Consecutive patients admitted with suspected AHF were invited to participate in an observational study. A confirmed diagnosis of AHF required typical clinical findings and a BNP>100pg/ml. Exploratory data analysis revealed PRC was positively skewed and was analysed as log(PRC) in a continuous fashion, or as ≤median/ >median (binary). The prognostic importance of PRC was analysed in a univariate Cox proportional hazard model and then in a multivariate model including independent markers of all-cause mortality (age, systolic blood pressure, history of chronic obstructive pulmonary disease, serum urea [BUN], troponin, log(BNP) and haemoglobin). These prognostic variables were identified by backwards selection in a multivariate model with predetermined variables not including PRC.

**Results:** 722 patients were enrolled in the study. The median (IQR) follow-up was 998 (365-1217) days. A PRC measured during hospital admission was available in 689 patients. The median (IQR) PRC was 47.3 (13.0-177.3) mIU/L. Univariate analysis demonstrated that higher log(PRC) and PRC >median predicted higher mortality (Table). In multivariate analysis both PRC variables remained predictive of mortality.

**Conclusion:** PRC adds independent predictive information to that obtained using established prognostic variables in AHF, including BNP. This finding raises questions about the contribution of incomplete renin-angiotensin system (RAAS) blockade or RAAS escape to the high mortality after hospitalization for AHF.

Table

Variable	HR (95% CI)	P-value
Univariate analysis		
≤ median PRC (vs > median)	0.62 (0.50 - 0.76)	<0.001
Log(PRC)	1.11 (1.06 - 1.15)	<0.001
Multivariate analysis		
≤ median PRC (vs > median)	0.72 (0.56 - 0.94)	0.015
Log(PRC)	1.08 (1.03 - 1.13)	0.003

**P1873**

**Hip fracture and heart failure**

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**Introduction:** The proximal femoral fracture or hip fracture is one of the major health problems of the elderly population. Lead to an increase in morbidity, mortality, functional impairment, costs and increases the degree of dependency and institutionalization of these patients a year of the fracture. Medical complications during hospitalization are usual. Episodes of heart failure are among the most frequent complications.

**Objectives:** Analyze the prevalence of episodes of heart failure among patients admitted for hip fracture and a history of heart failure based on whether they were monitored by Internal Medicine or Cardiology before decompensation.

**Material and methods:** A descriptive analysis of patients admitted for hip fracture in the Trauma and Orthopedic Unit that had a history of heart failure decompensation and performed an episode during hospitalization. Those patients who had a previous monitoring by Internal Medicine and Cardiology, with those cases were Internal Medicine and Cardiology were asked for dyspnea or edema, with the final diagnosis of decompensated heart failure: two groups were compared.

**Results:** From June 2008 to December 2014, 990 patients admitted for hip fracture were presented to Internal Medicine and Cardiology. Of these patients, 79 (7.9%) had a documented history of heart failure. 34.1% (27p) developed heart failure during admission, of which 44.4% (12p) were in prior to the episode monitoring and 55.6% (16p) developed in the acute phase.

**Conclusions:** There is a slight decrease in the prevalence of cardiac decompensation in patients admitted for hip fracture and a history of heart failure if a previous follow up is performed by Internal Medicine and Cardiology.

**P1874**

**Prognostic value of procalcitonin in a heart failure cohort**

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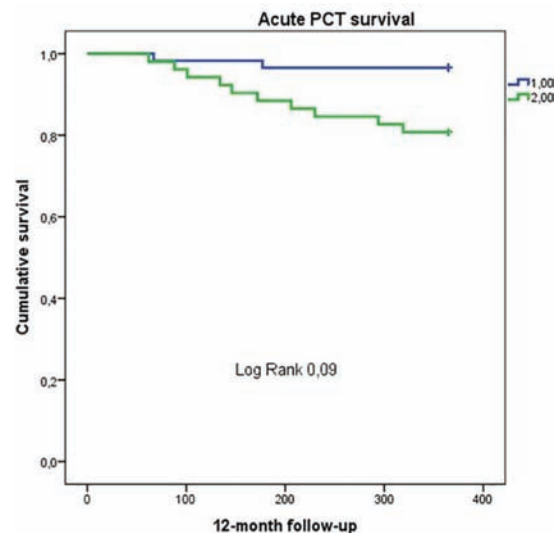
**Introduction:** Recent studies have shown that Procalcitonin (PCT) rises in some noninfectious inflammatory conditions such as Heart Failure (HF). Proinflammatory citoquines and endotoxines are released from congestive bowel and stimulate PCT synthesis, hence higher levels could be related to severity of HF.

**Purpose:** To analyse prognostic value of PCT concentrations measured during acute heart failure (AHF) and after stabilization.

**Methods:** Prospective study including patients consecutively admitted for an AHF. PCT was measured during first 24 hours of admission and one month after discharge. Patients were followed-up for unless 12 months. We assessed prognosis (one year mortality and readmission rate) according to concentrations of PCT during acute and stable phase of HF. SPSS 20.0 version was used for statistic analysis.

**Results:** One hundred and fourteen patients (47.4% men), mean age 78.32 years (CI 95% 77-80) were included. PCT was similar between patients admitted for decompensated AHF, either due to infectious or non-infectious disease (0.19 vs. 0.08, p 0.212). Total mortality at one-year was 10%. A concentration of PCT at admission above the median significantly correlated with mortality (19.2% vs 3.4%, p 0.012). Among patients whose PCT levels remained above the median one-month after discharge, there was a non-significant higher mortality (5.4% vs 16.4%, p 0.07), but significant mortality rate in the third tertile of PCT (20% in the 3rd tertile vs. 2.6% in the 1st tertile, p 0.018). A cut-off concentration of PCT at admission of 0.062 ng/ml had the best sensitivity (75%) and specificity (62%) in predicting short-term mortality.

**Conclusions:** Procalcitonin concentration measured during AHF, but not after stabilization, correlates with higher risk of death at one year. PCT may help stratify the risk of death after an acute decompensation of HF.



Acute PCT Survival

**P1875**

**Cardiogenic shock: what to expect?**

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**Purpose:** Cardiogenic shock (CS) is a state of end-organ hypoperfusion due to cardiac failure. The definition of CS includes hemodynamic parameters: persistent hypotension (systolic blood pressure < 80 to 90 mm Hg or mean arterial pressure 30 mm Hg lower than baseline) with severe reduction in cardiac index (< 1.8 L/min/m<sup>2</sup> without support or < 2.0 to 2.2 L/min/m<sup>2</sup> with support) and adequate or elevated filling pressure (eg, left ventricular [LV] end-diastolic pressure>18 mm Hg or right ventricular [RV] end-diastolic pressure>10 to 15 mm Hg). The incidence of CS according to the registries is between 4-11%. The leading cause is acute coronary syndromes (ACS). The purpose of our study was to describe the characteristics of patients from a single center with the diagnosis of cardiogenic shock.



## 61687. Patients characteristics and evolution

Case	Sex / Age	BMI (m2)	Duration of support (days)/ Number of devices	Diagnosis	LVEF (%)	Preimplantation support	Lactate (mmol/l)	Creatinine (mmol/l)	GPT (mg/dL)	Complications	Final situation
1	Female / 38	1.4	16 / 2	RCM	27	NA / DB	1.6	1.3	68	Hemolysis. IH	HT
2	Female / 48	1.5	17 / 2	STEMI. Killip IV	30	IABP/ NA	1.2	1.5	205	Hemolysis. Retroperitoneal bleeding.	HT
3	Male / 45	2.0	3 / 1	STEMI. Killip IV	25	IABP / NA	2.2	1.9	112	Acute arterial ischemia	Deceased
4	Male / 36	1.9	2 / 1	Idiopathic DCM	20	NA / DB	1.0	1.1	48	None	HT
5	Male / 65	1.6	2 / 1	Idiopathic DCM	20	DB	1.0	1.4	34	Hemolysis	HT
6	Male / 18	1.7	5 / 1	Idiopathic DCM	15	NA / DB	0.8	1.2	64	None	HT
7	Male / 32	1.6	4 / 1	Idiopathic DCM	18	DB	2.2	1.5	356	None	HT

BSA: Body surface area; RCM: Restrictive cardiomyopathy; STEMI: ST-segment elevation myocardial infarction; DCM: Dilated cardiomyopathy; LVEF: Left ventricular ejection fraction; NA: Noradrenaline; DB: Dobutamine; IABP: intra-aortic balloon pump; HT: Heart transplantation; IH: Intracranial hemorrhage

**Methods:** We reviewed retrospectively the medical records of 28 patients with CS who were hospitalized for heart failure in a single advanced heart failure unit between June 2009 and August 2013. Data regarding demographic, clinical, blood tests and echocardiograph parameters were collected in all patients. We measured the incidence of heart transplantation and cardiac death. Median follow-up time was 730 months.

**Results:** We retrospectively analyzed 30 patients (20 (66.7%) males) with a mean age of 64 +/- 15.8 years old. At admission, 25% of the patients had ACS, 14.3% ventricular arrhythmias and 14.3% valvular disease. The mean ejection fraction was 32 +/- 13.7% and atrial natriuretic peptide was 2457 +/- 666 pg/mL. The mean hospitalization time was 12 +/- 11 days. During the follow-up time, 8 patients (29%) with CS received a heart transplant. The long-term mortality was about 43%.

**Conclusions:** Despite improvements in reperfusion strategies and more frequent use of ventricular assist devices, mortality from CS remains high (around 50%). The heart transplantation can be a powerful tool in selected patients to reduce such catastrophic results.

## P1876

## "Should I stay should I go" is determined by beta blockers

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**Background:** Length of stay (LOS) remains as an important driver of heart failure (HF) hospitalization costs. The longer LOS also relates to higher rates of subsequent readmission and mortality. Therefore, it is important to determine those patients who will have longer LOS.

**Methods:** A total of 172 acutely decompensated, biventricular HF patients (33% females) were evaluated. Usage of Angiotensinogen Converting Enzyme Inhibitor/Angiotensin Receptor Blocker, Beta blocker, Mineralocorticoid Receptor Antagonist, diuretic before decompensation was recorded. The median LOS was six days, and the patients were classified into two groups: those with LOS ≤6 days and those with LOS >6 days

**Results:** The mean age was 69 ± 11 years. Patients with longer LOS were older (72 ± 9 vs 67 ± 12, p = 0.004) had significantly higher BUN [35 (6-97) vs 27 (8-92), p = 0.018], higher creatinine (1.6 ± 0.8 vs 1.3 ± 0.7, p = 0.014), higher systolic pulmonary artery pressure (48 ± 15 vs 42 ± 13, p = 0.015), and had significantly lower total cholesterol [115 (70-259) vs 151 (53-262), p = 0.004], lower triglyceride [70 (33-298) vs 91 (32-379), p = 0.006], lower hemoglobin and sodium levels (131 ± 3 vs 132 ± 4, p = 0.001; 12 ± 2 vs 13 ± 2, p = 0.047 respectively). Furthermore, the ratio of Atrial Fibrillation (AF) (60% vs 20%, p < 0.001) and moderate-severe Tricuspid regurgitation (74% vs 57%, p = 0.041) were higher in patients with longer LOS. Although the other medications prior to hospitalization were similar, the ratio of prior Beta Blocker (BB) usage were lower in patients with longer LOS than patients with shorter LOS (72% vs 89%, p = 0.008). In the multivariate logistic regression with forward stepwise model; older age (OR: 1.051, 95%CI: 1.009-1.096, p = 0.017), presence of AF (OR: 6.919, 95%CI: 2.867-16.696, p < 0.001), lower sodium (OR: 0.855, 95%CI: 0.758-0.964, p = 0.010) and lower hemoglobin levels (OR: 0.812, 95%CI: 0.669-0.986, p = 0.036) associated with increased risk of longer LOS, but prior usage of BB (OR: 0.245, 95%CI: 0.087-0.688, p = 0.008) associated with decreased risk of longer LOS in patient with biventricular HF after adjustment for variables found to be statistically significant in univariate analysis.

**Conclusion:** It would appear that in a cohort of acutely decompensated biventricular HF patients, prior usage of BBs independently predicted shorter LOS.

## P1877

## Early experience with percutaneous ventricular assist device Impella CP in cardiogenic shock

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**Introduction:** Cardiogenic shock (CS) is a therapeutic challenge with high mortality. Percutaneous ventricular assist devices (PVAD) are less invasive devices that could provide adequate hemodynamic support in these patients. The Impella CPTM is a new axial flow PVAD capable of providing up to 4L/min flow. The results of Impella CPTM support in CS are not disclosed.

**Methods:** We describe our initial experience with Impella CPTM in CS: Degree of support obtained, complications and final outcome of patients.

**Results:** From June 2014 to August 2015, 9 Impella CPTM were implanted in 7 patients with refractory CS (Average age 40 years [18-65]; 71% male). All patients were receiving combinations of catecholamine (71% noradrenaline) and 2 had intra-aortic balloon pump. The flow provided by the device was 2.9 ± 0.4 L/min (range 2-3.2). The mean duration of support was 7 days. Hemodynamic stabilization was achieved in 5 cases (71%) (patients with low body surface area [BSA], 1.4 to 1.7 m<sup>2</sup>), with mean arterial pressure between 65 and 94 mmHg two days post-implant, without increasing catecholamines. There was a device failure in two cases: One case presented acute arterial ischemia forcing its urgent withdrawal and in the second one the hemodynamic support provided was not enough (urgent heart transplant).

Complications were: hemolysis (5 cases), retroperitoneal bleeding (1), arterial ischemia (1), system dysfunction (1) and intracranial hemorrhage (1). Six patients got a heart transplant, they are all alive and without medium-term sequelae.

**Conclusion:** The Impella CPTM device provided sufficient hemodynamic support in 5 of 7 patients with CS of various etiologies, all with low BSA. The incidence of complications was significant. Larger series are necessary to establish the role of this PVAD.

## P1878

## Non invasive evaluation of hemodynamic effects of continuous positive airway pressure in patients with cardiogenic shock.

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**Background:** beneficial effects of continuous positive airway pressure (CPAP) in patients (pts) with acute pulmonary edema (APE) have been already demonstrated. However, few it is known regarding the effects of CPAP on pts with cardiogenic shock (CS). This lack of data is mainly due to concerns about possible harmful hemodynamic effects in this subgroup of pts. The purpose of our study is to evaluate the hemodynamic effects of CPAP, measured by echocardiography, in pts with CS.

**Methods:** we evaluated 10 pts with acute CS to our ICU department of which. Acute HF was defined as a left ventricular ejection fraction < 0.45 associated with at least one criteria between dyspnea at rest, pulmonary rales or radiological signs of pulmonary congestion. CS defined as presence of almost three criteria: urine output < 0.5ml/Kg/h, mean blood pressure < 65 mmHg,

cardiac index < 1,8 L/min/m<sup>2</sup> without pharmacological support or < 2,2 L/min/m<sup>2</sup> with support; LV filling pressures > 15-18 mmHg, arterial lactates > 2mmol/l, central venous oxygen saturation < 65%. Echocardiographic hemodynamic assessment was performed at presentation (T0) and at 30 minutes (T1), 24 h (T2) and 48 h (T3) after C-PAP beginning. Patients were treated with a different level of positive end expiratory pressure (PEEP 5-7,5-10 mmhg) chosen according to clinical needs.

**Results:** mean cardiac output (CO) significantly increased during CPAP therapy (3.5 l/min at T0 vs. 4.16 l/min at T2; p=0.02) as well as mean stroke volume index (19,1 ml at T0 vs. 26,2 ml at T2; p=0.04), while the mean cardiac index (CI) increased but not significantly (2.05 l/min/m<sup>2</sup> at T0 vs. 2.48 l/min/m<sup>2</sup> at T2; p=0.07). There were no significant variation of systolic, diastolic and mean systemic blood pressure during the two days of treatment while mean ejection fraction improved at 48 h (26.1 % vs. 31.6%, p=0.04). The WP is reduced already at 30 min but not significantly (21,8 vs 16,0 at T2 p=0.02). Right ventricular function did not deteriorate after application of PEEP (TAPSE 14,6 ± 3,1 at T0 compared to 15,2 ± 1 to T1) and central venous pressure (CVP) has increased but not significantly (mean 8.6 ± 4,6 at T0 compared to 9,8 ± 4,8 to T1). Systolic pulmonary pressure did not vary significantly after C-PAP (38,72 ± 13,66 vs 37,31 ± 13,15 p:0.8). We have not had adverse cardiovascular events. All patients were discharged alive.

**Conclusion:** C-pap is safe in pts with CS and provides significant hemodynamic support even in this subgroup of patients. These encouraging results should be confirmed with larger numbers or maybe dedicated trials.

### P1879

#### Urinary composition predicts diuretic efficiency of hypertonic saline solution with low-dose furosemide in patients with heart failure

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**Background:** We have reported that combination of hypertonic saline solution with furosemide enhances diuretic effect of furosemide in patients with acute decompensated heart failure (ADHF). However, it is not yet clear that which factors determine the diuretic efficiency of the combination therapy.

**Purpose:** The purpose of this study was to identify predictive factors for diuretic efficiency of the combination therapy.

**Methods:** This study was a prospective, observational. Consecutive 29 patients with ADHF were enrolled. At baseline, patients were underwent biochemical tests and echocardiography. 500ml of 1.7% hypertonic saline containing 40 mg of furosemide were administered at speed of 20 ml/hour along with oral standard heart failure medication. We explored the associations between 24-hour urinary volume (24-h UV) and the baseline examination data. Patients were divided into 2 groups according to the median value of 24-h UV (median: 3300 ml).

**Result:** Mean 24-h UVs were 4081 ± 602 ml and 1539 ± 696 ml for group over the medium and group the median and below, respectively. There were no significant differences in baseline, demographic data, serum creatinine levels, serum and urinary sodium levels, plasma osmolality, and echocardiographic parameters between 2 groups. There was a significant difference in urinary urea nitrogen-to-creatinine ratio (UUN/Cr) (7.2 ± 2.2, 4.9 ± 1.7 respectively, p < 0.05). Receiver operating characteristics analysis identified UUN/Cr 5.1 as the optimal cut-off point for the prediction of 24-h UV more than the median (AUC 0.80 with sensitivity of 0.57 and specificity of 0.93).

**Conclusion:** This study suggested that UUN/Cr at baseline can be a predictive factor for the diuretic efficiency of hypertonic saline solution with furosemide therapy in patients with ADHF.

### P1880

#### Defining the upper limits of "normal for their NT-proBNP" troponin T levels in acute decompensated heart failure patients

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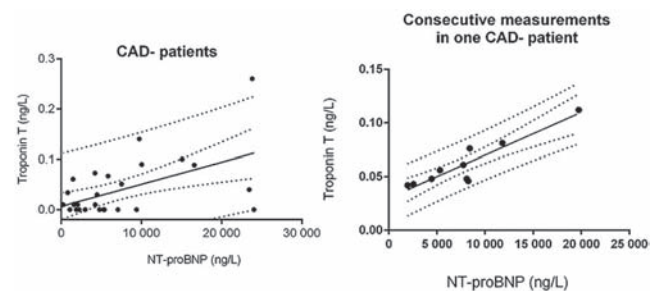
**Background:** Troponin T release is frequently observed in acute decompensated heart failure (ADHF) patients, and may be interpreted as the result of increased end-diastolic wall stress (EDWS), supply or demand ischemia, and/ or the result of obstructive coronary artery disease (CAD). As increased EDWS is the main determinant of natriuretic peptide release, troponin release that is only dependent on increased EDWS should correlate with NT-proBNP. If corrected for the level of

NT-proBNP, the level of troponin release may thus be better interpreted as 'being normal for the level of natriuretic peptide' or as indicative of the presence of CAD. We investigated this question in ADHF patients without obstructive epicardial CAD.

**Methods:** Our study population was assembled from 2 European cohorts with ADHF patients. Patients were selected with both troponin T and NT-proBNP measured at admission, and in whom in-hospital coronary angiography (CAG) was performed (n=80). We assessed the association between troponin T (4th generation and high sensitive) and NT-proBNP in patients without CAD (CAD-) using linear regression analysis. CAD was defined as >70% stenosis in at least one vessel on CAG.

**Results:** A total of 29 CAD- patients (median age 60 (51-70), 59% male) was studied. Median troponin T and NT-proBNP levels were 0,029 ng/L (0,03-0,06) and 4776 ng/L (1765-9562) respectively. In CAD- patients, troponin T and NT-proBNP were correlated (r<sup>2</sup> = 0.3, p = 0.003) and troponin T levels did not exceed 0.24 ng/L up to an NT-proBNP level of 25000 ng/ml (Figure). In one CAD- patient with 10 admissions over 5 years, troponin T (up to 0.11) and NT-proBNP (up to 20000) were highly correlated (r<sup>2</sup> = 0.84, p < 0.001).

**Conclusion:** In ADHF patients without obstructive epicardial CAD, there is a significant correlation between admission troponin T and NT-proBNP. Using upper troponin T limits that are 'normal for their NT-proBNP' may increase the diagnostic yield of CAD in ADHF patients suspected for CAD.



Troponin T & NT-proBNP in CAD- ADHF pts

### P1881

#### Serial measurement of ST-2 concentration in patients with decompensated acute heart failure (AHF)

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**Background:** Sulfotransferase 2 (ST-2) is an evolving marker for risk stratification in patients with cardiovascular disease. As a marker of cardiac stress and cardiomyocyte fibrosis it seems to yield benefits in risk stratification and may also be useful for therapy guidance in patients with heart failure.

**Methods:** Prospectively, 99 patients who attended the Emergency Department of the Charité Virchow Klinikum with acute decompensated heart failure were enrolled in this study. Blood samples were taken at admission and, if applicable, after 1, 2, 3, 5, 10 days and on the day of discharge if thereafter. ST-2 was measured in August 2015 in EDTA-Plasma using a monoclonal sandwich ELISA assay (Presage<sup>®</sup> Critical Diagnostics, San Diego, CA). A follow-up was conducted at discharge and after 1 year.

**Results:** Patients had a mean age of 74 years (± 10) and the majority was male (54.5%; n=54). Within 1 year, 20.0% of all patients died (n=17) and 68.4% were rehospitalized (n=54). Median ST-2 values were higher in non-survivors (median 53.17 ng/ml; IQR: 32.68-80.97) as compared to survivors (76.91 ng/ml; IQR: 59.94-194.22) at admission and in following blood draws. ST-2 showed a falling pattern with an increase on day 10 in non-survivors while survivors had in median constant ST-2 values (see figure 1).

**Conclusion:** ST-2 might be helpful in early risk-stratification of patients presenting to the Emergency Department with acute decompensated heart failure. Additionally ST-2 might add to current diagnostic criteria used for therapy guidance in these patients (BNP, LVEF) and serial measurements might support therapeutic decision making and identification of patients with a poor prognosis.

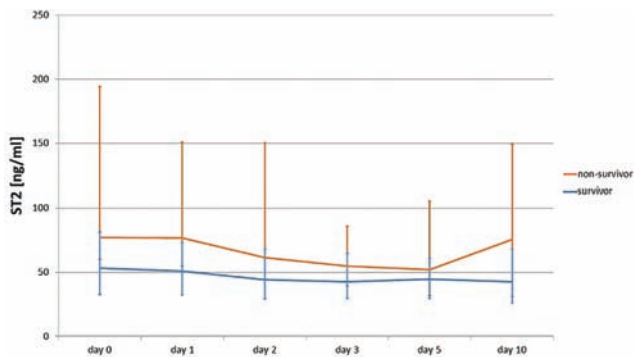


Figure 1: serial ST-2 concentrations in

### P1882

#### The effect of enhanced patient education and post discharge follow up on 30 day readmission rates after a heart failure admission.

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**Background:** Readmissions within 30 days after a heart failure (HF) discharge are associated with negative patient outcomes, increased hospital costs and likelihood of reimbursement penalties. With the goal of achieving greater patient engagement and knowledge, we implemented the HeartLink program; in this report, we analyzed the program's effect on the 30 day readmission rate.

**Methods:** Patients with the primary admission diagnosis of HF were identified through daily screening of the electronic medical record (EMR) or via consult order to the HeartLink nurses (1 registered nurse, 1 nurse practitioner). Patients discharged to care facilities or hospice were excluded. Between April and August 2015, 303 patients met the above criteria and received the standard HF care (written discharge instructions on core HF topics, daily HF education by staff nurses, 72-hour telephone follow up, and office follow up within 7 days of discharge). Of these patients, 75 were identified as being at higher risk of readmission based on chart review and a proprietary risk calculator that classifies patients as being low, medium, high and very high risk of readmission. These patients were personally seen by the HeartLink nurses for enhanced evaluation and treatment and formed the HeartLink group: 1) 15-60 minute one-on-one education session, featuring the teach-back method to focus on self-care. 2) screening for financial/social barriers to treatment plan (no scale, inadequate transportation, inability to fill medications, inability to read a food label), and 3) were referred to other disciplines (social work, dietician) as needed. All cause 30 day-readmissions to The our hospital were recorded for the control and intervention (HeartLink) groups.

**Results:** The 30 day readmission rates for the control (n = 228) and HeartLink (n = 75) groups were 18% and 12%, respectively. This reduction in readmissions is realized despite higher estimated risk in the HeartLink group: the proportion of patients assigned to high or very high risk of readmission was 21% for the control group and 41% for HeartLink.

**Conclusion:** In addition to existing best practice HF education and follow-up, incremental HF education provided prior to discharge by a certified HF RN/NP, is effective in reducing all-cause 30-day readmission rates.

### P1883

#### MAGGIC score in heart failure: does left ventricular ejection fraction matter?

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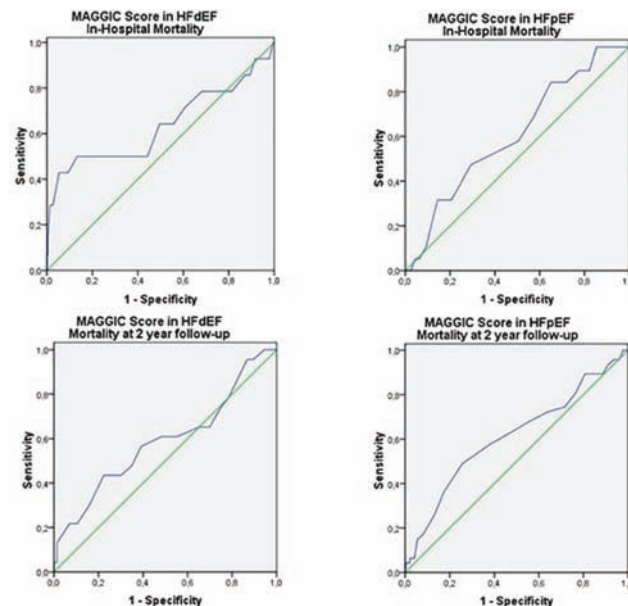
**Introduction:** In the MAGGIC meta-analysis<sup>†</sup>, Pocock et al proposed the application of a risk score capable of predicting which patients with heart failure (HF) would have a worse prognosis.

**Purposes:** Application of the MAGGIC score in a population of patients hospitalized for HF. Correlation of the results with in-hospital mortality and after 2 years follow-up. Comparison of the accuracy of the score in patients with HF with preserved ejection fraction (HFpEF) and depressed ejection fraction (HFdEF).

**Methods:** The MAGGIC Score was calculated in patients hospitalized for heart failure. Clinical, analytical, and echocardiographic parameters were evaluated. The patients were divided into two groups: Group A with HFdEF vs Group B with HFpEF. A cut-off value for ejection fraction of 40% was used, which was the reference value used in the meta-analysis.

**Results:** Total sample of 1007 patients, 50.8% male, mean age  $77 \pm 10$  years. When considering in-hospital mortality, the following ROC curves were ascertained: in the group with HFdEF, a AUC of 0.635 and  $p=0.091$  and in the group with HFpEF, a AUC of 0.607 and  $p=0.112$ . Regarding mortality at 2 years follow-up, the ROC curves reveal a AUC of 0.586 and  $p=0.180$  in the HFdEF and a AUC of 0.611 and  $p=0.013$  in the group with HFpEF.

**Conclusion:** In this population of patients with HF, the score proposed in the MAGGIC meta-analysis did not reveal statistical power in predicting poor prognosis in both HF groups. It is extremely difficult to create risk scores, particularly in patients with HF, since it is a very heterogeneous group. More studies are needed to develop scores with actual utility in the real world.



### P1884

#### Mechanical support by intra-aortic balloon pump in non-ischemic cardiogenic shock

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**Background:** Intra-aortic balloon pump (IABP) did not improve survival in cardiogenic shock complicating acute myocardial infarction (AMI) in the IABP-SHOCK II trial. However, the effect of IABP in other settings of drug-refractory heart failure deteriorating to cardiogenic shock has been less investigated.

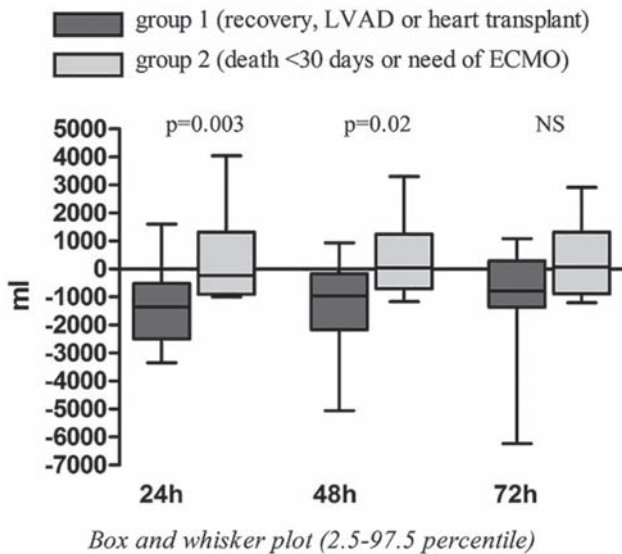
**Purpose:** Our aim was to evaluate haemodynamic changes and clinical outcomes of patients supported by IABP for non-ischemic cardiogenic shock.

**Methods:** We reviewed the charts of patients treated by IABP as the initial mechanical circulatory support between 2011 and 2015, excluding patients who had AMI or cardiac surgery in the past 30 days. We compared the patients who were successfully weaned or bridged to left ventricle assist device (LVAD) or heart transplantation (group 1) with those who died within 30 days or needed extracorporeal membrane oxygenation (ECMO; group 2). Continuous outcomes were evaluated by Mann Whitney U tests.

**Results:** We identified 27 patients supported by IABP for 5 days (interquartile range [IQR] 3-7). Lactate decreased from 3.2 (IQR 2.1-7.8) to 1.6 (IQR 1.2-3.5) mmol/L ( $p<0.001$ ) at 12 hours and hyponatremia was resolved at 48 hours. In group 1, 17 patients (63%) were bridged to either recovery ( $n=7$ ), LVAD ( $n=4$ ) or transplant ( $n=6$ ). In group 2, 10 patients (37%) died <30 days ( $n=8$ ) or needed support by ECMO ( $n=2$ ). The hemodynamic profile improved in group 1, as compared to group 2, already at 24 hours: lactate and heart rate were lower ( $p=0.009$  and  $0.006$ , respectively), and fluid balance was more negative ( $p=0.003$ ).

**Conclusion:** In severe heart failure sliding to cardiogenic shock, IABP can be used to improve the haemodynamic profile of patients, thus bridging them to recovery, advanced mechanical support or heart transplantation.





Fluid balance after IABP insertion

**P1885****The effects of urapidil and nitroglycerin in acute heart failure patients with hypertension: a randomized multi-center parallel-control study.**

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**Background:** Acute heart failure (AHF) is a common cause of hospitalization with high morbidity and mortality. Evidence based treatment of AHF is less and Urapidil improves cardiac function in heart failure (AHF) by reducing cardiac load.

**Objective:** To compare the hemodynamic responses, efficacy and safety of urapidil and nitroglycerin (NG) in acute heart failure patients with hypertension.

**Methods:** 248 patients with New York Heart Association class from II to IV were consecutively enrolled in 10 study centers from January 2012 to December 2013. The patients were randomized to receive urapidil(mrco-pump velocity:  $99.77 \pm 73.99 \mu\text{g}\cdot\text{min}^{-1}\cdot\text{kg}^{-1}$ , n=123) or nitroglycerin(micro-pump velocity:  $10.18 \pm 5.35 \mu\text{g}\cdot\text{min}^{-1}\cdot\text{kg}^{-1}$ , n=125) within 48 hours. All patients were monitored for blood pressure (BP), heart rate, NT-pro BNP levels and ultrasonic cardiogram at baseline, 48 hours and 7days; and major adverse cardiovascular events (MACE) at 7-day and 30-day following-up were recorded.

**Results:** Baseline characteristics of patients were similar between groups. (1) NT-proBNP decreased following the treatment of urapidil or nitroglycerin, although the difference of NT-proBNP level was't significant between the two groups(P=0.85); Urapidil group had higher left ventricular ejection fraction (EF) and end-diastolic volume (EDV) than the nitroglycerin group at 48 hours and 7 days(all P<0.05), the end-systolic volume (ESV) also decreased significantly (P=0.039) in urapidil group at 7 days. (2)The changes in total cholesterol (TCHO) and Low density lipoprotein (LDL) level were significant between the two groups at 48 hours and 7 days.( $\Delta$ TCHO: 48h, P=0.016; 7day, P=0.010;  $\Delta$ LDL 48h, P=0.031). (3) The creatinine level was significantly higher in urapidil patients at baseline (P=0.024), while the changes in creatinine at 48 hours and 7 days was similar among these two groups( $\Delta$ creatinine: 48h, P=0.69; 7day, P=0.74). (4) Within 30 days follow-up, the incidence of cardiac function deterioration and re-hospitalization was lower in urapidil group than in nitroglycerin group (P<0.001).

**Conclusions:** Urapidil was as safe and effective as Nitroglycerin on the treatment of acute heart failure patients with hypertension. Urapidil demonstrated better efficacy than nitroglycerin on improving cardiac function, and decreasing the rate of heart failure deterioration and re-hospitalization after 30 days follow-up. While urapidil also had the trend to better the lipid metabolism and renal function during the treatment. This contribution of urapidil may due to its attenuating cardiac pre-/after-load.

**P1886****Heart failure with preserved ejection fraction: patient characteristics, outcome and prognostic factors.**

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**Introduction:** Heart failure (HF) represents a major health concern. Classically associated with cardiac dilatation and impaired cardiac contractility, this clinical syndrome has been widely recognized to occur even when systolic function is preserved - HF with preserved ejection fraction (HFpEF). HFpEF is now known to be as frequent as HF with reduced ejection fraction (HFrEF) and is responsible for high morbidity and mortality. However, data on the prevalence, clinical characteristics, outcomes and risk factors of patients hospitalized with HFpEF are limited.

**Purpose:** This study was performed to analyze epidemiological features and outcomes of patients with HFpEF, comparing to those with HFrEF and to identify prognostic factors.

**Methods:** An observational study was conducted with data prospectively collected from an internal medicine department. All consecutive patients hospitalized with acute HF during the year 2014 were included. Demographic, clinical, laboratorial and transthoracic echocardiograms data were collected. To determine outcomes (rehospitalization, emergency admission, death), patients were followed for one-year. HFrEF was defined as ejection fraction  $\leq 50\%$  and HFpEF as ejection fraction  $> 50\%$ ,  $E/e' > 15$  or  $E/e' > 8$  and BNP  $> 220\text{pg/ml}$ .

**Results:** 255 patients included, with  $81 \pm 8$  years, 146 women. 61% had ejection fraction  $> 50\%$ . Patients with HFpEF were more likely to be older and female (p<0.01), to have history of coronary heart disease (CHD) (p=0.03), hypertension (p=0.05) or dyslipidemia (p=0.03) and to have an infectious disease as precipitating factor (p=0.01). Mortality and rehospitalization rates for patients with HFpEF (27.5% and 61.2%) weren't significantly different from those with HFrEF. The hospital length of stay was similar between the 2 groups. Patients with HFpEF had more episodes of decompensated HF requiring treatment at the emergency department (p=0.05). Univariate statistical analysis determined that dyslipidemia (p=0.03) and CHD (p=0.05) were associated with need of rehospitalization and chronic kidney disease (CKD) was also associated with mortality (p=0.02). Multivariate statistical analysis with logistic regression showed that mortality was related with CKD (OR(95% CI)=2.7 [1.1-6.5], p=0.03).

**Conclusions:** Preserved systolic function was found in the majority of patients. Those were more likely to be older and female, with coronary heart disease, hypertension or dyslipidemia and to have an infectious disease. One-year readmissions and mortality were high both in HFpEF and HFrEF groups but patients with HFpEF required more often emergency care. In this population CKD, CHD and dyslipidemia were related with poor prognosis.

**P1887****The association between cystatin c and in-hospital mortality in acute decompensated heart failure: 3-years follow-up study**

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**Objectives:** HF is often accompanied by impaired renal function, and the co-existence of both conditions is associated with an increase in cardiovascular risk and mortality. Cystatin C, an inhibitor of cysteine proteases of the cathepsin family has received considerable attention in recent years as a more accurate measure of renal function than serum creatinine based estimations. The present study aimed to investigate the relationship between in-hospital mortality in patients with ADHF and both cystatin C and N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels. Another aim was to assess if the out hospital mortality was related to in-hospital levels of cystatin C at a regular follow-up period (36 months).

**Methods:** Cystatin-C and NT-proBNP levels were measured in 57 consecutive patients hospitalized with acute decompensated heart failure (ADHF) with a glomerular filtration rate  $> 30 \text{ ml/min/1.73m}^2$  admission. Every patient was clinically followed for 3 years, and the primary clinical endpoint for this study was defined as the combination of any death from heart failure readmission and/or other reasons.

**Results:** During hospitalization 7 patients (12.3%) died. Patients who died during the in-hospital follow-up were more likely to be younger ( $47.4 \pm 17.5$  vs.  $60.8 \pm 15.8$ , p=0.043) and more likely to have a prior cerebrovascular accident (28.6% vs. 6.0%, p=0.048). Moreover, those patients who died had lower sodium concentrations ( $128.9 \pm 7.6 \text{ mmol/L}$  vs.  $135.5 \pm 5.1 \text{ mmol/L}$ , p=0.003), higher cystatin C ( $1.62 \pm 0.62 \text{ mg/L}$  vs.  $1.22 \pm 0.39 \text{ mg/L}$ , p=0.023) and NT-proBNP levels ( $1101.6 \pm 228.7 \text{ pmg/L}$  vs.  $577.2 \pm 585.5 \text{ pmg/L}$ , p=0.001) compared to survivors. In multivariate logistic regression analysis, no significant association was found between in-hospital mortality and NT-proBNP and sodium (p>0.05). However, cystatin C (OR: 12.311, 95% CI: 1.616- 93.764; p=0.015) and age (OR: 0.925, 95% CI 0.866- 0.990; p=0.023) were identified as independent predictors of mortality.

In correlation analysis, plasma cystatin C levels were correlated significantly with NT-proBNP ( $r=0.324$ ,  $p=0.014$ ) and GFR ( $r=-0.638$ ,  $p<0.001$ ) but not with age ( $p>0.05$ ). During a constant follow-up period (36 months), 38 patients died. In-hospital cystatin C levels were compared between the survivors and the patients who died. At 12-, 24- and 36-months follow-up the baseline cystatin C levels did not differ according to the survival ( $p>0.05$ ).

**Conclusions:** In patients with ADHF, assessment of in-hospital cystatin C levels may provide a better prediction of mortality compared to eGFR or NT-proBNP estimation. Although, higher cystatin C levels rendered relevant prognostic information in the setting of in-hospital adverse events, the prognostic significance of this marker did not persist during the post-discharge follow-up.

Table 1. Baseline characteristics of the study population.

Variables	In Hospital Survive n: 50	In Hospital Dead n: 7	p Value
Age (years)	60.8±15.8	47.4±17.5	0.043
Male gender n (%)	34(68.0%)	5(71.4%)	0.855
Diabetes Mellitus n (%)	15(30.0%)	4(57.1%)	0.154
Hypertension	24(48.0%)	5(71.4%)	0.246
Hyperlipidemia	12(24.0%)	1(14.3%)	0.566
Cigarette smoking	6(12.0%)	1(14.3%)	0.863
History of MI	9(18.0%)	2(28.6%)	0.507
History of SVD	3(6.0%)	2(28.6%)	0.048
History of PCI	5(10%)	1(14.3%)	0.729
History of CABG	6(12.0%)	1(14.3%)	0.863
New Diagnosis of HF	7(14%)	0(0.0%)	0.291
BMI (kg/m <sup>2</sup> )	26.1±4.9	22.4±3.8	0.062
Fasting Glucose (mg/dl)	113.6±48.7	124.7±49.1	0.559
Urea (mg/dl)	69.5±33.7	93.9±51.7	0.100
Creatinin (mg/dl)	1.15±0.43	1.27±0.61	0.784
Total Cholesterol (mg/dl)	136.5±35.8	127.0±38.9	0.518
Triglyceride (mg/dl)	85.6±34.5	106.6±38.2	0.138
Sodium (mmol/L)	135.5±5.1	128.9±7.6	0.003
Potassium (mmol/L)	4.3±0.6	4.2±0.7	0.794
Hemoglobin (g/dL)	12.4±1.9	11.5±1.2	0.218
LVDD (cm)	6.3±1.0	6.1±0.4	0.607
EF (%)	25.6±7.0	20.7±8.9	0.101
SPAP (mmHg)	43.0±11.5	40.9±10.2	0.638
Cystatin C (mg/L)	1.22±0.39	1.62±0.62	0.023
NT-proBNP (pg/mL)	577.2±585.5	1101.6±228.7	0.001
GFR (ml/dk)	72.8±30.0	74.3±44.8	0.907
Coceraft (ml/dk)	74.5±33.2	78.2±54.1	0.803
Follow-up time (day)	15.2±22.2	23.6±27.2	0.345

Table 1

## P1888

### Predictors of in-hospital mortality in a population of acutely decompensated heart failure patients

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**Background:** despite current therapeutic strategies organ (pulmonary, renal, hepatic) dysfunctions (AODs) are commonly encountered in the settings of ADHF patients (pts) leading to serious adverse implications on in-hospital clinical course and prognosis.

**Purpose:** the aim of our study was to investigate the levels of AODs in ADHF pts in a tertiary cardiology center; the main predictors of their in-hospital mortality and the influence of AODs in the complicated clinical course.

**Methods:** we prospectively analyzed in-hospital clinical and laboratory data on 937 ADHF pts from 2012 to November 2015: monitoring for cardio-renal syndrome type I (CRS), cardio-hepatic syndrome (CHS), diuretic resistance (DR), MELD score, dyspnea severity scale (DSS) was performed on a daily basis. Patients were stratified into four levels: 1 (absence of AODs), 2 (CRS present), 3 (CRS and CHS present); 4 (CRS & CHS & DR present). A composite endpoint (use of intravenous inotropes, DR, a prolonged in-hospital treatment-a week, pulmonary edema (PE), cardiac death) was defined a complicated clinical course; Cox proportional hazards models were used to define the role of AODs on the complicated clinical course and in-hospital mortality.

**Results:** between dead and alive groups there were significant differences in: age (69.7±0.6 vs 57.4±0.9,  $p<0.05$ ); CHS (70.1% vs 43.2%,  $p<0.0001$ ); cardiac index < 1.5 l/min/m<sup>2</sup> (63.6% vs 21.7%,  $p<0.0001$ ); MELD score (39.6±7.5 vs 17.3±8.5,  $p<0.0001$ ); DR (47.3% vs 12.4%,  $p<0.0001$ ); PE (81.6% vs 48.3%,  $p<0.0001$ ); no significant differences in sex (males)(65.7% vs 62.4%,  $p>0.05$ ); diabetes (32.7% vs 29.4%,  $p>0.05$ ); hypertension (18.7% vs 21.3%,  $p>0.05$ ), ischemic cardiomyopathy (67.2% vs 69.3%,  $p>0.05$ ). In Cox regression independent predictors of in-hospital mortality were: age HR 1.87 (95%CI: 1.15-2.34), hypotension on admission HR 2.3 (95%CI: 1.4-2.89), CRS HR 1.95 (95%CI: 1.3-3.04), CHS HR 2.1 (95%CI: 1.34-2.76), DR HR 2.43 (95%CI: 1.5-3.89), cardiac index < 1.5l/min/m<sup>2</sup> HR 2.64 (95%CI: 1.67-4.1). Comparing complicated clinical course HR (95%CI) of level

2 to 1 of ADHF pts was 1.57 (1.14-1.96), level 3 to 1 was 2.26 (1.62-3.78), and level 4 to 1 was 3.12 (1.89-4.37).

**Conclusions:** In our study main predictors of in-hospital mortality in ADHF patients were advanced age, hypotension on admission, cardio-renal syndrome and cardio-hepatic syndrome, diuretic resistance and low cardiac index. Presence of organ dysfunctions denotes an increased risk for complicated clinical course and should prompt adequate efforts to reduce costs, imposed by prolonged hospitalization and to improve survival.

## P1889

### Profile of patients admitted in emergency department with decompensated heart failure in a tertiary care centre in South India

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**Objectives:** India is fast becoming the diabetes capital of the world. With clustering of multiple risk factors, noncommunicable diseases is a major cause of morbidity, mortality and health burden in India. Heart failure (HF) is the converging point of many cardiovascular diseases and constitute a major public health problem. This study aims at analysing the profile of HF in patients coming to the emergency room (ER) with HF in a tertiary care centre in India.

**Materials and methods:** This is a prospective study conducted between April 2013 to March 2014 in an Hospital in India. Patients coming to the ER with complaints of breathlessness and having history and clinical examination suggestive of HF were included. Four sets of parameters - history, physical examination, laboratory investigations and imaging were collected. Patients with primary pulmonary, hepatic and renal cause of dyspnoea and those with glomerular filtration rate less than 30 ml/min were excluded.

**Results:** 153 patients were admitted during this period of which 132 were enrolled and 21 were excluded. 68(51.5%) were more than 65 years and 92(69.7%) were male. 76.55% had hypertension, 59.8% had diabetes, 73.5% had coronary artery disease (CAD) and 31.8% were smokers. 86.4% had pedal edema on presentation. 69.7% had desaturation on admission and 22% presented with cardiogenic shock. Anemia was found in 40.25%, hyponatremia in 35.6% and hyperurecemia in 56.1% cases. Mean value of NT Pro BNP was 27786+/-8258 in expired patients and 10838+/-1616 in survivors. 28% had LV ejection fraction (EF) less than 30%. 95.5% had LV systolic dysfunction (EF <50%). 28.7% had biventricular dysfunction. 22(16.7%) patients died. Length of hospital stay was 20.4days in expired patients and 7.9 days for the discharged patients.

**Conclusions:** In India diabetes and hypertension are the important comorbidities and CAD is much more frequent than dilated cardiomyopathy in patients presenting to ER with HF. NT Pro BNP values were very high and in-hospital mortality was also high. This may indicate that patients may present late in the course of their illness.

## P1890

### The blood pressure paradox in acute heart failure

nil

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**Background:** The lower blood pressure (BP) has been associated with poor outcome in patients with chronic heart failure, especially reduced ejection fraction (EF) and described as the "BP paradox". Whether that paradox is present in acute heart failure (AHF) remains changeable. We therefore investigated the rule of BP in patients hospitalized for AHF with both reduced and preserved EF.

**Methods and Results:** Our registry enrolled patients hospitalized for AHF. Hemographic and biochemistry data, echocardiographic characteristics, and BP on arrival were collected. Among a total of 2099 subjects (age 77±12 years, 66% men), 848 patients died during follow up. The group with higher BP had higher proportion of hypertension and diabetes, lower levels of hemoglobin and estimated glomerular filtration rate (eGFR), and higher left ventricular EF. As the systolic BP level was increased, the risk of mortality was decreased in those with reduced EF [HR and 95% CI per-1SD, 0.881 (0.778-0.998)] but not in those with preserved EF [0.951(0.860-1.051)]. The relation between systolic BP and mortality in the patients with preserved EF may be non-linear and U-shaped. (Figure 1)

**Conclusions:** The effect of systolic BP for mortality were different between those with reduced and preserved EF. The BP paradox might be absent in those patients hospitalized for AHF with preserved EF.

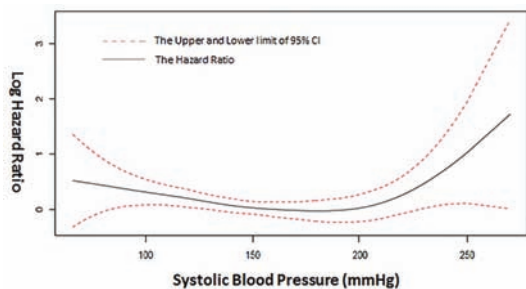


Figure 1

**P1891**

**A novel score for early risk stratification in acute heart failure**

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**Introduction:** Early risk stratification of patients admitted with acute heart failure (AHF) is important. As the prognostic value of admission BNP is limited, there is a need for an admission score to early risk stratify AHF patients.

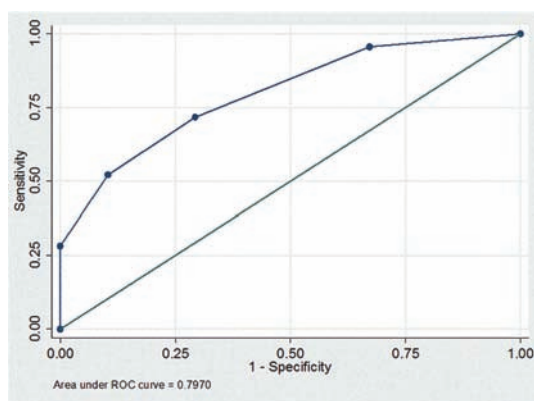
**Purpose:** To develop a risk score to early risk stratify patients admitted with AHF.  
**Methods-Design:** 104 consecutive patients (age, 73.5 ± 12.0 years; male gender, 55.8%; LVEF 38.9 ± 14.7%) admitted with AHF between January 2014 and July 2014 were enrolled in the study. Clinical, echocardiography and laboratory assessment were performed at admission. The endpoint of the study was the composite of death from any cause and/or rehospitalization for HF during 1-year of follow up.

**Results:** The independent prognostic factors of 1-year survival or rehospitalization are listed in the Table. Based on the odds ratios of the multivariable logistic regression we developed a model assigning 2 points for the absence of hypertension (HTN), 1 point for history of coronary artery disease or myocardial infarction (CAD/MI), and 1 point for an admission red cell distribution width (RDW) value ≥15.0 (median value). This simple score predicted the study end-point with an area under the curve of 0.80 (Figure).

**Conclusions:** These preliminary findings suggest that a simple admission score, consisting of HTN history, CAD/MI history, and RDW, may accurately risk stratify AHF patients. Further prospective validation of this score is necessary.

Variable	Odds Ratio (95% CI)	P Value
Hypertension	0.14 (0.05, 0.39)	< 0.0001
CAD/MI	3.88 (1.47, 10.24)	0.006
RDW ≥15.0	3.09 (1.22, 7.83)	0.02

Multivariable logistic regression



ROC curve for the prognostic score

**P1892**

**The use of lymphocyte-to-monocyte ratio in patients with heart failure**

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**Background and aim:** Leukocytes and their subpopulation have an important role in the progression of the heart failure (HF). Recent data show that the lymphocyte-to-monocyte ratio (LMR) have a prognostic value in patients with acute decompensated heart failure (ADHF). Our aim is to correlate LMR with the severity of disease in patients with HF.

**Methods:** We included 423 consecutive heart failure patients admitted to our clinic. LMR was analyzed in relation to NYHA class, NT-proBNP levels, ejection fraction (EF) and length of hospital stay (LOS), as markers of heart failure severity.

**Results:** The mean age was 69.47 ± 11.06 years. LMR was correlated with NYHA class (r = -0.451, p < 0.0001), NT-proBNP (r = 0.485, p < 0.0001), EF (r = 0.307, p < 0.0001) and LOS (r = -0.372, p < 0.0001).

In ROC curve analysis, LMR predicted ADHF with an AUC of 0.714 (95% CI 0.668-0.757, p < 0.0001), NYHA 4 class with an AUC of 0.745 (95% CI 0.700-0.784, p < 0.0001) and EF <35% with an AUC of 0.646 (95% CI 0.597 - 0.692, p = 0.0001) with a cut-off value calculated by the Youden index of LMR <2.79, <2.59 and <2.41, respectively. In multivariate logistic regression LMR <2.5 was an independent predictor of ADHF (OR 4.14, p < 0.0001), and NYHA 4 class (OR 4.64, p < 0.0001).

**Conclusion:** LMR, a cost-effective and easily-accessible biomarker, is an independent predictor of ADHF and NYHA IV class in patients with HF.

**P1893**

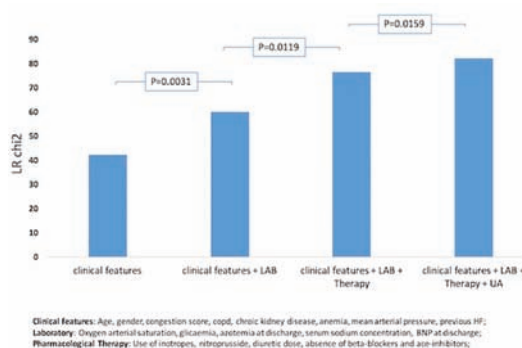
**Uric acid confers additive prognostic information in patients with acute heart failure**

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**Background:** Serum uric acid (UA) has been described as an important prognostic marker and useful for metabolic, and functional staging in both chronic and acute heart failure (HF). However, the predictive ability of serum UA when added to known predictors of HF mortality in the setting of acute HF is not well known.

**Methods and Results:** One-hundred and ninety-six patients (age 75 ± 11 years, 80% with ejection fraction ≤45%) admitted for acute HF were followed-up for a mean time of 20 ± 16 months after discharge. The primary end-point was a combination of all-cause death and/or admission for HF. Median UA values was 7.2 mg/dl (interquartile range 5.6 - 9.5). Serum UA was independently associate to the primary end-point (hazard ratio: 1.11, 95%CI: 1.05-1.18; p=0.001). Using Cox regression analysis, by adopting an interactive stepwise procedure, the prognostic value of serum UA was incremental to that of clinical features (age, gender, congestion score, mean arterial pressure, copd, anemia, chronic renal insufficiency, previous HF admission), laboratory data (oxygen arterial saturation, glycaemia, azotemia at discharge, serum sodium concentration, BNP at discharge), and therapy (use of inotropes, nitroprusside, diuretic dose, absence of beta-blockers and ace-inhibitors) (Figure).

**Conclusions:** High serum UA levels confirms to be strong and independent marker of poor prognosis in patients with acute HF. More importantly, the addition of uric acid to well established prognostic marker in this setting seems to confer incremental prognostic power.



Additive prognosi power of uric acid



**P1894****A case series of takotsubo cardiomyopathy from a southeast asian perspective**HS Hong Sang Chua<sup>1</sup>; I Jaafar<sup>2</sup>; DM Periasamy<sup>2</sup>; T Ganesan<sup>2</sup>; E Sim<sup>2</sup><sup>1</sup>Ripras Hospital, Department of Surgery, Bandar Seri Begawan, Brunei Darussalam;<sup>2</sup>Gleneagles JPMC Sdn Bhd, Bandar Seri Begawan, Brunei Darussalam**Objectives:** Our retrospective study looks at all patients who were diagnosed with Takotsubo cardiomyopathy in our centre over a 6 year period from 2007 to 2013.**Materials and Methods:** Patients diagnosed with Takotsubo cardiomyopathy were identified through the hospital cardiovascular patient database prior to clinical data collection. The data was then tabulated into a spreadsheet for analysis with a statistics software package.**Results:** The patient selection process identified 12 patients comprising 10 female patients (83.3%) and 2 male patients (16.7%) with a mean age of 62.3 years (range 38-78 years). The most common presenting complaints were chest pain and dyspnoea (Both with 66.7%). All patients had risk factors for coronary disease with 66.7% of patients presenting with at least 2 risk factors for ischaemic heart disease. 7 patients (58.3%) had documented psychological stressors with the most common being issues related to the home (41.7%). 11 patients (91.7%) had electrocardiographic changes and elevated serum troponin levels. All patients underwent coronary angiography with 8 normal studies (66.7%), 3 patients (25%) with minor coronary artery disease involving less than 30% stenosis of a single coronary artery and 1 patient (8.3%) with significant coronary artery disease involving 2 coronary arteries. Left ventriculography in all patients (100%) showed a similar presentation of a dilated left ventricle with akinetic mid to apical left ventricular segments and a hyperkinetic basal segment in all patients. Echocardiographic studies at the point of admission showed poor left ventricular ejection fractions of 30-50% (median 35%). Subsequent echocardiography showed a median change of 78% (Standard Deviation 55.4%) with the mean time between echocardiographic studies being 88.1 days (Standard Deviation 123.8 days). 7 patients required inotropic support and out of these patients, 2 required further support with an intra-aortic balloon pump. Follow-up data was available for all 12 patients with a median follow up of 463.5 days (Range 17 to 1234 days) post-presentation to the centre.**Conclusion:** In our centre, we describe a condition that presents similarly to an acute myocardial infarction with some patients in cardiogenic shock. Investigations show typical echocardiography and left ventriculography findings at the time of admission that appear to be reversible following conservative management measures only.**CHRONIC HEART FAILURE****P1895****Disorders of neurohumoral indicators and their correction in patients with chronic heart failure**Z D Zulfiya Rasulova<sup>1</sup>; UK Kamilova<sup>1</sup><sup>1</sup>Republican Specialized Scientific-Practical Medical Center Therapy and Medical Rehabilitation, Cardiology, Tashkent, Uzbekistan**Purpose:** to study the dynamics of brain natriuretic peptide levels of Nt-proBNP (BNP), aldosterone (Al) and noradrenaline (NA) in the serum of patients with chronic heart failure (CHF) II and III functional class (FC) during the treatment.**Methods:** There were examined in 46 patients with CHF with FC II - III, who on top of standard therapy including  $\beta$ -blockers (bisoprolol) took - lisinopril or losartan. The first group consisted of 23 patients with II (12) and III (11) FC CHF, who took over 6 months with standard therapy (spironolacton,  $\beta$ -blockers) - losartan (mean dose of this preparation was  $69,0 \pm 27$  6 mg/day); the second group - 23 patients with II (12) and III (11) FC CHF, took on a background of standard therapy - lisinopril (mean dose of this preparation was  $8,9 \pm 2,6$  mg/day).**Results:** Analysis of the neurohormonal factors in the dynamics of treatment showed a significant reduction in BNP, Al and NA in both groups. After 6 months of treatment, patients of the first group (n=23) had decreased levels of neurohormones (BNP, Al and NA) in patients with class II 43,7%, 21,2%, 22,5%, respectively; in patients with FC III by 31,7%, 42,6%, 9,9%, respectively. After 6 months of treatment, patients of the second group (n=23) had decreased levels of neurohormones (BNP, Al and NA) in patients with FC II by 36,5%, 21,2%, 22,5%, respectively; in patients with FC III by 35,2%, 31,2%, 8,3% respectively.**Conclusion:** The results showed that both groups had a significant decrease in BNP, Al and NA after 6 months of therapy. Combination therapy with  $\beta$ -blockers and ACE inhibitors or ARA has achieved no increase in activity studied neurohormones and significantly reduce BNP, Al, and NA 6 months of treatment. But at the same

time were no significant differences in the groups of patients treated with, losartan or lisinopril dynamics level of neurohormones.

**P1896****Right ventricular dysfunction in heart failure with either reduced or preserved LV function**S Ghio<sup>1</sup>; M Guazzi<sup>2</sup>; A Rossi<sup>3</sup>; FL Dini<sup>4</sup>; P Faggiano<sup>5</sup>; P L Pier Luigi Temporelli<sup>6</sup><sup>1</sup>Policlinic Foundation San Matteo IRCCS, Division of Cardiology, Pavia, Italy;<sup>2</sup>IRCCS, Policlinico San Donato, Heart Failure Unit, San Donato Milanese, Italy;<sup>3</sup>University of Verona, Department of Biomedical and Surgical Sciences,

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Cardiologia, Università di Brescia, Brescia, Italy;

<sup>6</sup>Cardiac Rehabilitation Unit, Salvatore Maugeri Foundation, IRCCS, Veruno, Italy**Aim:** Aim of the present study was to evaluate the clinical and echocardiographic determinants of right ventricular (RV) dysfunction and its prognostic significance in a population of chronic heart failure (CHF) patients with either reduced (HFrEF) or preserved (HFpEF) left ventricular ejection fraction (LVEF).**Background:** The reasons why RV dysfunction develops in CHF are still largely unclear.**Methods:** The study included 1663 CHF patients due to ischemic, hypertensive heart disease or to idiopathic cardiomyopathy. LVEF was  $\leq 40\%$  in 1130 patients (HFrEF), 41-49% in 149 patients and  $\geq 50\%$  in 384 patients (HFpEF). Imaging of the right ventricle was performed by echocardiography; RV function was defined on transtricuspid annular peak systolic excursion (TAPSE) and its normalization for pulmonary systolic pressure (PASP). All-cause mortality was the end point of survival analysis.**Results:** In the entire population, LVEF  $\leq 40\%$ , atrial fibrillation or ventricular stimulation, heart rate  $> 70$  bpm, ischemic etiology and E wave deceleration time  $< 140$  ms emerged as independent determinants of a reduced TAPSE at multivariate analysis. The same set of parameters was found to be statistically significant in HFrEF patients. Non sinus rhythm, heart rate  $> 70$  bpm and in particular PASP  $> 40$  mmHg which carried a sixfold increased risk, were the parameters associated with a reduced TAPSE in HFpEF patients. TAPSE/PASP proved to be a powerful predictor of prognosis both in HFrEF and in HFpEF patients.**Conclusions:** Non sinus rhythm and high heart rate are critical determinants of RV dysfunction in all CHF patients. In addition to these parameters, peculiar independent determinants in HFrEF are ischemic etiology and severity of the left ventricular disease, whereas in HFpEF pulmonary hypertension is strongly associated with reduced TAPSE. The normalization of TAPSE for PASP allows a powerful independent predictor of prognosis in all CHF patients, regardless of LVEF.**P1897****Circulatory power and exercise phenotypes: insights on disease severity in heart failure reduced ejection fraction**V Valentina Labate<sup>1</sup>; PL Laforgia<sup>1</sup>; V Donghi<sup>1</sup>; G Generati<sup>1</sup>; F Bandera<sup>1</sup>;M Guazzi<sup>1</sup><sup>1</sup>IRCCS Policlinico San Donato, heart failure unit, San Donato Milanese, Italy**Background:** Cardiopulmonary exercise testing (CPET) provides indexes of functional capacity. Circulatory power (CP=peak systolic BP X peak VO<sub>2</sub>) shows additional prognostic value to peak VO<sub>2</sub>. Ventilatory power (VP=peak systolic BP/VE/VO<sub>2</sub>, cutoff 3,5) combined with CPET derived CP (cutoff 1750 mmHg\* ml<sup>2</sup>\*kg<sup>-1</sup>\*min<sup>-1</sup>) allows to better stratify this population.**Aim:** To describe the relationship between peak exercise CP, VP and functional and echocardiographic phenotypes in HFrEF.**Methods:** 128 HFrEF patients (mean age  $64.39 \pm 11.88$ ; male 71.1%; ischemic etiology 56%; NYHA class I, II, III, IV 33.3, 34.4, 29.0, 3.2; mean EF  $32.4 \pm 7\%$ ) underwent maximal CPET on titable cycle-ergometer combined with exercise echocardiography.**Results:** We divided patients into three groups according to peak VP and CP using cutoff value of 3,5 and 1750 respectively: Group A=preserved VP and CP, B=impaired CP, C=both VP and CP impaired. Group C had worse bi-ventricular function already at rest. Group B showed lower right ventricular systolic function (peak TAPSE) and dynamic pulmonary hypertension (higher peak PASP) compared to group A patients, and more severe dynamic mitral regurgitation (MR). These echo-data corresponded to impaired exercise tolerance and ventilatory efficiency.**Conclusions:** Assessment of CP and VP, seems very useful to unmask different degree of impaired functional phenotypes. Patients exhibiting a combined CP and VP impairment are those with the worse phenotype of RV-pulmonary circulation uncoupling.

Population's Characteristics							
	A (n = 85)	B (n = 21)	C (n = 22)	p (AvsBvsC)	p (AvsB)	p (BvsC)	p (AvsC)
Rest LVEF, %	34,3 ± 6	30,5 ± 6	26,9 ± 9	< 0.001	0.03	0.126	< 0.001
Peak LVEF, %	37,4 ± 10,3	34,2 ± 10,0	31,4 ± 11,0	0.03	0.40	0.166	< 0.001
Rest MR ≥ 3/4+, n (%)	13 (15,2%)	5 (23,8%)	14 (63,6%)	< 0.001	0.35	0.03	0.01
Peak MR ≥ 3/4+, n (%)	25 (29,4%)	11 (52,3%)	15 (68,1%)	0.002	0.05	0.57	< 0.001
Rest TAPSE, mm	19,1 ± 4,4	17,1 ± 4,4	13,6 ± 3,3	< 0.001	0.16	0.014	0.004
Peak TAPSE, mm	21,7 ± 4,9	17,7 ± 5,2	15,1 ± 4,1	< 0.001	0.007	0.11	< 0.001
Rest PASP, mmHg	31,1 ± 8,7	34,8 ± 8,2	54,0 ± 18,5	< 0.001	0.04	0.001	< 0.001
Peak PASP, mmHg	54,0 ± 11,9	61,4 ± 14,0	69,7 ± 21,0	0.003	0.25	0.06	< 0.001
Workload, Watt	82 ± 33	51 ± 18	40 ± 14	< 0.001	< 0.001	0.04	< 0.001
Peak VO2, mlO2/kg/min	15,9 ± 4,7	9,4 ± 1,7	9,1 ± 1,6	< 0.001	< 0.001	0.57	< 0.001
VE/CO2 slope	29,8 ± 5,3	32,4 ± 4,5	45,9 ± 10,2	< 0.001	0.01	< 0.001	< 0.001
PETCO2, mmHg	35,2 ± 5,1	34,4 ± 3,8	28,4 ± 5,7	< 0.001	0.014	< 0.001	< 0.001

LVEF=Left Ventricular Ejection Fraction;

**P1898**

**Pattern of endothelial progenitor cells and apoptotic endothelial cell-derived microparticles differentiates preserved from reduced left ventricular ejection fraction chronic heart failure**

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**Background:** Chronic heart failure (HF) remains a leading cause of cardiovascular (CV) mortality and morbidity worldwide. The aim of the study was to investigate whether the pattern of endothelial progenitor cells (EPCs) with angiogenic capacity and apoptotic endothelial cell-derived microparticles (EMPs) would be able to differentiate HF with reduced (HF<sub>r</sub>EF) and preserved (HF<sub>p</sub>EF) ejection fraction.

**Methods:** One hundred sixty four chronic HF subjects met inclusion criteria. Patients with global left ventricular ejection fraction 50-59% were categorised as the HF<sub>p</sub>EF group (n=79) and those with ≤45% as the HF<sub>r</sub>EF group (n=85). All biomarkers were measured at baseline. The flow cytometric technique was used for predictably distinguishing circulating cell subsets depending on expression of CD45, CD34, CD14, Tie-2, and CD309 antigens and determining endothelial cell-derived microparticles. CD31+/annexin V+ was defined as apoptotic endothelial cell-derived MPs, MPs labeled for CD105+ or CD62E+ were determined as MPs produced due to activation of endothelial cells.

**Results:** In multivariate logistic regression model T2DM (R<sup>2</sup>=0.26; P=0.001), obesity (R<sup>2</sup>=0.22; P=0.001), previous MI (R<sup>2</sup>=0.17; P=0.012), galectin-3 (R<sup>2</sup>=0.67; P=0.012), CD31+/annexin V+ EMPs to CD14+CD309+ cells ratio (R<sup>2</sup>=0.16; P=0.001), CD31+/annexin V+ EMPs (R<sup>2</sup>=0.11; P=0.001), NT-proBNP (R<sup>2</sup>=0.11; P=0.046), CD31+/annexin V+ EMPs to CD14+CD309+Tie-2+ cells ratio (R<sup>2</sup>=0.102; P=0.001), CD14+CD309+ cells (R<sup>2</sup>=0.058; P=0.001), and CD14+CD309+ Tie-2+ cells (R<sup>2</sup>=0.044; P=0.028) were found as independent predictors of HF<sub>p</sub>EF. Using multivariate Cox-regression analysis adjusted etiology (previous myocardial infarction), cardiovascular risk factors (obesity, type 2 diabetes mellitus) we found that NT-proBNP (OR 1.08; 95% CI=1.03 - 1.12; P=0.001) and CD31+/annexin V+ EMPs to CD14+CD309+ cells ratio (OR 1.06; 95% CI=1.02 - 1.11; P=0.02) remained independent predictors for HF<sub>p</sub>EF.

**Conclusion:** We found that CD31+/annexin V+ EMPs to CD14+CD309+ cells ratio added to NT-proBNP, clinical data, and cardiovascular risk factors has exhibited the best discriminate value and higher reliability to predict HF<sub>p</sub>EF compared with NT-proBNP and clinical data / cardiovascular risk factors alone

**P1899**

**Reasons of under prescription in heart failure**

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**Introduction:** On 2014, 155 patients left our institute without recommended treatment for heart failure including converting enzyme inhibitor (CEI) and β-blocker. II.

**Purpose:** The objective of this study was to find reasons about those under prescriptions. III.

**Material and Method:** During the year 2014, 667 patients were admitted for HF. Among the 667, 121 patients left without CEI, and 64 left without β-blocker. We investigated likely reasons for no prescription of β-blocker or CEI. IV.

**Results:** On the 121 patients who left without CEI, 103 of them (85 %) had valid reasons: - Renal Failure (DFG < 30 ml/min: 43; DFG < 60 ml/min: 53; DFG defined by Cockcroft and Gault equation), - Renal Stenosis (1), - Hypotension (4), - Palliative treatment (1), - Bad hemodynamic tolerance (1). 17 patients (14%) didn't show any reason, and one (1%) showed an invalid reason. A CEI intolerance was reported but a Sartan could have been used which was not the case here. On the 64 patients who left without β-blocker, only 34 (53%) had valid reasons: - Bradycardia (19), - Severe Asthma (> 3) or severe chronic obstructive pulmonary disease, and β-mimetic treatment (6), - Severe Atrio Ventricular Block (4), - Under amines treatment (2), - Bad hemodynamic tolerance (1), - Under β-mimetic treatment (1), - Cardiogenic shock (1), - Palliative treatment (1). 16 patients (25 %) didn't show any reason and 14 (22%) showed invalid reasons: - 8 suffer from no severe asthma or no severe chronic obstructive pulmonary disease, - 3 suffered a cardiac decompensation, but β-blocker could have been used after the decompensation, (1 β-blocker at the admission not reintroduced when leaving; the others hadn't got β-blocker at the admission), - 2 suffer from no severe constrictive ventilatory disorders, - 1 had an allergic effect under β-blocker, but the effect was not detailed as minor or major. A minor effect could have been in favour of continuing the treatment. Accountability was not proven, allergy test or pharmacovigilance declaration hadn't been realised. We were interested to know if patients who left without β-blocker, could have left with Ivabradine instead. On 34 patients with valid reasons, 11 could take Ivabradine but only 1 get it. On 14 patients without valid reasons, 7 could take Ivabradine but only 2 get it. On 16 patients with unknown reasons, 11 could take Ivabradine but only 3 get it. V.

**Conclusion:** Most of patients who left without CEI or Sartan had valid reasons to not prescribe them. But prescriptions can still be improved. β-blockers prescriptions are less efficient and could be improved, and prescription of Ivabradine, when β-blockers can't be used, could be more considered. This work points out several under prescriptions with lack of information that could induce poor outcomes for patients. Better understanding underprescription should help us with improving our practices.

**P1900**

**Effect of levosimendan on cardiac output in stable chronic heart failure according to baseline cardiac output**

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**Background:** The intravenous inodilator agent levosimendan improves hemodynamics in acute decompensated heart failure. However, it is increasingly used for repetitive or intermittent infusions in advanced but stable chronic heart failure; without clear indication, selection criteria or effect. We tested the hypotheses that (1) levosimendan improves hemodynamics also in stable heart failure and (2) that the response is dependent on baseline cardiac output.

**Methods:** Twenty-three stable ambulatory patients (median age 56 [49-64] years, 4 women) with New York Heart association (NYHA) III or IV heart failure and reduced ejection fraction received a single 24-hour levosimendan infusion. Noninvasive hemodynamics with gas re-breathing technique, estimated glomerular filtration rate and N-terminal pro-brain natriuretic peptide (NT-proBNP) were measured before and after infusion.

**Results:** Levosimendan had the following effects overall: a significant increase in cardiac output (CO) ( $+9.8\% \pm 21.6\%$ ;  $p=0.026$ ) and decrease in NT-proBNP ( $-28.1\% \pm 16.3\%$ ,  $p < 0.001$ ), total peripheral resistance (eTPR) ( $-16.9\% \pm 18.3\%$ ,  $p=0.005$ ) and mean arterial pressure (MAP) ( $-5.9\% \pm 8.2\%$ ,  $p=0.007$ ) but no change in eGFR ( $+0.89\% \pm 14.0\%$ ,  $p=0.955$ ). In patients with baseline CO below median, there was an increase in CO ( $+15.8 \pm 20.2\%$ ,  $p=0.025$ ) and a decrease in NT-proBNP, MAP and TPR but no change in eGFR. In patients with baseline CO above median, there was a reduction in NT-proBNP but no change in CO, MAP, eTRP or eGFR.

**Conclusions:** In patients with stable advanced heart failure, levosimendan improves hemodynamics, but the effect may depend on baseline hemodynamics. Patients who started with CO below median showed a more favorable change in different variables compared to those who started with CO above median suggesting that the effect may be greater in patients with lower baseline CO. This has implications for patient selection and trial design for intermittent or recurrent levosimendan treatment.

### P1901

#### Ivabradine in the treatment of heart failure: effectiveness in heart rate

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Few drugs have demonstrated benefits on survival of patients with heart failure (HF) in the last decade, when added to standard therapy with ACE inhibitor, beta blocker (BB) and aldosterone antagonist. Ivabradine, to decrease heart rate (HR) acting on the sinus node If channels, significantly reduces morbidity and mortality in HF patients with systolic dysfunction of the left ventricle (LVSD) in sinus rhythm (SR) and HR > 70 bpm, and in Coronary Heart Disease.

**Objective:** To evaluate the early introduction of ivabradine in relocation and HR reduction at follow up. Population and

**Methods:** A retrospective observational study of patients consecutively admitted with HF LVSD, RS and HR > 70 bpm between February 2012 and December 2013 were studied demographic variables, cardiovascular risk factors and therapy at admission, discharge and follow up.

**Results:** 19 patients were identified with HF and LVSD, with RS and HR > 70 bpm, including 4 women (22%) and 15 men (78%) with a mean age of  $71.5 \pm 5$  years. In the pre-admission, 15.8% patients had already been treated with ivabradine BB +; 42% only with BB and 10% only with ivabradine. During hospitalization, 42% of patients taking BB started ivabradine and 31.6% patients started treatment with ivabradine BB +. At follow up, 5 patients (26%) remained Ivabradine+BB and there was a 28% decrease in CF; 4 (21%) with only ivabradine, HR decreased by 13%; only one patient remained only at BB, with a decrease of 15% HR. 2 patients discontinued the medication for bradycardia. Lost to follow up in 7 patients.

**Conclusions:** The data presented demonstrate that early introduction of ivabradine in hospital is safe and is an adjuvant drug to the beta blocker in HR reduction effectiveness. International recommendations advocating the addition of ivabradine to conventional therapy of IC to reduce the morbidity and mortality are discussed.

### P1902

#### Advantage of "nitrate centered" over "diuretic centered" treatment of acute decompensated heart failure on clinical congestion, NT-pro-BNP and renal function markers

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**Background:** Our purpose was to compare effects of prolonged optimal-dosed nitrate infusion plus low doses of iv diuretics ('nitrate centered strategy' - NC) and moderate doses of iv diuretics plus short intermittent nitrate infusion ('diuretic-centered strategy' - DS) on congestion symptoms, NT-proBNP and renal function markers (Cystatin C) in pts with acute decompensated heart failure (ADHF).

**Methods:** In single-blind parallel-group randomized study we assigned pts with 'wet-warm' ADHF to receive either optimal-dosed GNT infusion  $\geq 72$  hrs plus low doses of iv diuretic ( $\leq 80$  mg pd for furosemide, NC group,  $n=21$  per protocol, age  $58.7 \pm 1.1$  yrs or moderate doses of iv diuretic (41-120 mg pd plus short intermittent (< 0hrs pd,  $\leq 3$  days) GNT (DC group,  $n=54$  per protocol, age  $63.2 \pm 1.6$  yrs). Primary endpoints were CVP at D4-6, NT-pro-BNP (ELISA) and serum Cystatin C at D4-6 and Dsc.

**Results:** Total 1st week furosemide dose in NC group was  $194 \pm 20.7$ mg, in DC group -  $393 \pm 14.3$ mg, duration of NTG infusion -  $3.2 \pm 0.3$  vs  $0.76 \pm 0.07$  days ( $p < 0.001$ ). Symptomatic hypotension occurred in 3 (23%) and 2 (3.4%) pts, correspondingly, and transfer to p.o. diuretics in  $7.2 \pm 1.3$  and  $8.6 \pm 1.7$  days ( $p < 0.05$ ). At 1-st day NT-pro-BNP was comparable increased in both groups ( $1238 \pm 342$  and  $1172 \pm 304$  pg/ml,  $p > 0.05$ , between NC and DC groups respectively) but its on-treatment decrease was more significant in NC group (at D4-6 -  $871 \pm 244$  vs  $1061 \pm 271$  pg/ml,  $p < 0.04$ , and at Dsc -  $747 \pm 128$  vs  $871 \pm 249$  pg/ml,  $p < 0.05$ ). The same was true for CVP lowering from D1 (correspondingly,  $198 \pm 14.7$  and  $188 \pm 12.9$  mm H<sub>2</sub>O,  $p > 0.05$ ) to D4-6 ( $77 \pm 5.2$  vs  $96 \pm 5.8$  mm H<sub>2</sub>O,  $p < 0.05$  between NC and DC groups). Similar trend had changes of serum Cystatin C.

**Conclusion:** In ADHF patients 'nitrate centered' strategy compared to 'diuretic centered' one is associated with more pronounced and more early clinical decongestion, NT-pro-BNP lowering and better dynamics of serum Cystatin C.

### P1903

#### The association between the prognostic value and the Controlling nutritional status (CONUT) in elderly patients repeating hospitalization for decompensated heart failure.

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The association between the prognostic value and the nutritional CONUT scores in elderly patients repeating hospitalization for decompensated heart failure.

**Background:** Malnutrition is associated with poor prognosis in various setting of patients. Recently, controlling nutritional status (CONUT) score is emerging as a simple method for assessing nutritional status of a variety of disease. However, the association between CONUT score and outcome in patients with heart failure (HF) has not been clarified.

**Purpose:** This study aimed to investigate the clinical significance of CONUT score in predicting outcome in elderly patients with HF.

**Methods:** 53 consecutive patients (mean 85 years) admitted to our hospital with acute HF aged 75 or older were examined. All patients were evaluated nutritional status using CONUT score at discharge. Patients were classified into two groups according to the CONUT score at discharge: Low-CONUT score (<5) group ( $n=31$ ) and High-CONUT score ( $\geq 5$ ) group ( $n=22$ ). Clinical variables as well as cardiac outcomes after discharge, including cardiac death, admission for HF, was compared between the two groups.

**Results:** In all patients, LVEF on admission was  $51 \pm 16\%$ . BNP on admission level was  $804 \pm 620$  pg/ml, which was decreased to  $471 \pm 68$  pg/ml at discharge ( $p=0.0008$ ). BNP at discharge was negatively correlated with the time to re-admission for HF ( $r=-0.30$ ,  $p=0.04$ ). Of this patients, 49 patients (92%) were identified as having mild to severe nutritional disturbances. There were no significant differences between Low-CONUT score group and High-CONUT score group in setting of age, duration of hospitalization, and LVEF. Kaplan-Meier analysis revealed that the cardiac event free rate in Low-CONUT score group was significantly higher than in High-CONUT score group (log rank  $p=0.006$ ).

**Conclusions:** The results of this study suggested that the CONUT score at discharge is associated with cardiac outcome in elderly patients with HF.

### P1904

#### Preferences and therapeutic targets in patients with heart failure. an physicians survey in mexico

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Heart failure (HF) is a multifactorial disease with high prevalence and morbidity and mortality, there is diversity in drug treatment, as well as therapeutic targets.

**Objective:** To determine therapeutic preferences and goals to achieve in HF patients in Mexico.

Groups	NT-pro-BNP, M ± m, pg/ml	CVP, M ± m, mmH <sub>2</sub> O	Cystatin C, M ± m ng/ml						
	D4-6	Dsc	D1	D4-6	Dsc	D1	D4-6	Dsc	
NC	1238 ± 342	871 ± 244**#	747 ± 128**#	194 ± 14,7	78 ± 5,28**#	-	3271 ± 517	3528 ± 624 **#	2714 ± 478 **#
DC	1172 ± 304	1061 ± 271	871 ± 249**	186 ± 12,9	97 ± 5,89**	-	3314 ± 578	3895 ± 683 **	3071 ± 614 **

\* -  $p < 0,05$ , \*\* -  $p < 0,01$  compared to D1; # -  $p < 0,05$ , ## -  $p < 0,01$  compared to Group DC



**Material and Method:** A survey in different cities in Mexico, was attended by physicians from various specialties General Practitioners (GP), Internists (IM), Cardiologists (CA) and Others (Ot). All agreed voluntarily to their participation. Trained personnel interviewed personally to each physician. Questionnaire had closed and open questions. Interrogated: Monthly amount and proportion of patients with HF, patients with reduced Ejection Fraction (EF), Functional Class (NYHA), Their personal preference in: drugs and treatment target objectives. We declare any commercial bias. Data analysis made with SPSS statistical programme. Alpha error less than 0.05

**Results:** Interviewed 2053 physicians, in various Mexico cities. Their specialties were: GP 858 (41.8%), IM 461(22.5%), CA 439 (21.4%) Ot 295(14.4%). Monthly consultations average 178+2.64. observed in various pathologies. Most of respondents (98.1%) attended 75 patients with HF monthly, reported 42.9% of HF patients had reduced EF, 52.16% observed in cardiologists compared with other specialties (GP 40%, IM:43.8% and Ot:38.3%,  $p < 0.005$ ). NYHA Functional class were: Class I 383(18.7%) Class II 755(36.8%); Class III: 620(30.2%) and CF IV 295 (14.3%). 1758 patients (85.7%) were functional class I-III. The mostly used drug was Diuretics(DIU) followed by ARB's, Digital (DIG), ACE and Betablockers (BB). In dual combination was: ARB + ACE; ACE + DIU; ARB + Calcium Channel Blocker (CaCB). In triple combination ARB+CaCB+DIU. The objective of the treatment was: Quality of Life (28%) Improvement in NYHA Class (25%), Symptom Control (17.4%), Survival (8.5%). The Reduction of (Re)Hospitalizations (4.8%) and Improvement of EF (5.2%)

**Conclusions:** In this first survey in a Latin Country American, we observe that therapeutic behavior of cardiologists is different in the different specialties, there is similarity in the therapeutic objective.

## P1905

### Influence of telemedicine support to CHF patients on hospitalisation

United4Health

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Several international studies have confirmed that telemedicine- (TM) support to patients with Congestive Heart Failure (CHF) at home have positive effects for the patients and for a hospital providing the service. A telemedicine support service provided by a regional hospital was set-up in 2014 offering it to a population of 140.000 inhabitants in a rural region. Before inclusion into TM support services the patients in the intervention group were re-educated on their self-management possibilities. 134 CHF patients (intervention group) were receiving a TM support service for one year, in average for 402 days. The comparator group to them was the observed group itself, but in the period of one year prior to inclusion into the service. In the observed two-years period the patients received the recommended heart failure treatment. The TM services consisted of TM data capturing of blood pressure, heart rate, weight and oxygenation. Data were transferred to the hospital by a mobile phone without any intervention from the patient. Based on daily measurements the patients received, when needed, an advice or suggestion to change their therapy at home or to come for an unscheduled visit to a CHF clinic. Number of admissions (readmissions) to the hospital related to CHF and duration of hospitalisation (hospital days) was the primary clinical outcome observed. In the period of two years (one year prior to enrolment into TM support service and one year of using TM service) the observed cohort was hospitalised for 390.5 days with CHF as the primary diagnose, of which 316.7 were in the control period and 73.8 days in the intervention period. Number of admissions was 46 in the control and 13 in the intervention period. The results demonstrate a substantial reduction in number of admissions (readmissions) to the hospital (from 0.34 per year per patient to 0.1 ( $p < 0.001$ )) and a reduction in duration of hospitalisation for the patients in the intervention period (from 2.36 days/year/patient to 0.55 days ( $p < 0.001$ )). The results were achieved by early reactions to the worsening of the health condition detected through processing of TM service.

## P1906

### Low-dose anti-cytokine treatment impacts on heart failure with preserved ejection fraction in active rheumatoid arthritis

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**Background:** Recent data suggest that anti-cytokines can improve cardiovascular outcomes in RA. Heart failure with preserved ejection fraction (HF-PEF) is common cardiovascular condition in patients with rheumatoid arthritis (RA). In our previous studies we revealed the correlation between RA severity and functional class of HF. The purpose of this study was to assess the efficacy of combined anti-cytokine therapy with preparation arthrofoon (extra-low dose of antibodies against TNF- $\alpha$ ) and anaferon (extra-low dose of antibodies against IFN- $\gamma$ ) in RA pts regarding to clinical manifestation of HF-PEF.

**Methods:** 86 pts (67 female and 19 male aged 34-58 years) with determined active RA and HF-PEF had been randomized on two groups. The 1st group (46 pts) was

treated with arthrofoon+anaferon in addition to standard therapy of RA. The 2nd one (40 pts) received only standard anti-rheumatic drugs. We compared the symptoms and signs of RA activity and HF manifestation/deterioration in both group before and after 1 year course of the treatment.

**Results:** Baseline clinical and laboratory data were similar in compared groups. According to DAS28 index more prominent decrease of RA activity associated with decreased levels of TNF- $\alpha$ , IL-1, IL-6 had been revealed in the 1st group than in 2nd. 42 pts (91.3%) from the 1st group and 5 pts (12.5%) from the 2nd one demonstrated mild or moderate improvement of HF symptoms and life quality. The dynamics of mean distance in six-min walk test was from 232.6 m to 398.7m in the 1st group, from 233.7 m to 245.1m in the 2nd group. During 1 year period of monitoring none serious cardiovascular events were registered in the 1st group while in the 2nd one 3 pts (7.5%) were hospitalized due to complicated hypertensive crisis and deterioration of HF.

**Conclusion:** Combination of two preparations (arthrofoon+anaferon) with anti-cytokine properties can improve the course of HF-PEF in pts with active RA. The possible mechanism of this phenomenon may be associated with decreased activity of RA.

## P1907

### Development of bioartificial myocardium and ventricular support bioprosthesis using nanobiotechnologies

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**Background:** Post ischemic ventricular dilatation and adverse remodeling raises the need to assist the heart to decrease ventricular wall deterioration. In this way myocardial tissue engineering should play a key therapeutic role due to its capacity to reinforce or replace extracellular matrix.

**Purpose:** To develop biomimetic: 1) Cardiopatch, to reduce fibrosis and reinforce infarct scars, and, 2) Cardiac wrap bioprosthesis, for ventricular support and myocardial regeneration in chronic heart failure (HF). This will be done using semidegradable scaffolds manufactured with polymers and Nano biomaterials.

**Methods:** Cardiopatch and ventricular support bioprosthesis were evaluated in a sheep ischemic HF model. Biohybrid templates were created using semidegradable elastomers and self-assembling peptide nanofibers. Adipose Progenitor Cells (APC) was introduced inside the porous 3D membranes. Channeled scaffolds were proposed to guide the capillary network of the host tissue, a suitable microenvironment that mimics the extracellular matrix.

**Results:** Late gadolinium enhancement (LGE) on MRI was used to assess the volume of infarct scars related to ventricular mass. Results at 6 months showed in cardiopatch vs control group a significant reduction of the infarct volume size.

**Histopathology:** APC positive for red fluorescent protein were found inside the patch, into the infarct scars and healthy myocardium in treated group. Hence, APC were able to migrate from the cardiopatch to the nearby tissue. Integration of APC into the vessel structures was also observed in the patch, interconnected with myocardium. Thus, APC contributed to the formation of a capillary network between patch and myocardium.

Ultrasound studies of the treated group showed significant improvements in Stroke Volume, E/A ratio, EDT, E/E' ratio, LV VTI, and longitudinal strain compared with control group.

**Conclusions:** This study was designed for the creation of bioartificial myocardium. Firstly we have developed "cardiopatch" to reinforce or replace ischemic areas, and eventually repair congenital heart defects. Secondly we developed "bioprosthesis" for ventricular support and myocardial regeneration. Mechanical, chemical and biological characteristics of biomimetic scaffolds are adapted for the LV or RV geometry, physiology and pathology, designed with the concept of "helical myocardial bands". Bioprosthesis should limit ventricular dilatation and restore elliptical shape, reducing the risk of HF progression and the indication for heart transplantation

## P1908

### Comparison of angioedema in heart failure patients treated with sacubitril/valsartan or enalapril in PARADIGM-HF

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**Background:** The PARADIGM-HF study showed that sacubitril/valsartan (LCZ696) is beneficial in heart failure (HF) patients with reduced ejection fraction. Inhibition of neprilysin, angiotensin-converting enzyme (ACE) or aminopeptidase may lead to

bradykinin elevation and increased risk of angioedema. Therefore, this was considered an adverse event of special interest in the PARADIGM-HF study.

**Methods:** PARADIGM-HF included 10513 eligible class II-IV HF patients (ejection fraction  $\leq 40\%$ , and mildly elevated NT-proBNP/BNP) in the enalapril run-in phase. After a 36h wash-out, 9419 patients entered the LCZ696 run-in phase and 8442 patients were, after a further 36h wash-out, randomized to blinded twice-daily treatment with LCZ696 200mg or enalapril 10mg. Suspected angioedema or angioedema-like events were reported by the investigators or identified by the sponsor and were adjudicated by an independent angioedema adjudication committee (AAC).

**Results:** Prior to run-in 77.3% of patients used ACE-inhibitors and 22.9% ARBs. Investigators reported 25 angioedema events during the enalapril run-in period ( $18.6 \pm 6.3$  days) and 29 events during the LCZ696 run-in period ( $30.3 \pm 9.2$  days). During the double-blind period ( $27 \pm 11$  months), 45 events were reported for enalapril and 48 for LCZ696. Of all 147 reported events, 54 were confirmed by the AAC as angioedema (run-in period 25/54, double-blind period 29/93), with 25 confirmed events for enalapril and 29 for LCZ696. The incidence of confirmed angioedema was higher in black patients than in non-black patients (Table). The majority of events were of mild severity, requiring no treatment or antihistamines only. In 5 patients (enalapril: 2, LCZ696: 3) angioedema required hospitalization, including 1 black patient, but no patient required mechanical airway support.

**Conclusion:** In PARADIGM-HF, the incidence of confirmed angioedema was low, with no severe cases. Black patients were at higher risk of angioedema events with both treatments. A wash-out period when switching treatment is considered important to avoid the risk of overlapping ACE- and neprilysin inhibition.

	Run-in Enalapril n = 10513	Double-blind LCZ696 n = 9419	Enalapril n = 4229	LCZ696 n = 4203
Confirmed angioedema: n (%) patients	15 (0.14)	10 (0.11)	10 (0.24)	19 (0.45)
Confirmed angioedema in black patients: n (%)	2/559 (0.36)	2/493 (0.41)	1/214 (0.47)	5/213 (2.35)
Hospitalized but no mechanical airway support	1	0	1	3
Study drug permanently discontinued due to event	15	8	4	7

### P1909

#### Continuous flow left ventricular assist device for end-stage heart failure: mild-term outcome and quality of life.

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**Introduction:** Heart transplantation is actually the gold standard therapy for patients with end stage heart failure; unfortunately, the demands is much greater than the number of donors. The introduction of ventricular assist devices has changed the therapeutic possibilities for these patients. In this study, we evaluate the effectiveness and mild-term results of a continuous flow left ventricular assist device as definitive therapy.

**Methods:** We evaluate 178 patients who received a Jarvik 2000 FlowMaker between June 2008 and december 2015 as "destination therapy". Concerning the etiology of heart failure, 90 patients (50,4 %) had a post-ischemic heart disease, 69 patients (38,8 %) had an idiopathic dilated cardiomyopathy and 19 (10,7 %) other pathologies such as hypertrophic cardiomyopathy and muscular dystrophy. At LVAD implantation time, the average INTERMACS level was  $3 \pm 1.2$ . Post-operative clinical and instrumental evaluation of each patient was made every 3 month after implantation. The assessment of quality of life was carried out with the Short Form-36 Health Survey questionnaire, administered at 3, 6 and 9 months after LVAD implantation.

**Results:** In 49 patients (27,8 %) the device has been implanted in a minimally invasive approach; in 100 patients (56,8 %), the device has been implanted without the extra-corporeal circulation. In 160 patients (90,9 %) a retroauricular connection to driveline was used. The average time on system was 441 days and the average

support time of patients discharged out of hospital was 599 days. The cumulative support time was greater than 210 years. Concerning the survival rate, at 1 year is 82%, 60% at 2 years and 54 % at 3 years. Results show a significant progressive improvement in functional and mental status with results, at 9 months from LVAD implantation, similar to those of a healthy population.

**Conclusions:** Clinical data suggest that technological evolution and an interdisciplinary approach to the patient could propose in the next years VAD therapy as a "gold standard" for end-stage heart failure.

### P1910

#### Influence of the high blood pressure on the resistance to overload hypoxia

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The aim of the study was to evaluate the effect of high blood pressure on the performance of Serkin's sample.

**Methods:** Studies were conducted on 74 students, 56 of them where girls with systolic arterial pressure (APsyst) values recorded not more than 120 mmHg. The effect of increasing systolic blood pressure to 130 mmHg (n = 11) and up to 140 mmHg (n = 7) was studied. In students determination of the duration of breath holding on inspiratory (Stange's sample) or the first phase sample Serkin, the duration of breath holding immediately after 20 squats (second phase) and the duration of breath holding on inspiration after 1 minute of rest (third phase of Serkin's sample). Results. In girls with elevated systolic blood pressure up to 130 mmHg we observed shortening of the first phase to  $47 \pm 11,0$  min, the duration of the second phase was  $19 \pm 3,3$  min (39% of the first phase and the duration of the third phase was  $-34 \pm 12,9$  min (76%). In students with increased systolic blood pressure (140 mmHg), we observed shortening of the first phase of the sample until  $44 \pm 8,8$  min, the second phase - until  $15 \pm 2,7$  min (34%), the third phase - until  $27 \pm 6,7$  min (60%),  $p < 0,05$ .

**Conclusions:** The increasing of APsyst, contributes to poor Serkin's sample indicators characterizing the state of the respiratory and cardiovascular systems, which suggests that a correction of arterial hypertension, play a role in increasing the body's sensitivity to hypoxic load and promotes the development of heart failure.

#### Serkin's test indicators (20 squats) in

### P1911

#### Pharmacotherapy of the heart failure - what is the reality in the clinical practice in Slovakia.

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**Background:** Despite the possibilities of the current pharmacotherapeutic measures of the heart failure patients and the current national guidelines for the complex management of these patients the morbidity and mortality is still extremely high.

Aim of the study was to study the pharmacotherapeutic approaches of the followed patients in their daily clinical practice in the country, as well as the adherence to the therapy compared to the current clinical guidelines.

**Patients and methods:** 6584 heart failure patients have been followed-up for the period of one year (2014-2015). 5692 (83%) pts were older 60 years, 1162 (17%) were younger 60 yrs.

**Results:** 6463 pts (94%) took the drugs affecting the renin-angiotensin-aldosterone system, From this sample 3882 (60%) took ACE-inhibitors, (majority were the pts younger 60 yrs of age in 69%, 54% were older than 60 yrs). 2581 pts (40%) took ARBs. Therapy of beta-blockers were in 6584 pts (77%), with 84% using them among younger 60 yrs. Mineralocorticoid antagonists took 1568 pts (23%). 4324 pts (63%) were on diuretic treatment, with the majority among older 60 yrs (85%). 1012 pts (15%) took digoxin (90% among pts older 60 yrs). 1012 pts took vasodilators (isosorbide-dinitrate) and only 218 pts were on ivabradine treatment.

**Conclusion:** the gap between the international and national clinical guidelines and the current clinical practice was seen from the daily care physicians.

**P1912**

**Patients with non-ischemic heart failure in waiting list of heart transplant**

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**Purpose:** to estimate predictors of death in patients with non-ischemic etiology of heart failure in waiting list of heart transplant (WLHTx).

**Methods:** From 2010 to 2015 in a Medical Research Centre in WLHTx included 128 patients. WLHTx 67 patients with non-ischemic heart failure: DCM - 74,6% (n=50), non-compact myocardium - 13,4% (n=9), the other CM - 12% (n=8); men - 58,2% (n=39), CHF 4 [3;4] FC, LVEF 22 ± 10%, VO<sub>2</sub>peak < 12ml/kg/min, PCWP 19 [12;24]mmHg, TPG 9 [7;14] mmHg, the CI 1,9 ± 0,5 l/min/m<sup>2</sup>, PVR 2,8 [2,3;3,8] units Wood. Duration in WLHTx 87 [31;163] days, 38 patients (56,7%) performed HTx, 17 patients (25,4%) died, 7 patients (10,4%) had stabilized and was excluded from WLHTx. In WLHTx received therapy: combined diuretic therapy - 100%, spironolactone - 100%, beta-blockers - 82,1% (n=55), ACEI/ARA - 52,2% (n=35), ivabradine - 15% Amiodaron - 60%, dopamine or dobutamine - 49,3% (n=33), 7 patients (10,4%) implanted CRT-D, 16 patients (23,9%) - ICD, extracorporeal circulatory support EXCOR - 8 patients (11,9%), physical therapy - 100%. All patients were divided into 2 groups: 1 group (n=50) patients survived in WLHTx, 2 group (n=17) - patients who died.

**Results:** patients died compared with the surviving patients at the time of inclusion in WLHTx had higher CHF FC (4 [4;4], and 3 [3;4] FC, respectively, p=0,004), low GFR (64 ± 19 and 81 ± 24 ml/min/1,73m<sup>2</sup> respectively, p=0,008) greater frequency of use of inotropic support (70,6% (n=12) and 42% (n=21), respectively, p=0,04), high bilirubin level (34 [23;47] and 17 [14;28] mcmmol/L respectively, p=0,01), ALT (52 [22;502] and 22 [14;31] U/L respectively, p=0,008), low sodium (129 ± 8 and 139 ± 5 mmol/L respectively, p=0,03), shorter duration to outcome (29 [10;45] and 106 [63;204] days, respectively; p=0,0001). From the selected predictors (HF FC, GFR, RLA, hemoglobin, bilirubin, ALT, AST, sodium, inotropes, days WLHTx) in the patient's death WLHTx greatest force an outcome (death) were: bilirubin (r=0,49; p=0,01), HF FC (r=0,47; p=0,0001), Sodium (r=-0,43; p=0,03), ALT (r=0,37; p=0,006), GFR (r=-0,36; p=0,006).

**Conclusions:** WLHTx mortality in patients with CHF noncoronary pathology 25,4%. Predictor of death in patients WLHTx are symptoms of right heart failure (hepatic, renal dysfunction) and FC CHF. To increase the percentage of survival to HTx require increasing the frequency of implantation of mechanical circulatory support.

**P1913**

**Chronic Heart Failure acutely decompensated by a hypertensive urgency in an elderly population**

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**Purpose:** To describe and compare comorbidities of the elderly (80+ yrs) chronic heart failure (HF) patient with and without reduced ejection fraction admitted for an acute decompensation secondary to a hypertensive urgency in the clinical setting of an emergency hospital.

**Methods:** We included consecutive elderly chronic HF patients admitted to the Internal Medicine Clinic for an acute decompensation secondary to a hypertensive urgency from January through December 2015. We separated them in two groups - HF with reduced ejection fraction (HF-REF) and HF with preserved ejection fraction (HF-PEF) and compared the two groups in terms of presence of cardiovascular risk factors (smoking, obesity) and comorbidities - diabetes, dyslipidemia, coronary heart disease, atrial fibrillation (AF), chronic kidney disease stage>3, COPD, previous stroke, dementia.

**Results:** Coronary heart disease, AF and COPD were more frequent in the HF-REF group, however there were no significant differences between the two groups in terms of other CV risk factors and comorbidities. For other results see table.

**Conclusions:** Hypertension is a major risk factor for HF both with REF and PEF. Elderly patients admitted for chronic HF acutely decompensated by a hypertensive urgency had in 80% of the cases HF-PEF. However, in terms of CV risk factors and comorbidities there were very few differences between the groups.

	HF-REF	HF-PEF	Total	HF-REF vs HF-PEF	
No pts	53 (19.63%)	217 (80.37%)	270		
Males	24	45%	60	28%	84 p < 0.05
Smoking	14	26%	19	9%	33 p < 0.01
Obesity	19	36%	61	28%	80 ns
Diabetes	19	36%	73	34%	92 ns
Dyslipidemia	16	30%	83	38%	99 ns
Coronary Heart Disease	45	85%	97	45%	142 p < 0.01
Chronic Kidney Disease Stage > 3	36	68%	130	60%	166 ns
COPD	9	17%	17	8%	26 p < 0.05
Stroke	4	8%	32	15%	36 ns
AF	32	60%	94	43%	126 p < 0.05
Dementia	5	9%	18	8%	23 ns

**P1914**

**Factors associated with heart failure readmissions from skilled nursing facilities**

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**Background:** Despite guideline-driven pharmacological therapies and careful transitional care, the rates of preventable hospital re-admission of heart failure patients and associated costs remain unacceptably high in the SNF populations. Transfer to SNF is one strategy to limit hospitalisations. As such, 25% of patients are still symptomatic at time of discharge.

**Purpose:** The objective of this study is to identify patient factors affecting re-admissions of HF patients residing in SNF within 30-days.

**Methods:** A retrospective electronic chart review was completed on patients > 65 years with HF who were admitted into large medical center between 2012 and 2014. Descriptive statistics and univariate analyses using the chi-square test, Fisher's test and Mann-Whitney test was used to compare patients readmitted within 30 days vs. those who were not readmitted within 30 days. Significant factors associated with readmission in the univariate analysis (p < 0.10) were included for a multivariate logistic regression model.

**Results:** Fifteen variables: creatinine, weight difference, CKD, Angina, Arrhythmia, VHD, Tobacco, ADL, independent in bathing, independent in the toilet, S3 Heart sounds present, HJR, AF, Nitrates, and Hydralazine, were identified for the multivariate logistic regression as potential risk factors associated with "readmission within 30 days". Based on 23 readmissions within 30 days, our final model included only 2 predictor variables. Creatinine and ADLs were included in the final model as this subset of predictors was found to be the best for prediction of "readmission within 30 days". Creatinine (p < 0.0087) and ADLs (p < 0.0077) were both significantly associated with readmission within 30 days in the final logistic regression model. Every 1-unit increase in creatinine is associated with an 87% increase in the odds of being readmitted within 30 days (OR = 1.87). Those patients who require assistance with ADLs are over 9 times more likely to be readmitted within 30 days (OR = 9.25) as compared to patients who are independent.

Parameter	Estimate	Standard Error	Odds Ratio	95% Confidence Interval	Pr > ChiSq
Intercept	-1.69	0.57			0.0029
Cr	0.63	0.24	1.87	1.17	2.99 0.0087
ADL	1.11	0.42	9.25	1.80	47.49 0.0077



**P1915****RAAS genetic polymorphism association with clinical features of CHF**SU Volkova<sup>1</sup>; KA Tomashevich<sup>2</sup>; AU Efanov<sup>1</sup><sup>1</sup>Tyumen State Medical Academy, Tyumen, Russian Federation; <sup>2</sup>"Neftyanic" hospital, Tyumen, Russian Federation**Aim:** To estimate renin angiotensin aldosterone system (RAAS) genetic polymorphism association with clinical features of chronic heart failure (CHF).**Materials and methods:** The 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:** RAAS genotype distribution analysis in dependence of CHF clinical features taking into account stage and NYHA class together with left ventricular systolic dysfunction, estimated as ejection fraction less than 40%, found no 174M AGT and Cgenetic polymorphisms association with CHF clinical features. We also found no association of genetic polymorphisms with left ventricular systolic dysfunction. We found association tendency of 1166 allele (AA and AC genotypes) with lower CHF NYHA class (93.3% in 3-class NYHA Vs 66.7% in 4 class NYHA,  $\chi^2=4.26$ ,  $p=0.099$ ). The same association was found in Met235 allele (84.4% in 3-class NYHA Vs 50% in 4 class NYHA,  $\chi^2=43.99$ ,  $p=0.081$ ). This was concordant with less N-proBNP level in patients having Met235 allele (2086,6 [658,9;2996,5] Vs 3482,0 [1563,3;4487,3] in its absence,  $p=0.06$ ). The lowest N-proBNP level was found in heterozygotes, who had N-proBNP level 19882,0 [475,7; 2460,8] ( $=0.045$  compared to TT genotype and  $=0.092$  compared to genotype MM).**Conclusion:** During our investigation we found relatively small frequency of RAAS genes polymorphisms, which is responsible, according to literature data, for IHD and AH association. Quite an interesting fact was that in our research we found no genetic polymorphism candidates, associated with systolic dysfunction of left ventricular. Together with that there was a tendency to lower CHF NYHA class in patients having 1166 AGTR1 allele and Met235 AGT allele in genome. Although N-proBNP lower level was found in Met235 heterozygotes. Considering that modern literature data often give controversy information about genome influence on CVD development, especially in the researches that involved not very large population, further analysis of RAAS polymorphisms functional significance in CHF patients it is very actual.**P1916****Novel brilliant violet-based flow cytometric method for simultaneous assessment of monocyte subsets and telomere length in heart failure patients**

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S Roura<sup>1</sup>; I Alvarez<sup>2</sup>; E Elchinova<sup>3</sup>; MA Fernandez<sup>2</sup>; J Lupon<sup>3</sup>; A Bayes-Genis<sup>3</sup><sup>1</sup>ICREC research group, Institut d'Investigació en Ciències de la Salut Germans Trias i Pujol, Badalona, Spain; <sup>2</sup>Germans Trias i Pujol Health Science Research Institute, Flow Cytometry Facility, Badalona, Spain; <sup>3</sup>Germans Trias i Pujol Hospital, Cardiology Service, Badalona (Barcelona), Spain**Introduction:** Systemic monocyte subset counts are valuable as predicting factors in heart failure. Additionally, telomere length and telomere attrition are linked to genetic instability, pathogenesis and disease progression. Current analytical techniques, including Southern blot, qPCR, flow cytometry and Fluorescence In Situ Hybridisation (FISH), have limitations such as sample volume waste, number of available reagents, difficulty to conjugate antibodies and accuracy.**Purpose:** The aim of this study was to develop a novel and timely method for assessing simultaneously monocyte heterogeneity and ageing in patients with heart failure.**Methods:** Ninety-six consecutive patients diagnosed with heart failure and attended in the Cardiac Insufficiency Unit of our hospital were enrolled. Referral criteria were heart failure irrespective of the origin, at least 1 hospitalisation and/or reduced left ventricular ejection fraction of <40%. Methodologically, the study included standard procedures of peripheral blood extraction and Flow-FISH staining. The samples were incubated previously to telomere probe hybridisation with monoclonal antibodies conjugated with Brilliant Violet dyes (BV421, BV605 and BV786) against monocyte surface antigens CD86, CD14 and CD16, respectively. Data were acquired using a BD LSR Fortessa flow cytometer and analysed in BD FACSDiva software (v.6.0.2). Telomere length was expressed as Relative Telomere Length (RTL). The RTL value was calculated as the ratio between the telomere signal of each subset and the control cell (1301 cell line) with correction for the DNA index of G0/1 cells.**Results:** Percentage of monocyte subsets expressed as mean ± SD were CD14+CD16- (Classical Subset; 50.38 ± 17.29), CD14+CD16+ (Intermediate Subset; 42.02 ± 17.26) and CD14lowCD16++ (Non Classical Subset;

8.13 ± 4.21). In addition, RTL of monocyte subsets were CD14+CD16- (Classical Subset; 9.64 ± 2.51), CD14+CD16+ (Intermediate Subset; 9.68 ± 2.58) and CD14lowCD16++ (Non Classical Subset; 10.00 ± 2.43).

**Conclusions:** The use of Brilliant Violet dyes in FISH hybridisation protocol provides accurate measure of specific monocyte subpopulations and their respective telomere length done at the same time. Importantly, this novel methodology may be easily applied in broad patient populations to establish clinical associations between heart failure categories and/or progression and monocyte heterogeneity and ageing.**P1917****Risk factor for Heart failure admissions in adults with congenital heart disease in monocentric tertiary center**N Ben Moussa<sup>1</sup>; F Pontnau<sup>1</sup>; V Salles<sup>1</sup>; Y Boudjermine<sup>2</sup>; A Legendre<sup>2</sup>; L Iserin<sup>1</sup>; D Bonnet<sup>2</sup>; M Ladouceur<sup>1</sup><sup>1</sup>Hôpital Européen Georges Pompidou, Université Paris Descartes, congenital heart disease department, Paris, France; <sup>2</sup>Hospital Necker, Paris, France**Background:** Adult with congenital heart disease (ACHD) are now more important than children with heart malformation, and this population is rapidly growing. Heart failure (HF) is a serious complication in the long-term follow-up of ACHD, and is one of the main causes of death in these patients. Therefore, a substantial increase in hospitalizations because of heart failure in ACHD is observed, requiring specialized care and making this problem an important public health issue.**Aims:** we aimed to characterize HF in ACHD and its management in a tertiary center. We also wanted to identify risk factors of first HF-admission.**Methods:** We retrospectively assessed the medical records of 408 consecutive admissions of adults with CHD in our center. Risk factors for HF-admission were assessed using regression logistic models.**Results:** 408 patients were admitted in our center during a median follow up period of 14 months. HF criteria were met by 29 patients (7,1%). ACHD with HF were significantly older than other ACHD patients admitted (median age was 43 years vs 33 years,  $p=0.001$ ). They had more complex congenital heart disease (62%), they were mainly patients with history of right ventricle outflow tract surgery, single ventricle and pulmonary artery hypertension ( $p=0.007$ ). The aetiologies of HF were myocardial dysfunction ( $n=15$ ), valvular disease ( $n=5$ ), pulmonary hypertension ( $n=4$ ), arrhythmia ( $n=3$ ) and infective endocarditis ( $n=2$ ). Mean hospital stay of ACHD patients with HF was longer (13 days vs 5 days,  $p<0.0001$ ). Ten percent (3/29) died at a mean period of 23 days after their admission, one patient required circulatory support, and 2 patients were listed for heart transplantation. Independent risk factors for HF-admission were history of stroke (OR: 7,6 95%CI[2,4- 23,8],  $p$ ), abnormal rhythm conduction (OR: 4,2 95%CI[1,5- 11,6], heart failure (OR = 4,7 95%CI[1,6-13,7],  $p<0.01$ ), and atrial arrhythmia (OR: 3,5 95%CI[1,4 to 9,2). Number of cardiac surgeries was not a risk factor of HF. At admission systemic ventricle ejection fraction was the factor the most strongly associated with HF**Conclusions:** Mortality risk is substantially increased after HF-admission, which emphasizes the importance to identify patients at high risk of HF-admission. These patients might benefit from closer follow-up and earlier medical interventions. This may add in care of patients with ACHD in the community and streamline care at tertiary centers.**P1918****Epidemiology of chronic heart failure in Germany: a retrospective study of the health risk institute healthcare claims database**

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55.2% women) had CHF in 2011 and were included in the study, corresponding to an estimated prevalence of 3.87% in Germany. Out of those, a subgroup of 26 368 patients had newly diagnosed CHF, corresponding to an incidence of 655 per 100 000 persons at risk in Germany. The number of new CHF cases increased with age, and was similar in women and men. In the 2-year follow-up period, there were 48 159 hospitalizations among patients with newly diagnosed CHF; heart failure was the most common reason specified for hospitalization (7.5%). The most common comorbidities in the newly diagnosed CHF subgroup were primary hypertension (81.7%), dyslipidaemia (50.4%) and chronic ischaemic heart disease (44.4%). In the 2-year follow-up period, 16.3% (n=20 148) of all patients with CHF had died. In the same period, there were 5983 deaths in the newly diagnosed CHF subgroup (22.7%). Mortality was similar in women (22.6%) and men (22.8%), and increased with New York Heart Association class (14.6%, 16.9%, 30.8% and 53.3% for classes I, II, III and IV, respectively).

**Conclusions:** The high prevalence and incidence of CHF observed in this study underline the burden of CHF in Germany. Substantial mortality and hospitalization rates highlight the need for earlier diagnosis and appropriate treatment.

**P1919**

**Congestive heart failure quality markers: measures of gender-specific economic indicators (middle eastern population): data from a single centre heart failure registry**

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**Background/Introduction:** Identifying economic characteristics of congestive heart failure (CHF) measures is a vital component of resource allocation and clinical decision making.

**Purpose:** We aimed to identify the significant factors of economic and gender variability of CHF patients with a reduced ejection fraction (HFrEF).

**Methods:** We performed gender comparison of HFrEF patients hospitalised over a 12-month period.

**Results:** Of 174 consecutive patients, 78% were males and 22% were females. Compared to males, females had a statistically significant older age (64 vs. 58; P < 0.001). After one year, both males and females had similar all-cause and heart failure hospitalisation and re-hospitalisation rates. Females showed no differences in re-hospitalisation rates. Males were more likely to require defibrillator device implantation (34% vs. 12%; P = 0.008) and had higher gender-adjusted average annual expenses for single hospitalisation per patient (\$8,509 vs. \$6,232; P = 0.035), direct daily costs (\$967 vs. \$708; P = 0.038) and higher device implantation costs (\$3,714 vs. \$1,477; P = 0.002) than females. The total annual cost of \$2,142,186 was \$1,697,557 and \$444,629 from males and females, respectively.

**Conclusion:** Our findings showed that female HFrEF patients had similar annual costs; LOS; in-house mortality, hospitalisation and rehospitalisation rates; less resource utilisation for implantable devices and lower direct cost per patient per day in comparison to male patients.

**Gender-specific economic indicators**

Characteristics	Males (n = 135)	Females (n = 39)	P-value	95% CI for difference
Age	58, (13.5)	64, (9.04)	< 0.001	(-10.4, -3)
EF	23, (9.2)	28.2, (12.8)	0.02	(-9.6, -0.7)
Hospitalisation (all cause)	239%	236%	0.93	(-0.59, 0.64)
Hospitalisation (CHF)	144%	172%	0.20	(-0.7, 0.15)
Re-hospitalisation (all cause)	49%	79%	0.15	(-0.7, 0.11)
Re-hospitalisation (CHF)	34%	43%	0.33	(-0.2, 0.08)
Re-hospitalisation (30 day)	13%	17%	0.50	(-0.17, 0.08)
Average LOS (mean, SD)	8.5, (7.2)	10.08, (15.1)	0.55	(-6.5, 3.5)
Daily cost per patient	\$967 (667)	\$708 (676)	0.04	(14, 504)
Annual hospitalisation cost per patient	\$12,574 (13,080)	11,401, (16,360)	0.64	(-4,548, 6,895)
Single hospitalisation per patient	\$8,509 (5,873)	\$6,232 (5,951)	0.04	(121, 4,435)
Annual re-hospitalisation cost per patient	\$4,820 (9,156)	5,368, (13,161)	0.81	(-5,070, 3,973)

LOS, length of stay; EF, ejection fraction

**P1920**

**Eradication therapy for Helicobacter Pylori, an important tool to improve the heart function in patients with coronary heart disease.**

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**Background:** The pro-inflammatory and pro-coagulant status of Helicobacter Pylori (HP) and its involvement in ischemic coronary heart disease was studied largely in the last 20 years, but the literature data regarding the benefit of the curative treatment for HP and its repercussions on heart function was not explored sufficiently.

**Aim:** We aimed to investigate the benefit of eradication therapy for HP according to Maastricht IV/Florence Consensus 2010 in patients with different stages of heart insufficiency (HI) and coronary heart disease (CHD).

**Material and Methods:** During one year, between 2014 and 2015, 240 patients with CHD admitted in Cardiology and Gastroenterology Departments were explored according the HP infection status and found positive. The infection was determined by one of the most sensitive methods, including HP-Ag from feces, urea breath test or endoscopic biopsy. The CHD was assessed by electrocardiography (ECG) and HI was staged according to NYHA classification. According to the implementation of eradication therapy for HP, we divided the patients in two equal groups, matched by age, gender and severity of HI: one group of 120 patients with treatment and the other group of 120 patients without eradication therapy. We compared the heart function improvement after treatment for HP in both groups. We also compared the evolution of PCR, fibrinogen, IL-6 and other inflammatory cytokine.

**Results:** The eradication therapy for HP with one PPI and two antibiotics associated with cardiac treatment, improved the clinical status based on NYHA criteria in 96 patients with at least 1 stage decrease in NYHA staging compared with only 45 patients from the group with cardiac treatment but without eradication therapy (p = 0.03). The laboratory finding also revealed a favorable course of pro-inflammatory tests in treated patients compared with untreated patients, regarding protein C-reactive, leucocytes, IL-6 and fibrinogen (p = 0.023, p = 0.041, p = 0.03, respectively p = 0.017, ss).

**Conclusion:** Our study results demonstrate that eradication therapy for HP should be one of the treatment targets when managing infected patients with CHD in order to improve their cardiac function.

**P1921**

**Low hemoglobin, diabetes and renal impairment: the perfect cocktail for death in advanced heart failure patients.**

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**Introduction:** Patients with heart failure with reduced ejection fraction (HF-REF) are at higher risk of death. In the last decade, the progress made in the therapeutic approach has greatly improved the prognosis of HF-REF patients. However, there're baseline patient characteristics which are associated with higher rates of mortality and adverse events.

**Objective:** The aim of the study was to find independent variables with impact on death in stable HF-REF patients followed in an outpatient clinic.

**Methods:** Retrospective analysis of patients with advanced HF-REF. Clinical, laboratory and therapeutic variables were considered. A logistic regression model was performed to find the predictors of death in stable HF-REF patients.

**Results:** We evaluated 130 patients [99 (76.2% men)] with stable HF-REF whose mean age was 65.9 ± 14.8 years and mean follow up duration was 42 ± 7.7 months. The 16 patients (12.3%) who died had more previous emergency department's admissions. They were older, showed higher prevalence of diabetes, dyslipidemia, hypertension, coronary revascularization (percutaneous or surgery) and pulmonary disease. At laboratory findings, they had lower hemoglobin values and higher creatinine and urea values, leading to a lower GFR (MDRD calc). There were no statistically significant differences in therapeutic approach considering medical treatment and devices. Multivariate analysis showed diabetes, low hemoglobin value and renal impairment (MDRD calc) as independent predictors of death (Table). Despite its low specificity (22.2%), this adjusted model has high sensitivity (97.3%) and a good discriminating ability (AUC = 0.78; p < 0.001).

**Conclusions:** In spite of great achievements in the medical treatment, baseline characteristics still remain highly valuable in predicting death in HF-REF. According to the current data low hemoglobin, diabetes and renal impairment are independent predictor of death in patients with stable heart failure with reduced ejection fraction.

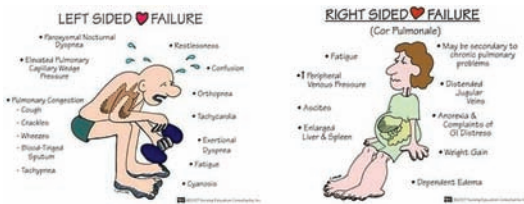
	OR	IC 95%	p-value
Diabetes	11.04	1.04 - 117.69	0.047
Low hemoglobin	1.77	1.08 - 2.92	0.025
Renal impairment	1.06	1.01 - 1.11	0.016

**P1922**

**Chronic heart failure management**

Heewad complex hospital (private) bust Helmand hospital (governmental)  
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Heart failure is a common syndrome that is increasing in incidence and prevalence. Optimal management of chronic heart failure includes combination medical therapies such as ACE inhibitors ,aldosterone antagonist,and B blocker. The treatment of heart failure is aimed at relieving symptoms, improving function status and preventing death and hospitalization. 1.diuretic therapy :- diuretic are most effective means of providing symptomatic relief to patients with moderate to severe heart failure. 2.ACE inhibitors reduce mortality by approximately 20% in patients with symptomatic heart failure and have been shown also to prevent hospitalization, increase exercise tolerance,and reduce symptoms in patients. 3.ARBs:- thus ARBs specifically candesartan or valsartan, provide important benefits as an alternative and in addition to ACE inhibitors in chronic heart failure with reduced LV EF. 4. B blockers : this has led to a strong recommendation that stable patients with mild moderate and even severe heart failure should be treated with a B blocker unless there is noncardiac contraindication. 5. Digitalis glycosides : based on these results digoxin should be used for patients who remain symptomatic when taking diuretics and ACE inhibitors as well as for patients with heart failure.



Lift and right side heart failure

**ARRHYTHMIAS AND TREATMENT**

**P1923**

**Prognostic markers of myocardial electric instability**

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**Purpose** of this study was assessment of the diagnostic significance of the complex of markers of myocardial electric instability: microvolt T-wave alternation (mTWA), HRT (TOVTS), intervals QTd and JTd dispersion, deceleration (DC) and acceleration (AC) indexes of heart rate to predict ventricular tachyarrhythmias (VTAs).

**Material and methods:** The study included 183 patients with systolic dysfunction (NYHA III) of different genesis (aged 51,2±12,3 years, male 77.6%; LVEF 36,7±10,8%); follow-up 35,3±9,6 months. All patients were examined: echocardiography; Holter monitoring (HM) ECG; 7-min ECG (Intekard-7) and telemetry of the implanted device (DDD, VVI, CRT, CRT-D, ICD) if in presence.

**Results:** In 86 (47%) patients according to the HM-ECG and devices telemetry the ventricular tachyarrhythmia (VTA) events (sustained and nonsustained ventricular tachycardias) have been registered. Correlative analysis revealed a positive correlation VTA events with a pathological test mTWA (% of pathological mTWA and average value mTWA; p=0.00001), the daily number of premature ventricular beats (PVEs\ 24h; p=0.0001), LVEF (p=0, 0001), the index of DC (p=0.003), HRT (TO; p=0.004) and interval JT dispersion (p=0.01). By the step discriminant analysis (F =5,58; p <0,0001) were confirmed the predictive value of LVEF (Wilks'-Lambda 0,90; p=0.00018), the percentage of pathological mTWA (Wilks' Lambda 0,87; p=0.006), and PVEs\ 24h (Wilks' Lambda 0,87; p=0.008). Data analysis and classification coefficients of the equations are presented in table.

**Conclusions:** The applying of classification matrix including markers of electric instability of myocardium (mTWA, PVEs\ 24h) and LVEF enabled to predict VTA events in patients with reduced ejection fraction (sensitivity 65%, specificity 70%).

Results of discriminant analysis

Predictors	Wilks' Lambda	Partial Lambda	F-remove (1,58)	p-level	Coefficients of the equations
Const. -4,52 (non VT)	Const. -5,14 (with VTA)				
LV EF	0,901462	0,924694	14,57743	0,000185	0,15101
Percent (%) of pathological mTWA	0,869567	0,958612	7,72830	0,006017	0,05068
PVEs\24h	0,866586	0,961909	7,08823	0,008466	0,00016

**P1924**

**Influence of pacemaker implantation in patients with heart rhythm disorders and heart failure without indications to cardiac resynchronization**

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There is a group of patients in different stages of heart failure and heart rhythm disorders which are qualified for standard right heart pacing without classic indications to cardiac resynchronization (CRT). Question, how pacemaker implantation influence the quality of life is still actual. Aim of this study was to evaluate the way on which pacemaker implantation influences the quality of life (QoL) in patients with heart rhythm disorders and heart failure without indications to cardiac resynchronization after six months of follow up.

**Methods:** 182 patients with heart rhythm disorders and heart failure (NYHA I - IV) qualified for pacemaker implantation (without indications to CRT) were included into this prospective single center study. A DDD pacemaker was implanted in each patient. The ventricular lead was positioned in the right ventricle outflow tract. QoL and was evaluated twice: 3-5 days before implantation and 6 months later using an MLWHF (Minnesota Living With Heart Failure) questionnaire - less points mean better QL.

**Results:** An overall statistical improvement in QoL was found in the global score (before 42.36±9.58, after 25.54±7.02; p=0.000), emotional components (before 9.56±4.15, after 7.75±3.41; p=0,000) and physical components (before 19.13±4.73, after 9.99±3.54; p=0.000) 6 months after implantation. QoL results according NYHA class are presented in the table below. Highly statistical improvements QoL was observed in all its components and in all NYHA classes.

**Conclusions:** Implantation of a pacemaker improves the quality of life in patients with heart rhythm disorders and heart failure.

**P1925**

**Left cardiac sympathetic denervation done by a video-assisted thoroscopic approach (VATS ) led to terminate electrical storm in ICD patients with ischemic cardiomyopathy.**

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**Introduction:** Electrical storm is a life threatening experience for the patients and it is a great therapeutic challenge for the physician. An electrical storm is usually associated with catecholaminergic hyperactivation. And requiring frequent shocks in patients with implantable cardioverter defibrillators. Deleviring repeated shocks induces myocardial damage and further worsens the arrhythmias, which are resistant to the antiarrhythmic drugs. Thus the management of an electrical storm by sympatholytic measures, other than the conventional pharmacologic beta adrenergic blockade , is of very significance.

**Methods:** We treated the electrical storm in 5 patients (4 men) , aged 42-58 years with ischemic cardiomyopathy. In all patients the conventional therapy failed. Cardiac sympathetic blockade was assessed by Left cardiac sympathetic denervation (LCSD) LCSD was done by video-assisted thoracoscopic approach(VATS).The pleural cavity was entered through three small incisions in the left subaxillary area; a double lumen endotracheal tube allowed ventilation of the contralateral lung while the ipsilateral lung was deflated and not ventilated to facilitate access to the sympathetic chain. The blockade was succeeded using 20ml of 2% xylocaine followed by an extra infusion of 20ml ropivacaine in the selected ganglion area.

**Results:** The effects of xylocaine and ropivacaine on hemodynamic parameters are minimal. The arrhythmia was tolerated by electrical storm termination. A partial Horner- s syndrome was developed in 3 patiens which is remained for one week. The patiens remained symptom-free without any incident of ventricular arrhythmias since 13-18 months now.

**Conclusions:** Sympathetic hyperactivity seems to play an important role during electrical storm in ischemic cardiomyopathy patients. Therefore neuroaxial modulation is an attractive option for the arrhythmia management. These treatment modalities can be considered when standard treatments fail. Large prospective randomized studies are needed to further define the clinical role of these therapeutic strategies in the future.



60856. QoL accoring NYHA class

	GLOBAL score		EMOTIONAL components			Physical components			
	Before	After		Before	After	p	Before	After	p
NYHA I	40,57 ± 7,84	26,83 ± 6,39	0,000	10,11 ± 4,54	8,51 ± 3,42	0,000	18,88 ± 4,91	11,08 ± 3,91	0,000
NYHA II	39,46 ± 8,11	23,98 ± 6,43	0,000	8,56 ± 3,88	7,46 ± 3,31	0,000	18,28 ± 3,95	9,41 ± 3,15	0,000
NYHA III	45,27 ± 11,07	26,25 ± 7,61	0,000	9,98 ± 4,09	7,65 ± 3,25	0,000	19,82 ± 5,17	9,87 ± 3,57	0,000
NYHA IV	47,18 ± 8,97	26,64 ± 7,77	0,000	10,86 ± 4,07	7,73 ± 4,09	0,000	20,50 ± 5,29	10,41 ± 3,77	0,000

Less points mean better QoL.

**P1926**

**Arrhythmic risk and genetic variations in dilated cardiomyopathy patients**

PTDC/BIM-MEC/0650/2012

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**Introduction:** Dilated cardiomyopathy (DCM), characterized by left ventricle (LV) enlargement and contractile dysfunction, is associated with high risk of arrhythmic sudden cardiac death (SCD) in a subgroup of patients. Until now, risk stratification has been based on the individual arrhythmic profile and LV ejection fraction (EF), even though SD may occur with EF > 35%. Family history of unexplained SD, especially in the young, is a raising concern, taking into account potential inheritable risk factors. Currently, with rare exceptions of lamina A/C mutations carriers, it remains unknown how genetic factors and respective tests can be used in clinical practice for SD prediction.

**Purpose:** We intend to assess the relation between the arrhythmic risk and genetic variations in dilated cardiomyopathy patients, to evaluate the potential role of genetic tests in clinical practice.

**Methods:** In this work we included idiopathic DCM patients (age ≤ 50 years) and familial DCM patients (irrespective of the age), and compared the presence of genetic variants between two subgroups with a priori distinct SD risk: those with family history of SD and/or previous implantable cardioverter-defibrillator (ICD) for primary or secondary prevention, versus those without any of the conditions. Molecular analysis included the search of mutations in LMNA/C, MYH7, MYBPC3, TNNT2, ACTC1, TPM1, CSRP3, TCAP, SGCD, PLN, MYL2, MYL3, TNNI3, TAZ and LBD3 genes using PCR technique with direct-sequencing (next-generation sequencing with at least a 30- fold coverage combined with Sanger sequencing). Pathogenicity was assessed by comparisons with mutations previously described, functional tests and segregations studies.

**Results:** We studied 112 patients, 46.4% with familial DCM; 58.3% males, mean age 47 ± 12 years, with mean age at diagnosis of 38 ± 13 years. Mean left ventricle ejection fraction was 32 ± 12% and LV end-diastolic diameter 64 ± 9 mm, and 37.4% of them presented left bundle branch block. Twelve (10.7%) patients had family history of unexplained SCD, 21 (18.8%) patients had implanted an ICD device and 3 patients (2.7%) presented both conditions. A total of 35 genetic variants were found in 29 (25.6%) patients. These mutations occurred in different genes: 10 in MYBPC3, 6 in TNNT2 and in LMNA, 3 in MYH7, in PLN, in TCAP and in LBD3, and one in TPM1 gene, with their relative distributions being similar between both groups (30.6% versus 23.7% in patients with and without family history of SCD/ICD, respectively; p=0.438).

**Conclusion:** In our DCM patients, family history and previous ICD implantation decision could not predict the genetic results. Follow-up of DCM patients with distinct genetic mutations is necessary to clarify how the genetic profile can be integrated in algorithms for SCD primary prevention.

**P1927**

**Incidence, associated factors and patient outcomes of heart failure complicated by ventricular arrhythmia in saudi arabia: from heart function assessment registry trial in saudi arabia.**

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**Introduction:** Arrhythmia is a common finding in heart failure (HF) patients. It has a greater impact on prognosis in those patients, especially ventricular arrhythmia type. Although there are some studies about premature ventricular contractions (PVCs) and non-sustained ventricular tachycardia (NSVT) in heart failure, few data

are available regarding sustained ventricular tachycardia (VT)/ ventricular fibrillation (VF) in heart failure.

**Purpose:** In this study, our aim was to investigate the incidence of sustained VT/VF, the factors associated with its occurrence and prognosis in hospitalized heart failure patients.

**Methods:** This is sub-study of prospective study of 2610 patients admitted in 18 government hospitals with HF between October 2009 and December 2010. Patients were categorized as having ventricular arrhythmia (VA) if they experienced either sustained VT or VF or both during hospitalization.

**Results:** Of 2610 patients with HF enrolled in Heart Function Assessment Registry Trial in Saudi Arabia (HEARTS), 110 (4.2%) were diagnosed with VA. The vast majority (97%) occurred in patients with heart failure with reduced ejection fraction (HFrEF). Factors associated with an increased risk of developing VA during hospitalization for HF are arrhythmia (OR 7; 95% CI 2.4-19.3), STEMI (OR 4.7; 95% CI 1.6-14), infection (OR 3; 95% CI 2.4-19.3) as precipitating factors for HF, and low SBP (<90 mm Hg) at presentation (OR 3.6; 95% CI 1.2-11). Adverse in-hospital outcomes including recurrent HF, hemodialysis, shock, sepsis, major bleeding, intra-aortic balloon pump (IABP) and pacing were higher for patients with VA (P≤.001 for all comparisons) and signified a poor prognosis. The in-hospital, 30-days, 1-year, 2-year, and 3-year mortality rates were significantly higher in VA patients compared with non-VA patients (P≤.001 for all comparisons).

**Conclusions:** VA was found in a small percentage of hospitalized heart failure patients. However, it was associated with remarkably high rates of adverse events and increased mortality rate. Information from patient's medical history and clinical presentation parameters can predict VA development in HF patients. Evaluating those associated factors would help in identifying patients at high risk for VA.

Factors associated with in-hospital VA

Associated Factor	Odds ratio	95% CI	P value
Arrhythmia	7	2.4-19.3	<.001
STEMI	4.7	1.6-14	0.006
Infection	3	1.2-7.6	0.024
SBP < 90 mmHg	3.6	1.2-11	0.023

**P1928**

**The relation between digoxin and appropriate shocks in patients with ischemic heart failure and implantable cardioverter defibrillator**

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**Objective:** Although digoxin improves heart failure symptoms, its potential proarrhythmic effects on ischemic myocardium has been debated. In this cross-sectional study, we investigated the relation between appropriate shocks in patients with ischemic heart failure (HF) and implantable cardioverter defibrillator (ICD).

**Material and Method:** In between January 2014 and August 2015, patients who were admitted to our hospital for routine ICD controls were evaluated according to the presence of appropriate ICD therapy. All patients included into the study provided ventricular pacing <5%.

**Results:** A total of 139 patients were included in the present study. Of these 35 patients (25.1%) experienced appropriate ICD shocks. In patients with ICD shocks, baseline left ventricular ejection fraction (LVEF) was significantly lower (p=0.009). When patients were compared according to the medications used, the number of the patients using aspirin and diuretic was significantly higher in the shock-received group whereas, statin usage was significantly lower in the shock-received group (p=0.030, p=0.046, p=0.044; respectively). Digoxin usage did not differ between the groups (p=0.388). In logistic regression analysis, aspirin usage and LVEF were found as independent predictors of ICD shocks (p=0.032 and p=0.045).

**Conclusions:** Baseline LVEF independently predicts ICD shocks. However, digoxin has no effect on ICD shocks in patients with ischemic HF and ICD. Moreover,

patients with ICD shocks require more diuretic therapy and were less treated with statins compared to patients without shocks.

Variables	Univariate			Multivariate		
	OR	CI 95%	p-value	OR	CI 95%	p-value
GENDER	0,357	0,140-0,910	0,031	0,361	0,128-1,020	0,054
AGE	0,994	0,959-1,029	0,718			
CABG	1,086	0,463-2,545	0,850			
PCI	2,308	1,049-5,076	0,038	2,158	0,919-5,068	0,077
Hypertension	1,500	0,615-3,360	0,373			
Diabetes mellitus	1,244	0,540-2,867	0,608			
Cigarette	1,283	0,593-2,777	0,527			
LVEF	1,115	1,023-1,215	0,013	1,102	1,002-1,212	0,045
ACEI/ARB	0,783	0,255-2,403	0,668			
Spiromolaktone	1,819	0,835-3,963	0,132			
Aspirin	3,291	1,071-10,116	0,038	3,784	1,125-12,725	0,032
Digoxin	1,448	0,623-3,367	0,389			
Furosemid	2,500	0,999-6,258	0,050			
Statin	0,452	0,207-0,987	0,046	0,455	0,189-1,092	0,078
Beta-blocker	2,833	0,342-23,495	0,335			

TABLE 1

**P1929****Permanent junctional reciprocating tachycardia: a cause of heart failure during pregnancy**SN Naccache<sup>1</sup>; FH Halimi<sup>1</sup><sup>1</sup>Hôpital privé de Parly II, le chesnay, France

Permanent junctional reciprocating tachycardia (PJRT) is a rare form of supraventricular arrhythmia, more common in the pediatric than in the adult population. This type of accessory-pathway-mediated tachycardia is usually incessant and can lead to tachycardia-induced cardiomyopathy. We describe the case of a 38-year old woman, consulting during the 17th week of pregnancy for dyspnea and progressive fatigue. Physical examination was unremarkable. A long RP narrow complex supraventricular tachycardia with inverted P waves in inferior leads was noted on her ECG. Transthoracic echocardiography revealed a dilated cardiomyopathy with depressed left ventricular ejection fraction. Since this arrhythmia became life-threatening for both mother and foetus, ablation was discussed. This was a challenging task because fluoroscopy at this stage of pregnancy is associated with a considerable risk of congenital malformation. In the electrophysiology laboratory, initiation of the clinical tachycardia occurred after sinus rhythm acceleration. Catheters were placed in the right atrium, without using fluoroscopy, guided by Carto 3D system. The earliest retrograde atrial activation during tachycardia was present at the proximal-to-mid coronary sinus. Paced ventricular extrastimuli, timed to His bundle refractoriness, advanced the atrial electrogram approximately 20 ms and reset the tachycardia. On the basis of these findings, diagnosis of orthodromic reciprocating tachycardia utilizing a slowly conducting posteroseptal accessory pathway, or PJRT, was made. A mapping of the right atrium was performed. Radiofrequency ablation of the right posteroseptal pathway was accomplished and stopped definitively the tachycardia. Radiofrequency ablation of the accessory pathway is the only real curative treatment in PJRT. It prevents side effects of such incessant tachycardia and allows total cardiac recovery after ablation. During pregnancy, zero fluoroscopy ablation represents an advantageous technique that must be considered.

**P1930****Appropriate therapies in patients with implantable cardioverter-defibrillator for primary prevention of sudden death: how to identify patients who benefit the most?**S Sofia Alegria<sup>1</sup>; O Simoes<sup>1</sup>; AR Almeida<sup>1</sup>; R Miranda<sup>1</sup>; S Almeida<sup>1</sup>; G Morgado<sup>1</sup>; I Rosario Cruz<sup>1</sup>; L Brandao<sup>1</sup>; H Pereira<sup>1</sup><sup>1</sup>Hospital Garcia de Orta, Cardiology, Almada, Portugal

**Introduction:** Left ventricular (LV) ejection fraction (EF)  $\leq 35\%$  is a major determinant for implantable cardioverter-defibrillator (ICD) therapy for primary prevention of sudden death, in patients with ischemic cardiomyopathy or dilated non-ischemic cardiomyopathy. However, LVEF presents limited sensitivity and specificity as a risk marker of sudden death, since a significant amount of patients with poor LV function never present malignant ventricular arrhythmias.

**Purpose:** Characterization of a population submitted to ICD implantation for primary prevention of sudden death; analysis of the occurrence of appropriate therapies and its predictors.

**Methods:** Retrospective analyses including patients with ischemic cardiomyopathy and non-ischemic dilated cardiomyopathy who implanted ICD, with associated

cardiac resynchronization therapy (CRT) or not, for primary prevention of sudden death, between 2011 and 2014.

**Results:** 59 patients were included (mean age  $61 \pm 10$  years, 68% male sex), 66% with ischemic cardiomyopathy and 29% with associated CRT. The mean baseline EF was  $28 \pm 6\%$ , 48% of patients were on NYHA class II and 44% on NYHA class III. During a mean follow-up of  $825 \pm 412$  days, 17% of patients had appropriate therapies (3.4% shocks, 10.2% ATP and 3.4% both) and the mortality rate was 15%. Among the 43 patients in whom a follow-up transthoracic echocardiogram (TTE) was available, 34.9% recovered LV function (defined as improvement of EF  $\geq 5\%$ , with final value  $> 35\%$ ). The occurrence of appropriate therapies was not associated with the etiology (ischemic vs. non-ischemic), baseline EF, functional class, presence of CRT-D, evidence of delayed enhancement in the cardiac MR and aneurysm in the TTE. However, there was a trend to the increase in appropriate shocks in patients with severe compromise of LV function (11% vs. 0% in patients with moderate compromise,  $p=0.098$ ). In this population the only variable associated with the occurrence of appropriate therapies was the EF post-implantation; patients who maintained EF  $< 30\%$  had an increased risk of dysrhythmic events (29% vs. 4%,  $p=0.028$ ; OR=9.17). In addition, the occurrence of appropriate therapies was associated with higher mortality during follow-up (40% vs. 10%,  $p=0.017$ ; OR 5.9 95% CI 1.2-28.1).

**Conclusion:** In this population of patients with compromised LV function submitted to ICD implantation for primary prevention of sudden death, appropriate therapies, although not common, were associated with higher mortality. Since the etiology, EF or functional class were not associated with the occurrence of appropriate therapies, our results reinforce the need to identify new risk markers of sudden death in this population. Taking into consideration that the only variable associated with appropriate therapies was the EF post-implantation, the identification of predictors of function recovery might contribute for a better risk stratification of these patients.

## ATRIAL FIBRILLATION

**P1931****Influence of metoprolol and diltiazem on diastolic function in patients with recurrent atrial fibrillation and heart failure with preserved ejection fraction**IM Irina Balabanenko<sup>1</sup>; AA Shavarov<sup>1</sup>; GK Kiyakbaev<sup>1</sup><sup>1</sup>Peoples Friendship University of Russia (PFUR), Moscow, Russian Federation

**Objective:** Heart failure with preserved ejection fraction (HF-PEF) is presumed to be due to diastolic dysfunction (DD) and is an independent predictor of atrial fibrillation (AF) in the elderly. Positive impact of beta-blockers has been studied and proven, but data for the effects of diltiazem on DD are limited.

**Aim:** The purpose of this study was to compare parameters of echocardiography and DD in AF patients with HF-PEF under metoprolol (M) and diltiazem (D) treatment.

**Methods:** The study included 55 patients (40% men) aged 66 (62; 73) years with mild-to-moderate AH, recurrent AF and HF-PEF ( $>50\%$ ). Clinical characteristics of M group patients ( $n=31$ ) and D group patients ( $n=24$ ) were similar. Average duration of AF was 11 (9; 13) months. All patients underwent echocardiography before and 3 months after treatment.

**Results:** Forty one patient (75%) had diastolic dysfunction, in 76% of these cases it was impaired relaxation. There were no significant differences in  $e'$  and  $E/e'$  medians in M and D groups, but comparison of delta showed significant opposite changes of these parameters.  $\Delta e'$  increased by 0,01 m/s in M group and reduced by -0,2 m/s in D group ( $p=0,002$ );  $\Delta E/e'$  increased by 0,01 in M group and decreased by -0,8 in D group ( $p=0,04$ ).  $E/e'$  had significant direct correlations with left ventricular myocardial mass index (LVMMI) ( $r=0,34$ ) and left atrial (LA) volume index ( $r=0,24$ ), and indirect correlations with LA emptying fraction ( $r=-0,31$ ) and LA expansion index ( $r=-0,31$ ). Changes of LVMMI and LA structural and functional parameters, as well as AF recurrence rate, were not significant in both groups during follow-up.

**Conclusion:**  $E/e'$  was correlated with structural and functional LA parameters in patients with AF and HF-PEF. Diltiazem improved cardiac diastolic function in comparison with metoprolol but it didn't lead to difference in AF recurrence rate.

**P1932****Relation of the severity of mitral regurgitation to thromboembolic risk in patients with atrial fibrillation**A Metwally<sup>1</sup><sup>1</sup>Al-Azhar University, cardiovascular department, Cairo, Egypt

Atrial fibrillation (AF) is the commonest sustained cardiac rhythm disorder and is responsible for substantial mortality and morbidity due to stroke, thromboembolism, heart failure, reduced quality of life and impaired cognitive function. This arrhythmia is commonly seen in everyday practice. The most important threats patients with atrial fibrillation face are stroke and heart failure. Furthermore, quality of life

grades of MR			
	mild	moderate	severe
specific signs	vena contracta width <0.3 cm, with small central jet (<4 cm <sup>2</sup> or <10% of LA),no or minimum flow convergence.	MR more than mild, without any criteria for severe MR.	Vena contracta width ≥0.7 cm , with large central MR jet(area > 40% of LA) or with a wall-impinging jet of any size; large flow convergence; systolic reversal in pulmonary veins; prominent flail leaflet or ruptured papillary muscle.
supportive signs	Systolic dominant flow in pulmonary veins;A-wave dominant mitral inflow; low-density doppler MR signal; normal left ventricle (LV) size.	MR more than mild, but no criteria for severe MR.	Dense, triangular doppler MRsignal; E-wave dominant mitral inflow (> 1.2 m/s); enlarged LV and left atrium (LA), particularly with normal LV function.
quantitative variables Rvol (mLper beat) RF ERO area (cm2)	<30 <30% <0.20	30–44; 45–59 30–39; 40–49% 0.20–0.29;0.30–0.39	≥60 ≥50% ≥0.40

is diminished due to AF symptoms as well as frequently associated cardiovascular diseases like hypertension, heart failure, coronary artery and valvular diseases. In the present study, the relationship between severity of mitral regurgitation (MR) and thrombo embolic risk in patient with AF was studied. Forty five patients (21M/24F) 30 patients with AF and MR referred to our cardio. dep., and 15 patients with atrial fibrillation without MR between Oct. 2012 and April 2013. Patients were subjected to full history taking, clinical evaluation, ECG., Transthoracic and transesophageal Echocardiographic (TEE) assessment was done. The severity of MR was assessed based on American Society of Echocardiography (ASE) guidelines (listed in a table down). Multiple standard tomographic planes were imaged by (TEE) for assessment of left atrium, spontaneous echo contrast (SEC), left atrial appendage (LAA) emptying velocities and LAA thrombi. Data were coded & entered using the statistical demo version of the graph Pad InStat, P value < 0.05 was considered statistically significant. It was found that thrombo embolic risk has been shown to increase significantly in patients with AF without MR compared to patients with AF with MR. SEC is increased significantly in patients with mild MR than patients with moderate and severe MR and no significant changes between SEC grade in moderate and severe MR. The prevalence of LAA thrombus is increased in patients with mild MR than patients with severe MR. LAA emptying velocity is decreased in patients without MR than patients with MR and decreased in patients with mild MR compared to patients with severe MR.

**P1933**

**Clinical characteristics of patients treating heart failure with and without atrial fibrillation under oral anticoagulant therapy.**

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**Background:** Oral anticoagulant (OAC) therapy is usual in patients with heart failure (HF), and atrial fibrillation (AF) is a common indication to prevent embolic complications. Clinical characteristics may influence therapeutical choices and modulate treatment response.

**Purpose:** To evaluate clinical characteristics of patients treating HF using OAC and to explore clinical differences between patients with AF and without AF (No-AF).

**Method:** A cross-section observational study analyzed 50 patients randomly selected from 417 treating HF and using OAC in referral service for cardiology in Brazil (29 AF and 21 No-AF). Variables as age, gender, weight, height, heart rate, heart disease etiology, functional class, history of hypertension, diabetes mellitus, use of alcohol, tobacco, previous occurrence of intracardiac thrombus, pulmonary embolism, stroke, presence of coronary artery disease confirmed by coronary angiography, echocardiography data, blood count, seric urea, creatinine, sodium, potassium, thyroid hormone level and BNP, dose of medication, time of follow-up, number of visits, hospitalizations, and free time for complications were compared between the groups. Statistical analysis: the t-test was applied to the continuous variables and the chi-square in categorical variables. P value less than 0.05 was considered significant.

**Results:** Among patients treating HF and using OAC, males were more prevalent in AF than No-AF (93% vs. 57%, p < 0.0001). Heart disease etiology showed more prevalence of hypertension and alcoholic cardiomyopathy in AF group and more prevalence of heart Chagas disease and ischemic cardiomyopathy in No-AF group (see the table below, p = 0.02). In AF group were more prevalent previous alcohol use (34.5% vs 14.3%, p = 0.03) and history of hypertension (69% vs 52.4%, p = 0.04).

In No-AF group were more prevalent previous occurrence of intra-cardiac thrombus (23.8% vs. 0%; p = 0.04) and pulmonary embolism (9% vs 0%, p = 0.03). The mean of left atrial diameter was higher in AF group (50.8 ± 7.0 vs 46.6 ± 7.3 mm, p = 0.047). There was no significant difference in the other variables analyzed.

**Conclusion:** Despite of the same condition of HF and OAC therapy, AF and No-AF groups shows some clinical differences. These distinct characteristics should be considered in therapeutic decision.

**P1934**

**Pulmonary vein isolation with cryoablation versus ablation with radiofrequency in the treatment of atrial fibrillation: a comparative analysis**

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**Introduction:** Atrial fibrillation (AF) is the most frequent sustained arrhythmia and is associated with a poor quality of life. Electric isolation of the pulmonary veins aims to prevent the occurrence of AF and represents a treatment option for symptomatic patients, refractory to antiarrhythmic drug therapy. Radiofrequency and cryoenergy are two used sources of energy; however, there is no consensus on which is the best choice. The authors present the initial experience of the Centre in pulmonary veins isolation (PVI) using cryoablation, analysing its efficacy and safety compared to ablation with radiofrequency.

**Methods:** Retrospective analysis of the PVI procedures using cryoablation and ablation with radiofrequency (ARF), based on review of clinical and interventional data of the procedures undertaken between August 2014 and October 2015. Follow-up was done by telephonic interview and clinical files consultation.

**Results:** 119 procedures, 42 (35.3%) with cryoablation and 77 (64.7%) with ARF, were performed in 118 patients (mean age 54.4 ± 11.2 years-old, 71.2% men). In the ARF group, 4 procedures included cavotricuspid isthmus ablation. There were no significant differences in age, comorbidities, left atrium diameter, ejection fraction, type of AF (paroxysmal or persistent), duration of AF, antiarrhythmic drug therapy or CHA2DS2-VASc score between the groups. Isolation of the 4 pulmonary veins was achieved in 73 (94.8%) of the procedures in the ARF group and in 38 (90.5%) in the cryoablation group, with similar acute complication rates (one small pericardial effusion in the ARF group and one transient phrenic nerve palsy in the cryoablation group). Procedural time was significantly inferior in the cryoablation group (98.5 ± 17.8 vs 109.1 ± 23.3 minutes, p = 0.01) and fluoroscopy time was higher (22.7 ± 10.2 vs 15.2 ± 6.1 minutes, p < 0.001). After a mean follow-up of 7.4 ± 4.2 months, AF recurred in 5 patients (11.9%) in the cryoablation group and 18 (23.4%) in the ARF group (p = 0.12), in a mean of 3.2 ± 2.5 vs 3.3 ± 3.5 months after the PVI procedure (p = 0.45), respectively. After multivariate logistic regression (adjusted for age, cardiovascular risk factors, echocardiographic parameters, type and duration of AF), the type of energy source used in the PVI was not a predictor of recurrence of the AF. There was a significant improvement in the palpitations, dyspnea, dizziness and fatigue symptoms in both groups, after the intervention.

**Conclusion:** The cryoablation and ARF methods in PVI showed comparable results in acute success and complication rates. Procedural time was significantly shorter in the cryoablation group and fluoroscopy time was longer. At short-term follow-up, recurrence rate was similar in both groups, mostly occurring during the blanking period. Patients experienced a significant improvement in the arrhythmia-related symptoms, irrespective of the method used.



## P1935

**Risk factors of the atrial fibrillation progression in patients with recurrent atrial fibrillation**TZ Tohir Ganiyev<sup>1</sup>; NU Zakirov<sup>1</sup>; RD Kurbanov<sup>1</sup>; DB Irssov<sup>1</sup><sup>1</sup>Specialized Cardiology Center of the Republic of Uzbekistan, Cardiac arrhythmia, Tashkent, Uzbekistan**Background:** HATCH score - acronym for hypertension, age>75, TIA or stroke, chronic obstructive pulmonary disease and heart failure are stratifies patients with paroxysmal AF according to their risk for AF progression during 1 year.**Purpose:** to evaluate the accuracy of the HATCH score to predict progression and to identify some other possible factors leading to permanent AF within 1 year in patients with recurrent AF.**Methods:** We retrospectively studied 203 patients (mean age 55 ± 13 years; 143 of men, 137 of them had paroxysmal AF (>2 onset per 3 months) and 66 had persistent AF (mean AF duration 81 ± 9 days) after cardioversion. Antiarrhythmic drugs administered to 88% patients in addition to upstream therapy. Progression of AF was defined, if paroxysmal or persistent AF at baseline becoming permanent AF. The primary end point was rhythm status at 1 year. We constructed a receiver operating characteristic (ROC) curve and calculated the area under the curve to estimate the HATCH score's accuracy of predicting AF progression.**Results:** Among 203 patients 43(22%) had progression to permanent AF (8.8% for paroxysmal and 47% for persistent AF). The mean HATCH score was 1.79 ± 1.58 and was significantly higher in patients whose AF progressed than who had no AF progression (2.95 ± 1.8 vs 1.48 ± 1.4, P=0.0001). According to HATCH score 50 (24%) patients had 0 points, 63 (31%) patients had score=1, and 78 (38%) patients had score 2-4. Only 12 (6%) patients had score>5 (4 patients had 6 points and no patients with score 7). High risk patients in paroxysmal AF subgroup were 8 and 4(50%) of them had progression versus 4 patients (100%) in persistent AF subgroup (n/s). According to logistic regression analysis, only 2 items of the HATCH score was associated with a risk of AF progression: HF (OR: 3.89, 95% CI: 1.46-10.35, P=0.006) and history of stroke or TIA (OR: 3.32, 95% CI: 1.45-7.62, P=0.004). In addition to HF and previous stroke or TIA, the history of persistent AF (OR: 11.84, 95% CI: 4.68-29.91, p<0.0001), and the presence of obesity or overweight at baseline (OR: 8.01, 95% CI: 1.49-43.08, p=0.015) were independently associated with AF progression. The HATCH score's ROC area under the curve was 0.732 (95% CI, 0.64-0.83, p<0.0001).**Conclusions:** At baseline, the HATCH score was a significant, but predictive accuracy was modest. Only 4 patients had a HATCH score>5 points and this recommended tool wasn't useful in identifying high-risk patients in this cohort. Independent predictors were the presence of HF, previous stroke or TIA and obesity or overweight and history of persistent AF.

## P1936

**Change in peak left atrial longitudinal strain predicted atrial fibrillation recurrence after cardioversion**AA Andrey Shavarov<sup>1</sup>; GK Kiyakbaev<sup>1</sup>; VS Moiseev<sup>1</sup><sup>1</sup>Peoples' Friendship University of Russia, Moscow, Russian Federation**Background:** Several echocardiographic studies have demonstrated that left atrial (LA) strain and strain rate imaging is a very useful to assessing atrial function before and after cardiovascular procedures. We hypothesized that speckle tracking imaging could be superior to traditional echocardiography in predicting atrial fibrillation (AF) recurrence after electrical cardioversion (CV).**Purpose:** To compare the predictive value of baseline echocardiographic parameters and its changes after CV for AF recurrence at 3 months.**Methods:** Thirty one patients [mean age 64 (60; 72) yrs, 48% men] with paroxysmal and persistent non-valvular AF were included in study comparing echocardiographic measurements before and 10 days after CV. All pts underwent conventional and speckle tracking echocardiography and received III class antiarrhythmic drugs after CV. 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:** Sinus rhythm maintenance was observed in 13 (42%) patients (group 1) throughout follow-up period whereas 18 (58%) patients (group 2) experienced at least one AF recurrence. Baseline echocardiographic and speckle tracking parameters were comparable between the 2 groups excluding PALSRc that was higher in group 1 than in group 2 (-1.87 vs -1.49 1/s, p=0.03, respectively). Change ( $\Delta$ ) in PALSR and PALSc 10 days after CV were significantly higher in group 1 to compare with group 2 (1.9 vs 0.5%, p=0.01, and -1.8 vs -0.7%, p=0.001, respectively). Regression analysis showed that  $\Delta$ PALSc was associated with AF recurrence ( $\beta$ =-0.67, =0.011). The AUC of  $\Delta$ PALSc in discriminating AF recurrence was 0.85 (95% CI 0.71-0.99, =0.001). An optimal cut-off value for  $\Delta$ PALSc of -1.96% predicted AF recurrence with sensitivity of 88.9% and a specificity of 61.5%.**Conclusions:** Improvement of PALSc within 10 days after CV was independently associated with AF recurrence. Baseline echocardiographic measurements did not reveal predictive ability regarding recurrent AF.

## P1937

**Effect of chronic kidney diseases on mortality among digoxin users treated for non-valvular atrial fibrillation: a nationwide register-based retrospective population-based cohort study.**M Sessa<sup>1</sup>; A Mascolo<sup>1</sup>; MP Andersen<sup>2</sup>; G Rosano<sup>3</sup>; F Rossi<sup>1</sup>; A Capuano<sup>1</sup>; C Torp-Pedersen<sup>2</sup><sup>1</sup>Second University of Naples, Department of Experimental Medicine, Naples, Italy;<sup>2</sup>Aalborg University, Department of Health, Science and Technology, Aalborg,Denmark; <sup>3</sup>San Raffaele Pisana Hospital IRCCS, Rome, Italy**Introduction:** After the post-DIG trial era, digoxin is commonly used worldwide as heart rate control agent for the treatment of atrial fibrillation. Current clinical practice guidelines recommend administering digoxin to patients with or without chronic kidney disease, if the clinical condition permits the treatment. However, no single study have directly evaluated the effect of chronic kidney disease on mortality in patients receiving only digoxin as the treatment for atrial fibrillation. Taking into account that patients with chronic kidney disease typically were excluded from clinical trials, register-based observational studies could potentially improve knowledge on this topic.**Purpose:** The objective of this study was to investigate the impact of chronic kidney disease on mortality across non-valvular atrial fibrillation patients treatment-naïve with digoxin.**Methods:** All patients with non-valvular atrial fibrillation and/or atrial flutter as hospitalization diagnosis from January 1, 1997 to December 31, 2012 were extracted through Danish nationwide administrative registries. Among these patients we selected only digoxin treatment-naïve users who have initiated pharmacological treatment for non-valvular atrial fibrillation in the period. A "new user" design was applied, to remove bias due to the inclusion of prevalent drug users. Patients were excluded if they started digoxin in co-administration with other antiarrhythmic drugs. Treatment initiation date of digoxin was used as the index date for each patient, as all patients should be diagnosed with non-valvular atrial fibrillation within this index date. The study population was divided into two cohorts: patients with or without chronic kidney disease. Cox proportional hazard model was used to estimate the adjusted risk of all-causes and cardiovascular mortality between the cohorts.**Results:** We identified 37981 patients treated for non-valvular atrial fibrillation receiving digoxin. Of these, 1884 patients had the diagnosis of chronic kidney disease. The study population of 37981 patients was followed up in the Patient Register for 10294 person-year (median = 99 days; range = 0-180), 22536 (59.3%) patients died. Among these, 14862 (39.1%) patients died for cardiovascular disease. Kaplan-Meier survival curves differed between the two cohorts for all-causes and cardiovascular mortality (log-rank test, p-value < 0.05). However, Cox regression analysis showed no statistically significant differences in all-causes (p-value = 0.110) and cardiovascular mortality (p-value = 0.146) among patients with chronic kidney disease compared to those without within both 180 days and 2 years from the index date.**Conclusions:** This study suggesting no effect of chronic kidney disease on all-causes and cardiovascular mortality within both 180 days and 2 years from the first prescription of digoxin in patients treatment-naïve with digoxin for non-valvular atrial fibrillation.

## CARDIOMYOPATHY

## P1938

**Long-term outcome of patients with virus-negative inflammatory cardiomyopathy after immunosuppressive therapy**F Felicitas Escher<sup>1</sup>; U Kuehl<sup>1</sup>; D Lassner<sup>2</sup>; D Westermann<sup>3</sup>; B Pieske<sup>1</sup>; C Tschöpe<sup>1</sup>; HP Schultheiss<sup>2</sup><sup>1</sup>Charite - Campus Virchow-Klinikum (CVK), Berlin, Germany; <sup>2</sup>Institute of CardiacDiagnostics and Therapy (IKDT), Berlin, Germany; <sup>3</sup>University Heart Center Hamburg, Hamburg, Germany**Aim:** To analyse the long-term outcome after immunosuppressive treatment of patients with virus-negative inflammatory cardiomyopathy (CMI).**Methods and Results:** We investigated 114 patients with endomyocardial biopsy (EMB)-proven virus-negative CMI, who were treated with prednisone and azathioprine for 6 months. Myocardial inflammation was assessed by quantitative immunohistology (IH). We examined hemodynamic measurements after 6 month and long-term follow-up periods of up to 10 years (mean 35.4 ± 127.9 months).

At follow-up, the patients altogether showed a significant improvement of left ventricular ejection fraction (LVEF) compared to baseline after 6 month and in the long-term follow-up (p = 0.006). Simultaneously, EMB-analysis revealed significant reduction of quantified inflammatory infiltrates (CD3+, CD2+, perforin+ cells), and cell-adhesion molecule HLA-1.

In a subgroup analysis, Patients with initial LVEF ≤45% (n=74) significantly increased with LVEF at follow-up (29.3 ± 8.8% to 41.7 ± 13.2% to 42.1 ± 13.1%, p &lt; 0.0001). Patients with initial LVEF &gt;45%-60% (n=25) significantly improved further (hemodynamically) or recovered completely, regarding LVEF (53.0 ± 3.6% to 59.0 ± 9.4% to 59.8 ± 10.0%, p = 0.03). Patients with initial LVEF &gt;60% (n = 15) remained stabilized and did not deteriorated over long-term follow-up (68.8 ± 6.7%

to  $67.5 \pm 10.9\%$  to  $68.8 \pm 10.7\%$ ,  $p=0.5$ ). Our data imply, that all patients can benefit from an immunomodulatory treatment, even in cases where initially only a slightly impaired LV function is present.

**Conclusions:** In patients with CMi we could show the effectiveness and beneficial effects of immunosuppressive treatment. This LVEF improvement is lasting for a long-term period of time.

#### P1939

##### Benefit of heart failure treatment in left ventricular non-compaction of the myocardium

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**Introduction:** Up until now there is no specific therapy for patients diagnosed with left ventricular non-compaction of the myocardium (LVNC). In the clinical practice if these patients present systolic dysfunction, standard heart failure treatment is initiated, however, its efficacy and clinical benefit is not studied among this group of patients.

**Methods:** We have included in our study all patients (pts) who fulfilled criteria for LVNC of the myocardium with decreased ejection fraction (EF < 50%) measured by echocardiography and magnetic resonance in the non-invasive cardiology laboratory of our tertiary hospital between January 2012 and February 2014. All of them received medical therapy for heart failure, including anti-remodeling agents according to the last recommendations. Clinical follow-up and control echocardiography study was carried out in order to determine the benefit of standard heart failure therapy in this patient population.

**Results:** We identified 11 pts fulfilling current criteria for LVNC and presenting decreased EF. Seven of them (63.6%) were males. Our study population had a mean age of  $54.4 \pm 14.9$  years and a mean ejection fraction of  $32.9\% \pm 10.4$ . Five pts (45.5%) had a previous heart failure episode. Two pts were in NYHA class  $\geq$  II, and the resting 9 patients were in NYHA class I. Ten pts (91%) received beta-blockers, 10 pts (91%) angiotensin converting enzyme inhibitors or angiotensin receptor blockers (91%), and 6 pts anti-aldosterone agents (54.5%). A resynchronization device was implanted in 1 patient. After a mean follow-up of  $29.6 \pm 8.4$  months, the mean ejection fraction was  $37\% \pm 18.2$  in the study population. Five patients presented a significant increase (>10%) of the EF after initiating the anti-remodeling treatment and 3 of them achieved a complete normalization of the EF (>55%). All these patients were alive and asymptomatic at the end of the follow-up. All 6 patients who did not present improvement of the EF were alive, and 50% of them was in NYHA class II at the end of the follow-up.

**Conclusions:** A significant percentage of our patients on anti-remodeling therapy presented increase of the left ventricular EF and in some of them the LVEF normalized. Anti-remodeling therapy can be beneficial in patients with LVNC and left ventricular systolic dysfunction.

#### P1940

##### Effect of combined treatment with ozonotherapy on the structural and geometric parameters of the myocardium in patients with hypertension and metabolic syndrome

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Hypertensive heart disease is the most common diseases of the cardiovascular system, being one of the causes of disability, morbidity and mortality. Also, the attention of clinicians focused on metabolic syndrome.

The aim of the study was to investigate the influence of complex medical treatment with the inclusion of ozonotherapy (OT) on the structural, geometric and functional parameters of left ventricular myocardium in hypertensive patients with metabolic syndrome.

The study involved 90 patients (44.2% men, 55.8% women) with essential hypertension II degree, concentric left ventricular hypertrophy, heart failure of 0-I and metabolic syndrome. The average age of the patients was ( $55.98 \pm 2.29$ ) years. The control group consisted of patients (30 persons), receiving standard medical therapy. The study group included 60 patients who in addition to standard medical therapy conducted in drip ozonated physiological sodium chloride solution with a concentration of ozone in the solution 3000 mg / l, 200 ml infusion lasting 60 minutes every other day, 10-12 procedures a course of treatment.

After treatment, there was a significant decrease of End Diastolic Volume (EDV) in all subgroups. Left Ventricular Ejection Fraction (LVEF) in the control and basic groups after treatment has not changed much. Increased Stroke Volume (SV) in the study group compared with the results before the treatment and was statistically significant. An increase in Minute Volume (MV) in the main group compared with the results before the treatment and was more pronounced, statistically significant nature than in the control group.

Thus, for the intergroup comparison showed a trend to improved left ventricular systolic function.

In analyzing the structure and geometric parameters of the left ventricle, found that after treatment the dynamics of changes in these indicators in the control groups and the main character was one-way with a tendency to their normalization. Also, significantly decreased indicators such as Interventricular Septal Thickness (IVST), the thickness of the posterior wall of the left ventricle (PWT), the index of left ventricular mass (LVMI).

Based on the above, we can conclude that the effect of ozonotherapy has its own character, which is not dependent on the use of antihypertensive drug base to optimize medical treatment of these patients.

Thus, comprehensive medical treatment including ozonotherapy improves the pumping function and reduces diastolic dysfunction of the left ventricle in hypertensive patients with metabolic syndrome.

#### P1941

##### Acute heart failure complicating takotsubo syndrome

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**Introduction:** Takotsubo syndrome (TS) has generally been regarded as a relatively benign disease; however growing evidence suggests it is a more serious acute cardiac disorder with a high incidence of acute heart failure (HF).

**Purpose:** To characterize a population with TS and acute HF and to determine the predictors of HF.

**Methods:** Retrospective study of 57 patients (pts) consecutively admitted for TS in a cardiology department over a period of 5 years. We define HF as Killip class  $\geq$  2. We analyzed the demographic and clinical characteristics, biomarkers and electrocardiographic and echocardiographic parameters.

**Results:** The mean age of the pts was  $67.3 \pm 11.6$  years and there were 46 (80.7%) female pts. The prevalence of HF was 43.9% and 8.8% of the pts developed cardiogenic shock. There were no differences in the demographic characteristics and cardiovascular risk profile of these pts. The presence of atrial fibrillation/flutter on admission was more common in pts with HF (28 vs 3.1%,  $p=0.007$ ). There was no difference in other electrocardiographic parameters. Pts with HF had, at admission, higher levels of creatinine ( $1.1 \pm 0.4$  vs  $0.8 \pm 0.3$  mg/dl,  $p=0.01$ ) and NT-proBNP ( $12750 \pm 14869$  vs  $3827 \pm 2767$  pg/ml,  $p=0.007$ ), as well as lower glomerular filtration rate ( $70.1 \pm 29.5$  vs  $89.1 \pm 33.3$  ml/min/1.73m<sup>2</sup>,  $p=0.03$ ). The peak troponin I was also superior in these pts ( $6.0 \pm 5.1$  vs  $3.6 \pm 3.3$  ng/ml,  $p=0.03$ ). In echocardiographic evaluation, the pts with HF had a higher prevalence of severe depression of left ventricular systolic function (LVSF) (36% vs 12.9%,  $p=0.04$ ), left ventricular outflow tract obstruction  $\geq$  40 mmHg (12% vs 0%,  $p=0.04$ ) and mitral regurgitation (grade > II/IV) (25% vs 3.1%,  $p=0.01$ ). The mean left ventricular ejection fraction was lower in these pts ( $34.2 \pm 7.4\%$  vs  $38.5 \pm 7.2\%$ ,  $p=0.03$ ). Most had the apical variant, with no difference between groups regarding anatomical variant. After multivariate analysis, we established as independent predictors of heart failure: atrial fibrillation/flutter at admission ( $p=0.03$ , OR = 15.2 95% CI 1.3-186) and severe depression of LVSF ( $p=0.04$ , OR = 6.5 95% CI 1.2-39.2).

**Conclusion:** In our population, HF is a frequent in-hospital complication, with a cardiogenic shock prevalence of 8.8%. Severe depression of LVSF and the presence of atrial fibrillation/flutter were found to be independent predictors of HF.

#### P1942

##### Clinical features of peripartum cardiomyopathy

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**Objective:** To study the clinical features and prognosis of patients with peripartum cardiomyopathy (PCM).

**Materials and Methods:** The study involved 50 patients with PCM in the age from 20 to 41 years (mean age  $28.2 \pm 0.8$  years). All patients underwent ECG, HMECG, echocardiogram, a 6-minute walking test with definition of functional class (FC) of heart failure (HF) by NYHA, and also studied life prognosis. The study of the dynamics of the disease lasted from 3 to 175 months (average,  $5.4 \pm 67.4$  months), the mortality was 17 cases (34%). Patients were divided into 2 groups: I-Group amounted 17 patients died in the period from 3 to 131 months of observation ( $36.6 \pm 7.2$  months). II group of patients – 33 patients, survivors in the process from 31 to 175 months (average  $83.1 \pm 5.7$  months;  $p < 0.001$ ) surveillance. Therapy in these groups did not differ.

**Results:** A group of patients with lethal outcome, compared with patients surviving in the reference period was characterized by significantly higher FC of the CHF:  $3.6 \pm 0.1$  and  $3.2 \pm 0.1$  ( $p=0.01$ ), and disease duration was  $7.8 \pm 1.8$  and  $6.2 \pm 1.2$  months., respectively ( $p > 0.05$ ). The walk distance (WD) in the reference period

in the I group was 25.6% lower than in the II group, and amounted  $170,3 \pm 15,7$  m and  $214 \pm 12,1$  m ( $p=0.02$ ). When comparing the parameters of intracardiac hemodynamics revealed that the I group of patients have decrease of ejection fraction (EF) of LV ( $32,6 \pm 1,7\%$  and  $37,6 \pm 1,8\%$ ;  $p=0.01$ ) was associated with significant differences in the linear dimensions of the heart; EDV  $6.8 \pm 0.2$   $6.4 \pm 0,09$  sm ( $p=0.04$ ), ESD  $5,9 \pm 0,1$   $5,5 \pm 0,3$ sm ( $p=0.01$ ). In the analysis of ECG, a worst performance recorded in I group; violation of AV conduction of I degree found in 5 (29.4%) and 4 (12.1%) patients, atrial fibrillation in 3 (17.6%) and 1 (3.03%), pseudo - Q wave at 3 (17.6%) and 1 (3.03%), respectively, in I and II groups, but which did not have a statistically significant character. Analysis of the HMECG results showed that comparative aspect, high grade of VE; pair 12 (70.6%) and 12 (36.4%), Groups 6 (35.3%) and 3 (9.1%) significantly more frequently recorded in the group of died patients (both  $p < 0.05$ ), unstable ventricular tachycardia (less than 30 sec) are set at 2 (11.8%) and 4 (12.1%), sustained at 1 (5.9%) (30 sec).

**Conclusions:** Results of the study patients' life expectancy PCM with prolonged follow-up (average  $67,4 \pm 5,4$  months) revealed that mortality rates amounted to 17 (34%) cases. In case of death, heart failure is characterized by relatively severe, accompanied by a deterioration in the basic parameters of intracardiac hemodynamics and accompanied by a significant increase in the incidence of ventricular arrhythmias high gradation.

### P1943

#### Incidence, risk factors, and clinical characteristics of peripartum cardiomyopathy in south korea

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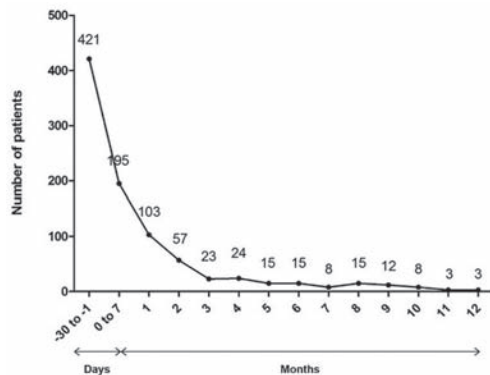
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**Background:** Peripartum cardiomyopathy (PPCM) is a rare disorder associated with pregnancy that can lead to a life threatening conditions. Because of its rarity, the incidence and the clinical characteristics of this condition remain poorly understood.

**Objective and methods:** The purpose of this study was to produce the first population-based study for PPCM in South Korea using the Korea National Health Insurance Claims Database of the Health Insurance Review and Assessment Service. Patients were identified from International Classification of Diseases, tenth edition (ICD-10) who fulfilled diagnostic criteria of PPCM by searching for a pregnancy and heart failure related codes from 2009 to 2013. To discriminate the PPCM from other causes of heart failure (HF), we exclude who already have HF related ICD-10 codes in 2009 and performed investigations between 2010 and 2012.

**Results:** During 2010 and 2012, a total of 838 cases were identified as PPCM by discharge ICD-10 codes and there were 1,385,902 deliveries in South Korea. Thus, the overall incidence of PPCM was 1 in 1667 deliveries. Patients with PPCM were older ( $p < 0.01$ ), had a higher prevalence of preeclampsia ( $p < 0.01$ ) and gestational DM ( $p < 0.01$ ), and more likely to occur in primiparous ( $p=0.02$ ) and multiple pregnant women ( $p < 0.01$ ) compared with control. Moreover, not only cesarean section ( $p < 0.01$ ) was more common during delivery but related complications were also more common (Uterine arterial embolization,  $p < 0.01$ ; peripartum hysterectomy,  $p < 0.01$ ) in PPCM patients. Intriguingly, contrary to the classic criteria for the diagnosis of PPCM, quite large number of PPCM patients were still reported until 9 months (figure).

**Conclusions:** The incidence of PPCM was 1 per 1667 deliveries in South Korea. PPCM patients were older, more associated with primiparity and multiple pregnancy, and had more pregnancy related complications than control. In addition, the current traditional criteria of PPCM is too strict and that patients who develop HF after the 5 months of delivery might also be considered as a continuum of PPCM.



Time of diagnosis of PPCM

### P1944

#### Meta-analysis on the clinical effects of colchicine in recurrent pericarditis

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**Background:** Colchicine inhibits microtubule self-assembly by formation of tubulin-colchicine complexes, and thereby ultimately decreases leucocyte motility and phagocytosis, thereby reducing the inflammatory response. Recurrent pericarditis is partly responsive to colchicine treatment, as elucidated in several randomized controlled trials.

**Purpose:** Meta-analysis of RCTs on the clinical effects of colchicine treatment for recurrent pericarditis.

**Results:** We identified  $n=7$  RCTs eligible for inclusion to this meta-analysis, with 1,832 patients (mean age: 57.1 years; range: 18-85 years; men: 56%), presenting with recurrent pericarditis under nonsteroidal anti-inflammatory drugs, (NSAID) and partly also corticosteroids. The mean follow-up period was 13.1 months (range: 3-22 months). The patients treated with colchicine were prescribed colchicine 1.0 to 2.0 mg on the first day, followed by a maintenance dosage of 0.5 to 1.0 mg/d for 3-6 months. Compared with the control group, colchicine treatment reduced the risk of recurrent pericarditis (OR: 0.42; 95% CI: 0.33-0.52;  $p < 0.001$ ). Pericarditis-associated re-hospitalizations and persistence of symptoms at 72 hours were reported in 5 RCTs. The rate of symptom persistence at 72 hours (OR: 0.29; 95% CI: 0.21-0.41;  $p < 0.001$ ), and pericarditis-associated re-hospitalizations (OR: 0.29; 95% CI: 0.16-0.53;  $p < 0.001$ ) were significantly reduced by colchicine treatment compared with the control group, respectively. Compared with the control group, colchicine treatment was associated with a higher rate of adverse events (OR: 1.48; 95% CI: 1.06-2.07;  $p=0.02$ ). The most frequent adverse event was gastrointestinal intolerance / diarrhea (mean incidence: 9%).

**Conclusions:** The results of this meta-analysis of RCTs confirm that colchicine treatment decreases significantly the rate of pericarditis recurrence, as well as the hospitalization rate resulting from recurrent pericarditis.

### P1945

#### Advanced left ventricular diastolic dysfunction in uremic patients with type 2 diabetes on maintenance hemodialysis.

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**Background:** It is generally difficult to determine whether myocardial dysfunction in diabetic patients on hemodialysis is due to diabetes or kidney disease and whether the association of these two conditions will worsen again myocardial disease. The aim of the study is to identify the impact of diabetes on the left ventricular diastolic dysfunction in uremic patients on hemodialysis.

**Methods:** A total of 72 patients on maintenance hemodialysis with normal LV systolic function were studied. We compared the diastolic function in 2 groups: group 1 = with diabetes (11 patients) and group 2 = without diabetes (61 patients).

**Results:** The conventional LV diastolic echocardiographic parameters did not differ between the 2 groups, except for the left atrial size ( $p=0,02$ ) and volume index ( $P < 0.001$ ). The ESRD patients with DM, however, had significantly decreased mitral annular early diastolic peak velocity ( $<0.001$ ) and ratio of early to late diastolic mitral annular velocity ( $e'/a'$ ;  $P < 0.016$ ). Additionally, diabetic patients had markedly higher estimated LV end-diastolic filling pressure ( $E/e'$ ;  $p=0.03$ ).

**Conclusions:** In End stage renal disease patients with type 2 DM undergoing hemodialysis, TDI indicated more advanced LV diastolic dysfunction. Also, TDI offers a feasible means of evaluating subclinical alterations of LV function, possibly allowing for the early detection of diabetic heart disease in severe uremic patients.

### P1946

#### Inflammatory cardiomyopathy detected by immunohistological methods - a meta-analysis

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**Background:** Chronic intramyocardial inflammation has been associated with the pathogenesis of dilated cardiomyopathy. Whereas the histological diagnosis of myocarditis according to the Dallas criteria has no prognostic and diagnostic value, the immunohistological diagnosis of inflammatory cardiomyopathy (DCMI) in endomyocardial biopsies (EMB) has endorsed a novel entity within the clinical presentation of DCM patients.



**Purpose:** Meta-analysis on the immunohistological and histological diagnosis of intramyocardial inflammation in EMB.

**Results:** We identified n=61 investigations eligible for inclusion in this meta-analysis, with 10,491 patients (mean age: 47.1 years; men: 66%) who underwent EMB obtainment and immunohistological quantitative diagnostics for infiltrate density and endothelial cell adhesion molecule (CAM) expression. In these studies, n=460 control patients were reported. The mean detection rate of DCMi by immunohistology was 50.8 % (95 %-CI: 47.7–53.8%). A substantial publication bias was excluded by linear regression / Funnel Plot (p = 0.4264). The positivity rate of the immunohistological proof of intramyocardial inflammation in patients with clinically suspected acute myocarditis (AMC: mean: 58.6%; 95 %-CI: 51.2–65.0%) was significantly (p = 0.0053) higher compared with patients presenting with chronic DCM (mean: 47.0 %; 95%-CI: 42.3–51.7 %). This immunohistological detection rate was significantly (p<0.001) higher compared to the mean detection rate of myocarditis according to the Dallas criteria (mean: 13.6 %; 95%-CI: 11.3–16.3%).

**Conclusions:** The results of this meta-analysis confirm that the immunohistological detection technique is significantly more sensitive in the detection of intramyocardial inflammation in patients presenting with AMC or DCM compared to the histological Dallas criteria. The proof of the adverse prognostic impact, and the suitability of the immunohistological approach for selection of candidates profiting from immunosuppression, as shown in 2 randomized trials, as opposed to the histological Dallas criteria, may be due to the observer-independent, methodologically determined higher detection robustness.

#### P1947

##### Reverse left ventricular remodeling after cardiac resynchronization in patients over 75 years.

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**Background:** little data exist on the benefit of cardiac resynchronization therapy (CRT) in the elderly since the number of these patients was limited in large trials. We aimed to describe predictors of response to CRT in a group of elderly patients (≥ 75 years old).

**Methods:** A total of 41 patients undergoing CRT implantation between June 2006 and October 2014 were included. Left ventricular reverse remodeling was defined as reduction of ≥ 15% in left ventricle end diastolic diameter (LVEDD).

**Results:** mean age was 79.2 ± 2.9 years and 20.4% were women. At the time of the implant left ventricle was dilated (mean LVEDD 60.4 ± 6.6 mm) and impaired (mean left ventricular ejection fraction (LVEF) 23.4 ± 6.7 %). Almost half of the patients suffered non-ischemic cardiomyopathy (51%) and mostly were in NYHA III-IV (54.2%). Medical treatment was optimized (Beta blockers: 87.5%; ACEI (angiotensin-converting enzyme inhibitors): 64.6% and aldosterone antagonists: 68.8%). Left bundle branch block (LBBB) was present in 67.3% of the overall population, and mean QRS duration was of 155.4 ± 25ms. After a mean follow up of 37.2 ± 19.3 months, a reduction in LVEDD (57.3 ± 9.3mm) and an improvement in LVEF (30.8 ± 13.7%) were observed. 60.5% of patients were in NYHA I-II. Significant reverse left ventricular remodeling (positive response) was observed in 11 patients (26.8%). Responders not only showed greater reduction in LVEDD (baseline LVEDD 61.3 ± 4.1 mm; final 47.6 ± 5.9 mm; p = 0.024 in responders Vs baseline LVEDD 59.9 ± 7.1 mm; final 60.8 ± 7.8mm; p = 0.286 in non-responders) but also showed greater improvement in LVEF (baseline LVEF 23.4 ± 7.1%; final 44.1 ± 12.9%; p = 0.02 in responders Vs baseline LVEF 22.9 ± 6.7%; final 24.7 ± 9.6%; p = 0.212 in non-responders). A positive remodeling was associated with female sex (OR 50.5; IC 95%: 1.96-1296,03); QRS duration ((OR 1,1; IC 95%: 1,02-1,19).

**Conclusion:** left ventricular dilatation reversed in a 26.8% of elderly patients after CRT. Given the high costs of the implant, defining strategies to select elderly patients who are more suitable for CRT, is necessary. QRS duration and female sex were good predictors of reverse remodeling.

#### P1948

##### Assesment of bioelectrical impedance indicators among the patients with dilated cardiomyopathy

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**Introduction:** Dilated cardiomyopathy is one of the cardiomyopathies a group of diseases that affect primarily the myocardium. In DCM, a portion of myocardium is dilated, often without any obvious cases. So far volemia has not been examined by BIA (bioelectrical impedance) parameters among the patients diagnosed with this disease.

**Purpose:** Assesment of selected bioelectrical impedance indicators among the patients affected with dilated cardiomyopathy.

**Methods and materials:** In the Cardiology Department in the Medical University of Lublin 106 patients with DCM and 103 healthy persons have been examined. For the assesment of bioimpedance parameters the WBIA method has been applied and used by means of bioelectrical impedance analysis measurements by BCM Body Composition Monitor (Fresenius Medical Care Deutsche and GmbH) with frequency from 5 to 500 kHz. The following correlations of parameters have been set: OH (overhydration), ECW (extracellular water), ECW/TBW indicator (extracellular water/total body water), ICW/TBW indicator (intracellular water/total body water).

**Results:** Parameters OH was significantly higher in patients with DCM than in the control group, 0,2 vs 0,1 (p=0,02). ECW was significantly higher in patients with DCM than in the control group, 16,6 vs 14,1 (p < 0,000001). ECW/TBW was higher in patients with DCM, 0,47 vs 0,43 (p < 0,000001). ICW/TBW was lower in patients with DCM, 0,53 vs 0,57 (p < 0,000001).

**Conclusions:** The analysis of bioelectrical impedance indicators make signifiant importance in volemia and potential overhydration among the patients with DCM.

#### P1949

##### Left ventricular dysfunction (burn-out phase) in hypertrophic cardiomyopathy: prevalence and associated factors

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**Introduction:** Left ventricular hypertrophy (LVH) in hypertrophic cardiomyopathy (HCM) is usually associated with a normal LV ejection fraction. However, a small minority of patients progress to a dilated stage with LV systolic dysfunction, known as “burnout phase”. The prevalence of this phase in HCM patients varies from 2.4% to 4.9%.

**Purpose:** Describe a HCM Portuguese population and determine the prevalence of “burn-out” phase among those patients. Define any clinical, genetic, electrocardiographic or imagiologic factors related with advancement to “burnout phase”.

**Methods:** A multicentre Portuguese study involving 10 hospital centres and including all patients diagnosed with HCM. Clinical, genetic, electrocardiographic, echocardiographic and magnetic resonance (MR) characteristics were evaluated. “Burnout phase” was defined as the presence of an ejection fraction <50%.

**Results:** 476 patients with HCM were included (58% were male and mean age 62 ± 15 years). HCM was predominantly septal asymmetric (72%), but concentric symmetrical in 13% and apical in 15% of patients. The most common symptoms were dyspnoea (57%), angina (19%) and syncope (13%). Cardiac death occurred in 11 patients (2.3%) after a mean follow up of 6 years. Family history of HCM was identified 15% and of sudden death in 14%. Genetic study was done in 244 patients (51%), and 34% presented with pathogenic genetic mutations. 21% had a history of atrial fibrillation and 16% of non-sustained ventricular tachycardia. Pacemaker was implanted in 6% and ICD in 16% of this patients. The mean ejection fraction was 66 ± 9%. MR late gadolinium enhancement was found in 58%. 2.9% of patients were in “burnout phase”. They had most frequently chronotropic incompetence in 24 hour Holter (p<0,001). There were no significant differences in the remaining clinical, genetic, electrocardiographic, echocardiographic and MR characteristics.

**Conclusion:** In this Portuguese population, the prevalence of “burnout phase” was 2.9%, which is consistent with previous studies. Chronotropic incompetence was significantly associated with “burnout phase”.

#### P1950

##### Predictors of cardiopulmonary responses to exercise in hypertrophic cardiomyopathy

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**Background:** Inconclusive evidence exist about the main determinants of exercise intolerance, ventilatory inefficiency and chronotropic incompetence in hypertrophic cardiomyopathy (HCM). Aim of this study was to investigate the main demographic, clinical and echocardiographic predictors of cardiopulmonary responses to exercise in patients with HCM.

**Methods:** Exercise capacity (maximal oxygen consumption/predicted [%peakVO<sub>2</sub>]), ventilatory efficiency (ventilation/carbon dioxide output [VE/VCO<sub>2</sub>] slope) and chronotropic index (heart rate reserve/220-age-heart rate at rest [%HRR]) were evaluated in 154 consecutive HCM patients (age at first evaluation 43 ± 14 years; 72% male) that underwent cardiopulmonary exercise testing.

**Results:** A total of 78 (50.6%) of 154 patients had impaired exercise tolerance (%peakVO<sub>2</sub> <80% of predicted), 81 (52.6%) reduced chronotropic response

Predictors of cardiopulmonary responses						
	Exercise capacity ( $R^2 = 0.37$ )		Ventilatory efficiency ( $R^2 = 0.21$ )		Chronotropic index ( $R^2 = 0.21$ )	
	B	p value	B	p value	B	p value
Female gender	-17.90	<0.001	1.63	0.048	NA	NA
NYHA class > I	-13.01	<0.001	2.17	0.005	-0.13	<0.001
Age	0.39	0.001	NA	NA	NA	NA
Maximum wall thickness	-7.39	0.01	NA	NA	NA	NA
Obstructive phenotype	-8.80	0.01	NA	NA	NA	NA
B-blocker	NA	NA	NA	NA	-0.13	<0.001
Left atrial diameter	NA	NA	2.13	<0.001	NA	NA
NA:	not applicable,	$\nu\eta\alpha$ :	New York	Heart	Association	

(%HRR <80% of predicted), and 17 (11%) ventilatory inefficiency (VE/VO<sub>2</sub> slope > 34). Forward stepwise multivariate regression analysis resulted in female gender, NYHA class > I, younger age, higher maximum wall thickness and obstructive phenotype as main independent determinants of reduced %peakVO<sub>2</sub> ( $R^2 = 0.37$ ). Furthermore, independent predictors of higher VE/VO<sub>2</sub> slope were increased left atrial diameter, NYHA class > I and female gender ( $R^2 = 0.21$ ), whereas of lower %HRR were NYHA class > I and b-blockers administration ( $R^2 = 0.21$ ) (Table).

**Conclusions:** The prevalence of exercise intolerance, ventilatory inefficiency and chronotropic incompetence was high in our HCM population. Patients' functional status was the only common independent determinant. Female gender independently correlated with reduced %peakVO<sub>2</sub> and higher VE/VO<sub>2</sub> slope whereas younger age seem to have a negative effect on exercise capacity. Echocardiographically, obstructive phenotype and increased left atrial diameter were associated with lower %peakVO<sub>2</sub> and higher VE/VO<sub>2</sub> slope, respectively.

#### P1951

##### The risk factors of advanced heart failure in hypertrophic cardiomyopathy

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**Background:** Hypertrophic cardiomyopathy (HCM) is the most common genetic cardiomyopathy worldwide of which diastolic heart failure is the dominant clinical manifestation. Proportion of patients progress into burnt out dilated cardiomyopathy (DCM), which have very poor prognosis. However, very little is known about its clinical risk factors, echocardiographic features and therapeutic strategies.

**Purpose:** The hypothesis is that subgroups of HCM depending on heart failure syndromes have heterogeneous prognosis. The prognostic markers of the subgroups are searched by comparing clinical and echocardiographic risk factors. Next, we searched for prognostic markers of clinical outcomes of total death, cardiac death, heart failure admission and VT in total HCM patients.

**Methods:** Medical record of 520 HCM patients in a large cardiovascular center in Korea from January 2000 to December 2013 are retrospectively reviewed. The total HCM patients are classified into three groups (1) systolic heart failure (2) diastolic heart failure (3) neither (1) nor (2). The risk factors and clinical outcomes of total death, cardiac death, heart failure and VT were compared with each group. Cox regression analysis was performed in regard to clinical outcomes of all the HCM patients.

**Results:** 520 patients are enrolled. 453 patients are followed up for more than 1 year. Average follow up period is  $90 \pm 60$  months. Baseline characteristics of total HCM are as follows. Average age  $58 \pm 14$  years-old, male is 289 (55.6%) patients. Apical hypertrophy is the most frequent (34%), followed by septal hypertrophy (21%), septal-anterior-lateral hypertrophy (18%), septal and apical(mixed) hypertrophy (22%). Maximal wall thickness is  $20.5 \pm 4$  mm, obstructive HCM is in 21% of patients. Total death occurred in 89(17%) patients during follow up, cardiac death in 36(7%), heart failure admission in 61(12%), VT in 26(5%). Group 1 had significantly decreased survival rate for total death, cardiac death and heart failure. With multivariable logistic regression, LA volume, HCM types are significant risk factors for HCM progression to DCM. With Cox regression analysis, age, AF are significant risk factors for total death, cardiac death and heart failure admission. Age, maximal wall thickness and AF are significant for VT.

**Conclusion:** We retrospectively documented poor prognosis of HCM into DCM progression group and risk factors, which are LA volume, HCM type. In addition, age and AF are significant prognostic markers for total death, cardiac death, and heart failure admission.

#### P1952

##### Vascular endothelial growth factor is associated with the morphologic and functional parameters in patients with hypertrophic cardiomyopathy

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**Purpose:** Hypertrophic cardiomyopathy (HCM) is mostly autosomal dominant disease of the myocardium, which is characterized by myocardial hypertrophy. Vascular endothelial growth factor (VEGF) is involved in myocyte function, growth, and survival. The aim of study was to analyze the clinical significance of VEGF in structural and functional changes in patient with non-obstructive type of HCM.

**Methods:** In a group of 21 patients ( $58.4 \pm 13.2$  years, 6 female) with non-obstructive HCM, we assessed serum VEGF and analyzed its association with morphological and functional parameters.

**Results:** Compared to healthy controls, serum VEGF was increased: 199 (IQR: 120.4–260.8) ng/L versus 20 (IQR: 14.8–37.7) ng/L,  $p < 0.001$ . In patients with New York Heart Association (NYHA) functional classes III and II, serum VEGF values were lower compared to patients with NYHA classes I and IV: 146.4 (IQR: 113.6–235.2) ng/L versus 328.1 (IQR: 286.7–406.3) ng/L,  $p < 0.01$ . The mean left ventricle mass was  $408.4 \pm 11.8$  g, and it exceeded reference values for two-dimensional method (female: 150 g, male: 200 g) in all patients. The mean left ventricle mass index was  $202.4 \pm 53.9$  g·m<sup>-2</sup>, and it exceeded reference values for two-dimensional method (female: 88 g·m<sup>-2</sup>, male: 102 g·m<sup>-2</sup>) in all patients. The mean of the left ventricle ejection fraction was  $65.4 \pm 12.2\%$ . The mean of the left ventricle fractional shortening was  $0.32 \pm 0.09$ , and it exceeded the reference values (female: 27–45, male: 25–43) in 3 (15%) patients. The mean peak tricuspid regurgitation gradient was  $22.6 \pm 11.8$  mmHg. The inferior vena cava diameter was  $18 \pm 3.7$  mm. None of the patients had left ventricle outflow tract obstruction. The peak left ventricle outflow tract gradients were 6 (IQR: 1–7.5) mmHg during at rest measurement and 15 (IQR: 2.2–29) mmHg during Valsalva maneuver. The median values for the peak LVOT pressure gradient were 3 (IQR: 2.2–5) mmHg for at rest measurements and 14 (IQR: 2–22) mmHg during Valsalva maneuver. VEGF levels were associated with left atrium diameter ( $= 0.51$ ,  $p = 0.01$ ), left ventricle ejection fraction ( $= -0.56$ ,  $p = 0.01$ ), fractional shortening ( $= -0.54$ ,  $p = 0.02$ ), left ventricular mass ( $= 0.61$ ,  $p = 0.03$ ), LV mass index ( $= 0.46$ ,  $p = 0.04$ ), vena cava inferior diameter ( $= 0.65$ ,  $p = 0.01$ ), and peak gradient of tricuspid regurgitation ( $= 0.46$ ,  $p = 0.03$ ).

**Conclusions:** Increased VEGF level is associated with structural and functional parameters in patients with HCM and serves as a potential tool for diagnostic process of these patients.

## CO-MORBIDITIES

#### P1953

##### Elderly patients with heart failure, how do they go?

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**Intro:** Heart failure (HF) has been studied for many years, it has high incidence and it seems to be increasing. However, in every paper, elderly patients (p) are excluded.

**Objective:** 1- Describe characteristics and evolution of 75 years old or older p admitted for decompensated HF (DHF). 2- Compare these p with younger ones.

**Method:** It is a prospective analysis of 370 p admitted for DHF, consecutively, in our Cardiology Service, from June 2012 to November 2015, with a median follow-up of

23 months (Q1 13 - Q3 33). We divided p into 2 groups according to their age: G1  $\geq 75$  years old (151 p) and G2  $< 75$  years old (219 p). Quantitative variables with normal distribution were expressed with mean and with standard deviation (analyzed by Fisher's Test); those with not normal distribution, were expressed with median (m) and quartiles (analyzed by Mann Whitney's Test). Dichotomous variables were analysed by Chi2.

**Results:** G1 showed a mean age of 82 years old, 48% were males (vs 77.7% in G2,  $p < 0.001$ ), 83.4% had HTA, 29.1% were diabetics (vs 34.9%,  $p = 0.01$ ), 24.5% smokers (vs 62.4%,  $p < 0.0001$ ). Etiology was predominantly ischemic, but we only had statistically significance difference (SSD) in valvular etiology (G1 17.1% vs G2 10%,  $p = 0.04$ ). In the echocardiography, elderly p had smaller left ventricular diameters (diastolic 52 mm vs 58 mm,  $p < 0.0001$ , systolic 35 mm vs 47 mm,  $p < 0.0001$ ), and they present better ejection fraction (EF) than younger p (45% vs 34%,  $p = 0.0003$ ). Older p also had more prevalence of moderate mitral regurgitation (37% vs 27.6%,  $p = 0.04$ ). Clinically, both G had similar presentation, but G1 had more males (80.1% vs 68.5%,  $p = 0.006$ ).

At labs, renal function was worse in G1, as well as with glomerular filtration rate by MDRD as by creatinine clearance in 24 hs. (44.5 ml/min/1.73 m<sup>2</sup> vs 57 ml/min/1.73 m<sup>2</sup>,  $p < 0.01$ ). We also noted lower values in T3, bilirubin, uric acid, proteins, albumin, hematocrit and hemoglobin (every one with SSD), but with no clinical significance. At the EKG, G2 had had more sinus rhythm (67.3% vs 39.3%, SSD), and G1 more atrial fibrillation/flutter or pacemaker rhythm (both SSD). Also width of QRS complex was longer in G2 (105 msec vs 80 msec, SSD), with more LBBB (32.7% vs 20.4%, SSD).

There were no differences in previous treatment, except for more diuretics in G1 (59.6% vs 41.5%, SSD).

G1 had more mortality (MRT) at hospital (7.9% vs 2.8%,  $p < 0.0001$ ) as well as at the following up (52.2% vs 22.8%,  $p < 0.0001$ ). Readmission were about 35% in both G ( $p = 0.58$ ).

**Conclusions:** We see that our population had similar characteristics to those in international registries. Older p had worse evolution even they had better EF; we think this could be due to comorbidities. It would be interesting to analyze each one.

#### P1954

##### Variation in the clinical profile of women with acute myocardial infarction and an ejection fraction lesser than 40% over the last 10 years

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**Introduction:** The clinical profile of women patients has varied greatly over the past few years, particularly with regard to demographic characteristics and comorbidities.

**Aims:** Assess the profile variation of women with acute myocardial infarction (AMI) and an ejection fraction (EF) lesser than 40% (EF  $< 40\%$ ) over the past ten years.

**Methods:** Retrospective study, including 1138 women with AMI and an EF  $< 40\%$ , from 2006 to 2015. The population was divided in three groups: A, including patients with AMI between 2006 and 2009 (n = 498); B, including patients with AMI between 2010 and 2012 (n = 388); C, including patients with AMI between 2013 and 2015 (n = 252). Differences between groups were evaluated regarding the clinical profile.

**Results:** There has been an important reduction of time interval between onset of symptoms and hospital admission over time ( $p < 0.001$ ). Smoking habits have become a more prevalent risk factor in the last years ( $p = 0.042$ ). Previous history of AMI and the prevalence of AMI without ST elevation have declined ( $p < 0.05$ ), with growing reperfusion therapy ( $p < 0.001$ ). A severe EF (under 30%) and decompensated heart failure have become less prevalent ( $p < 0.001$ ). There was not significant change in hospital mortality or mortality at 6 months follow-up.

**Conclusions:** The clinical profile of women with AMI and an EF lesser than 40% has changed over time. This is a result of a modification of lifestyle habits, with growing smoking habits, and an improvement of health care, which translates into improved diagnosis of ischemic heart disease and a better ability to optimize therapy in these patients.

#### P1955

##### Comorbidities and prognostic factors associated with 1-year mortality and hospital admission in heart failure outpatients based on ejection fraction findings.

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**Background/Introduction:** The presence of comorbidities is very common in patients with heart failure, making more difficult the clinical management and being associated with poor prognosis. The prognostic factors should be stratified according to currently recommended ejection fraction (EF) findings. We conducted this study in order to know the prevalence and type of comorbidities in heart failure outpatients and to determine prognostic markers.

**Methods:** We studied all the heart failure outpatients included in the ESC Heart Failure Registry in our Hospital, recording their clinical characteristics, comorbidities, and mortality and hospital admissions during 1-year follow-up. Preserved EF was defined as  $\geq 45\%$ .

**Results:** Of the 245 patients (67 years, 31.4% women), 139 (56.7%) had reduced EF and 94 (38.4%) had preserved EF. The group of patients with preserved EF presented a significantly higher mean age (69 vs 65 years,  $p < 0.024$ ), higher percentage of women (51.1% vs 19.4%,  $p < 0.001$ ), and lower prevalence of ischemic heart disease (17% vs 37.4%,  $p = 0.001$ ). The patients with reduced EF practiced less regular physical activity (39.3% vs 55%,  $p = 0.041$ ) and had higher prevalence of prior admission for heart failure (43% vs 16.3%,  $p < 0.001$ ). There were no significant differences in both groups with regard to comorbidities (Charlson index 4.86 of reduced EF patients vs 4.84 of preserved EF patients,  $p = 0.929$ ). Older age and Charlson index were independent predictors of 1-year mortality for all study patients. Atrial fibrillation and high heart rate were associated with 1-year mortality and 1-year hospital admission in outpatients with reduced EF, and high heart rate and regular physical activity were associated in outpatients with preserved EF.

##### Conclusions:

1. Heart failure outpatients have high prevalence of comorbidities, independently of EF.
2. Older age and Charlson index were independent predictors of 1-year mortality for all study patients.
3. Atrial fibrillation and high heart rate were associated with 1-year mortality and 1-year hospital admission in outpatients with reduced EF, and high heart rate and regular physical activity were associated in outpatients with preserved EF.

#### P1956

##### Heart in the air piacenza project: correlation between air pollution and heart failure hospitalisation in the po valley

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**Background:** Air pollution is a heterogeneous, complex mixture of gases, liquids, and particulate matter. Epidemiological studies have demonstrated a consistent increased risk for cardiovascular events in relation to both short- and long-term exposure to present-day concentrations of ambient particulate matter. The Po valley located in the Northern Italy is one of the most polluted area in the world due to geographic and demographic characteristics.

**Aim and Methods:** In order to evaluate the impact of air pollution on the occurrence of cardiac morbidity in our region, we correlated the increment in air pollutant and admission to Emergency Dept. at our General District Hospital for acute coronary syndrome, supraventricular arrhythmias, heart failure, hypertension, syncope, in the years 2007-2008. Preliminary a test of homogeneity was performed by computing three coefficients of correlations (Pearson, Lin, Bland-Altman). Therefore a correlation analysis using the Poisson model for the disease frequency was used.

**Results:** The study population was represented by 2810 patients admitted for cardiac causes, (72.61  $\pm$  14.2 years, 1404 males (49.96%): arrhythmias 6.6%, acute coronary syndrome 23.7%, hypertension (27%), heart failure (35.8%), syncope (6.5%). A significant correlation was detected among the rate of admission for supraventricular arrhythmias, syncope and increases in the air concentration of benzene ( $P < 0.05$ ), while a no-significant correlation were detected between increases in the air concentration of NO<sub>2</sub>, SO<sub>2</sub> and O<sub>3</sub> and admission for acute coronary syndrome.

**Conclusion:** We confirm the evidence of a relationship between cardiac disease and increment in air pollution. Several plausible mechanistic pathways have been described, including enhanced coagulation/thrombosis, a propensity for arrhythmias, acute arterial vasoconstriction, systemic inflammatory responses, and the chronic promotion of atherosclerosis.

#### P1957

##### Hyperuricemia is a determinant of mortality in heart failure patients irrespectively of age, ejection fraction, or renal function

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**Purpose:** Serum uric acid is a predictor of cardiovascular mortality in heart failure with reduced ejection fraction (HFrEF). We studied the prognostic value of serum uric acid (sUA) in patients hospitalized for acute heart failure (AHF), with specific focus on age, ejection fraction, and renal function.

**Methods:** The CCU Network Database is an on-going emergency medical service registry supported by 71 hospitals. Among 7573 patients hospitalized for AHF in



2012 and 2013, data of sUA and serum creatinine (sCre) were available in 5193 patients (75.6 ± 13.6 years; men, 59%).

**Results:** In-hospital mortality rate during hospital stay was 7.0%. Mean sUA was 7.2 ± 2.9 mg/dl. sUA correlated with sCre, and very weakly correlated with BNP and LV ejection fraction. Logistic regression analysis with in-hospital mortality as a dependent variable showed that sUA, sCre, systolic blood pressure, body mass index (BMI), and hemoglobin concentration (Hb) at admission were independent factors after adjusting age and sex. We, then, subdivided the AHF patients dependent on the LV ejection fraction (<or ≥40%, median) or on the age (<or ≥78 years old, median). After adjusting age, sex, and sCre, sUA was still an independent predictor of mortality both in patients with HFREF and in those with heart failure with preserved ejection fraction (HFpEF), as well as in younger patients (YOUNG) and older patients (OLD).

**Conclusion:** Hyperuricemia in AHF patients is one of the strongest predictors of mortality either in younger or older patients, or in patients with HFREF or those with HFpEF, respectively of renal function.

Logistic regression of mortality (p)				
Independent variables	HFREF (EF<40%)	HFpEF (EF≥40%)	YOUNG (<78yrs)	OLD (≥78yrs)
Age	0.0000*	0.003*	0.018*	0.005*
Sex	0.0769	0.0756	0.9126	0.002*
BMI	0.8671	0.006*	0.1437	0.2167
sCre	0.1685	0.0637	0.2614	0.007*
Systolic blood pressure	0.0000*	0.0000*	0.0000*	0.0000*
sUA	0.034*	0.007*	0.025*	0.012*
Hb	0.0000*	0.0665	0.0001*	0.028*
Ejection fraction	0.0661	0.2621	0.429	0.9393

\*p < 0.05

#### P1958

##### Respiratory drive in patients with chronic heart failure and central sleep apnea

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**Background:** Patients with chronic heart failure (CHF) are characterized by exercise intolerance and ventilatory abnormalities that are related to poor prognosis. We hypothesized that CHF patients with Cheyne-Stokes Breathing (CSB) have increased respiratory drive. The aim of this study was to evaluate the respiratory drive in patients with CHF and CSB.

**Methods:** Outpatients with CHF underwent nocturnal polygraphy to evaluate the presence of sleep apnea and CSB. Then, the respiratory drive was evaluated in all patients, measuring by mouth occlusion pressure (P0.1) while breathing room air and during CO<sub>2</sub> rebreathing.

**Results:** 19 outpatient with CHF (60.6 ± 10.3 years; mean LVEF: 37.94 ± 9.37%) were enrolled in the study. 12 subjects were classified as CSB negative (CSB-) while in 7 patients (36%) there was high percentage of central sleep apnea and CSB and were classified as CSB positive (CSB+). These two groups were not different for age, BMI and LVEF. Subjects with evidence of CSB were characterized by higher values of resting P0.1 than CSB- patients (4.42 ± 2.42 vs 2.32 ± 0.91, p=0.04) and higher value of P01/PetCO<sub>2</sub> slope (0.65 ± 0.53 vs 0.29 ± 0.29, p=0.01).

**Conclusions:** outpatients with CHF and CSB have increased activity of respiratory drive. This increased activity might greater tendency to develop central apnea and CSB, over the stage of heart failure.

#### P1959

##### Enhanced adaptive servo-ventilation improves echocardiographic parameters of diastolic and right ventricle function in patients with sleep apnea and heart failure with preserved ejection fraction

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**Background:** Enhanced adaptive servo ventilation (eASV) is a ventilator device with a new feature-auto-adjustment of expiratory positive airway pressure used to normalize ventilation in patients with sleep disorders breathing (SDB) and central sleep apnea (CSA). Very limited data are available on heart failure with preserved ejection fraction (HFpEF) and use of eASV.

**Purpose:** To test eASV in HFpEF patients with SDB and CSA.

**Methods:** 10 consecutive acute HFpEF (LVEF > 45 %) subjects with moderate to severe SDB (apnea-hypopnoea index, AHI > 15/h with prevalence of CSA) were enrolled and randomly assigned to two groups: 5 patients treated for 7 days with eASV (group 1) on the top of standard care and 5 patients treated only with standard care for acute HF (group 2). Echocardiographic parameters of diastolic function and right ventricle (RV) function were assessed. Brain natriuretic peptide (BNP) was measured at baseline and after 7 days of treatment.

**Results:** eASV therapy markedly reduced AHI and CSA (36 ± 9 to 3 ± 1, p < 0.001 and 32 ± 7 to 1 ± 0.6, p < 0.0001 respectively). A beneficial effect on cardiac diastolic function was observed in group 1 versus group 2 (E/E': 17.5 to 9.6, p < 0.02 vs 18.5 to 14.5, p = 0.4; S wave: 0.19 to 0.34 m/sec, p < 0.04 vs 0.23 to 0.28 m/sec, p < 0.4; pulmonary artery pressure: 36 to 23 mmHg, p < 0.05 vs 35 to 29 mmHg, p = 0.07). In addition, BNP decreased significantly in group 1 compared to group 2 (298 to 84 pg/ml, p < 0.02 vs 280 to 120 pg/ml, p > 0.05). RV function, calculated with tricuspid annulus plane systolic excursion (TAPSE) and fractional area change (FAC) of the RV, improved in group 1 (15 to 17 mm, p = 0.05 and 39 to 43 %, p = 0.03), while in group 2 no significant differences were observed.

**Conclusions:** eASV device may improve cardiac diastolic parameters, RV function and BNP in acute HFpEF patients with SDB and prevalence of CSA, with respect to standard treatment. These early and encouraging findings suggest that long-term application of eASV in HFpEF patients with SDB should be evaluated in larger prospective studies.

#### P1960

##### Daytime oscillatory breathing patterns and sleep disordered breathing in patients with heart failure: are they related?

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**Background:** Sleep disordered breathing (SDB) is a highly prevalent but under-recognized comorbidity in patients with heart failure (HF). Daytime oscillatory breathing patterns (DOBP) have also been frequently reported in HF patients. The relationship between SDB and DOBP has not been addressed in large series. Particularly it is not known whether DOBP and SDB represent a continuum and the presence of DOBP might be related to an increased SDB burden.

**Methods:** We studied 302 patients with clinically stable, optimally treated moderate-to-severe HF (age 58 ± 9 years, NYHA class 2.7 ± 0.5, LVEF 33 ± 10%) who were submitted to a 10-minute daytime supine respiratory recording and to a standard polysomnography (PSG) on the same or subsequent night. DOBP was defined as a repeated oscillation of instantaneous tidal volume with regularly recurring hyperventilation and apnea or hypopnoea, with a greater than 25% variation in peak to trough values of tidal volume occurring in more than 75% of the 10 min record. The severity of SDB was quantified by the apnea-hypopnea index (AHI).

**Results:** DOBP was observed in 140/302 (46%) patients, while SDB (AHI ≥ 5/h) was present in 263/302 (87%). The AHI was significantly different according to the presence or absence of DOBP (25 ± 17 vs 18 ± 14, p < 0.001). The presence of DOBP was significantly associated with the presence of SDB (p = 0.0004). As shown in the table, 90% of the patients with DOBP had SDB but SDB was also present in 85% of patients who did not show DOBP.

**Conclusions:** Although DOBP and SDB are significantly related, the presence or absence of DOBP cannot be used to infer the severity of SDB.

	AHI < 5	AHI ≥ 5 - <15	AHI ≥ 15 - ≤30	AHI > 30
DOBP yes	10%	26%	27%	37%
DOBP no	15%	37%	32%	16%

#### P1961

##### The frequency of anemia among patients with heart failure

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**Background:** HF is a socially significant problem throughout the world, according to statistics, about 1-2% of the adult population in developed countries suffers from HF. More than 5 million Americans suffer from HF and, according to the AHA, annually identify 550,000 new cases of HF. The prevalence of anemia in patients with CHF is from 10 to 50% or more. Most often, (80%) it develops in patients with NYHA IV.

**Purpose:** to evaluate the prevalence of anemia among the HF patients which were hospitalized to our institution.

**Methods:** retrospective analyze of clinical cases of patients with CVD that were hospitalized to our Institution in 2014.

**Results:** 3,089 patients were hospitalized with CVD in 2014. Six hundred nineteen (20, 03%) of them were with LVEF below 50%. According to the WHO definition of anemia, (Hb concentration is below 130 g/l in men and below 120 g/l in women) there were 128 patients with HF, which amounted 20, 67%. The number of women and men with HF and anemia was 46 (25.55%) and 80 (18.22%), respectively. The amount of HF patients with anemia over 70 years occurred in 17 (20, 98%) cases among men and 20 (43, 47%) among women.

Furthermore, the number of patients with LVEF 40-50% was 116 (64,44%) among women and 240 (54,67%) among men, the frequency of anemia among these groups of patients was 24 (20,08%) cases among women and 41 (17,08%) cases among men. As for LVEF 30-39% - these number was 41 (22,77%) among women and 136 (30,98%) among men, the prevalence of anemia in these groups of patients was 16 (39,02%) and 24 (17,64%), respectively. The total amount of the patients with LVEF below 30 % was 23 (12,7%) among women and 63 (14,35%), the prevalence of anemia was 6 (26%) among woman and 15 (23,80%) among men. So, we can see that percentage of HF patients with anemia is depending on the severity of HF.

**Conclusion:** Thus, the retrospective analyze shows that the prevalence of anemia among the HF patients is high and depends on severity of HF.

### P1962

#### Does anaemia in Heart Failure correlate with chronic anticoagulant and antiplatelet therapies?

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**Introduction:** Anaemia is a frequently reported co-morbidity of Heart Failure (HF), it has a prognostic role and it is an independent risk factor for HF hospitalization and mortality. Several conditions are associated with anaemia in HF, such as iron deficiency, renal failure, chronic inflammation, hemodilution, bone marrow dysfunction and drug therapy including anticoagulant and antiplatelet therapies.

**Purpose:** It is known the prevalence of anaemia increases with HF severity and other co-morbidities (advanced age, female gender, renal disease, diabetes mellitus). We investigated a possible correlation between anaemia/iron deficiency in HF and chronic anticoagulant and/or antiplatelet therapies, either alone or in combination.

**Methods:** We retrospectively studied 280 patients hospitalized for HF. We collected values of haemoglobin, Mean Corpuscular Volume (MCV), iron status, creatinine, International Normalized Ratio (INR) and Brain Natriuretic Peptide (BNP) in different groups based on either anticoagulant or antiplatelet therapy or both. In details: group 1 (no therapy, n = 37), group 2 (Vitamin K Antagonists (VKAs), n = 105), group 3 (either a VKAs or a Novel Oral Anticoagulants (NOACs), plus antiplatelet therapy, n = 30), group 4 (NOACs alone, n = 13) and group 5 (antiplatelet therapy alone, n = 86). We used Ancova analysis corrected by confounding factors (creatinine, age, sex, left ventricular ejection fraction, diabetes mellitus and others) to obtain a comparison between all groups variables.

**Results:** BNP shows a trend representing the severity of HF, with the highest value of adjusted mean in group 4 (1186 pg/mL; C.I. 615.3-1756.1) and the lowest value in group 1 (961 pg/mL; C.I. 588-1334.6). There are no significant differences among the groups regarding haemoglobin, MCV, ferritin, transferrin and transferrin saturation. Instead, there are significant differences among the groups on INR ( $p < 0.0001$ ) and blood iron ( $p < 0.014$ ). Then we have also made a post hoc Anova analysis (adjusted for confounding factors) for blood iron and haemoglobin to check differences in multiple comparison. Blood iron shows statistically significant differences between group 1 and all the other groups (p values: group 2, 3, 4, 5 respectively 0.002, 0.013, 0.034, 0.0006). Haemoglobin has a significant difference only between group 3 and 4 (11.84 mg/dL and 13.32 mg/dL,  $p < 0.023$ ).

**Conclusion:** Iron is an important co-factor in mitochondrial respiration complexes and so in physiologic cardiac function. We demonstrate that antiplatelet and anticoagulant therapies correlate with iron deficiency as independent factors. Haemoglobin in patients with NAOs therapy alone reaches the highest value compared to the other group (adjusted mean 13.32 mg/dL; C.I. 12.2-14.4).

### P1963

#### Establishing a heart failure unit for decompensated HFrEF patients with CKD class IV and diuretic resistance or deteriorating kidney function : a pilot project.

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**Background:** Patients with decompensated HFrEF and CKD are difficult to treat. A substantial portion of these patients deteriorate despite adequate medical treatment. Others have diuretic resistance. These patients are often referred for dialysis.

**Purpose:** Establishing a dedicated heart failure unit on the CCU with a pre-specified hemodynamics based protocol for the above mentioned patients, to provide recompensation with improvement of kidney function and avoid dialysis.

**Methods:** 7 patients with HFrEF and CKD stage 4 admitted to the conventional

ward for decompensation with deteriorating kidney function were enrolled in this program.

The protocol for recompensation was based on PAC measurements, which was inserted at the cath lab.

The protocol consisted of measurements of cardiac pressures and SvO<sub>2</sub>. Diuretics were stopped and nitroprusside drip was started and stepwise uptitrated every 5 minutes till the MAP was 60-65. If SvO<sub>2</sub> <40% in presence of anemia (Hb <10), transfusion was given.

The maximum dose of nitroprusside was given for > 6 hours. If CVP still was > 8, diuretics in combination with nitroprusside drip was started. Once CVP was < 8, nitroprusside was changed to hydralazine and oral nitrates. Thereafter, patients were readmitted to the conventional ward.

**Results:** 7 patients were included. Mean age 78 years; 5/7 ischemic CMP; mean EF 30%; 7 on b-blokkers and diuretics, 2 on ACE-inhibition and 1 on spironolactone. None with ICD or CRT.

3 patients had transfusion. 2 patients were started on dialysis because of persistent congestion without improvement of kidney function. One of them died on the second session of dialysis.

In all patients, hemodynamic parameters improved; mean PCWP (27,4 to 20,1), mPAP (41,4 to 34,4) and CVP went down (17,7 to 10,1), while CI remained stable (2,5 to 2,5) with increased MAP (75 to 81).

In the 5 patients without dialysis, kidney function either improved (1) or were less congested (4) with the same baseline creatinine levels. One of these patients later developed septic shock during hospital stay and died.

5 patients were able to leave the hospital. 2 out of 5 patients died suddenly (d37 and d52 after discharge). The other 3 are currently in FU > 1 year after hospital discharge.

**Conclusion:** The heart failure unit for patients with HFrEF, CKD 4 and worsening kidney function during recompensation was a valuable and feasible pilot project. In 5 patients, initiation of long-term dialysis or ultrafiltration could be avoided. However, 4 patients died within 3 months after discharge. Future research in patients with HFrEF and preterminal kidney failure should probably not focus on improved mortality, but on quality of life and dialysis-free survival.

### P1964

#### B-type natriuretic peptide, congestion, and acute kidney injury in heart failure: incidence and relationship to outcomes

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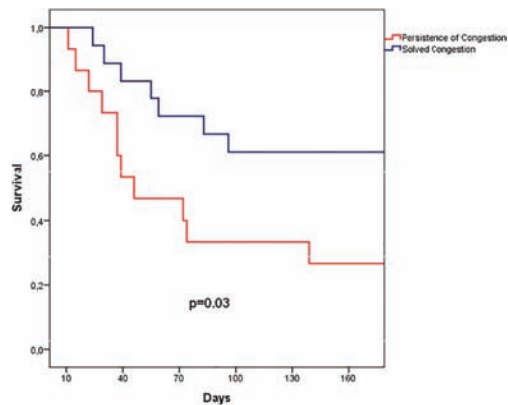
**Background:** While baseline B-type natriuretic peptide (BNP) and its change over time and the presence of pulmonary/systemic congestion have been related to inpatient mortality, their relationships to acute kidney injury (AKI) and outcomes are not well understood.

**Purpose:** The aim of this study were: 1- to investigate the relationship among BNP, congestion, and AKI in AHF; 2- to evaluate the independent prognostic role of BNP, renal dysfunction, and congestion in this setting to longer term outcomes after discharge.

**Methods:** In this study, we enrolled 157 patients admitted to our department with diagnosis of acute HF (BNP levels more than 400 pg/ml, echocardiography and chest-ray). At admission and at discharge two clinicians performed a standardized congestion assessment giving one point for each of the following signs: pulmonary rales, jugular venous distention, third heart sound, peripheral edema, hepatomegaly (total 5 points). All the patients underwent to laboratory assessment to measure blood levels of the following markers: BNP, creatinine, estimated glomerular filtration rate (eGFR). AKI was defined as creatinine increase  $\geq 0.3$  mg/dL or reduction 20% in eGFR during hospitalization. All patients were followed for six months for death or re-hospitalization due to cardiovascular causes.

**Results:** Of 157 patients, 146 completed the follow-up. In our population, 110 patients displayed effective decongestion (discharge congestion score  $\leq 2$ ), 116 patients experienced BNP decrease  $\geq 30\%$  and 28 patients developed in-hospital AKI. BNP decrease  $\geq 30\%$  rate was significantly higher in patients who showed good decongestion compared to persistent congestion at discharge (63% vs 22%;  $p < 0.001$ ); no significant differences were found in the rates of AKI according to the degree of decongestion (15% vs 4%;  $p = 0.526$ ). BNP reduction in the overall sample was not associated with a difference in rehospitalization or death. In those with a BNP decrease  $\geq 30\%$ , Kaplan-Meier survival plots showed better survival in terms of freedom from rehospitalization or death in patients with good decongestion at discharge ( $p = 0.03$ ). In the same subgroup, AKI was not associated with a difference in outcomes.

**Conclusions:** BNP reduction in AHF is associated with decongestion. It appears that both BNP reduction and decongestion in the same patients is a favourable sign for long term survival irrespective of transient AKI.



### P1965

#### The prevalence of renal dysfunction and its influence on the prognosis of patients with heart failure

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The aim was to evaluate the prevalence of renal dysfunction and a prognostic impact of estimated glomerular filtration rate (eGFR) in patients with heart failure (HF).

**Methods:** 85 patients (mean age  $54.4 \pm 0.91$  years, 88.2% 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. N-terminal pro-B-type natriuretic peptide (NT-proBNP) levels were measured by CARDIAC proBNP assay. Renal function was classified into 6 categories ( $\geq 90$ , 60–89, 45–59, 30–44, 15–29, and < 15 mL/min/1.73 m<sup>2</sup>) 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:** 51.7% patients had eGFR less 60 mL/min/1.73 m<sup>2</sup>. During the follow-up time (follow-up median 18 months), 33 patients (38.8%) 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 ( $p = 0.04$ ). We analyzed the end point onset frequency depending on the eGFR and microalbuminuria. Analysis of the and eGFR in relation to clinical condition of patients revealed that 33 patients had primary end point. 25 patients had eGFR less than 45 mL/min/1.73 m<sup>2</sup> and frequency end points increased with a decrease eGFR ( $p = 0.005$ ) and increase microalbuminuria ( $p = 0.013$ ). We investigated the OR of adverse events depending on eGFR. eGFR from 45 to 59 mL/min/1.73 m<sup>2</sup> 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 m<sup>2</sup> increases the OR of end point onset several more (OR 95% 5.8 (1.09 – 30.6),  $p < 0.004$ ). The development of acute kidney injury during hospitalization is associated with an increase in the frequency end points ( $p = 0.010$ ).

**Conclusion:** Renal dysfunction is one of their most important comorbid conditions in HF. Reduced eGFR is an important predictor of cardiovascular morbidity and mortality. Renal dysfunction is associated with a higher incidence of cardiac events (unplanned hospitalization due to HF or death related).

### P1966

#### The role of BUN changes and its influence on worsening renal function in patients hospitalized for heart failure

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**Background:** Blood urea nitrogen (BUN) may not only be a measure of renal function but also neuro-hormonal activation and adverse events in decompensated heart failure (DHF). Worsening renal function (WRF) is conventionally considered an unfavourable prognostic factor but may also reflect the effectiveness of decongestive therapy.

**Purpose:** In patients with DHF we would evaluate the prognostic significance of isolated increases in BUN compared to an increase associated with respect to congestion score at discharge and prognosis

**Methods:** We enrolled patients admitted to our department with DHF and assessed

the severity of congestion by clinical and laboratory assessments (BNP, creatinine, BUN) at admission and at discharge. WRF was defined as an increase in creatinine by  $\geq 0.3$  mg/dL and increasing BUN as an increase by  $> 20\%$  during hospitalization. Congestion score was defined by five traditional signs (peripheral oedema, pulmonary rales, jugular venous distention, third heart sound, hepatomegaly). Effective decongestion was considered when  $\geq 3$  signs disappeared by discharge. All patients were followed for six months for re-hospitalization due to cardiovascular causes or death.

**Results:** Of 161 patients, 149 completed the study and 77 (52%) had events during follow-up. Patients who had both an increase in BUN and WRF had a higher rate of events (77%;  $p < 0.01$ ) compared to those with isolated WRF (43%), isolated BUN increase (67%) or neither (45%). Absolute changes in BUN predicted outcome (AUC: 0.65 [0.57–0.74]  $p = 0.002$ ) but changes in creatinine did not (AUC 0.57 [0.48–0.67]  $p = 0.12$ ). Increases in BUN were also associated with a lower likelihood of achieving decongestion (62%;  $p = 0.004$ ) compared to those with WRF (72%) or those who had neither (78%). Univariate analysis showed that BUN increase and persisting congestion were the only variables related to worse prognosis (HR 1.85 [1.16–2.96]  $p = 0.01$ ; HR 1.84 [1.18–2.85]  $p = 0.007$ ). Multivariable analysis adjusted for chronic kidney disease, LVEF and aetiology showed similar findings.

**Conclusions:** Increasing BUN during hospitalization predicts greater difficulty in decongestion and a higher rate of cardiovascular events independently from WRF.

### P1967

#### Acute cardiorenal syndrome in patients with IE

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**Goal:** To study the features of acute kidney injury (AKI) in patients with infective endocarditis (IE).

**Material and methods:** 125 patients (77 men) with IE (Duke 2015) were included, median age was 50 [33–72] years. 70 (56.0%) patients had native valve IE, 37 (29.6%) had IE associated with heart valve disease, 16 (12.8%) had prosthetic valve IE and 2 (1.6%) had IE attendant on pacemaker implantation. We evaluated the anamnesis, echocardiogram, renal function (GFR, proteinuria, microscopic hematuria, serum Cystatin C, urinary KIM-1), heart failure (NYHA) rates and NT-proBNP levels, AKI (KDIGO 2012) and mortality rates. Early AKI was defined as AKI at the hospital admission, late AKI — as AKI developed during hospitalization.

**Results:** Median GFRCKD-EPI at hospital admission was 58.8 [40–90] mL/min/1.73 sq.m. GFR > 60 mL/min was presented in 62 (49.6%) patients, 59–30 mL/min — in 45 (36.0%), 29–15 mL/min — in 14 (11.0%), < 15 mL/min — in 4 (3.0%). AKI was diagnosed in 63 (50.4%) patients with IE. Early AKI was detected in 23 (36.5%) patients, late AKI — in 40 (63.5%) patients. Active IE increased the chances of both early [OR 5.33 (95% CI 3.61–7.88),  $p < 0.001$ ] and late AKI [OR 2.8 (95% CI 2.03–3.87),  $p < 0.001$ ]. The chances of late AKI was increased in the presence of HF [OR 1.58 (95% CI 1.05–2.38),  $p = 0.03$ ], using of vancomycin [OR 1.53 (95% CI 1.03–2.27),  $p < 0.05$ ] or gentamicin [OR 1.67 (95% CI 1.14–2.34),  $p < 0.01$ ]. Patients with AKI more often had NYHA FC III/IV HF [36 (57.1%) vs. 20 (32.3%),  $p < 0.05$ ] and higher NT-proBNP levels — 3804 [1895–4709] pg/ml vs. 875.5 [424.5–1989.5] pg/ml ( $p < 0.05$ ); more frequently had urine laboratory changes [59 (93.7%) vs. 41 (66.1%),  $p < 0.05$ ], proteinuria [53 (84.1%) vs. 38 (61.3%),  $p < 0.05$ ], had higher values of KIM-1 [2.7 (2.5–2.8) ng/ml vs. 1.5 (1.4–1.7) ng/ml,  $p < 0.05$ ] and serum Cystatin C [2.8 (1.5–3.2) mg/ml vs. 1.9 (1.3–2.2) mg/ml,  $p < 0.05$ ]. In AKI group prevailed *S. aureus* [20 (31.7%) and 20 (32.3%),  $p > 0.05$ ], more often occurred embolic syndrome [39 (61.9%) vs. 22 (35.5%),  $p < 0.05$ ] and was revealed higher mortality rate [21 (33.3%) vs. 11 (17.7%),  $p < 0.05$ ]. AKI increased the chances of death [OR 1.52 (95% CI 1.02–2.31),  $p < 0.05$ ].

**Conclusion:** The AKI complicates IE in 50% of patients and is presented mainly by late AKI associated with the activity of IE, HF and use of nephrotoxic antibiotics. In the group of IE with AKI more often occur NYHA FC III/IV HF, urine laboratory changes, proteinuria. These patients have higher values of NT-proBNP, Cystatin C and KIM-1, higher incidence of embolic syndrome and mortality rate of 33.3%.

## CYTOKINES AND INFLAMMATION

### P1968

#### The relationship in blood levels of proinflammatory cytokines and antibodies to myocardial tissue in patients with dilated cardiomyopathy depending on the severity of heart failure

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**Objective:** To assess the concentration of antibodies to the myocardial tissue, and proinflammatory cytokines (TNF- $\alpha$  and interleukin-6) in the blood and their



relationship with the severity of heart failure (HF) in patients with dilated cardiomyopathy (DCM).

**Materials and Methods:** The study included 100 pts with DCM at the age of 18 to 61 years (mean  $37.7 \pm 1.1$ ). Preclinical stage was diagnosed in 8 (8%) pts, NYHA class II was put up at 15 (15%), III - 42 (42%), IV FC -35 (35%) pts. All pts had made Complex conventional studies, the concentration of antibodies (Abs) to myocardial tissue and inflammatory cytokines were measured by ELISA. Instrumental studies conducted ECG, echocardiography. Assessment of the severity of heart failure was performed using 6-MWT. A control group comprised 29 healthy subjects matched for sex and age. Levels of IL-6, TNF- $\alpha$  and antibodies to myocardial tissue in the serum of pts in the control gr were, respectively,  $3.4 \pm 0.2$  pg / ml,  $4.58 \pm 0.8$  pg / ml and  $33.3 \pm 2.6$  pg / ml.

**Results:** Immunologic monitoring depending on the severity of NYHA classes revealed the following: compared with control gr, the titer of antibody to the tissues of the myocardium in DCM pts in preclinical stage showed a fourfold increase ( $150.8 \pm 33.3$ ;  $p=0.001$ ), in pts with II and III - a threefold increase ( $92.6 \pm 17.8$  and  $92.9 \pm 21.3$ ;  $p=0.001$ ) with minimum values of this indicator in pts with IV NYHA classes ( $69.5 \pm 12.4$ ;  $p>0.05$ ). Through analysis between the concentration of pro-inflammatory cytokines in the blood and the severity of heart failure found that pts with DCM NYHA class IV the level of TNF- to  $64.5\%$  ( $12.7 \pm 1.9$  pg / ml versus  $4.5 \pm 0.8$  pg / ml;  $p=0.01$ ), with a class III  $32\%$  ( $6.6 \pm 0.3$  pg / ml;  $p=0.02$ ), with class II to  $13.4\%$  ( $5.2 \pm 0.6$  pg / ml;  $p>0.05$ ) in the gr of preclinical stage exceeded by  $21\%$  ( $5.7 \pm 1.4$  pg / ml;  $p<0.05$ ) higher than in control group. It revealed a dynamic increase in the level of IL-6 with an increase in the severity of heart failure, amounting to  $4.5 \pm 0.2$  pg / ml ( $p>0.05$ );  $5.5 \pm 0.1$  pg / ml ( $p>0.05$ );  $7.4 \pm 0.8$  pg / ml and  $10.5 \pm 1.5$  pg / ml (Both  $P<0.01$ ), respectively, in pts with HF of NYHA class II, III and IV respectively.

**Conclusion:** The most high concentrations of antibodies to tissue have been reported in patients with DCM identified in preclinical stage, at the same time as the worsening of heart failure characterized by gradually reduced titer of antibodies to the myocardial tissue, and the level of proinflammatory cytokines progressively increased.

## P1969

### Predictive value of circulating ve-catherin in patients with symptomatic ischemic-induced moderate-to-severe chronic heart failure

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**Background:** Chronic heart failure (CHF) is considered as a leading cause of morbidity and mortality worldwide. VE-catherin is a component of endothelial cell-to-cell adherens junctions, and it has a key role in the maintenance of vascular integrity appeared to be a marker of endothelial dysfunction.

**Aim:** To evaluate the prognostic value of circulating VE-catherin for cumulative survival in patients with ischemic-induced chronic heart failure (CHF).

**Methods:** A total of 154 patients with ischemic symptomatic moderate-to-severe CHF were enrolled in the study on discharge from the hospital. Observation period was up to 3 years. All the patients have given their written informed consent for participation in the study. Blood samples for biomarkers measurements were collected. ELISA method for measurements of circulating level of VE-catherin was used. Concentration of VE-catherin for cumulative survival cases due to advanced CHF was tested. Additionally, all-cause mortality, and CHF-related death were examined.

**Results:** During a median follow-up of 2.18 years, 21 participants died and CHF-related death was defined in 18 patients. Additionally, 106 subjects were hospitalized repetitively due to advance CHF (17 cases in died cohort and 89 cases in survival cohort). Medians of circulating levels of VE-catherin in survived and died patient cohort were  $0.63$  ng/ml (95% confidence interval [CI] =  $0.55$ - $0.64$  ng/ml) and  $1.03$  ng/ml (95% CI =  $0.97$ - $1.07$  ng/ml) ( $P<0.001$ ). VE-catherin plasma levels were directly related to NYHA functional class of CHF ( $r=0.474$ ,  $P=0.006$ ), NT-pro-BNP ( $r=0.344$ ,  $P=0.001$ ), T2DM ( $r=0.42$ ,  $P=0.006$ ), gender ( $r=0.366$ ,  $P<0.001$  for male), multi-vessel lesion of coronary arteries ( $r=0.362$ ,  $P=0.001$ ), /m( $r=0.362$ ,  $P=0.001$ ), /Em( $r=0.35$ ,  $P=0.001$ ), TC ( $r=0.32$ ,  $P=0.001$ ), age ( $r=0.28$ ,  $P=0.001$ ), smoking ( $r=0.26$ ,  $P=0.001$ ) and inversely to LVEF ( $r=-0.426$ ,  $P=0.001$ ) and eGFR ( $r=-0.416$ ,  $P=0.002$ ). No significant association between the levels of circulating VE-catherin with fasting plasma glucose, HbA1c, mean systolic and diastolic BP, premature CAD in family anamnesis, and medications for both cohorts of the patients was found. ROC analysis has been shown that cutoff point of VE-catherin concentration for cumulative survival function was  $0.755$  ng/ml. It has been found a significantly divergence of Kaplan-Meier survival curves in patients with high ( $>0.755$  ng/ml) and low ( $<0.755$  ng/ml) concentrations of VE-catherin. Circulating VE-catherin independently predicted all-cause mortality (OR =  $1.27$ ; 95% CI =  $1.08$ - $1.59$ ;  $P=0.002$ ), CHF-related death (OR =  $1.16$ ; 95% CI  $1.02$ - $1.50$ ;  $P<0.001$ ), and also CHF-related rehospitalisation (OR =  $1.12$ ; 95%CI =  $1.07$  -  $1.25$ ;  $P<0.001$ ) within 3 years of observation period.

**Conclusion:** Increased circulating VE-catherin associates with increased 3-year CHF-related death, all-cause mortality, and risk for recurrent hospitalization due to CHF

## P1970

### Anti-inflammatory effects of metformin in diabetic patients and non-diabetic heart failure patients

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**Background & Aim:** Metformin has been shown to reduce cardiovascular events in randomized controlled trials; however, the underlying molecular mechanisms remain poorly understood. Accumulating evidence suggests that diabetes (DM), and heart failure (HF) share a metabolic milieu characterized by chronic sub-acute inflammation. In this bench-to-bedside study, we studied the anti-inflammatory effects of metformin on inflammatory biomarkers in animal tissues, followed up these findings in a population cohort analysis of treatment naïve DM patients and in a group of non-diabetic HF patients from a randomised controlled trial (RCT).

**Methods:** In the molecular study, anti-inflammatory effects of metformin were studied in hepatic (primary mouse hepatocytes) and extrahepatic tissues (bone marrow derived macrophage/BMDM) of C57/BL6 mice. In the clinical study, we identified treatment naïve diabetic patients from the GoDARTS diabetes registry who had been commenced on metformin ( $n=498$ ) or sulphonylurea (SU; as control;  $N=172$ ), and examined the impact of diabetic therapy on change in Neutrophil-to-lymphocyte ratio (NLR), a marker of inflammation after 12 months of metformin/SU therapy. We followed up these findings in an RCT of metformin in non-diabetic HF patients (Age  $63 \pm 7.0$  years; 85% male; NYHA I/II/III/IV, 04/28/01/0) who were randomized to receive either 4 months of metformin ( $n=20$ , 2 g/day) or placebo ( $n=13$ ).

**Results:** Molecular study: Metformin inhibited the expression of pro-inflammatory cytokines IL-6, IL-1 $\beta$ , VEGF & CXCL1/2 in primary mouse hepatocytes and also reduced IL-12p40 and IL-6 secretion in macrophages (BMDM) suggesting that the effects of metformin on anti-inflammatory signalling pathways are separable from its actions on metabolism and are likely to be different from conventional non-steroidal anti-inflammatory drugs.

**Clinical Study:** In a large treatment naïve diabetes population cohort, we observed differences in NLR, following incident treatment with either metformin or SU monotherapy. Compared to SU exposure, metformin reduced the mean log-transformed NLR after 8-16 months by 0.09 units (95% CI =  $0.02$ - $0.17$ ,  $p=0.013$ ), and increased the likelihood that NLR would be lower than baseline after 8-16 months (OR 1.83, 95% CI =  $1.22$ - $2.75$ ,  $p=0.00364$ ). Following up these findings in a double blind placebo controlled trial in non-diabetic heart failure patients, metformin suppressed plasma inflammatory cytokines such as CCL11, IL-2, IL-4, CCL22 and CXCL12 ( $p<0.01$ ).

**Conclusion:** Cross-species evidence from cells, plasma, patient records and a randomized placebo controlled study strongly suggest that metformin exerts anti-inflammatory effects, irrespective of diabetes status. This apparent anti-inflammatory effect of metformin including its utility in non-diabetic 'at risk' cardiovascular disease groups warrants further investigation.

## P1971

### The effects of tumour necrosis factor on bone metabolism in patients with chronic heart failure

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In recent years, there has been growing evidence that tumor necrosis factor is associated with the progression of chronic heart failure (CHF) and bone resorption.

**Aim:** To investigate if circulating markers of bone tissue and tumor necrosis factor are associated with severity of heart failure and hemodynamic in patients with CHF.

**Methods:** Seventy outpatients suffering from CHF (40 women and 30 men, age 56-88 years) due to coronary heart disease or arterial hypertension entered the study. Forty subjects with cardiovascular diseases but without CHF (30 women and 10 men, age 57-88 years) were selected as sex- and age-matched controls. Spine and femoral neck bone mineral density (BMD) (expressed as T-score), calciotropic hormones (parathyroid hormone, PTH; 25-hydroxycholecalciferol, 25(OH)D3) and biochemical markers of bone turnover (osteocalcin, OC; type I collagen C-terminal telopeptide, CTX); N-terminal pro-B-type natriuretic peptide (N-proBNP) and tumour necrosis factor- $\alpha$  (TNF) were evaluated.

**Results:** Spine and femur T-scores were higher in the CHF patients (spine:  $-1.2$  ( $0.4$ - $2.3$ ); femur:  $-2.5$  ( $1.6$ - $2.7$ )) compared to subjects of control group (spine:  $-0.7$  ( $0.1$ - $1.3$ ),  $p=0.003$ ; femur:  $-1.6$  ( $0.9$ - $2.3$ );  $p=0.060$ ). CTX and OC concentrations were not significantly different between patients with HF and control group, whilst 1,25(OH)D3 concentrations were significantly lower in HF patients [ $9.6$  ( $5.0$ - $14.4$ ) ng/ml compared with controls [ $16.8$  ( $10.7$ - $22.3$ ) ng/ml],  $<0.001$ . PTH were significantly higher in HF patients [ $7.7$  ( $4.5$ - $9.4$ ) pmol/l] compared with controls [ $4.5$  ( $3.7$ - $5.7$ ) pmol/ml],  $<0.001$ . TNF was increased in HF patients [ $18.7$  ( $5.1$ ) pg/ml] but not in controls [ $3.5$  ( $0.8$ ) pg/ml]. The significant correlation was established between serum TNF and BMD in femur ( $p=0.016$ ,  $r=-0.35$ ), N-proBNP ( $=0.017$ ,  $r=0.43$ ), low

concentration of 1,25(OH)<sub>2</sub>D<sub>3</sub> ( $p < 0,001$ ,  $r = 0,50$ ); LV EDD ( $=0,015$ ,  $r = 0,36$ ), LV ESD ( $=0,022$ ,  $r = 0,35$ ), left atrium ( $=0,031$ ,  $r = 0,33$ ), right ventricular diameter ( $=0,013$ ,  $r = 0,38$ ), LV EDV ( $=0,016$ ,  $r = 0,37$ ), LV ESV ( $=0,016$ ,  $r = 0,37$ ) and LV EF ( $=0,031$ ,  $r = -0,33$ ).

**Conclusion:** These data show that HF patients have an osteopenia, the degree of which is different in controls; however, bone turnover is not significantly higher in HF patients. These findings confirm the association between the TNF and BMD and N-proBNP. TNF may serve as a marker of severity of disease in concomitant osteopenic syndrome among HF patients. Properly controlled long-term trials are needed to fully evaluate the impact of TNF on bone mineral density in heart failure.

#### P1972

##### Role of interleukin-18 in estimation of hospital complications in subjects with coronary artery disease who underwent coronary artery bypass grafting

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**Purpose:** To estimate the clinical significance of interleukin-18 (IL-18) in blood serum for predicting the risk of hospital complications development in subjects with coronary artery disease (CAD) who underwent coronary artery bypass grafting (CABG).

**Materials and methods:** The study included 720 subjects who underwent CABG in RI for CICVD in the period since March 2011 till April 2012. All the subjects before performing CABG and on the 7th day after surgical interference were measured the blood serum creatinine concentration, glomerular filtration rate (GFR) by MDRD (Modification of Diet in Renal Disease) formula and also interleukin-18 concentration in blood serum. We evaluated the incidence of adverse outcomes of surgical interference (myocardial infarction, stroke or transient ischemic attack, acute or chronic renal disease progression, reoperation) during in-hospital period. All the subjects were measured a score by EuroSCORE-II additive risk scale.

**Results:** In the present study we didn't receive significant differences in blood serum creatinine level and GFR both as before surgery and on the 7th postoperative day among subjects of different risk groups by EuroSCORE-II, as well as in subjects with complicated and uncomplicated course of postoperative period. Whereas the IL-18 level in the blood serum before surgery and on the 7th postoperative day was significantly higher in subjects of high and medium risk groups by EuroSCORE-II scale, as compared to low-risk subjects. Detection of IL-18 in the blood serum in preoperative period proved to be useful for estimation the risk of certain cardiovascular complications development in postoperative period. It was found out that in subjects with development of myocardial infarction (MI) or stroke after CABG preoperative IL-18 values were definitely higher as compared to subjects without MI or stroke. IL-18 values in the blood serum of subjects with the development of acute renal failure were also higher as compared to subjects without acute renal failure (ARF). Analysis of IL-18 levels in subjects with the development of postoperative adverse outcomes also showed its statistically significant higher values, both in preoperative and in postoperative periods, while such indicators of renal dysfunction as creatinine and GFR didn't show any significant differences in subjects with favorable and adverse outcomes.

**Conclusion:** Thus preoperative quantitative estimation of IL-18 in the blood serum which is a preclinical marker of acute kidney injury, allows to predict more accurately the hospital risk of development of adverse cardiovascular and renal complications of CABG.

## VALVULAR HEART DISEASE (DIAGNOSIS, MANAGEMENT AND INTERVENTIONAL THERAPIES)

#### P1973

##### Transcatheter aortic valve replacement: a new opportunity for elderly patients

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**Background:** Aortic stenosis is the most common acquired valve disease in elderly patients. Surgical aortic valve replacement remains the standard therapy to reduce symptoms and improve survival. However, in patients who are not suitable or are at very high surgical risk percutaneous transcatheter aortic valve implantation (TAVI) offers a new therapeutic option. We aim to assess the feasibility and safety of this technique and evaluate periprocedural, short and mid-term outcomes.

**Methods:** Clinical, echocardiographic and procedural data were analyzed from patients referred for TAVI in a single tertiary centre between November 2014 and November 2015.

**Results:** Forty eight patients were consecutively referred for TAVI at our hospital, after Heart Team evaluation. Two refused the procedure, 5 died in the meantime

and 41 underwent TAVI and only those were included in our analysis. Transfemoral approach was used in 90% of cases, 68.3% implanted third-generation percutaneous self-expanding CoreValve. The mean age of the patients was  $80 \pm 7.4$  years, 41.5 % of them were men. The median of EuroSCORE II 3.5% (1.25-15.75%). Of this high-risk patients, porcelain aorta was the indication for TAVI in 60% of patients. The mean aortic valve orifice area was  $0.69 \pm 0.19$  cm<sup>2</sup> and the mean transvalvular gradient was  $51.5 \pm 13.9$  mmHg before the intervention. The mean duration of the intervention was  $80 \pm 20$  minutes and the screening time  $18.8 \pm 7.4$  minutes. The procedure was technically successful in all patients. The post-interventional mean transvalvular gradient was  $9.8 \pm 5.8$  mmHg ( $p < 0.001$ ). Significant residual aortic regurgitation (more than grade II/IV) was present in only two cases. Contained aortic root rupture was diagnosed in 1 patient and one vascular complication was immediately treated by catheter angioplasty. Mean hospital stay was  $10 \pm 5$  days. A permanent pacemaker was implanted in 9 of the patients. All patients were discharged alive from hospital. Median follow-up time was 1 month (1-12 months). During this period no deaths occurred and there was one re-hospitalization from cardiovascular cause. NYHA functional class at follow-up was significantly improved (NYHA > II 34.1% vs 7.3%;  $p < 0.001$ ).

**Conclusions:** The burden of severe symptomatic aortic stenosis among the elderly patients with co-morbidities is substantial. Although challenging, TAVI is creating a window of opportunity that should be considered to add quality-of-life and improve functional status for those who have contraindications to surgical valve replacement. In this first year of experience we obtained excellent results during hospitalization and short-term follow-up which encourages our center for further development of this promising technique.

#### P1974

##### Percutaneous transvenous mitral commissurotomy in patients with calcific mitral stenosis: immediate and in-hospital clinical, echocardiographic and hemodynamic outcome

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**Objectives:** To see Immediate and In-hospital Clinical, Echocardiographic and Hemodynamic Outcome of Percutaneous Transvenous Mitral Commissurotomy in Patients of Mitral Stenosis with and without fluoroscopically visible mitral valve calcification.

**Background:** Rheumatic fever and rheumatic heart disease continue to be the major health problem in all developing countries including Bangladesh. Rheumatic mitral stenosis is a very common problem in our population having an incidence of 54 percent among rheumatic heart disease with a female preponderance of 2:1. Mitral valve calcification has shown to be an important factor in determining immediate outcome of patients undergoing surgical mitral commissurotomy. Percutaneous balloon mitral commissurotomy is appealing because the mechanism of valve dilation closely parallels the mechanism of surgical mitral commissurotomy. The technique of balloon mitral commissurotomy has evolved rapidly, with improvements in balloons, guide wires, and the application of double-balloon techniques. Percutaneous transvenous mitral commissurotomy (PTMC) using an Inoue balloon catheter is of established efficacy and safety and is an alternative to surgical valvotomy in selected patients with rheumatic mitral stenosis.

**Methods:** A prospective study was done during the period of August 2003 to November 2015. Nineteen hundred and eighty (1980) patients with rheumatic mitral stenosis who underwent PTMC were evaluated clinically, by echocardiography and by catheter during and after procedure. Out of 1980 patients 80 patients had fluoroscopically visible mitral valve (MV) calcification (Group-1) and rest 1900 patients had no fluoroscopically visible mitral valve (MV) calcification (Group-2).

**Results:** Mean age of the study population was  $44.25 \pm 08.40$  years in group-1 and  $29.14 \pm 12.31$  years in Group-2. Most of the population are female, 72% in Group-1 and 75% in group-2. After PTMC mean mitral valve area increased from  $0.70 \pm 0.15$  cm<sup>2</sup> to  $1.46 \pm 0.34$  cm<sup>2</sup> as measured by echocardiography in group-1 and from  $0.82 \pm 0.22$  cm<sup>2</sup> to  $1.81 \pm 0.33$  cm<sup>2</sup> in group-2. Mitral valve gradient reduced to  $12.73 \pm 4.19$  mm Hg from  $33.56 \pm 04.94$  mm Hg after PTMC in group-1 and  $11.75 \pm 3.67$  mm Hg from  $27.34 \pm 04.34$  mm Hg after PTMC in group-2. Mean left atrial pressure as recorded by catheter before PTMC was  $32.99 \pm 08.58$  mm Hg while after PTMC it was  $22.72 \pm 05.38$  mm Hg in group-1 and in group -2,  $29.72 \pm 06.27$  mm Hg before while after PTMC it was  $22.76 \pm 05.12$  mm Hg in group-2. In Group-1 had higher NYHA class, higher atrial fibrillation, High Wilkins Echo score and higher age.

**Conclusions:** PTMC can be performed effectively and safely in patients had fluoroscopically visible mitral valve (MV) calcification with good immediate result but result is inferior to patients had no fluoroscopically visible mitral valve (MV) calcification.

#### P1975

##### Heart failure class at presentation: a predictor of prognosis in patients with infective endocarditis

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**Purpose:** Despite diagnostic and therapeutic advances infective endocarditis remains an important cause of morbidity and mortality worldwide. To recognise predictors of poor prognosis at presentation is crucial in the management of these patients.

**Methods:** Retrospective, single center study, of patients admitted for infective endocarditis (EI) in a tertiary hospital, during a ten years period. The patients were divided in two groups according to heart failure classification by New York Heart Association (NYHA) criterions at admission: Group 1 (NYHA class I/II) and Group 2 (NYHA class III/IV). For each group we analyse clinical, echocardiographic parameters and in-hospital and one year outcomes.

**Results:** 103 patients with EI were included, 62,1% men, mean age  $65,8 \pm 17,2$  years. Native valve EI was present in 85% of cases with same prevalence of aortic and mitral valve involvement (40%). Perivalvular complication were reported in 17,6% (14,7% abscess and 2,9% fistulas). According to division in heart failure NYHA class at presentation Group 1 included 72 patients and Group 2 31 patients. There were no significant differences between groups regarding gender, type and location of EI or perivalvular complication, but with a higher proportion of severe valvular regurgitation in Group 2 (18,3 vs 28,7%  $p=0,027$ ). Patients in Group 2 were older ( $62,6 \pm 17,1$  vs  $73,2 \pm 15,1$  years  $p=0,003$ ), had a lower creatinine clearance at admission ( $68,1 \pm 29,4$  vs  $44,6 \pm 23,9$   $p<0,001$ ) and developed more frequent acute kidney injury (25,4 vs 51,6%  $p=0,010$ ), with no significant differences in diabetes, immunosuppression or use of IV drugs. Group 2 had also a higher percentage of patients with atrial fibrillation (28,2% vs 44,8%  $p=0,010$ ) and with moderate to severe left ventricular dysfunction (4,3% vs 20%  $p=0,020$ ). We found same proportion of embolic events, but with higher rates of sepsis and cardiogenic shock in Group 2. In-hospital and one year mortality rate were higher in Group 2 (21,4% vs 45,2%  $p=0,015$  and 6,0% vs 28,6%  $p=0,036$ , respectively). After multivariate analysis acute kidney injury and NYHA class remained as independent predictors of mortality (OR: 3,44; 95% CI: 1,22 to 9,66;  $p=0,019$  and OR:2,37; 95% CI:0,72 to 7,83;  $p=0,043$ ).

**Conclusion:** NYHA class at admission proved to be a strong predictor of prognosis in patients with EI. Presentation in class III/IV NYHA reflects a type of patients with higher comorbidities and in-hospital complications, with a consequent higher mortality rates.

#### P1976

##### Comparison of the effectiveness of transcatheter aortic valve implantation in patients with degenerated bioprosthetic surgical valves versus. aortic stenosis

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Reoperation, the current standard of care for failed bioprosthetic tissue 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 of this study was to evaluate the clinical results of this technique using the CoreValve prosthesis in patients with degenerated bioprosthesis surgical valves and comparing them with patients with aortic stenosis.

**Methods:** The CoreValve prosthesis (Medtronic, Minneapolis, MN, USA) was implanted in 18 patients with symptomatic degenerated surgical aortic valves (SAV) and in 482 patients with aortic stenosis (AS).

**Results:** The mean age was lower in SAV compared with AS  $74,1 \pm 16$  vs.  $79,3 \pm 6$  years,  $p=0,002$  and logistic EuroSCORE was higher by SAV  $27,5 \pm 17\%$  vs.  $17 \pm 11$ ,  $p=0,001$ . TAVI procedure was successful in all patients with degenerated bioprosthesis. In two patients required to implant a second valve prosthesis. After procedure and 1-year, the mean gradient was higher in patients with SAV than AS,  $19,7 \pm 14$  mmHg vs.  $8,8 \pm 4$  mmHg, and  $15,1 \pm 9$  vs.  $9 \pm 4$  mmHg,  $p<0,001$ , respectively. The aortic regurgitation grade post procedure in patients with SAV was: absent in 66.7%, middle in 22.2% and moderate in 11.1% and there were not 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 (73.3% vs. 38.3%,  $p=0,024$  and 40% vs. 8.7%,  $p=0,001$ , respectively). There were tend to lower requiring pacemaker after procedure (13.3% vs. 24.8%,  $p=0,310$ ). In the follow-up, after  $34,3 \pm 23$  months, the total mortality was similar in both groups, 3.5 vs. 3.6%,  $p=0,936$  and 80 % of patients was at an Association functional class I-II.

**Conclusions:** The valve-in-valve procedure is clinically effective in patients with degenerated bioprosthesis aortic valves. The procedure and outcomes are similar in some aspects to TAVI in the setting of native aortic valve stenosis.

## DEVICES / CRT / ICD

#### P1977

##### Cardiac remodeling after percutaneous intervention for mitral regurgitation using the MitraClip system

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**Introduction:** Reverse remodeling of the cardiac chambers can be seen in most patients undergoing mitral valve repair surgery. Percutaneous mitral valve treatment with the MitraClip system is considered an alternative intervention for symptomatic patients with severe mitral regurgitation (MR) and high surgical risk and has shown favourable clinical results. However, data regarding cardiac remodeling after this percutaneous intervention are sparse.

**Methods:** Retrospective study including patients with moderate to severe MR and high surgical risk undergoing MitraClip implantation, between May 2014 and November 2015. Clinical and echocardiographic follow-up was achieved at discharge, 1, 6 and 12 months. The echocardiographic parameters analysed included: left atrium (LA) indexed volume, short axis/long axis ratio of LA, LA and right atrium area, left ventricle (LV) telesystolic and telediastolic indexed volumes, LV sphericity index, LV ejection fraction (EF), right ventricle (RV) basal and longitudinal diameters and RV systolic function evaluated by tricuspid annular plane systolic excursion (TAPSE).

**Results:** The studied population included 22 patients: 21 with functional MR and one with MR of a mixed etiology. 9 patients (40.9%) had and an EF<30% and 10 (45.5%) were in sinus rhythm. Comparing to pre-procedural evaluation, there was a significant improvement in the degree of MR at discharge ( $p<0,001$ ), after implantation of a median of 2clips [IQR 1-2]. Comparing to discharge, at one month follow-up there were no significant differences in the echocardiographic parameters evaluated. At 6 months, there was a significant reduction in the short/long axis ratio of the LA (from 0.84 [IQR 0.79-0.88] to 0.78 [IQR 0.75-0.89];  $p=0,03$ ). At 12 months, a significant reduction in LV telediastolic indexed volume (from 108.0mL/m<sup>2</sup> [IQR 94.3-122.7] to 100.0mL/m<sup>2</sup> [IQR 91.6-114.0];  $p=0,04$ ) and a decrease in the LV telesystolic indexed volume (from  $78,3 \pm 31,6$  mL/m<sup>2</sup> to  $73,1 \pm 10,6$  mL/m<sup>2</sup>;  $p=0,08$ ) were seen. There were no significant differences in the remaining evaluated parameters at 6 and 12 months.

**Conclusion:** In this population of patients, MitraClip implantation was associated with a reduction in the short/long axis ratio of the LA and LV telediastolic indexed volume at short term follow-up. There were no significant differences in the other echocardiographic parameters evaluated. The addition of a greater number of patients to this initial experience and a long term follow-up will be relevant in the re-evaluation of the impact of this intervention in cardiac chambers size and function.

#### P1978

##### Obstructive sleep apnea in continuous flow LVAD supported patients: incidence and therapeutic implications

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**Background:** Obstructive Sleep apneas (OSA) and hypopneas result from complete or partial collapse of a narrowed pharynx. The reported prevalence of OSA in the healthy population is approximately 4% in women and 9% in men. In the heart failure (HF) populations, prevalence of OSA varies between 37% up to 54%. However, only a minority of the HF patients complain of excessive daytime sleepiness, suggesting that many patients with HF have relatively asymptomatic OSA. The incidence of sleep apnea in HF patients supported with continuous flow LVAD is unknown. The aim of this study was to assess the incidence and therapeutic implications of sleep apnea in LVAD supported patients.

**Methods:** Sleep study was performed in 12 continuous flow LVAD supported patients. The participating patients were 6 months post operation, stable with no changes planned in their medical management and had no OSA related symptoms

**Results:** OSA was present in 11 patients (91%). According to the apnea-hypopnea index, OSA was mild (5 to 15) in 4, moderate (15 to 30) in 6 and severe (more than 30) in 1 patients. CPAP treatment was offered to the entire group with OSA but was tolerated in only 8 patients who used it for more than 3 months. After 3 months of CPAP therapy a mild improvement in kidney function (decrease in mean creatinine from 1.30 to 1.18 mmol/l), mean pulmonary pressures (from 22.75 to 18.5 mmHg) and mean cardiac index (from 2.05 to 2.70 l/min/m<sup>2</sup>) was observed.

**Conclusion:** OSA is very frequent in continuous flow LVAD supported patients. The use of CPAP in LVAD supported patients has a significant hemodynamic effect. Due to the low symptomatology of OSA in the LVAD supported patients and the benefits of CPAP therapy; we propose to perform sleep study in all LVAD patients.



Baseline characteristics (12 patients).	
Age (years)	63
Sex (male)%	66
Etiology (ischemic)%	41
Creatinine (mg/dl)	1.3
Hemoglobin (mg/dl)	12.1
Doppler blood pressure (mmHg)	90
Pulmonary pressure (mmHg)	22.75
Cardiac index (l/min)	2.05

### P1979

#### Improving long-term results of mechanical circulatory support in crash-and-burn patients

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**Purpose:** Crash-and-burn patients are still challenging group of patients. We sought to find preimplant factors which may improve long-term results of mechanical circulatory support in this cohort.

**Methods:** Fifty-seven adult patients in crash-and-burn status (15 females, 40.2 years of age) were treated by paracorporeal VAD (Nipro-Toyobo) since 2003. Thirty-four patients were on ECMO support before VAD implant. DCM was seen in 21, AMI in 14, and fulminant myocarditis in 9. Bridge strategy to continuous-flow VAD after stabilization of general condition was adopted in 2011. Actuarial survivals were analysed and compared.

**Results:** Survivals at 1, 3, 5 years were 68.4%, 55.0% and 42.9% in the whole population. Survival of recent cases (2010-2015) was superior to that of early cases (5-year survival: 70.3% vs 32.9%). Successful endpoints (weaning from the system and alive, bridged to continuous-flow VAD and alive and transplanted) were met in 22 cases in recent cases, whereas only 11 cases in the other. ECMO support before implant and BiVAD requirement were significant risk factors for unfavorable outcomes.

**Conclusions:** Long-term results of VAD implantation in crash-and-burn patients were improving in recent years thanks to our recent bridge strategy. Preimplant ECMO and BiVAD requirement were still big hurdles.

### P1980

#### Right heart failure post LVAD therapy - timing of RVAD placement predicts survival

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**Purpose:** Right ventricular (RV) support in the case of RV failure after left ventricular assist device (LVAD) implantation is a well-established surgical therapeutic option and remains an important cause of mortality. We sought to review our practice of RVAD implantation post LVAD insertion and the association between time in hours from LVAD implantation until the need for RVAD and survival in hospital discharge or long term survival.

**Methods:** Retrospective analysis was performed of a prospectively collected database of all LVAD implantations between March 2011 and October 2015. The study cohort included patients who required post-operatively RVAD support post LVAD implantation. Demographic and clinical characteristics were compared in patients in survivors and non-survivors.

**Results:** Out of 171 adult patients with a heartware H-VAD implantation, 20 received RVAD support for post-operative right heart failure (12%). The median time on LVAD support was 28 days (1-1000). 10 (50%) patients had inpatient deaths, 2 were transplanted, 1 was successfully de-commissioned and 7 remain on support. Univariate analysis of basic demographic and clinical data performed no significant differences for age, gender, height, weight, bilirubin at the time of LVAD insertion and measurement of central venous pressure, pulmonary artery systolic pressure. Out of the 20 supported patients, 14 had RVAD support instituted at the time of LVAD insertion. 30 day survival for those 14 patients was 55 +/- 15% versus 20 +/- 18% (p=0.031)

**Conclusion:** Our data supports the use of good pre-operative evaluation of right heart function with timely insertion of RVAD support leading to increased survival.

### P1981

#### Impact of a new less invasive ventricular restoration system on ischemic mitral regurgitation

BioVentrix Inc.

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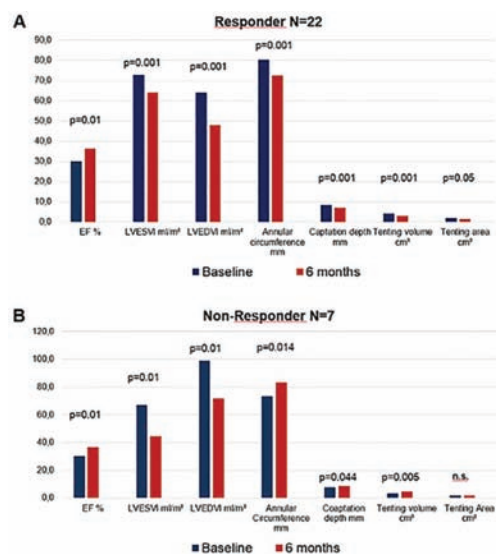
**Background:** The frequency of secondary mitral regurgitation (MR) which originates from LV dysfunction is up to 90% in a population with CHF. It could be demonstrated that associated secondary MR is an independent predictor of mortality. An altered LV geometry constitutes the main factor for the development of secondary MR. Left ventricular reconstruction (LVR) has the potential to improve MR. Compared to surgical LVR, this new system is a less invasive device which enables LV volume reduction through scar exclusion. This system excludes akinetic or dyskinetic scars located in the antero-septal LV. The device replicates the geometric reconfiguration achieved through surgical LVR, but on a beating heart.

**Purpose:** The aim of this multicenter study is to assess the impact on mitral valve geometry of a less invasive LV restoration therapy for ischemic heart failure. Multiple MV geometric parameters were assessed by the use of echocardiography.

**Methods:** Retrospective core laboratory analysis of 29 patients treated for ischemic cardiomyopathy following an anterior myocardial infarction. Patients underwent the LV volume reduction procedure using a series of micro-anchors. Patients with paired (before and after implant) echocardiographic acquisitions were included into analysis. MV geometric parameters were measured before and 6 months after implantation.

**Results:** Twenty-nine patients were included in the analysis. There was significant reduction in annular circumference (80.3±13.8 mm vs 72.6±10.6 mm; p=0.001) coaptation depth (8.5±1.9 mm vs 7.2 ±1.8 mm; p=0.001), tenting volume (4.3±2.1 cm<sup>3</sup> vs 3.1±1.5 cm<sup>3</sup>; p=0.001) and tenting area (2.2±0.7cm<sup>2</sup> vs 1.6±0.5 cm<sup>2</sup>) in 22 patients (76%=Responders) at 6 months follow-up. Seven patients (24%=Non-Responders) showed no significant reduction (or even an increase) in annular circumference (73.4±12.4 mm vs 83.4±15.8 mm ; p=0.014), coaptation depth (7.8±3.1 mm vs 8.6±2.7 mm; p=0.044), tenting volume (3.6±1.9 cm<sup>3</sup> vs 4.8±2.3 cm<sup>3</sup>; p=0.005) and tenting area (1.8±0.8 cm<sup>2</sup> vs 2.1±0.8 cm<sup>2</sup>; n.s.) at 6 months follow-up. Ejection fraction (EF) and LV Volume indices improved significantly in both groups (Responders: EF 29.0±7.4% vs 32.2±5.1%, p=0.01; LVEDVI 89.3±22.9ml/m<sup>2</sup> vs 72.7±23.3ml/m<sup>2</sup>, p=0.001; LVESVI 64.2±21.4 ml/m<sup>2</sup> vs 48.0±21.5ml/m<sup>2</sup>, p=0.001/ Non-Responders: EF 30.2±7.4% vs 36.5±7.9%, p=0.01; LVEDVI 98.9±26.5 ml/m<sup>2</sup> vs 71.8±12.8 ml/m<sup>2</sup>, p=0.01; LVESVI 67.1±19.8 ml/m<sup>2</sup> vs 44.7±6.5 ml/m<sup>2</sup>, p=0.01).

**Conclusions:** This less invasive, off pump, ventricular restoration system shows a favorable impact on MV geometry. In 76% of patients at 6 months post implantation there were beneficial geometric changes to the mitral apparatus. The observed geometric changes have the potential to improve MR. This technology is unique in that it directly addresses the underlying ventricular origin of ischemic mitral regurgitation.



Mitral geometry after less invasive SVR

## P1982

**Preoperative severe mitral valve regurgitation resolves after continuous-flow left ventricular assist device implantation and is not associated with adverse outcomes**

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**Background:** The presence of severe mitral valve regurgitation (MR) at the time of left ventricular assist device (LVAD) implantation is prevalent and its clinical importance remains still unclear.

**Purpose:** The impact of an untreated preoperative severe MR on outcomes after LVAD implantation should be evaluated.

**Methods:** Between November 2008 and October 2014 235 patients underwent first time implantation of a continuous-flow LVAD in our center. We excluded 11 patients with prior mitral valve replacement and 2 patients with mitral valve reconstruction during LVAD implantation. Based on availability of echocardiography with good image quality before and after LVAD implantation (n = 110 HVAD, n = 18 HeartMate II), 128 patients of our outpatient clinic were divided into 2 groups according to the presence of severe pre-operative MR: group A with severe MR (n=65) and group B with none to moderate MR (n=63; 28 of 63 with moderate MR). We evaluated the transthoracic echocardiography preoperative (mean ± SD 24 ± 33 days pre LVAD) and postoperative: first postoperative (19 ± 15 days post LVAD), second postoperative (353 ± 83 days post LVAD), and the last follow-up available (574 ± 457 days (5-2213 days) post LVAD). We registered deaths, complications, and clinical status in the entire population.

**Results:** Patients in group A were more likely to have a dilated cardiomyopathy, increased left ventricle diameters, and higher pulmonary pressure before LVAD implantation. We observed a significant decrease in severity of MR after LVAD implantation (severe MR 51% pre vs 6% post, p < 0.0001). There was no difference between groups regarding right heart failure, rate of urgent heart transplantation due to any cause, pump thrombosis or ventricular arrhythmias. Finally there was no difference in 1- and 3-years survival (87.7% vs. 88.4% and 71.8% vs. 66.6% for group A and B respectively, p = 0.97)

**Conclusions:** Preoperative severe MR resolves in the majority of patients after LVAD implantation and is not associated with worse clinical status, increased risk for right heart failure or long-term survival.

## P1983

**Minimally invasive LVAD implantation - initial two years single centre experience**

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**Introduction:** Left ventricular assist device (LVAD) as a bridge to transplant strategy is well established. However, the implantation of LVAD is invasive and associated with significant peri-operative complications in these critically ill patients. Lower invasiveness of implantation might have the potential to enhance results of these high risk patients. The aim of this study is to present our two years experience with minimally invasive approach to implantation of left ventricular assist device HeartWare HVAD.

**Methods:** Seventeen patients underwent minimally invasive implantation of left ventricular assist device HeartWare HVAD between November 2013 and November 2015 as a bridge to heart transplantation in our centre. Sixteen patients were males, one patient was female. Mean age of patients was 57 ± 8,9 years. Basic diseases were dilated cardiomyopathy in 13 patients (76%), ischemic cardiomyopathy in 4 patients (24%). The mean value of left ventricular ejection fraction was 13,5 ± 3.8%, right ventricular ejection fraction was 30,9 ± 5.4%. Access to the left ventricular apex was reached by small left anterior thoracotomy (approximately 8 cm incision). To access the ascending aorta we used upper J ministernotomy.

**Results:** Minimally invasive implantation was successful in all patients. In one patient closure of foramen ovale was simultaneously performed. Most patients (76%) were extubated on the first postoperative day. Only in one case (6%) a failure of the right ventricle occurred with the need for temporary percutaneous right-sided circulatory support device Centrimag. Overall thirty-day survival was 94%, one year survival was 82%. Nine patients (53%) underwent successfully heart transplantation, five patients (29%) remain on LVAD support.

**Conclusion:** Minimally invasive LVAD implantation is feasible, safe and allows easier re-entry for subsequent transplantation. There is also a promising tendency for lower incidence of perioperative right heart failure. After initial experience with this technique it has become the method of choice in our centre.

## P1984

**Impact of remote monitoring on clinical outcomes in chronic heart failure: our experience.**

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**Introduction:** The increasing worldwide prevalence of heart failure (HF) is associated with numerous and protracted hospital admissions. The increasing number of patients with implantable cardiac devices raises the need for more efficient outpatient follow-up care. Remote monitoring (RM) concept has been proposed to optimize medical management of the patients with chronic HF to decrease the hospitalizations.

**Purpose:** To assess the benefits on clinical outcomes of RM compared to standard outpatient follow-ups.

**Methods:** 558 consecutive outpatients with chronic HF with left ventricular ejection fraction (LVEF) <45% with single- or dual-chamber implantable cardioverter defibrillator (ICD) implanted (58,8% ischemic etiology, 66,8% primary prevention) were divided into a group of patients followed through standard outpatient visits (AMBULATORY group) and a group followed by the RM-system (REMOTE group). Emergency room accesses and delivered shocks were evaluated in both groups.

**Results:** During the 18-months follow-up, it was considerably reduced the number of emergency room accesses in the REMOTE group compared to the AMBULATORY group (38 and 125 respectively, p=0.05). A comparable number of patients experienced one or more shocks (14.1 and 15 respectively in the AMBULATORY and REMOTE group, p=0.34).

**Conclusions:** RM offers a unique opportunity to maintain device surveillance and improve patient outcomes in patients with chronic heart failure.

## P1985

**Role of non-invasive home telemonitoring (HTM) in diastolic heart failure treatment.**

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**Introduction:** Heart Failure (HF) is the leading cause of hospitalization in older people and health costs are increasing. We sought to identify whether HTM improves therapies outcomes for patients with diastolic HF who are at high risk of hospitalization and death.

**Purpose and Methods:** We studied for 1 year patients with a recent clinical admission for HF with preserved left ventricular ejection fraction (LVEF) and with diastolic dysfunction. Patients sent and received data via internet with telematic support. HTM consisted of 6 months weekly remote monitoring of vital signs, blood pressure and ECG, with feed-back instructions for the management of drug therapy and way of life. Quality of life was measured by means of Minnesota Living with Heart Failure Questionnaire (MLHFQ). **Results:** We enrolled 30 patients from 55 to 90 years (mean 73.7, median 74, mode 61), males (66%), females (34%). The aetiology of diastolic heart disease was: hypertension (68%), post-ischemic (21%), post-myocardial inflammation (6%), post-ischemic associated with immunologic disease (5%). Mean LVEF at the beginning was 50.3% and after 6 months became 54.9%. The rate of mortality at 6 months was extremely low (5%) and the rate of hospitalization too (26%). Mean MLHFQ score at the beginning was 54.8 (30-76, range 46), after 6 months became 21.3 (5-70, range 65). Considering titration, beta blockers use increases from 67% to 88%, ACEi from 60% to 69%, AT1 from 47% to 80% and Diuretics from 90% to 98%. The rate of mortality at 6 months was extremely low (6%). With HTM patients in NYHA Class IV underwent: 48% in III, 37% in II-III, 5% in II and 5% remained stable in IV; patients in NYHA Class III became II (18%), II-III (18%) and 64% remained stable. We also observed after 1 ys a significant increase in home blood pressure control (MAP 150+30 mmHg vs 135+15.5 mmHg, p < 0.001).

**Conclusions:** The results of this study support the compliance and effectiveness of HTM for the management of diastolic HF in the early months after heart failure admission. In particular we obtained a successful optimization of the therapy according to Guidelines, a significant increase in LVEF, sensible decrease in III-IV NYHA patients, MLHFQ score and improvement in blood pressure control.

## P1986

**New possibilities of quadripolar left ventricular leads to optimise CRT**

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The maximal value of cardiac resynchronization therapy (CRT) is developed when left ventricular (LV) stimulation is provided from the LV latest activation area (LAA). A quadripolar LV lead offers multiple additional pacing vectors (PV) to optimize CRT. The purpose of this study was to evaluate whether pacing from the pole of the LV

lead closest to the LAA evaluated by device based algorithm (DBA) could enhance cardiac output.

**Methods:** Six patients with ischemic (33%) and dilated (67%) cardiomyopathy (4 males, 54 (53; 57.3) years; NYHA III; LV EF 30 (25; 31)%; LBBB with QRS duration 140 (119; 156) ms) with implanted CRT-D featuring multipolar LV stimulation were included in the study for retrospective data analysis. Patients were equipped with quadripolar coronary sinus leads, implanted into an antero-lateral (1 patient) and lateral coronary sinus branch (5 patients). LV pacing evaluations were performed in all patients at baseline (BL) and during follow-up (FU) at 6 (FU1) and 7 months (FU2) after implantation. Cardiac output enhancement was estimated by transthoracic echocardiography. At FU1 the pole of the LV lead closest to the LAA was determined by DBA. LV PV was chosen according to these data. AV and VV delay optimization was performed using automatic device based optimization algorithm. All patients received optimal drug therapy including beta-blockers, ACE inhibitors and diuretics. Non-parametric statistical methods were used, all the quantitative characteristics were described as Me (IQR 25%; 75%).

**Results:** One patient died due to heart failure decompensation. At FU1 we registered an increasing of LV EF (from 29 (25; 31)% to 33 (32; 38)%,  $p < 0.05$ ) and an ESV decreasing (from 195 (170; 230) ml to 183 (156; 209) ml,  $p = 0.04$ ). According to a study protocol we changed LV PV at 80% of patients. In 1 case DBA showed LV LAA to be closer to basal LV lead pole (Proximal), in other cases it was closer to apical poles (Tip 1 or Mid 2). At FU2 we recorded further cardiac output enhancement: LV EF 40 (33; 47)%, ESV 141 (125; 159) ml ( $p = 0.03$ ).

**Conclusions:** DBA can determine a pole of quadripolar LV lead which is closest to LV LAA. Changing a PV according to these data may be a novel way to optimize CRT and to enhance cardiac output.

#### P1987

##### Quality of life and long follow-up efficacy of biventricular pacing in heart failure patients

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Atrial fibrillation (AF) and congestive heart failure (HF) are highly prevalent diseases in modern society, with considerable morbidity and mortality.

**Aim:** To assess heart failure (HF) long-term dynamics on biventricular pacing (BP) in patients with AF.

**Methods:** Study involved 127 patients (pat) (59 females), middle age  $60.7 \pm 10.1$  years, all of them were on BP (CRT-D – 109 pat, 85/8%). Coronary artery disease had 51 pat (42/2%). Dilated cardiomyopathy had 76 (57.8%). NYHA HF stratification: III – 108 pat (85%); IV – 20 (15%). Sinus rhythm in 42 (33%) pat, drug resistant atrial fibrillation in 85 pat. EchoCG showed ventricular dyssynchrony in all pat. All patients were on optimal HF medication, pat with AF were anticoagulated. Pat with AF were performed AV-nodal ablation (63, 74/1%) or pulmonary vein isolation (22, 25/9%). QOL by SF-36 scores were assessed.

**Results:** After  $36 \pm 3.6$  months positive dynamics was shown in 93 (73.2%): NYHA HF class decreased at average  $1.4 \pm 0.6$ ; Ejection Fraction (EF) increased from  $25.7 \pm 6.4\%$  to  $33.5 \pm 5.2\%$ ; End diastolic volume (EDV) of left ventricle decreased on  $77 \pm 8.4, 43$  ml; lung circulation time decreased on  $8.7 \pm 3.6$  s; 6 minute walking test distance increased on  $45.5 \pm 18.6$  m. There also was improvement in quality of life (SF-36 questionnaire) in physical and mental functioning. Patients seemed to perform better in the physical functioning domain and possibly also in the general health domain. From the rest, 8 pat. died (total mortality 6.3%), 19 didn't show dynamics in NYHA HF class. Although, 6 of them showed an improvement in quality of life. For the follow-up period in 33 (26%) patients a ventricular tachycardia was registered, that wasn't revealed before implantation.

**Conclusion:** Biventricular pacing in patients with ventricular dyssynchrony on EchoCG decreases symptoms of HF, improves left ventricular function and quality of life in 73.2% of the pat. Responders had significantly better SF-36 scores than patients with advanced heart failure in terms "bodily pain," "general health perceptions" and "vitality."

#### P1988

##### The effects of CRT on arterial stiffness and ventricular-arterial coupling

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**Background:** cardiac resynchronization therapy (CRT) is indicated for patients with heart failure HF and left ventricular ejection fraction (LVEF)  $< 35\%$  in sinus rhythm and wide QRS. It can improve LVEF and reduce mortality. Arterial stiffness and ventricular-arterial coupling (VAC) are independent prognostic factors in HF patients. No studies to date have investigated the role of CRT regarding these parameters.

**Purpose:** we aimed at evaluating arterial stiffness and VAC before and early after CRT.

**Methods:** 23 patients scheduled for CRT were enrolled. Within 3 day before and at least 3 day after the procedure they underwent radial artery applanation tonometry to evaluate central blood pressures and augmentation index (Alx@75), and transthoracic echocardiography to calculate the aortic elastance (Ea), the end-systolic left ventricular elastance (Ees) and their ratio, namely VAC.

**Results:** mean age was  $73 \pm 11$  years. 16 (69.6%) were male. LVEF was  $32 \pm 17\%$ . Hemodynamic parameters are reported in Table 1. After CRT there was a great improvement in central pressure and Ea. On the other hand, no effects were seen on left Alx@75, Ees or VAC. These results are independent from LVEF.

**Conclusion:** CRT is associated to an early improvement in central pressure and Ea, without effects on VAC or peripheral arterial stiffness. This may be due to a regularization of blood flow through the ascending aorta. Considering the prognostic role of these factors in patients with HF, CRT is of growing importance under different points of view.

Table 1

Variable	Before CRT	After CRT	p
Aortic SBP (mmHg)	113 ± 14	106 ± 12	0.028
Aortic DBP (mmHg)	76 ± 11	72 ± 10	0.054
Aortic MAP (mmHg)	91 ± 10	85 ± 9	0.016
Aortic PP (mmHg)	37 ± 14	33 ± 11	0.147
Alx@75 (%)	24 ± 16	20 ± 13	0.353
Stroke volume (mL)	58 ± 17	67 ± 22	0.101
Ea (mmHg/mL)	2.1 ± 0.7	1.7 ± 0.5	0.020
Ees (mmHg/mL)	2.5 ± 1.0	2.1 ± 0.9	0.131
VAC	0.9 ± 0.4	0.9 ± 0.4	0.961

SBP=systolic blood pressure; DBP=diastolic blood pressure; MAP=mean arterial pressure; PP=pulse pressure; Alx@75 augmentation index corrected for 75 bpm; Ea=aortic elastance; Ees=end-systolic left ventricular elastance; VAC=ventricular-arterial coupling

#### P1989

##### The Burden of scar and fibrosis is the strongest predictor for the early to midterm need for ICD-therapies in patients with primary prophylactic CRT-D

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**Purpose:** Indications for primary prophylactic ICD-implantation as well as those for cardiac-resynchronisation-therapy (CRT) are generally based on severe LV-dysfunction. A high number of pts with CRT-D will never profit from ICD-therapy but experience complications. A parameter independent from LVEF to predict which patient with CRT will need adequate ICD-therapies is required.

**Methods:** We studied 74 pts who underwent CRT-D implantation and had complete follow up of device interrogations at our institution for 3 years. Pts with secondary prophylactic indication for ICD or upgrade from existing devices were excluded. Following characteristics were investigated: modified Selvester-ECG-score (MSES), which correlates with LV scar burden and fibrosis, every one point raise counts for 3% additional scar or fibrosis), "true" left bundle branch block (LBBB, defined by the method of the modified Selvester-ECG-score), LVEF, ischemic (ICM) vs dilatative cardiomyopathy (DCM), myocardial infarction prior to implant (MI), sinus rhythm (SR) vs. atrial fibrillation (AF), occurrence of ICD-therapy.

**Results:** 25/74 pts suffered an adequate ICD-therapy. Calculation of the relative risk for the characteristic subgroups revealed the following results (table 1). Only 1 pt with a MSES  $\leq 3$  and LBBB suffered an ICD-therapy.

**Conclusion:** The burden of scar and fibrosis, measured by the modified Selvester-ECG-score is a promising approach to predict the necessity of ICD-therapy in pts with indication for CRT. It is superior to other routinely assessed parameters. Pts with low MSES and true LBBB are under the lowest risk.

	relative risk	confidence interval	p
SR vs. AF	0.82	0.41 - 1.64	0.57
DCM vs. ICM	0.87	0.46 - 1.65	0.67
EF > 25% vs. < 25%	0.80	0.37 - 1.72	0.56
LBBB vs. no LBBB	0.54	0.29 - 0.99	0.05
MSES $\leq 3$ vs. $> 3$	0.21	0.07 - 0.65	< 0.01



BETA BLOCKERS

P1990

**Heart rate reduction or ventricular reverse remodeling associated with beta-blocker therapy is accompanied widespread, distinct changes in the beta1-adrenergic receptor gene signaling network**

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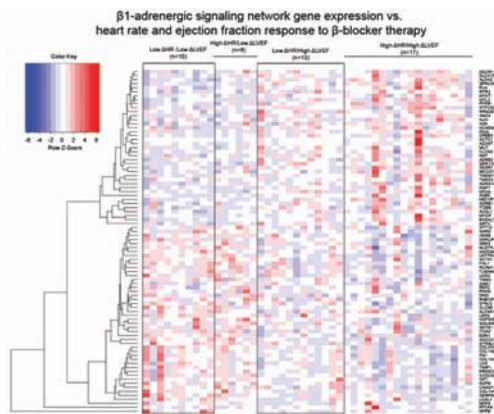
**Background:** Beta-blocker (BB) therapy of HF with reduced EF is lowers resting heart rate (HR). We hypothesize that changes in the beta-1-adrenergic receptor gene signaling network (B1GSN) are distinctly associated with HR lowering or reverse remodeling.

**Objective:** To describe HR response in reverse-remodeling and associated myocardial gene expression changes.

**Methods:** Forty-six nonischemic dilated cardiomyopathy patients were treated with BB for 12 months. Ventriculography and RV endomyocardial biopsies were performed at baseline, 3 and 12 months. LVEF response was defined as improvement of  $\geq 8$  EF units (EFU) at 12 months or  $\geq 5$  EFU at 3 months. mRNA expression was measured by microarray. Differences in gene expression change between LVEF Responders (Rs) and Nonresponders (NRs) were stratified by 3 month HR decrease above and below cohort median (18 bpm).

**Results:** In 30 (65%) Rs, EF increased by  $21 \pm 10$  vs.  $1 \pm 5$  EFU in NRs ( $p < 0.001$ ). At 3 months, HR decreased by  $18 \pm 21$  in Rs, vs.  $5 \pm 13$  bpm in 16 NRs ( $p < 0.001$ ). EF change correlated inversely with HR change at 3 months in all patients ( $r = -0.44$ ,  $p < 0.01$ ). There were 17 (37%) Rs with HR decrease  $> 18$  bpm vs. 10 (22%) NRs with HR decrease  $< 18$  bpm. Of 87 B1GSN genes, 46 (53%) were differentially expressed between these groups ( $p < 0.05$ ) with 65 (75%) trending toward significance ( $p < 0.10$ ). In comparison 1913/19586 (10%) non-B1GSN genes were differentially expressed ( $p < 0.05$ ) and 3395 (17%) trended toward significance ( $p < 0.01$ ). Favorable changes in B1GSN expression increased progressively from NR/HR decrease  $< 18$  bpm to NR/HR decrease  $> 18$  bpm to R/HR decrease  $< 18$  bpm to R/HR decrease  $> 18$  bpm (Figure).

**Conclusions:** The B1GSN remodeling subnetwork is strongly associated with HR reduction and LV reverse remodeling in response to beta-blockers.



B1-AR gene expression changes

P1991

**Effect of beta blockers on exercise capacity in patients with heart failure undergoing cardiac rehabilitation**

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**Background:**  $\beta$ -blockers ( $\beta$ B) are the mainstay of medical therapy in heart failure. Aim of this study was to compare the exercise training response of patients with chronic heart failure (CHF) receiving or not  $\beta$ B therapy at admission.

**Methods and Results:** Sixty-two consecutive patients with CHF were included in a 3-week training program. Patients underwent a cardiopulmonary exercise and a 6 minute walk test (6MWT) test before and after training. Oxygen uptake (VO<sub>2</sub>) at peak exercise and at VT increased in both groups with a

trend towards a greater improvement in those patients not receiving  $\beta$ B but receiving ivabradine for heart rate control. A greater VT improvement was detected in patients not receiving  $\beta$ B but with heart rate  $< 70$  bpm. A better improvement in exercise capacity was detected in those patients receiving  $< 50\%$  of  $\beta$ B target dose.

**Conclusions:**  $\beta$ B therapy may impair the improvement in functional capacity obtainable with a rehabilitation program in patients with CHF.

P1992

**Association of beta-blocker usage with mortality following myocardial infarction in patients with COPD: a propensity score analysis from the high-risk myocardial infarction database initiative**

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**Background/Introduction:** Concerns that beta-blocker treatment may be harmful in patients with chronic obstructive disease (COPD) still limits their usage in this subset of patients, even in post-myocardial infarction (MI), where they have been shown to be highly effective in reducing mortality.

**Purpose:** The aim of the study was to assess the association between baseline beta-blocker intake and long-term prognosis of MI survivors with heart failure (HF) or with left ventricular dysfunction and a history of COPD.

**Methods:** In the 28,771 patients high risk MI collaborative database, we identified 1573 patients with a baseline history of COPD. We evaluated the association between beta-blocker usage at baseline (822 with a beta-blocker and  $n = 751$  without) on the rate of all-cause death and cardiovascular death.

**Results:** By univariable Cox analysis, beta-blocker intake was associated with lower rates of both all-cause death (HR = 0.61, 0.51-0.75,  $p < 0.0001$ ) and cardiovascular death (HR = 0.63, 0.51-0.78,  $p < 0.0001$ ). After extensive adjustment for confounding including 24 baseline covariates, beta-blocker usage was associated with a lower risk in COPD patients (HR = 0.73, 0.60-0.90,  $p = 0.002$  for all-cause death; HR = 0.77, 0.61-0.97,  $p = 0.025$  for cardiovascular death) (Table). Propensity scores (PS), estimating probability of beta-blocker treatment on 24 baseline characteristics, were calculated; when entering these scores as covariate for adjustment in Cox models, the survival in the treatment group remained significantly higher. A cohort of 561 pairs of patients taking or not a beta-blocker was obtained by 1:1 nearest neighbor matching method. Among matched pairs of patients, treated group experienced less all-cause deaths (HR = 0.71, 0.56-0.89,  $p = 0.003$ ) and cardiovascular deaths (HR = 0.76, 0.59-0.97,  $p = 0.032$ ).

**Conclusions:** in the specific setting of a well-treated cohort of high-risk MI survivors, beta-blocker treatment was associated with better outcomes in patients with a history of COPD.

Cox proportional hazard models

	All-cause mortality HR (95%CI)	p-value	Cardiovascular death HR (95%CI)	p-value
Univariable analysis	0.61 (0.51-0.75)	< 0.0001	0.63 (0.51-0.78)	< 0.0001
Model 1	0.66 (0.54-0.80)	< 0.0001	0.68 (0.54-0.84)	< 0.0001
Model 2	0.72 (0.59-0.88)	0.001	0.75 (0.60-0.93)	0.010
Model 3	0.73 (0.60-0.90)	0.002	0.77 (0.61-0.97)	0.025

Model 1: age and gender and smoking habits. Model 2: model 1 + Killip class  $\geq 3$ , co-morbidities (MI, HF, hypertension, renal failure, AF, PAD, diabetes, history of stroke), and biological variables (systolic and diastolic BP, HR, eGFR). Model 3: model 2 + LVEF and treatment (digoxin, ACE-I/ARB, diuretics, aspirin, CCB, statin).

P1993

**The effect of beta-blocker therapy in HF patients with high comorbidity burden: interpreting data in community setting**

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**Background:** Older adults are often excluded from clinical trials. The benefit of HF-related treatments tested in younger trial populations may be diluted when applied to older adults with higher comorbidity burden in the clinical setting.

**Purpose:** To study whether the co-morbidity burden had an impact on the treatment effects of beta-blockers, we investigated the hazard ratios for outcome according to comorbidity burden in the community-based population.

**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. Overall population were divided into groups with different co-morbidity burden (1, 2,  $\geq 3$  of comorbidities) taking into account 15 non cardiac comorbidities.

**Results:** The study population comprised 2,321 HF patients (mean age 78  $\pm$  8, 57% men). Of these, 914 (41 %) patients with LVEF <50% were identified as HFREF; 1,380 (59%) patients as HFpEF. The high mean age and comorbidity rates (mean 3.2  $\pm$  2.5; 54% patients with  $\geq 3$  non cardiac comorbidities) were similarly between EF-HF phenotypes. 1198, 52% of overall population were treated with beta-blockers (536, 57% - HFREF; 662, 48% - HFpEF); 53% showed heart rate (HR) <70 bpm (73% in sinus rhythm). All cause mortality, HF hospitalization, non cardiovascular hospitalization significantly increased ( $p < 0.0001$ ) with comorbidity burden irrespective of beta-blocker therapy. According to increased comorbidities rate, there was a progressive significant reduction of the effect of beta-blocker treatment for all-cause mortality and morbidity outcomes. No significant impact of beta-blocker was achieved in HF patients with  $\geq 3$  comorbidities for overall mortality, and morbidity end point (HF hospitalization, overall hospitalizations). This trend was maintained unchanged after adjustment for EF-HF phenotypes.

**Conclusion:** In an elderly real-world HF population, the high comorbidity burden may diluted the benefit of beta-blocker, even though HFREF.

### P1994

#### Beta blockers up titration in patients with chronic heart failure and ICD/CRT-D: A single center study

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**Background:** Clinical trials have shown the unequivocal benefits of beta blockers (BBs) in patients with chronic heart failure with reduced ejection fraction (HFREF). These benefits include improved survival (30-35%) and a reduced need for hospitalization. Cardiac resynchronization therapy (CRT) has emerged as an important device-based therapy for symptomatic patients with HFREF despite optimal pharmacologic therapy. The extent to which BBs are being utilized in patients receiving implantable cardioverter defibrillator (ICD) and/or CRT is not well known.

**Aims:** In this study we evaluate the effect of BBs doses on clinical outcome in an unselected cohort of HFREF patients receiving ICD/CRT capable defibrillator system (CRT-D).

**Methods:** Adults who received their first ICD/CRT-D at our center between July 2008 and July 2015 were identified. Using hospital data, BBs use was determined at time of discharge, and during follow-up. A composite end point of cardiovascular mortality, CRT-D appropriate intervention (discharge or anti tachycardia pacing) and hospitalization for acute heart failure was recorded.

**Results:** The study cohort comprised 202 patients, 126 patients (62%) had an optimized BBs doses according to ESC guidelines (group A). 78 patients (38%) had a BBs doses higher than that recommended by European Society of Cardiology (ESC) guidelines (group B). The two groups were similar in terms of demographics characteristics, heart failure NYHA class, others pharmacologic HF therapy, and comorbidities. Comparing the two groups Group A have a better clinical outcome than group B (Table 1).

**Conclusion:** After ICD/CRT-D implantation, BBs therapy can be up-titrated, in a good percentage of patients, at higher doses than that recommended by international guidelines and this strategy confers advantages in terms of mortality and morbidity respect the use of standard doses.

Table 1

	Group A (n 126)	Group B (n 78)	P value
Overall cardiovascular events	95	20	< 0,001
Cardiovascular death	6	3	< 0,001
Acute heart failure related hospitalization	44	7	< 0,001
CRT-D appropriate intervention	45	10	< 0,001

Difference of cardiovascular events between the two study groups

## RENIN-ANGIOTENSIN-ALDOSTERONE ANTAGONISTS

### P1995

#### Improvement in central haemodynamic parameters by association of angiotensin II receptors blockers and canrenone therapy in obese hypertensive patients

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**Introduction:** Hypertension and obesity are strong risk factors for heart failure (HF). It is associated with activation of the renin-angiotensin-aldosterone system (RAAS). Obesity is an inflammatory disease increased plasma aldosterone levels through leptin. A large body of evidence links aldosterone, now consider a major cardiovascular risk hormone, to development and progression of arterial stiffness, left ventricular hypertrophy, left ventricular post-load, and HF. Thiazide diuretics can activate the neurohormonal system, impair glucose metabolism, increase new-onset diabetes, and are potentially harmful.

**Purpose:** Could be obese hypertensive patients both sexes with normal kidney function, benefit from the association of Angiotensin II Receptors Blockers (ARBs) and canrenone (Cr) therapy better than with ARBs associated to hydrochlorothiazide (Hct).

**Methods:** In a retrospective cross-sectional study, data were collected from 448 obese hypertensive patients, normal kidney function, both sexes (female 64%), aimed to compare the effect of two therapy groups: ARBs+Cr (female/male average age 60/56) and ARBs+Hct (female/male average age 64/57). Were measured in female (ARBs+Cr/ARBs+Hct) BMI (36.3/35.6), and WC (107.8/108.3), and in male (ARBs+Cr/ARBs+Hct) BMI (33.2/33.8), and WC (112.1/113.4). The averages dose used in both genders were Cr 37 mg and Hct 16 mg. Were measured central haemodynamics parameters by the SphygmoCor System, according system's standard methods. Also was measured the difference between the observed values and the expected values of Augmentation Index (Diff-Alx) according to normal levels by age.

**Results:** The averages of BMI and WC were similar in both therapy groups. Interestingly, were found better results from ARBs+Cr than ARBs+Hct therapy, both female/male with the following differences (mmHg): Central Aortic Pressure (17.7/14.8), End-Systolic Pressure (15.5/15.3), Mean Arterial Pressure (12.3/11), Pulse Pressure (11.1/6.1), Augmentation Pressure (5.9/3.2), and Diff-Alx (6%/6.4%), with a statistically significant difference. Partly, this fact, could be explained by the phenomenon named "escape of aldosterone" by Hct.

**Conclusions:** In obese hypertensive patients, has been obtained better haemodynamic results by use ARBs+canrenone therapy. This association could prevent or reduce in short- and long-time the harmful effect of the RAAS, the development of HF and its serious complications such as atrial fibrillation.

### P1996

#### Safety and benefits of the use of an uptitration protocol in patients with heart failure and reduced ejection fraction followed in an heart failure unit

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**Background:** Current guidelines recommend that patients with heart failure are enrolled in a multidisciplinary-care management programme to reduce the risk of heart failure hospitalization (level of recommendation IA). This will permit patients to reach dosages of Angiotensin converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB) and beta blockers (BB) achieved in the randomised controlled trials that have demonstrated their efficacy

**Purpose:** To assess the influence of achieving higher dosages of recommended pharmacological treatment of heart failure with reduced ejection fraction, in terms of quality of life and safety, using an established protocol of uptitration

**Methods:** Data from 103 consecutive patients (80 men, 77.7%) referred to the Heart Failure Unit of our hospital between June 2014 and August 2015 were analyzed. We used the Pearson correlation test to establish the relationship between doses of recommended pharmacological treatment and the incidence of worsening renal function (increase of serum creatinin) as well as with the quality of life, using the Minnesota Living with Heart Failure Questionnaire (MLHFQ)

**Results:** The etiology of the left ventricular dysfunction was ischaemic heart disease in 31.1% of patients, with a mean left ventricle ejection fraction of 30.8% (SD 8,7). An ACEI, ARB and BB were prescribed in 59.2, 34.9 and 96.1% of the cases, respectively. No relationship between dose of ACEI, ARB or BB and changes in serum creatinin was found. Only in two patients, an increase >50% regard the basal level was observed, and in only one was necessary to stop the ACEI. We found a correlation between dose of ACEI and lower score in the MLHFQ (meaning better quality of life) performed 6 months after uptitration

**Conclusions:** In our study, we have demonstrated that using an established protocol of uptitration of pharmacological treatment, designed by the physician and performed by specialized nurses, is safe and effective. In addition, reaching higher dosage of ACEI is related with a better quality of life in patients with heart failure and reduced ejection fraction

Table 1

	MLHFQ
BB Pearson Correlation Sig. (2-tailed) N	-0,108 0,405 99
ACEi Pearson Correlation Sig. (2-tailed) N	-0,336* 0,045 61
ARB Pearson Correlation Sig. (2-tailed) N	-0,212 0,343 36
Age Pearson Correlation Sig. (2-tailed) N	0,096 0,434 103

\*correlation is significant at the 0,05 level (2-tailed)

### P1997

#### Mineralocorticoid receptor antagonists: do we use them enough in very elderly patients with heart failure and severe left ventricular dysfunction?

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**Background and objectives:** Mineralocorticoid receptor antagonists (MRAs) significantly reduce the risk of morbidity and mortality among patients with heart failure (HF) and severe left ventricular dysfunction (SLVD). In this study, we aimed to measure the use of this group of drugs among the elderly population.

**Methods:** Between 2008 and 2013, all patients aged >75 years revealed to have ejection fraction <35% following imaging studies were recruited by the cardiac imaging laboratory that had performed the analyses. Clinical variables and echocardiography results were gathered, among other data. A prospective follow-up study was performed by consulting either the electronic medical history of patients or by telephone interview.

**Results:** A total of 802 patients were included in the study. Men comprised 66.2% of all the participants, and the mean age was  $82 \pm 4.9$  years. Mean ejection fraction (EF) was  $28 \pm 6.5\%$ . Ischemic etiology was found in 51.1% of the cases. Hypertension was observed in 79.2% of patients, while 31.3% were diabetic, and 35.7% presented chronic renal insufficiency (CRI). According to the New York Heart Association (NYHA) classification system, 55.4% of the patients were in Class II at the time of inclusion. The mean duration of follow-up was  $32.7 \pm 22.6\%$  months. The percentage of deaths was 47.5%, and 61.84% of patients developed a cardiac event (death or admission due to HF).

At the conclusion of follow-up, 45.1% of patients were undergoing treatment with MRAs. Of all patients not receiving MRA treatment, in 24.3% the cause was presence of CRI that contraindicated use of the drugs or because of worsening of existing CRI. Treatment was suspended in 4.9% of cases due to hyperpotassemia, and 35.7% did not receive MRAs due to absence of clinical indication (i.e. NYHA Class I status, normalization of EF). MRA administration was indicated in as many as 29% of patients who did not receive the treatment.

**Conclusions:** MRAs were shown to be underused in our population of very elderly patients with HF and SLVD. This finding is due in part to the presence of side effects and comorbidities, although no justified cause was found in a high percentage of patients. Strict adherence to the care guidelines may lead to improved prognosis in this population.

### P1998

#### Causes and impact on survival of omission of ACE-inhibitors and angiotensin II receptor blockers in heart failure.

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**Background:** Large epidemiological studies have demonstrated that a sizable portion of patients with newly diagnosed heart failure (HF) are prescribed neither angiotensin-converting enzyme inhibitors (ACEi) nor angiotensin II receptor blockers (ARB), mainly because of concomitant kidney dysfunction, and that this therapeutic choice results in higher mortality. It is likely that this holds even more true when ACEi/ARB are withheld for a long period of time. However, there are few data to confirm this assumption. Furthermore, other reasons may also lead to the omission of ACEi/ARB.

**Purpose:** We investigated the correlates and the effect on survival of never-use vs. use of ACEi/ARB in a cohort of chronic HF patients referred to a single tertiary outpatient clinic in Italy.

**Methods:** Among all first visits between Jan. 1st 2004 and May 31st 2015, those with a serum creatinine concentration (sCr) available and <3.5 mg/dL were retrospectively selected. Patients not on ACEi/ARB at the time of both the first and the last visit were considered as never treated with ACEi/ARB. Clinical, biochemical, and echocardiographic data were compared between ACEi/ARB recipients and not. A multivariate logistic regression model with backward selection was created to

identify independent correlates of ACEi/ARB therapy. The risk of all-cause mortality was assessed by multivariate Cox regression and Kaplan-Meier analysis.

**Results:** Of 711 eligible patients, 117 (17.4%) never received ACEi/ARB. Compared to subjects on ACEi/ARB, never-users were older and more often women, had lower systolic blood pressure (SBP) and higher sCr, had more frequently an history of anemia and tumor and less frequently of ischemic heart disease (IHD), and were less commonly on  $\beta$ -blocker (all  $p < 0.05$ ). In multivariate analysis, male gender (OR 0.41, 95%CI 0.26-0.66), SBP (0.98, 0.97-0.99), higher sCr (3.53, 2.26-5.52), a history of tumor (1.96, 1.07-3.58), the presence of IHD (0.62, 0.39-0.98) and  $\beta$ -blocker therapy (0.61, 0.37-0.99) were independently related to ACEi/ARB never-use. The same correlates were found when estimated glomerular filtration rate was substituted for sCr. At about 1-year follow-up, LVEF improved by  $\geq 10\%$  in 30% vs. 17% of subjects on ACEi/ARB or not ( $p = 0.005$ ), while sCr increased by more than 25% of baseline in 11% vs. 7%, respectively ( $p = 0.20$ ). Overall mortality was 37% over a 5-year period ( $58 \pm 30$  months), and never-use of ACEi/ARB was associated with an almost 2-fold increased risk of death [adjusted HR 1.82, 1.33-2.50]. Patients not taking ACEi/ARB were more likely to die over the course of our extended follow-up (Figure 1).

**Conclusions:** In our population, a history of tumor and increased sCr were independent causes of ACEi/ARB omission. While renal function worsened similarly in ACEi/ARB recipients vs. not, never-use of ACEi/ARB was associated with lower rate of LV remodeling and dramatically raised risk of mortality.

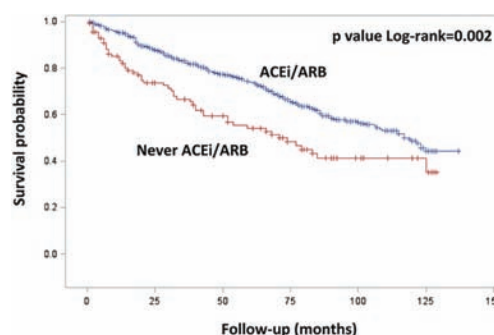


Figure 1

## METABOLISM / DIABETES MELLITUS / OBESITY

### P1999

#### Chronic heart failure induces changes in the serum blood profile of lipids containing choline - results of the validation study.

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**Introduction:** Heart failure (HF) is a common clinical syndrome which constitutes the final stage of a variety of the cardiovascular diseases.

**Aim:** The use of untargeted metabolomics to identify and validate changes in the blood metabolites profile, occurring as a result of heart failure development.

**Methods and Results:** We prospectively studied a group of optimally treated patients with stable chronic HF (n=69) and subjects without the disease (n=40). Both groups were divided into the derivation (36 HF patients:  $61.4 \pm 13.9$  yrs, 58% ischemic etiology-IE, ejection fraction-EF  $23.6 \pm 6.3\%$ , New York Heart Association Class - NYHA II/III 47/53% and 20 age-matched controls:  $60.5 \pm 12.8$  yrs, EF  $64.1 \pm 5.2\%$ ) and validation group (33 HF patients:  $63.9 \pm 10$  yrs, 55% IE, EF  $25.2 \pm 5\%$ , NYHA II/III 36/64% and 20 age-, gender- and concomitant disease-matched controls:  $65.5 \pm 7$  yrs, EF  $58.6 \pm 5\%$ ). All of the enrolled patients were assessed clinically (NYHA class), biochemically (natriuretic peptide - BNP, C reactive protein - CRP, estimated glomerular filtration rate - eGFR) and echocardiographically (left ventricle EF). Acute and chronic inflammatory diseases (rheumatoid arthritis, diabetes mellitus, asthma) were excluded. Additional fasting serum samples were collected and fingerprinted by liquid chromatography-mass spectrometry (LC-QTOF-MS). Final identification of significant features, which occurred in both a derivation and validation study, was performed based on MS/MS spectra. In the validation study we focused on statistically significant lipids containing choline. Considering the derivation and validation studies lower levels of phosphatidylcholine-PC 34:4 ( $-30 \pm 12\%$ ,  $p = .002$ ), lysophosphatidylcholine-LysoPC 15:0 sn1 ( $-26 \pm 10\%$ ,  $p = .005$ ), LysoPC 14:0 sn1 ( $-25 \pm 8\%$ ,  $p = .008$ ), LysoPC 15:0 sn2 ( $-22 \pm 6\%$ ,  $p = .008$ ), LysoPC 20:3 ( $-24 \pm 8\%$ ,  $p = .009$ ), and LysoPC 14:0 sn2 ( $-24 \pm 8\%$ ,  $p = .012$ ) were characteristic for heart failure patients. LysoPC 20:3 and LysoPC 14:0 sn2 were moderately correlated with total blood cholesterol level ( $r = .40$ ,  $r = .38$ ; respectively). The



positive correlation ( $r=.44$ ) between LysoPC 20:3 and low density lipoproteins (LDL) were also observed. There were no significant differences in the median intensity of each of the metabolites between patients treated with statins and those without the medication (for each metabolite, statin use vs no statin use  $p>.05$ ).

**Conclusions:** Serum metabolites profile of stable HF subjects differ from controls especially in terms of decreased levels of lysophosphatidylcholines, its isomers and PC 34:4. Changes in LysoPC 20:3 and 14:0 sn2 may be dependent on total cholesterol and LDL metabolism.

## P2000

### How do we treat diabetic patients with heart failure?

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**Purpose:** If we try to assess if the treatment is adequate for heart failure in diabetic patients, using as quality index the percentage of patients treated with ACE inhibitor-ARA II and beta blockers.

**Methods:** Observational prospective cohort study including a total of 1824 patients presenting to emergency departments in acute decompensated heart failure (acute decompensated heart failure and chronic heart failure). Sociodemographic features, cardiovascular risk factors, comorbidities, history of heart disease (ischemic cardiomyopathy, valvular, arrhythmia) and analytical and echocardiographic data were collected during emergency episode and hospital admission. We compared the 1824 at discharge treatment in diabetic and non-diabetic patients diagnosed with heart failure admitted to three hospitals of our Health Service between 2011 and 2013. 609 patients (33.39%) were diabetic and 1215 (66.61%) patients were not diabetic.

**Results:** 338 (27.82%) non-diabetic patients (PND) and 185 (30.43%) diabetic patients (PD) treated with an ACE inhibitor ( $p=0.24$ ). 272 (22.39%) PND and 173 (28.45%) PD treated with ARA II ( $p=0.004$ ). 437 (35.97%) and NDP 255 (41.94%) PD treated with beta-blockers ( $p=0.013$ ). 0.721 (59.34%) and NDP 410 (67.43%) PD treated with loop diuretics ( $p=0.0008$ ). 379 (31.19%) PND and 235 (38.65%) were treated with antiplatelet PD ( $p=0.001$ ). 418 (34.40%) and 349 PND (57.40%) PD treated with statins ( $p<0.001$ ). 259 (21.32%) PND and 175 (28.78%) were treated with calcium antagonists PD ( $p=0.0004$ ). There were no significant differences regarding treatment with digoxin, antiarrhythmics, ivabradine, aldosterone and anticoagulation among others. Associated cardiovascular risk factors: hypercholesterolemia in 65% vs 44% in PD PND ( $p<0.0001$ ), hypertension in 90% vs 80% PND PD ( $p<0.0001$ ) and obesity in PD 45.89% vs 32.97% in PND ( $p=0.0002$ ). Ischemic etiology of heart failure: 30% vs 21% in PD in PND with  $p<0.0001$

**Conclusions:** 1. There is not a minor use of ACEI-ARA II and beta blockers in diabetic patients compared to non-diabetics. On the contrary, there is a difference in favor to diabetics compared to non diabetics for treatment with ARBs and beta-blockers, with no significant differences in ACE.2. There are a greater number of diabetic patients treated with antihypertensives and statins because of the largest association of cardiovascular risk factors in diabetic patients.3. A greater number of diabetic patients treated with antiplatelets reflects the higher percentage of ischemic etiology of heart failure in these patients.

## P2001

### Determination of the metabolic syndrome risk factors in adults in turkey

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**Background:** Metabolic syndrome (MetS) is an important public health problem starting with insulin resistance and including systemic disorders such as abdominal obesity, glucose intolerance or diabetes mellitus, dyslipidemia, hypertension and coronary artery disease together. MetS continues to be an important cause of mortality and morbidity increasing day by day all around the world. In this growth, basic changes in the nutritional habits, increase in sedentary lifestyle and some hereditary features have a role.

**Purpose:** This study intended to determine the prevalence and risk factors of metabolic syndrome in adults in line with the diagnosis criteria determined by International Diabetes Foundation (IDF).

**Methods:** This study was conducted with a total of 201 persons who admitted to a family health center due to any health problem between June 2015 and August 2015. Fasting blood glucose, triglyceride, LDL-cholesterol and HDL-cholesterol measurements were obtained from the laboratory results of the patients. Weight, height, body mass index, waist circumference, blood pressure measurements, on the other hand, were obtained from the measurements made by the researchers. Number, percentage, average, frequency, standard deviation and chi-square were used in the statistical evaluation. Statistical significance was accepted as  $p<0.05$ .

**Results:** Age average of the individuals participating in the study was  $58.5\pm 2$ , 50.7% of which were male and 49.3% of which were female. Average of waist

circumference of the males was  $98.2\pm 2$ cm, average of HDL values was  $38.2\pm 8$  mg/dl; average of waist circumference of the females was  $91.7\pm 17.8$  cm and average of HDL values was  $43.4\pm 11$  mg/dl. Average of BMI of all the groups was  $26.3\pm 5$ , average of systolic blood pressure was  $126.65\pm 20.85$ , average of diastolic blood pressure was  $77.59\pm 16.1$ , average of triglyceride value was  $169.9\pm 66$  mg/dl, average of LDL values was  $126.12\pm 37$ , and average of fasting blood glucose was  $116.35\pm 50.57$ . MetS was present in 56.21% of the individuals according to IDF criteria. 63.68% of the individuals were under risk in terms of waist circumference, 67.66% and 58.7% of them were under risk in terms of HDL and triglyceride values, respectively. There was not any significant difference between the groups in terms of metabolic syndrome presence ( $p=.62$ ). 82.3% of the individuals with MetS were equal to and above 50 years of age. There was not any significant difference between sexes in terms of metabolic syndrome presence ( $p=.39$ ).

**Conclusion:** It was found that individuals participating in the study were under risk with regards to waist circumference, HDL values, triglyceride values and diabetes. The frequency of metabolic syndrome is high and increases with age.

## P2002

### The differences between two metabolic syndrome diagnostic criteria in predicting clinical severity and prognosis of acute myocardial infarction

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**Introduction:** Metabolic syndrome (MetS) is defined as a group of interrelated factors (hyperglycemia, abdominal obesity, atherogenic dyslipidemia, hypertension, prothrombotic and proinflammatory states), which significantly increases the risk of coronary artery disease and other forms of atherosclerotic cardiovascular diseases.

**Purpose:** To investigate the importance of two MetS diagnostic criteria (the revised National Cholesterol Education Program - Adult Treatment Panel III (NCEP-ATP III) and International Diabetes Federation (IDF)) in predicting clinical severity and prognosis of acute ST-elevation myocardial infarction (STEMI).

**Methods:** This prospective study included 250 acute STEMI patients treated with primary percutaneous coronary intervention. They were classified into two groups (with/without MetS) which were analyzed by baseline (medical history and demography), severity (clinical presentation, laboratory, echocardiography, coronary angiography and in-hospital complications) and prognostic parameters (major adverse cardiovascular events (MACE) and sick leave duration (SLD) during 12-month follow up).

**Results:** MetS (NCEP-ATP III) patients (54.4%) had longer hospitalization, higher rates of total in-hospital complications, higher number of significantly stenosed coronary arteries (CAs), wider stents, higher rate of significantly stenosed proximal/middle CAs segments, and longer SLD ( $p<0.05$ ). MetS (IDF) patients (58.8%) only had wider stents ( $p<0.05$ ). MetS (NCEP-ATP III) increased the risk of total in-hospital complications and  $>1$  significantly stenosed CAs ( $p<0.05$ ). Hyperglycemia increased the risk of heart failure and the number of significantly stenosed CAs as the risk of total MACE ( $p<0.05$ ).

**Conclusions:** MetS (NCEP-ATP III) has a role in predicting acute STEMI severity (total in-hospital complications, severity of coronary disease), while MetS (IDF) have no influence on it. They all have no influence on prognosis (MACE and SLD).

## P2003

### Galectin-3 and metabolic syndrome components in non-diabetic patients with heart failure with preserved left ventricular ejection fraction

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**Background:** Galectin-3 (Gal-3) is a marker of cardiac fibrosis and predicts incident heart failure. Recent studies suggested an important role for metabolic syndrome components in development and progression of heart failure with preserved left ventricular ejection fraction (HFpEF).

**Purpose:** To evaluate the association of circulating Gal-3 levels and metabolic syndrome components in non-diabetic patients with HFpEF.

**Methods:** Forty four non-diabetic patients (27 males and 17 females; mean age  $60.45\pm 9.8$  years) with HFpEF of ischemic genesis were examined. Patients with diabetes mellitus were excluded. The serum Gal-3, TNF-alpha, Nt-proBNP and insulin levels measured in serum by ELISA, according to manufacturer's instructions. Homeostasis Model Assessment (HOMA) index was calculated as a measure of IR at fasting state ( $IR=fasting\ glucose \times fasting\ insulin/22.5$ ). The echocardiographic parameters were measured with M- and B-mode and calculated following the American Guidelines of Echocardiography Society. Continuous variables are expressed as median (25th, 75th percentile). To distinguish the significance of the variation among the subjects for nonparametric data Spearman's correlation analysis and Mann-Whitney U test were used. The categorical variables were compared with a

$\chi^2$  test. All statistical tests were 2-tailed, and  $p < 0.05$  was considered statistically significant.

**Results:** Twenty two patients (50%) had Gal-3 serum levels above the median value of 3.13 ng/mL (interquartile range, 2.68 –3.60). In the high Gal-3 levels group all patients were overweight. Compared with a low Gal-3 levels group there was significantly higher TNFa and glucose levels in the high Gal-3 levels group ( $P = 0.001$ ,  $P = 0.05$ , respectively). Moreover, incidence of IR and co-occurrence cardiovascular risk factors in high Gal-3 levels group was significantly higher ( $P < 0.05$ ,  $c2 = 5.53$ ,  $P < 0.05$ ,  $c2 = 13.37$ , respectively) compared with those in low Gal-3 levels group. Gal-3 levels were associated with systolic blood pressure (SBP) ( $r = 0.371$ ,  $P = 0.05$ ), higher SBP values were found in patients with higher levels of Gal-3. Gal-3 was also associated with diastolic dysfunction - E/A ratio ( $r = -0.316$ ,  $P = 0.05$ ). There were neither a significant correlation between Gal-3 levels and left ventricular ejection fraction and NTproBNP levels.

**Conclusions:** It was found, that increasing Gal-3 serum levels associated with higher incidence of metabolic syndrome components in non-diabetic patients with HFpEF. This fact may to provide complementary information about mechanisms development and progression of HFpEF.

**P2004**

**Short- and long-term adverse outcomes associated with diabetes in patients with acute heart failure. Results from the esc-hfa long term heart failure.**

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**Background:** Diabetes mellitus and heart failure (HF) are two common diseases that often coexist. However, despite the high frequency of diabetes among patients with HF, there are few contemporary, comparative data on the short- and long-term survival outcomes from multi-national cohorts of patients with and without diabetes who have been admitted to hospital for acute HF, out of the context of randomized clinical trials. Additionally, the few studies that explored the impact of diabetes on short- and long-term adverse outcomes in patients hospitalized for acute HF have reported discrepant results.

**Purpose:** To evaluate the short- and long-term prognostic impact of diabetes and elevated blood glucose levels at hospital admission for an acute HF episode.

**Methods:** We studied a multinational cohort of 6,926 hospitalized patients with acute HF included in a Society of Cardiology and a Heart Failure Association Long-Term HF Registry, of whom 49.4% ( $n = 3,422$ ) had known or newly diagnosed diabetes. Two multivariable regression models were applied to estimate the risk associated with diabetes status in terms of in-hospital mortality (by logistic regression analysis), 1-year all-cause or cardiac mortality and 1-year re-hospitalization for HF (by Cox regression analysis).

**Results:** Compared with those without diabetes, patients with diabetes had higher cumulative rates of short- and long-term adverse outcomes that occurred independently of multiple clinical risk factors: in-hospital mortality (6.8 vs. 4.4%; adjusted HR - 1.79; 95% CI 1.31-2.44,  $p < 0.001$ ), 1-year all-cause mortality (27.5 vs. 24.0%; adjusted-HR 1.179; 95% CI 1.03-1.32,  $p = 0.014$ ) and 1-year re-hospitalizations for HF (23.2 vs. 18.5%; adjusted-hazard ratio 1.33; 95% CI 1.15-1.53,  $p < 0.001$ ). Elevated blood glucose concentrations at hospital admission were powerfully prognostic for in-hospital mortality, but not for 1-year mortality or re-hospitalization rates, both in patients with and in those without diabetes.

**Conclusion:** Among patients hospitalized for acute HF, presence of diabetes is independently associated with an increased risk of short- and long-term mortality and re-hospitalizations for HF, underscoring the need for investigating a more individualized management of diabetes in this patient population.

**P2005**

**The exercise has beneficial effects on circulating endotoxin levels in obese women.**

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**Introduction:** Obesity is worldwide pandemic and associated with high cardiovascular risk. Metabolic endotoxemia (ME) is thought to be involved in these associations as underlying molecular mechanism. ME triggers toll-like receptor 4-mediated inflammatory adipokines and leads to a chronic low grade inflammatory status,

which results in CV risk increase and target organ damage. Exercise is the best nonpharmacological treatment to improve prognosis for obesity.

**Purpose:** In this study, we examined the circulating endotoxin levels in Korean obese women and investigated effects of exercise on them.

**Methods:** Women ( $n = 20$ ) who met obesity criteria of BMI 25 kg/m<sup>2</sup> or greater were included and participated in a resistance training exercise (with an intensity of 60-80% of their maximum heart rate, a frequency at least three days per week and duration of 30 minutes) for 12-weeks. After 0 (baseline) and 12 weeks, tests including anthropometric measurements, fasting blood samples and postprandial blood samples were conducted in all participants.

**Results:** In Korean obese women ( $n = 20$ ,  $27.9 \pm 0.5$  kg/m<sup>2</sup>), the fasting circulating endotoxin was  $1.45 \pm 0.11$  EU/mL. Ingestion of a high calorie meal led to a peak level at 2 hour in endotoxin ( $1.78 \pm 0.15$  EU/mL for 2 hour;  $1.75 \pm 0.14$  EU/mL for 4 hour,  $p < 0.05$  vs. for 0 hour). After 12 week exercise, BMI and Hip circumference were reduced significantly. The total cholesterol at fasting, postprandial 2 and 4 hour was decreased significantly. Although the circulating endotoxin levels showed reduction at fasting state, they were not significant. The serum glucose and endotoxin levels at postprandial 2 hour were significantly declined in similar pattern ( $117.7 \pm 6.4$  at 0 week vs.  $100.7 \pm 5.1$  mg/dL for glucose;  $1.78 \pm 0.15$  at 0 week vs.  $1.48 \pm 0.06$  EU/mL at 12 week for endotoxin,  $p < 0.05$ ).

**Conclusions:** In conclusion, our data reports the circulating endotoxin levels in Korean obese women for the first time. Also, we suggest that exercise exerts beneficial effects on the endotoxin and it has an impact on the better prognosis in obese women who follow regular exercise.

(n = 20)	0 week	12 weeks	p value	
Glucose (mg/dL)	0 hour	85.9 ± 9.1	88.0 ± 2.0	0.076
	2 hour	117.7 ± 6.4**	100.7 ± 5.1**	0.011
	4 hour	86.0 ± 3.0	81.9 ± 3.3	0.455
Endotoxin (EU/mL)	0 hour	1.45 ± 0.11	1.27 ± 0.08	0.098
	2 hour	1.78 ± 0.15*	1.48 ± 0.06	0.045
	4 hour	1.75 ± 0.14*	1.43 ± 0.06*	0.055

**P2006**

**Features of the diabetic population with acute heart failure in our reference area**

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**Introduction:** This study aims to determine the differential characteristics of patients with Diabetes Mellitus (DM) and acute heart failure admitted to the Emergency Services 3 hospitals in the Osakidetza network between 2011 and 2013.

**Methods:** Observational prospective cohort study including 1824 patients presenting to the emergency room of our hospital for acute decompensated heart failure. Outcome variables were considered short-term mortality and readmissions during 3 months.

**Results:** The sample included 1824 patients, of whom 609 are diabetics (33.39%). 47% were male and 51% female. The diabetic population was younger at the time of diagnosis :77.68 vs 80.58 years ( $p < 0.0001$ ) and presented more cardiovascular risk factors: hypercholesterolemia 65% vs 44% ( $p < 0.0001$ ), hypertension 90 % vs 80% ( $p < 0.0001$ ) and obesity 45.89% vs 32.97% ( $p = 0.0002$ ). In addition, diabetic patients more frequently have coronary artery disease as etiologic diagnoses (30% vs 21 %  $p < 0.0001$ ) and higher comorbidity with the Charlson index significantly higher (3 vs. 2 vs.  $p < 0.0001$ ) with a higher degree of chronic kidney disease (7.55% vs. 5.1%  $p = 0.036$ ), anemia (27% vs. 19.84%  $p = 0.0002$ ) and COPD (27.09% vs. 22.8%,  $p = 0.0435$ ). Despite these data in our study we found no significant differences in short-term mortality (5.09% vs 4.44% with  $p 0.5371$ ), mortality at 3 months (11.66 vs 12.67%  $p 0.5336$ ) and readmissions (22.9% vs. 21.07% with  $p 0.3486$ ) compared to patients without diabetes.

**Conclusions:** Diabetic patients in our study had significantly more cardiovascular risk factors and greater comorbidity than non-diabetic patients. However, no significant differences were found in short-term mortality or readmissions in 3 months. However, we cannot say that the risk of poor outcome is higher in a longer time frame. It would require a longitudinal study to establish the risk of adverse outcomes in those patients for a longer period of time.

patients with DM and HF			
	non DM	DM	p
Average age	77,68	80,58	p<0,00001
Dyslipemia	65 %	44%	p<0,00001
Hypertension	90%	80%	p<0,00001
Obesity	45%	38%	p=0,0002
Coronary disease	30%	21%	p<0,00001
Charlson index	3	2	p<0,00001

characteristics of patients with Diabetes Mellitus (DM) and acute heart failure

## HEART FAILURE IMAGING

### P2007

#### Right ventricular outflow tract m-mode echocg in congestive heart failure

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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) M-mode EchCG fractional shortening (FS%) in patients with congestive heart failure (HF).

**Material and Methods:** We studied 230 healthy volunteers and 110 patients with HF. RVout M-mode EchCG was registered from parasternal short axis view. It was measured RV outflow diastolic (RVd) and systolic (RVs) diameters. RVout FS% was calculated by formula  $(RVd-RVs)/RVd$ %.

**Results:** The RVd and RVs was significantly greater ( $30.4 \pm 4.9$ mm versus  $33.6 \pm 5.4$ mm and  $13.2 \pm 5.4$ mm versus  $21.0 \pm 5.3$ mm respectively,  $p < 0.001$ ) and RV FS% was significantly lower ( $57.2 \pm 5.4$ % versus  $37.6 \pm 10.4$ %,  $p < 0.001$ ) in patients with heart failure compared to normal persons. If we take for RV FS% <50% as reference point the sensitivity and specificity of this parameter in diagnosis of heart failure is 0.88 and 0.95 respectively.

**Conclusion:** In patients with HF the RV outflow tract systolic and diastolic diameters and FS% was significantly different compared to normal persons.

### P2008

#### Right ventricular outflow tract tissue doppler parameters in congestive heart failure

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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 outflow tract of RV (RVout) was actively studied by different EchoCG methods in normal and pathologic state, but there is little information about RV outflow tract.

**Aim:** To investigate RV outflow tract (RVout) pulsed wave TDI qualitative and quantitative parameters in patients with congestive heart failure (HF).

**Material and Methods:** We studied 140 healthy volunteers and 75 patients with HF. RVout pulsed wave TDI was registered from subcostal position with sample volume on RV lateral wall, near the pulmonary valve. RV in TDI was registered in apical 4 chamber view with the sample volume positioned at lateral wall near the pulmonary valve.

**Results:** The pattern of TDI from RVout was quite different from pattern of TDI of RV free wall. 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 RVout were significantly greater in normal persons than corresponding waves on RVout TDI in patients with HF. The Sict ( $4.2 \pm 1.6$  versus  $6.5 \pm 1.9$  cm/sec), S ( $7.7 \pm 2.0$  versus  $9.2 \pm 2.3$  cm/sec), Eict1 ( $-4.0 \pm 1.7$  versus  $-6.1 \pm 2.1$  cm/sec) and E ( $5.1 \pm 1.8$  versus  $7.4 \pm 1.8$  cm/sec) on TDI from RVout were 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 were significantly lower compared to the normal persons.

### P2009

#### 2D speckle tracking of the left ventricle for early detection of myocardial involvement in patients with systemic sclerosis

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**Aims:** Systemic sclerosis (SSc) is a connective tissue disease characterized by vascular inflammation and fibrosis. Visceral involvement particularly myocardial involvement is associated with poor prognosis. Two-dimensional speckle-tracking echocardiography is a useful sensitive tool to detect left ventricular systolic dysfunction that, so far, has not been diagnosed in SSc patients. The aim of this study was to evaluate deformation analyses derived from 2D speckle-tracking echocardiography for early detection of left ventricular dysfunction in patients with SSc.

**Methods and results:** 25 patients with SSc ( $53.64 \pm 13$  years, LVEF (Left ventricular ejection fraction)  $64.58 \pm 8.87$  %) and 25 gender and age matched healthy subjects ( $35.8 \pm 8.72$  years, LVEF  $68.2 \pm 7.41$ %) underwent echocardiography with STE to assess global and regional left ventricular function. Despite a preserved and comparable LVEF, the global longitudinal strain of the left ventricle was significantly lower in the SSc group compared with controls:  $-17.42 \pm 1.62$  vs.  $-19.24 \pm 8.85$  ( $P < 0.0001$ ). This was mainly driven by a reduced strain in the medial and apical segments.

**Conclusion:** ventricular deformation analysis by 2D speckle-tracking echocardiography is a sensitive method to detect early left ventricular dysfunction in patients with SSc.

### P2010

#### Left ventricular diastolic function: the effect of exercise training in young athletes

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**Introduction:** Regular training induces structural myocardial adaptation, so-called "athlete's heart". The aim of this study was to assess the impact of regular sport activity in left ventricular (LV) diastolic function in young athletes.

**Patients and methods:** Thirty-three young athletes (football players) regularly trained at least three times a week for at least 9 months a year and 20 young controls were evaluated by 2D echocardiography (echo). The diastolic LV function was evaluated by 2D conventional echo parameters and Doppler method.

**Results:** All the found values were within the normal range. The LV End Diastolic Diameter (LVED  $37.24 \pm 2.08$  mm/m<sup>2</sup>) and the LV Mass index (LVMI:  $97.93 \pm 15.58$  g/m<sup>2</sup>) were significantly higher in young athletes as compared with controls. There was no significant difference regarding the LV systolic function assessed by conventional echo parameters in the 2 study groups. Comparison of the standard transmitral Doppler parameters yielded similar E-wave and E-wave deceleration time for the 2 study groups. The A-wave was significantly lower in the athletes group ( $p < 0.001$ ) and the E/A ratio was significantly higher in athletes ( $E/A = 2.10 \pm 0.49$  versus  $1.64 \pm 0.26$ ,  $p < 0.001$ ). Comparison of TDI parameters measured from the lateral mitral annulus also demonstrated similar S' and E' rates for all 2 groups ( $p = 0.377$  and  $p = 0.177$ , respectively). But there was no difference in the filling pressure in the 2 groups.

**Conclusion:** Conventional functional echocardiographic parameters could distinguish some adaptations in the athlete's heart and showed a different pattern of LV diastolic function in young footballers versus controls.

### P2011

#### Carotid intima-media thickness and arterial stiffness are the best determinants of left atrial reservoir function

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Left atrium (LA) dysfunction is associated with atrial fibrillation and heart failure (HF). However, LA function is often neglected, as well as the potential role of medication for improving atrial function and subsequently lower HF incidence by targeting the arteries.

**Aim:** To test the hypothesis that LA reservoir function is related to the arterial function.

**Methods:** We studied 120 subjects ( $44 \pm 27$  years, 63 males): 20 athletes, 20 normals, 20 patients with risk factors, 20 with growth hormone deficiency, 20 with multiple sclerosis, and 20 with dilated cardiomyopathy, with an ejection fraction (EF) from 12 to 76%. LA reservoir function was assessed from total LA strain (TLAS) and LA expansion index (LAEI), LA conduit function from positive global LA strain (pGLAS) and passive LA emptying fraction (PLAEF), while LA pump function from LA active emptying fraction; LV global systolic function from EF; longitudinal



systolic function from mitral annular systolic velocity (Sa) and MAPSE; LV diastolic function from mitral annular diastolic velocity (Ea). Arterial function was assessed from intima-media thickness (IMT) and stiffness parameters (elastic module - Ep and local wave speed - LWS); endothelial function from flow mediated dilation (FMD).

**Results:** All parameters of LA reservoir function correlated with both LV systolic and diastolic functions, FMD, and arterial stiffness (table), whereas LA conduit and pump functions correlated only for some of the parameters. By stepwise multivariate analysis, the best determinants of the LA reservoir function were Ea ( $\beta = 0.40$ ) and IMT ( $\beta = -0.37$ ) (both  $p < 0.01$ ).

**Conclusions:** LA reservoir function is related to the LV longitudinal function, arterial stiffness, and endothelial function. This emphasizes the arterial-ventricular-atrial interaction, and role of medication in targeting both the heart and arteries, in an attempt to improve arterial and atrial function and prevent progression to HF.

Correlations				
	TLAS	LAEI	pGLAS	PLAEF
LVEF	0.52	0.45	0.46	0.43
MAPSE	0.61	0.55	0.61	0.51
Sa	0.67	0.46	0.71	0.57
Ea	0.63	0.53	0.51	0.61
IMT	-0.63	-0.38	-0.62	-0.42
Ep	-0.45	-0.31	-0.44	NS
LWS	-0.56	-0.25	-0.56	NS
FMD	0.43	0.25	0.43	0.36

$p < 0.01$  for all correlations, except NS = non-significant

**P2012**

**The value of tissue doppler imaging in left ventricular diastolic function assessment**

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**Background:** Diastolic dysfunction is common in cardiac disease and contributes to the signs and symptoms of heart failure. Noninvasive assessment of diastolic filling by Doppler echocardiography provides important information about left ventricular (LV) status only in selected subset of patients.

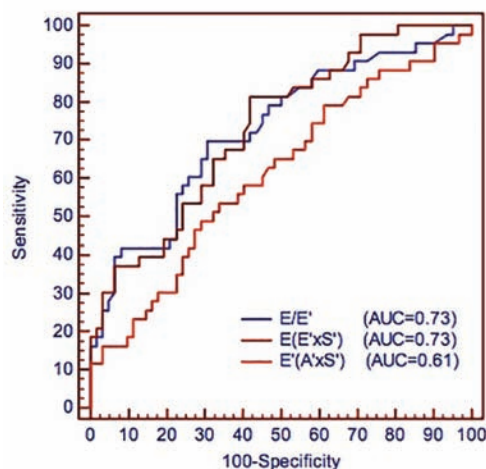
The purpose of this study was to evaluate the reliability of different tissue Doppler imaging indexes in prediction of high LV filling pressures.

**Methods:** 105 patients underwent echocardiographic examination prior to cardiac catheterization. They were divided in two groups according to left ventricular end-diastolic pressure (LVEDP) and left ventricular ejection fraction (LVEF). LVEDP was obtained before coronary angiography and ventriculography. An elevated LV filling pressure was defined as LVEDP  $\geq 16$  mmHg. 42 patients had elevated LV filling pressures. Doppler signals from the mitral inflow and TDI of the mitral annulus were obtained.

**Results:** The parameters of transmitral flow correlated with LVEDP only when EF was reduced. In the subgroup of patients with normal EF, only E/E' ratio correlated with LVEDP. The ratio of E/E' showed a better correlation with LVEDP for all levels of systolic function. For predicting high LVEDP an E/E' ratio  $> 7.7$  provided a sensitivity and specificity of 70%, E/(E'xS')  $> 75$  provided a sensitivity of 81% and a specificity of 58%, E'/A'xS'  $> 10.4$  provided a sensitivity of 49% and a specificity of 71%.

**Conclusion:** The E/E' ratio is the best predictor of LV filling pressure for all levels of systolic function, but it can't be used in isolation for the assessment of left ventricular diastolic dysfunction.

Correlation of TDI variables with LVEDP			
Variable		EF <50%	EF $\geq 50\%$
E	0.40	0.54	0.25
A	-0.32	-0.54	-0.05
E/A	0.50	0.66	0.2
DTE	-0.37	-0.27	-0.31
E' mean	-0.22	-0.06	-0.07
A' mean	-0.30	-0.37	0.04
E/E' mean	0.46	0.42	0.41
E/(E'xS')	0.45	0.40	0.14
E'/A' mean	0.04	0.28	-0.02
E'/(A'xS')	0.37	0.44	0.06



ROC curve for prediction of LVEDP > 16mmHg

**P2013**

**Cardiac magnetic resonance late gadolinium enhancement in patients with genetic dilated cardiomyopathy**

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**Introduction:** Dilated cardiomyopathy (DCM) has an estimated prevalence of 1:2500 in adult population, with genetic etiology explaining 30-50% of "idiopathic" cases. Genetic causality is difficult to identify because of the scarcity of distinctive red flags. In recent years, cardiac magnetic resonance (CMR) has emerged as a valuable imaging modality in this field. However, it's utility in diagnosing genetic DCM remains largely unknown.

**Purpose:** In this work we aimed to describe CMR findings in genetically characterized DCM patients.

**Methods:** We included patients with idiopathic and familial DCM, that underwent a comprehensive CMR with a 3-T scanner (Siemens, Erlangen, Germany), as part of their diagnostic work-up. Left ventricular (LV) volumes, ejection fraction (LVEF) and mass were measured using dedicated software (ARGUS Software™, Siemens Healthcare Global). LV late gadolinium enhancement (LGE) presence, pattern and location were assessed; extensive fibrosis was defined as LGE presence in  $\geq 3$  LV segments. Molecular analysis included the search of mutations in LMNA/C, MYH7, MYBPC3, TNNT2, ACTC1, TPM1, CSRP3, TCAP, SGCD, PLN, MYL2, MYL3, TNNT3, TAZ and LBD3 genes. Pathogenicity was assessed by comparisons with mutations previously described, functional tests and segregations studies.

**Results:** We analyzed 73 patients, 46.6% with familial DCM, 52.8% men. Mean LVEF was  $34 \pm 11\%$  and LV end-diastolic volume of  $128 \pm 34$  mL. We identified 18 genetic variants in 17 distinct patients. Eleven patients presented variants with pathogenicity criteria. Comparing patients with or without genetic variants, we observed no difference in CMR parameters. Focusing on patients with mutations in MYBPC3, TNNT2 and MYH7 genes, we found only a trend toward an association of MYH7 mutations with LGE ( $p = 0.057$ ) – with a significant predilection for septum involvement ( $p = 0.042$ ), and with the presence of non-compaction ( $p = 0.057$ ). There was no relationship between the remaining CMR variables.

**Conclusion:** LGE might have some utility in the clinical recognition of patients with genetic DCM, namely those with MYH7 mutations, although additional studies are warranted to confirm these findings. Nevertheless, the exclusion of other causes of LV dysfunction and the use of more recent CMR tools, as interstitial fibrosis assessment, support the continued exploration of this technique in the evaluation of genetic/familial DCM patients.

**P2014**

**Acute coronary syndrome with normal coronary angiography: a gender issue?**

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**Introduction:** Acute coronary syndrome (ACS) with normal coronary angiography (CA) is a challenging medical condition with an uncertain prognosis. It has been reported that women are the most affected.

**Purpose:** The aim of this study was to compare women and men with ACS with normal/near-normal (stenosis <50%) CA (NCA) and describe the clinical profile, final diagnosis and outcome in these two groups.

**Methods:** This study was based on a retrospective analysis of 108 consecutive patients (pts) admitted in a tertiary centre from January 2007 to December 2014 with ACS suspected and NCA. All pts did a cardiac magnetic resonance (CMR) for additional evaluation. The pts were divided by gender.

**Results:** In our cohort, 56 (51.9 %) pts were female. The women were older than men (59.9 ± 14.5 years vs. 44.0 ± 15.4,  $p < 0.001$ ). Within cardiovascular risk factors, hypertension was more often in women (60.7% vs. 30.8%,  $p = 0.002$ ), while smoking was more common in men (28.8% vs. 10.7%,  $p = 0.017$ ). The presence of recent emotional stress was more often in women (30.4% vs. 5.8%,  $p = 0.001$ ) and prior infectious symptoms were more common in men (40.4% vs. 7.1%,  $p < 0.001$ ). The changes in initial EKG were similar in both groups. Mean value of maximal I troponin was greater in women, but without significance. The echocardiography showed moderate to severe left ventricular dysfunction in 33 patients, with no significantly difference according to sex. The findings in CA were no different as well. Myocardial edema and late enhancement in CMR was more common in men (48.1% vs. 23.2%  $p = 0.007$ ; 80.8% vs. 48.2%,  $p < 0.001$ ). Concerning to final diagnosis, ACS and Tako-Tsubo cardiomyopathy were more frequent in women (44.6% vs. 15.04%,  $p = 0.001$  and 32.1% vs. 3.8%,  $p < 0.001$ , respectively). Acute myocarditis was more often in men (3.5 vs. 32.1%). During follow-up of 3.0 ± 2.0 years, readmission and all-causes mortality were rare, without differences between both genders.

**Conclusions:** Surprisingly, the number of female and male pts with ACS suspected and NCA did not differ significantly. While women were more hypertensive and had more often emotional stress factor, men were more smokers and had more frequently infectious symptoms. In work-up diagnosis, the most difference observed between both sexes was in CMR results, focusing the importance of this exam in etiologic diagnosis. ACS and Tako-Tsubo syndrome was the leading final diagnosis in women, while acute myocarditis was the main diagnosis in men.

## P2015

### Assessment of the left ventricle during heart failure : cardiac magnetic resonance or echocardiography ?

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**Introduction:** Echocardiography is commonly used to assess heart failure. This technique is facing many challenges that can be solved by the magnetic resonance imaging. However, this exam remains understudied in our country. Our objectives were to study the correlation between echocardiography and cardiac magnetic resonance imaging in evaluation of the left ventricle during heart failure.

**Results:** Thirty patients were collected consecutively. The mean age of our patients was 50 ± 16 years with a sex-ratio of 14. Ischemic cardiomyopathy was found in 50 % of cases. An atrial fibrillation was observed in 27% of patients. The mean follow-up was 11.53 months. The overall mortality rate was 17%. There was a good correlation between echocardiography and magnetic resonance imaging measurements of the diameters of the left ventricle with  $r = 0.84$  and  $p < 0.0001$ . The correlation between the end-systolic and the end-diastolic volumes of the left ventricle was good with respectively  $r = 0.66$  ( $p < 0.0001$ ) and  $r = 0.73$  ( $p < 0.0001$ ). There was also good agreement between the 2 exams for measuring the ejection fraction of the left ventricle with  $r = 0.73$  and  $p < 0.0001$ . The correlation between echocardiography and magnetic resonance imaging was good for the diagnosis of left ventricular hypertrophy with  $r = 0.67$  and  $p < 0.0001$ . However, magnetic resonance imaging had a sensitivity of 70 % and a specificity of 100 % in comparison to echocardiography. Three left ventricular thrombi had not been detected by echocardiography. Myocardial fibrosis was observed in 73 % of cases. There was no correlation between fibrosis and the symptoms, diastolic function or mortality.

**Conclusion:** In our national context, magnetic resonance imaging allows reliable measurements of diameters, volumes and ejection fraction of the left ventricle with excellent correlation with echocardiography evaluation. This exam was showed to be the gold standard imaging technique for the detection of myocardial necrosis. The main limitation of magnetic resonance imaging remains its availability and cost.

## P2016

### Comparative study of coronary computed tomography versus coronary intravascular ultrasound and virtual histology for the diagnosis of cardiac allograft vasculopathy after heart transplantation

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**Background:** Cardiac allograft vasculopathy (CAV) is currently one of the leading causes late graft-related death after heart transplantation (HT). CAV is characterized by diffuse and progressive coronary arteriopathy with concentric intimal hiperplasia. The exact pathophysiology of CAV remains poorly understood as the diagnosis is complex mainly at initial stages of the disease, when it is also usual lack of symptoms. Coronary angiography supported by intravascular ultrasound (IVUS) is widely used as the "gold standard" for routine surveillance to identify signs of CAV. Moreover, analysis of spectrum of the radiofrequency data obtained by IVUS has recently allowed the development of virtual histology techniques (IVUS-VH), bringing added value to the IVUS. Coronary computed tomography (cCT) has joined the diagnosis of ischemic heart disease by direct visualization of the coronary vessel wall and lumen, and identifying the presence of atherosclerosis and the stenosis degree.

**Methods:** 45 heart transplanted patients were prospectively included with a within-subject design in order to compare both tests (VH-IVUS vs cCT) and determine the diagnostic performance of cCT. 51% were male, ages 55 ± 9.6 years (range 32-70 years). Presence of CAV was defined as International Society for Heart and Lung Transplantation (ISHLT) score of ≥1. Sensitivity and specificity found for the diagnosis of presence or absence of disease were 100%. When patients were adequately classified according to Stanford scale of CAV severity, sensitivity was 85.7%, specificity of 100%, positive predictive value of 100% and negative predictive value of 97.4%. The area under the ROC curve was 0.83

**Conclusions:** cCT have a high sensitivity, specificity and negative predictive value, which may support its inclusion in CAV screening protocols. cCT has also proven to be cost-effective, with direct costs attributable more than 10 times lower than the cost of IVUS, and has shown to be safe in patients undergoing HT.

## BIOMARKERS

## P2017

### The association of galectin-3 and clinical parameters in patients with chronic heart failure

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**Background:** Galectin-3 is a novel biomarker of fibrosis and cardiac remodeling that represents an intriguing link between inflammation and fibrosis.

**Aim of the study:** to assess the association of circulating galectin-3 levels with other clinical parameters and functional performance indicators of patients with chronic HF NYHA II-III.

**Methods:** 53 patients with HF NYHA II-III were enrolled into single-centre prospective cohort study. Patients underwent echocardiographic evaluation of cardiac structure as well as systolic and diastolic function. Estimated glomerular filtration rate (eGFR) was calculated using the standard 4-variable Modification of Diet in Renal Disease equation (MDRD). Plasma levels of galectin-3 and NT-proBNP were assessed at baseline. Galectin-3 levels were assessed on baseline samples, using enzyme-linked immunosorbent assay. The relationship between galectin-3 levels and other baseline variables of interest was analyzed using Pearson (Spearman for non-parametric data) correlation analysis. A  $p < 0.05$  was regarded as statistically significant.

**Results:** Galectin-3 levels were associated with higher NYHA class (Table 1) and correlated to other risk factors such as, higher creatinine ( $r = 0.26$ ,  $p = 0.04$ ), higher NT-proBNP ( $r = 0.30$ ,  $p = 0.02$ ) and lower EF ( $r = -0.26$ ,  $p = 0.04$ ). Association was found between galectin-3 levels and scale of evaluation of clinical state in CHF (as modified Mareev VY 2000) ( $p = 0.025$ ). Other variables, including age, sex, age, heart failure etiology, left ventricular myocardium mass, 6-min walk test were not significant independent predictors of galectin-3 levels.

**Conclusion:** in a small cohort of patients with systolic heart failure galectin-3 levels were associated with known markers of disease severity. Thus galectin-3 testing may provide prognostic information complementary to other established HF biomarkers, such as NT-proBNP.

Tab 1 Gal-3 and NYHA class association

Parameter	n	Gal-3, ng/ml, median	Gal-3, ng/ml, Q25	Gal-3, ng/ml, Q75
HF NYHA II	14	6,86	3,67	10,02
HF NYHA III	39	9,61	7,75	12,57

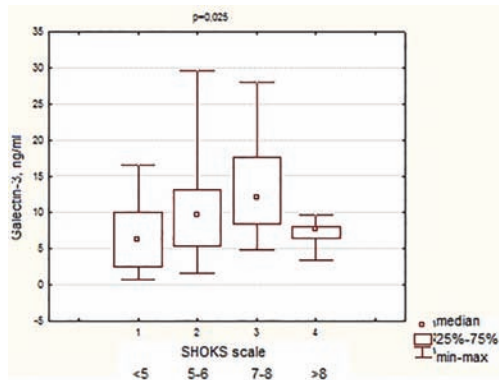


Fig 1 Gal-3 and SHOKS Association

**P2018****Association between neutrophil gelatinase-associated lipocalin (NGAL) and ventricular function in patients with chagas cardiomyopathy. Nephron or cardiomyocyte?**

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**Purpose:** The Neutrophil gelatinase-associated lipocalin (NGAL) is a 25kDa glycoprotein covalently linked to matrix metalloproteinase-9, produced by a variety of cells including respiratory cells, intestinal epithelial cells, endothelial cells, renal tubular cells and cardiomyocytes. In patients with chronic heart failure (CHF) elevated levels of NGAL are associated with worse functional class, higher levels of NT-proBNP, readmissions, and increased mortality. Global longitudinal strain (GLS) has proven to be a marker of myocardial dysfunction with a great prognostic value. In the present study, the correlation between the levels of NGAL and GLS in patients with chronic chagas disease was determined, which has not been previously reported in the literature.

**Methods:** Analytical cross-sectional study. Patients older than 18 years with chagas disease were included. Those patients with uncontrolled hypertension, diabetes, history of coronary artery disease and valvular disease were excluded. The GLS was established by speckle tracking electrocardiography and blood levels of NGAL were determined, both measures were taken the same day. A descriptive analysis was performed, the correlation between the GLS and NGAL was evaluated by scatter plot and Spearman's rank correlation coefficient. Finally, a multiple linear regression analysis adjusted by sex, age and Glomerular Filtration Rate (GFR) was performed.

**Results:** A total of 100 patients were analyzed, 55% (55/100) were men; the mean age was 61 years (SD  $\pm$  12 years); the median and interquartile range of LVEF was 42% (Q1 = 27; Q3 = 56), of NGAL was 96.5 ng / mL (Q1 = 69; Q3 = 145); of GLS was -12.6% (Q1 = -17.8; Q3 = -8.1); 40% (40/100) of the patients had a GFR  $<$ 60 mL / min / 1.73 m<sup>2</sup>. A positive correlation between GLS and NGAL values ( $\rho = 0.584$ ,  $p = 0.000$ ) was established; on the other hand, NGAL and LVEF presented a negative correlation ( $\rho = -0.584$ ,  $p = 0.000$ ). In addition, an association between GLS and NGAL ( $\beta = 0.031$ ,  $p = 0.005$ ) adjusted by sex, age and GFR was established.

**Conclusions:** NGAL is a biomarker traditionally used to determine tubular necrosis. In studies in patients with CHF it has shown to be an independent marker of mortality. In patients with Chagas cardiomyopathy, the GLS showed a moderate positive correlation with NGAL. The finding of an association between these two variables in a model adjusted for age, sex and GFR suggests that it is a marker of myocardial dysfunction in the presence or absence of renal dysfunction in chagas disease.

**P2019****Low circulating microRNA levels in heart failure patients are associated with peripheral arterial disease**

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**Background:** Several circulating microRNAs (miRNAs) were found to be downregulated in patients with heart failure. Further characterisation of the heart failure population and corresponding circulating miRNA profiles would be valuable for future clinical application of miRNAs as biomarkers. Here, we aimed to study differences

in these circulating miRNAs between heart failure patients with and without evidence of atherosclerotic disease.

**Methods:** A panel of 11 heart failure specific circulating miRNAs was measured with quantitative reverse transcription-polymerase chain reaction (qRT-PCR) in plasma from 114 patients hospitalized for heart failure, at time of discharge. MiRNA levels were compared in heart failure patients with different manifestations of atherosclerosis including coronary artery disease, stroke/transient ischemic attack and peripheral arterial disease. In addition, associations between differentially expressed miRNAs and biomarkers related to the atherosclerotic disease process were assessed.

**Results:** From the 114 heart failure patients, 54.5% had a medical history of coronary artery disease. Cerebrovascular disease was present in 13.2% of the patients and 21.1% had a prior diagnosis of peripheral arterial disease. There was no consistent trend in plasma levels of the selected miRNAs in patients with and without coronary artery disease, stroke and/or transient ischemic attack. In contrast, consistently lower levels of miRNAs were found in patients with peripheral arterial disease ( $n = 24$ ), of which 7 miRNAs (miR-18a-5p, miR-30e-5p, miR-106a-5p, miR-27a-3p, miR-223-3p, miR-199a-3p and miR-652-3p) were significantly lower compared to heart failure patients without peripheral arterial disease. Further, low levels of these miRNAs were significantly associated with high levels of multiple biomarkers related to inflammation and endothelial dysfunction (ESAM, LTBR, PIGR, pentraxin-3, troy, syndecan-1, galectin-3, NGAL, GDF-15, RAGE, TNFR-1, VEGFR-1, neuropilin-1 and angiogenin).

**Conclusion:** A consistent pattern of low circulating miRNAs were found in heart failure patients with peripheral arterial disease. In addition, lower levels of miRNAs were related to higher levels of several biomarkers related to inflammation and endothelial dysfunction.

**P2020****The influence of the standard heart failure treatment on the RDW variation in patients with decompensated heart failure**

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**Background and aim:** Red blood cell distribution width (RDW), which is routinely reported in complete blood counts, is a measure of the variability in size of circulating erythrocytes. Studies have already shown that an increase in RDW is associated with a poor prognosis in patients with both acute and chronic heart failure (HF). The aim of our study was to determine the effect of the standard HF therapy on the RDW variation.

**Material and method:** 170 patients with acute decompensated CHF admitted in Cardiology Unit were included; mean age of the cohort 72.89  $\pm$  11.11 years, 44% male, 55% with preserved ejection fraction. Age- and sex-matched 50 control subjects without HF were also evaluated. Patients with cancer, moderate to severe anemia, COPD, infectious diseases or autoimmune disorders were excluded from both groups.

**Results:** RDW was significantly higher in HF group compared to control group (13.64  $\pm$  2.14 % vs. 12.61  $\pm$  0.95 %,  $p < 0.0001$ ), with a mean value of 14.23  $\pm$  2.73 % in NYHA class IV patients. 83.53 % were treated with ACEI/ARBs, 78.25 % with beta-blockers, 75% with statins, 71.76 % with diuretics and 53.53 % with antialdosterone diuretics. RDW values were statistically significantly lower in patients treated with ACEI or ARBs (13.01  $\pm$  1.48 %  $\pm$  2.70 vs. 13.39 %,  $p = 0.009$ ) and higher in patients treated with loop (13.29  $\pm$  1.19 % vs. 12.87  $\pm$  1.34 %,  $p = 0.004$ ) or antialdosterone diuretics (13.49  $\pm$  2.12 % versus 12.81  $\pm$  0.18 %,  $p = 0.01$ ). There were no statistically significant differences between the values of RDW in patients treated with statin ( $p = 0.07$ ), betablockers ( $p = 0.693$ ), oral anticoagulants ( $p = 0.122$ ) or antiplatelet therapy ( $p = 0.126$ ).

**Conclusion:** RDW was significantly lower in patients receiving ACEI or ARBs suggesting the role of angiotensin on the mechanism involved in the RDW increase in patients with HF and the possible inhibitory effect of this class of drugs on these mechanisms.

**P2021****Influence of body mass index on laboratory and biomarkers in acute heart failure patients**

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**Background:** It is known plasma concentrations of natriuretic peptide decline with obesity in patients with heart failure. Whether this is true for other biomarkers is unknown. We investigated biomarker profiles in acute heart failure across the body mass index (BMI) spectrum.



**Methods:** We acquired data and baseline plasma samples from 2033 patients in PROTECT; a trial comparing the effects of rolofylline to placebo in patients with acute heart failure, and measured 48 biomarkers, assessing multiple pathophysiological pathways. Patients were classified into four BMI groups (<25, 25-30, 30-35 and > 35 kg/m<sup>2</sup>).

**Results:** Of 2003 patients with known weight and height, the mean age was 70 ± 12 years and 67% were men. Patients with a higher BMI (> 35 kg/m<sup>2</sup>) had higher blood pressures, were younger and more often women. Median levels of BNP were 550 pg/ml in patients with a BMI <25 kg/m<sup>2</sup> and 319 pg/ml in patients with a BMI > 35 kg/m<sup>2</sup> (p < 0.001). Multivariable regression analysis revealed that BNP ( $\beta = -0.250$ , p < 0.001) and RAGE ( $\beta = -0.095$ , p < 0.007) were strongly inversely correlated to BMI, whereas higher levels of uric acid ( $\beta = 0.164$ , p < 0.001), proADM ( $\beta = 0.171$ , p < 0.001), creatinine ( $\beta = 0.118$ , p = 0.003), sodium ( $\beta = 0.101$ , p = 0.006) and bicarbonate ( $\beta = 0.094$ , p = 0.009) were associated with higher BMI. All betas are per standard deviation. Patients with a higher BMI had a lower 180-day mortality although this relationship was no longer significant on multivariable analysis.

**Conclusions:** When assessing the clinical utility of biomarkers for patients with acute heart failure, BMI should be taken in to account. These findings suggest that these markers should be interpreted with caution in obese patients, and BMI should be included in multivariable analyses assessing the prognostic value of biomarkers in acute heart failure.

## P2022

### The role of circulating miR-21, miR-34a, miR-423, miR-208a and miR-499a in ischemic and dilated cardiomyopathy

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**Background:** Despite growing evidence of the pivotal role of microRNAs in cardiovascular disease, primarily in aspect of myocardial remodeling, there is still great inconsistency about certain microRNA contribution to heart failure (HF), particularly of different origin. We assessed circulating levels of miR-21, miR-34a, miR-423 and two abundantly expressed in heart microRNAs - miR-208a and miR-499a in patients with HF with reduced ejection fraction (HFrEF) and healthy individuals.

**Methods:** We included patients with symptoms and signs of heart failure who had left ventricular ejection fraction (LVEF) ≤ 40%, 9 of whom had dilated cardiomyopathy (DCM) and 7 - ischemic one (ICM). The control group consisted of 10 healthy individuals. Circulating microRNAs levels were quantified by real-time reverse transcription polymerase chain reaction for all participants. Tissue microRNA levels were obtained from 2 myocardial biopsy samples of patients with DCM.

**Results:** 10 healthy individuals and 16 patients with HFrEF (10 males, aged 52 ± 16 years) were analyzed (LVEF % 32.6 ± 8.0). We found that plasma levels of miR-21, miR-34a and miR-423 were higher in the HF group when compared to control group (p < 0.0001, p < 0.002 and p < 0.001 respectively). On contrast, levels of muscle-specific microRNAs (miR-208a, miR-499a) were similar in both groups. The differences in microRNAs levels between patients with DCM and ICM did not reach statistical significance. Noticeably miR-423 appeared to be the only microRNA for which bioplat/plasma ratio was < 1 (0.54). Correlation analysis showed no significant association with both - LVEF and NYHA class.

**Conclusions:** These results suggest that miR-21, miR-34a and miR-423 may be novel diagnostic biomarkers for patients with HFrEF, while the implication of muscle-specific microRNAs may turn up beneficial in the setting of acute myocardial injury. The ability of these microRNAs to distinguish the etiology of HF was not approved.

## P2023

### Prognostic value of high sensitivity troponin-T to identify patients at risk of primary graft dysfunction after heart transplantation

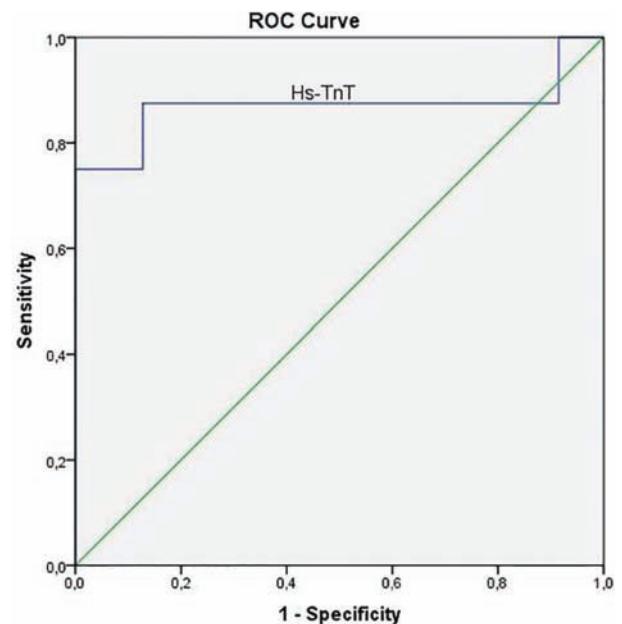
A Ana Belen Mendez Fernandez<sup>1</sup>; J Ordonez<sup>2</sup>; S Mirabet<sup>1</sup>; J Galan<sup>3</sup>; ML Maestre<sup>3</sup>; V Brossa<sup>1</sup>; L Lopez<sup>1</sup>; T Koller<sup>3</sup>; A Sionis<sup>1</sup>; E Roig<sup>1</sup>

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Primary graft dysfunction (PGD) after heart transplantation (HT) has a very high mortality especially if the left ventricle is involved. Early diagnosis is important to select the appropriate therapy to improve prognosis. The value of high sensitivity troponin T (hs-TnT) obtained at the arrival of the patient at the intensive care unit to identify patients at risk of PGD was analyzed in 71 HT. PGD was defined by hemodynamic compromise with systolic blood pressure < 90 mmHg and/or CI < 2.2 l/min/m<sup>2</sup>, need of > 2 inotropic drugs or mechanical support and left ventricular dysfunction by echocardiography.

Mean recipient age was 54 ± 12 years (73% men) and mean donor age was 47 ± 11 years. Ischemic time was 200 ± 51 min. and cardiopulmonary bypass (CPB) 122 ± 31 min. Nine HT (13%) patients were diagnosed of having PGD post-HT, 8 with biventricular dysfunction. Four patients died, 2 with PGD (15%) and 2 without PGD (3%). Mean hs-TnT before HT was 158 ± 565 ng/L and post-HT 1621 ± 1269 ng/L. The area under the curve (ROC) of the hs-TnT to detect patients at risk of PGD was 0,86 (p < 0.001). A value of TnT-hs>2000ng/L had a sensitivity of 75% and specificity of 87% to identify patients at risk of PGD. Multivariate analysis identified hs-TnT>2000 ng/L (p < 0.02) and CPB time (p < 0.01) as independent predictors of PGD.

**Conclusions:** hs-TnT>2000ng/L at intensive care admission after HT and prolonged CPB time were the most powerful predictors of PGD. Hs-TnT may be helpful to identify HT patients at risk of PGD and worse prognosis.



## P2024

### Galectin-3 in different phenotypes of heart failure

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**Purpose:** Galectin-3 has in heart failure (HF) been linked to inflammation, fibrosis and ventricular remodeling. We investigated levels of galectin-3 and its correlation to disease severity and prognosis in HF with preserved (HFpEF) and reduced (HFrEF) ejection fraction.

**Methods:** Galectin-3 was measured in HFpEF patients with ejection fraction ≥ 45% (n = 86) and in advanced stable HFrEF, < 40% (n = 85), post left ventricular assist device (LVAD; n = 24) and post heart transplantation (HTx; n = 34). In HFpEF patients the composite endpoint consisted of HF hospitalization and death and in HFrEF, implantation of LVAD, HTx and death.

**Results:** Levels of galectin-3 was in HFpEF median (interquartile range) 17.1 (13.0;21.4) µg/L and in HFrEF 16.8 (13.0;21.4; p = 0.825) µg/L and decreased post LVAD 15.1 (11.1;17.9) and post HTx 12.2 (9.2;15.8) µg/L (HFrEF-LVAD-HTx p = 0.0004). In both HFpEF and HFrEF galectin-3 correlated with creatinine clearance but with NT-proBNP in HFrEF only (Table 1). Among comorbidities in HFpEF galectin-3 correlated with previous hypertension beta coefficient 0.21 (95% CI 0.00-0.42; p = 0.048) and in HFrEF with atrial fibrillation 0.26 (0.04-0.40; p = 0.017). Galectin-3, adjusted for age, gender and creatinine clearance, did not predict the composite endpoint in HFpEF (per log increase: 1.14, 0.47-2.77; p = 0.776) whereas in HFrEF it was numerically but not significantly associated with the composite endpoint (1.96, 0.83-4.62; p = 0.125).

**Conclusions:** HFpEF appears associated with increased galectin-3, which may reflect renal dysfunction but not HF prognosis. In HFrEF galectin-3 may more distinctively mirror the HF syndrome itself as demonstrated by falling levels after LVAD and HTx and may thus have a potential prognostic role.

Table 1

Galectin 3	HFrEF n=86 Correlaton	HFrEF n=84 p-value	LVAD n=24 Correlaton	HTx n=34 p-value	Correlaton	p-value	Correlaton	p-value
Age	0.142	0.193	0.435	< 0.0001	0.523	0.009	0.477	0.004
BMI	0.273	0.011	0.080	0.474	0.170	0.426	0.151	0.393
Systolic BP	-0.105	0.336	-0.027	0.814			0.005	0.979
LVEF	0.015	0.896	-0.124	0.264	-0.094	0.761	0.046	0.794
E/e'	0.334	0.007						
NTproBNP (ng/L)	0.206	0.059	0.454	< 0.0001	0.474	0.019	0.358	0.038
Creatinine clearance (mL/min)	-0.446	< 0.0001	-0.631	< 0.0001	-0.446	0.029	-0.361	0.036
Uric acid (umol/L)	0.244	0.025	0.343	0.139	-0.600	0.285	0.094	0.662

Correlation between galectin 3 and selected variables

**P2025**

**High-sensitivity troponins are the most effective predictors of mortality after heart transplantation when compared to other cardiac and renal biomarkers**

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**Background:** Troponins, natriuretic peptides, galectin-3, creatinine, cystatin C, and NGAL are recognized as biomarkers of heart and renal function and/or injury. However, careful selection of biomarkers with focus on the predictive power is necessary.

**Purpose:** We aimed to compare the prognostic power of selected cardiac and renal biomarkers in the early posttransplant period after heart transplantation (HTx).

**Methods:** In the prospective study, a total of 116 patients after heart transplantation (HTx) was evaluated. The group consisted of 97 men and 19 women. The standard immunosuppressant therapy was used together with other medication according to the common posttransplant regimen. Blood samples were taken on the 30th day after HTx, urine (for NGAL) on the 1st day after HTx. 11 patients (10 %) died during the first year after HTx, total mortality reached 16 % during follow-up period (up to 1800 days, 4.9 years). Total survival (together with the survival interval) was selected as the main end-point. BNP, galectin-3, cystatin C, hs-cTnI, and urinary NGAL were measured with Abbott Architect diagnostic kits, NT-proBNP and hs-cTnT were measured with Roche Elecsys diagnostic kits on Cobas 6000 analyzer.

**Results:** We tested 9 clinical variables (age, EuroScore, infection, sex, renal replacement therapy, diabetes mellitus, the use of ventricle assist device, BMI, smoking) and 8 laboratory variables (hs-TnI, hs-TnT, BNP, NT-proBNP, galectin-3, creatinine, cystatin C, NGAL) assessed before or up to 30 days after HTx. Cox proportional hazard regression analysis revealed 6 variables with significant hazard ratios (HR; 95% CI): diabetes mellitus (3.02; 1.2 – 7.6), BMI (1.14; 1.01 - 1.29), smoking (2.52; 1.11 – 5.59), hs-TnI (1.76; 1.12 – 2.77), hs-TnT (2.82; 1.44 – 5.50), NGAL (1.43; 1.1 – 1.87). Two multivariate Cox models based on four significant variables together with either hs-TnT or hsTnI were tested. Only hs-TnT (HR 2.41; 1.10 – 5.29) or hs-TnI (HR 1.67; 1.05 – 2.66) were significant predictors of death.

**Conclusions:** Cardiac troponins measured with high-sensitivity methods 30 days after heart transplantation are the best predictors of prognosis when compared to other clinical and laboratory variables.

**P2026**

**Prognostic utility of ST2 level as a predictor of clinical outcomes in incidental dialysis patients.**

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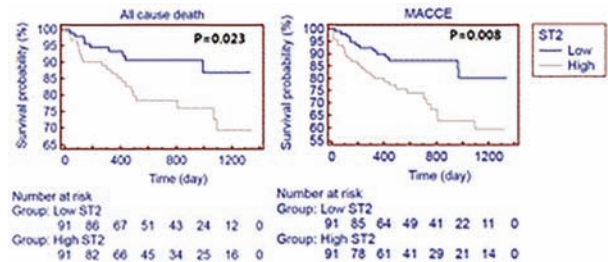
**Background:** The ST2 is associated with cardiac remodeling and tissue fibrosis. It is well known as a novel biomarker on predictor of cardiovascular events in patients with heart failure. In patients needed to start dialysis, 64~83% had congestive heart failure. However, the prognostic implications of serum ST2 level are unknown in incidental hemodialysis.

**Methods:** A total 182 patients undergoing incidental hemodialysis were consecutively enrolled from November 2011 to December 2014. We can analyze the serum ST2 level, and compared major adverse cardiac and cerebral events (MACCE)

including all-cause death, heart failure admission, acute coronary syndrome, and nonfatal stroke.

**Results:** Median follow up duration was 628 days (interquartile range 382 to 1,052 days). All patients were divided into two groups according to median ST2 level (59.5 ng/ml, interquartile range 40.0 to 102.5); high ST2 group (n=91) and low ST2 group (n=91). High ST2 group had significantly higher incidence of all-cause mortality, and composite of MACCE. High ST2 was a significant independent predictor of MACCE (adjusted hazard ratio 2.513, 95% confidence interval 1.02 to 6.20, p=0.046).

**Conclusion:** The higher ST2 is associated with higher cardiovascular and cerebral events in incidental dialysis patients. The serum ST2 level may serve as a predictor of cardiovascular and cerebral events in incidental dialysis patients.



Kaplan-Meier Curve

**P2027**

**Serum neprilysin and recurrent hospitalizations after acute heart failure**

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**Background:** Prediction of recurrent hospitalizations after an episode of acute heart failure (AHF) remains a challenge. The soluble form of neprilysin (sNEP) has been recently postulated as a promising biomarker in heart failure. We sought to evaluate the association between sNEP and long-term recurrent hospitalizations.

**Methods:** We measured at admission sNEP of 210 consecutive patients admitted for AHF. Negative binomial regression method was used to determine the association between sNEP and the risk of recurrent hospitalizations. Estimates were reported as incidence rate ratios (IRR).

**Results:** At a median follow-up of 2.1 years (IQR: 1.2-2.8), 94 deaths, 307 all-cause rehospitalizations in 144 patients (68.6%) and 130 AHF-rehospitalizations in 82 patients (39.1%) were recorded. The multivariable analysis showed that sNEP, from lower to higher quartile, had a stepwise increase of rates for both end-points, although with lesser effect on all cause-rehospitalizations. In reference to the first quartile, the IRRs for all-cause rehospitalizations were: Q2=0.96 (0.61-1.51); p=0.860, Q3=1.21 (0.77-1.88); p=0.407, and Q4=1.94 (1.28-2.94); p=0.002 [Omnibus p-value=0.004]. For AHF-rehospitalizations, the IRRs were: Q2=1.28

60154.	Clinical	Events	in	Patients	with	high	ST
	Low ST2 (n=91)	High ST2 (n=91)		Unadjusted HR (95% CI)	p value	Adjusted HR <sup>a</sup> (95% CI)	p value
All-cause death	9 (9.9)	21 (23.1)		2.41 (1.10-5.26)	0.021	2.62 (0.93-7.33)	0.067
Cardiac death	5 (5.5)	13 (14.3)		2.68 (0.96-7.53)	0.061	3.58 (0.73-17.5)	0.115
Heart failure admission	5 (5.5)	9 (9.9)		1.98 (0.66-5.91)	0.221		
Acute coronary syndrome	2 (2.2)	3 (3.3)		1.67 (0.28-10.0)	0.573		
Nonfatal stroke	1 (1.1)	3 (3.3)		3.09 (0.32-29.7)	0.329		
Composite of MACCE	13 (14.3)	28 (30.8)		1.59 (1.24-2.05)	0.012	2.52 (1.02-6.20)	0.046

<sup>a</sup>Adjusted covariates included age, sex, hypertension, diabetes mellitus, current smoker, BMI, ejection fraction, hemoglobin, albumin, C-reactive protein, high sensitivity troponin T, galectin-3, B type natriuretic peptide. HR = hazard ratio; CI = confidence interval

(0.63-2.58;  $p=0.491$ ,  $Q3=1.99$  (1.09-3.62);  $p=0.024$ , and  $Q4=4.31$  (2.34-7.97);  $p < 0.001$  [Omnibus  $p$ -value  $< 0.001$ ].

**Conclusion:** In patients with AHF, sNEP was positively associated with long-term recurrent hospitalizations.

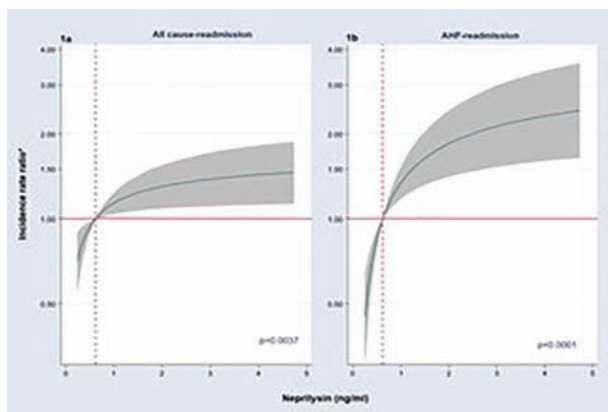


Figure 1

## P2028

### Plasma neutrophil gelatinase-associated lipocalin and long-term mortality in acute heart failure

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**Background:** Neutrophil gelatinase-associated lipocalin (NGAL) has emerged as a tubular marker related to early renal dysfunction. In heart failure (HF), contradictory results have been reported and some ambiguity still prevails about the prognostic utility of NGAL beyond standard prognosticators and traditional renal markers.

**Purpose:** We aimed to evaluate the independent ability of serum NGAL for predicting long-term mortality in patients admitted for acute HF (AHF).

**Methods:** 206 patients consecutively admitted for AHF were prospectively enrolled. Chronic kidney disease (CKD) was defined as  $eGFR < 60$  ml/min/1.73m<sup>2</sup>. Outcomes rates were depicted across NGAL median value and the presence of CKD using the Kaplan-Meier method. Multivariable analysis for all-cause mortality was performed by using regression Cox model. The discriminative accuracy and calibration of the model were assessed by the Harrell's C-statistic and the Hosmer-Lemeshow test, respectively

**Results:** During a median follow-up of 36 months (12-46), 97 deaths were registered (47.1%). 51% were female and 53.4% exhibited LVEF  $> 50\%$ . The median (interquartile range) for eGFR, BUN, serum creatinine and NGAL were 64.1 ml/min/1.73m<sup>2</sup> (37), 22.9 mg/dl (13.1), 1.02 mg/dl (0.5), and 85 ng/ml (98,7), respectively. NGAL above median showed higher rate of death (1.25 vs. 2.70 per 10 persons-year,  $p < 0.001$ ). Among renal biomarkers, BUN showed the higher discriminative accuracy followed by eGFR, creatinine, and NGAL (Harrell's C-statistics 0.650, 0.618, 0.612, and 0.610, respectively). When the sample was stratified across CKD, a differential prognostic effect was found. NGAL was related to long-term mortality in

patients without CKD but not in those with CKD (Figure 1). In the adjusted analysis, NGAL, dichotomized by its median, was borderline associated with risk of death in the whole sample (HR = 1.49; CI 95%:0.96-2.31,  $p=0.077$ ). Likewise, in the univariate setting the differential prognostic effect of NGAL across CKD was also identified after adjustment (adjusted  $p$ -value for interaction = 0.021). In patients with CKD, NGAL above median did not show any prognostic effect (HR = 0.94; CI 95%:0.53-1.66,  $p=0.818$ ); conversely, NGAL was powerfully associated with the risk of long-term mortality in those with  $eGFR \geq 60$  ml/min/1.73m<sup>2</sup> (HR = 2.56; CI 95%:1.34-4.88,  $p=0.004$ ). The final multivariate model showed an adequate discriminative ability and calibration (Harrell's C-statistics and Hosmer-Lemeshow were 0.720 and 0.811, respectively).

**Conclusions:** In patients admitted for AHF, circulating NGAL levels were associated with an increased long-term risk of death in patients with normal eGFR but not in those with decreased renal function. Further studies are warranted in order to confirm present findings.

## P2029

### The lymphocyte count and neutrophil/lymphocyte ratio as independent predictors for cardiac events in heart failure only in ischemic heart disease patients

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**Background:** The predictive value of some biomarkers in heart failure (HF) is not well established. Recent data suggests that some specific types of leucocytes have different predictive value in cardiovascular risk. The predictive value is improved by using neutrophil/lymphocyte ratio (NLR).

**Purpose:** To evaluate the predictive values of white blood cell (WBC) count, WBC differential formula (WBC-DF) and NLR for cardiovascular events (cardiac adverse outcome and rehospitalisation) in heart failure patients with ischemic heart disease (IHF) and without ischemic heart disease (NIHF).

**Methods:** Our prospective study included 323 HF patients (185 with IHF and 138 with NIHF), NYHA class II-IV ( $66.7 \pm 14.7$  yrs), 47.3% male and 52.7% female. They signed informed consent and underwent clinical and laboratory assessment: lipid profile, N-terminal pro-brain natriuretic peptide (NT-proBNP), C reactive protein (CRP), total WBC, WBC-DF and NLR. The patients were followed for one year. The study methodology was approved by the Ethical Committee. Statistical data processing was performed with SPSS.

**Results:** There were no significant differences regarding gender, age and body mass index (BMI) between the subgroups. Patients with NIHF had significantly higher levels of total cholesterol and LDL-cholesterol ( $p < 0.001$ ) whereas patients with IHF had significantly higher levels of NT-proBNP ( $p < 0.001$ ), CRP ( $p < 0.005$ ), WBC ( $7.68 \pm 3.07 \times 10^9/l$  vs  $6.71 \pm 2.08 \times 10^9/l$ ,  $p < 0.005$ ), lymphocyte count ( $16.9 \pm 10.2\%$  vs  $13.8 \pm 10\%$ ,  $p < 0.05$ ), neutrophils index ( $57.8 \pm 29.4\%$  vs  $52.6 \pm 31.3\%$ ,  $p < 0.005$ ) and NLR values - 1.27 (1.2-1.36) vs 0.99 (0.4-1.15) ( $p < 0.02$ ). A significant difference between NLR values was found in patients in NYHA class II vs III, while no difference of NLR was found between patients in NYHA classes III and IV. A positive correlation between NLR and NT-proBNP level was found ( $r = 0.43$ ,  $p < 0.05$ ). The lymphocyte count, NLR and NYHA class ( $p < 0.001$ ) are independent predictors for the free interval until rehospitalisation for cardiovascular events. After adjusting for NYHA class, the lymphocyte count and NLR remained predictors only for IHF.

**Conclusion:** For patients in the same NYHA class, the lymphocyte count and NLR are independent predictors for cardiovascular events in IHF but not in NIHF.



**P2030**

**Higher urinary hydrogen peroxide levels are associated with increased plasma renin activity and aldosterone concentration in patients with chronic heart failure**

T. Sousa was supported by a Ciência 2008 Contract, funded by FCT and POPH/FSE (EC) and by a Postdoctoral fellowship from FCT (SFRH/BPD/112005/2015).

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**Background:** Renin-angiotensin-aldosterone system activation and oxidative stress are known to contribute to the pathogenesis of chronic heart failure (CHF) (1,2). Hydrogen peroxide (H2O2) is a non-radical oxidant and an established downstream mediator of RAAS activation that also appears to regulate the levels of RAAS components (3). Recent studies suggest that oxidative stress and H2O2 may stimulate renin release from juxtaglomerular cells (4,5).

**Purpose:** Therefore, we investigated the relationship between H2O2, oxidative stress and RAAS activation in patients with CHF.

**Methods:** Urinary H2O2, plasma and urinary isoprostanes, plasma renin activity and aldosterone concentration were evaluated by commercial kits in 60 CHF patients (New York Heart Association, NYHA, class I to IV) recruited from the Heart Failure Clinic of our hospital.

**Results:** Patients were first stratified into mild-to-moderate CHF (NYHA classes I and II) and severe CHF (NYHA classes III and IV). Severe CHF patients had higher levels of urinary isoprostanes (3.94 ± 0.68 vs 2.55 ± 0.34 ng/mg creatinine, p < 0.01) but no significant differences were observed in plasma isoprostanes (0.88 ± 0.10 vs 0.66 ± 0.05 ng/mL), urinary H2O2 (0.017 ± 0.0038 vs 0.012 ± 0.0015 micromol/mg creatinine), plasma renin activity (460.3 ± 158.2 vs 283.7 ± 112.2 microU/L) or aldosterone (16.58 ± 3.97 vs 10.56 ± 1.22 mg/dL). To evaluate the relationship between oxidative stress or H2O2 with RAAS activation, we analysed plasma renin activity or aldosterone levels by tertiles of urinary H2O2, urinary isoprostanes or plasma isoprostanes. Linear trend analyses revealed that both plasma renin activity and aldosterone increased across urinary H2O2 tertiles (Log plasma renin activity: 1st tertile: 1.82 ± 0.16; 2nd tertile: 2.10 ± 0.13; 3rd tertile: 2.39 ± 0.17, p = 0.012; Log aldosterone: 1st tertile: 0.77 ± 0.10; 2nd tertile: 1.12 ± 0.07; 3rd tertile: 1.07 ± 0.06, p = 0.0089). No differences in plasma renin activity or aldosterone were observed between tertiles of urinary or plasma isoprostanes.

**Conclusion:** Our results show that CHF patients with higher urinary excretion of H2O2 exhibit increased RAAS activation and thus reinforce the hypothesis of H2O2 being a modulator of renin release.

**P2031**

**Correlation between N-terminal pro-brain natriuretic peptide levels and myocardial involvement detected with 2D speckle tracking echocardiography in systemic sclerosis**

habib thameur hospital

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**Aims:** Systemic sclerosis (SSc) is a severe tissue disorder characterized by frequent myocardial involvement which is associated with poor prognosis. The aim of this study is to identify the relation between serum levels of N-terminal pro-brain natriuretic peptide (BNP) and the severity of cardiac involvement assessed with 2D speckle tracking echocardiography (STE) in patients with systemic sclerosis (SSc).

**Methods and results:** 25 patients with SSc (53.64 ± 13 years, LVEF 64.58 ± 8.87 %) and 25 gender and age-matched healthy subjects (35.8 ± 8.72 years, LVEF 68.2 ± 7.41 %) underwent echocardiography with STE to assess global and regional ventricular function. Dosage of serum BNP was done for all patients and controls. There was a significant increase in the mean values of serum levels of BNP in SSc patients compared to controls (p = 0.03), parallel to an alteration of myocardial function assessed by 2D SST (left ventricle global longitudinal strain -17.42 ± 1.62 vs. -19.24 ± 8.85 (P < 0.0001)). BNP values were correlated to ventricular strain impairment.

**Conclusion:** The results of this study provide confirmation that high BNP levels over time are associated with myocardial involvement progression.

**P2032**

**Brain natriuretic peptide guided transthoracic doppler 2D echocardiography requests is cost saving and effective way to rule out heart failure.**

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**Introduction:** Brain Natriuretic Peptide (BNP) is a useful test to rule out heart failure with high negative predictive value. NICE guidelines(2) suggests referral for patients with suspected heart failure and a BNP level between 100 and 400 pg/ml (29–116 pmol/litre) or an NT-proBNP level between 400 and 2000 pg/ml (47–236 pmol/litre) to have echocardiography. ESC guidelines (1) suggests an optimal level of NT-proBNP of less than 300 pg/ml as a cut off point in patients presenting with acute onset or worsening of heart failure symptoms.

**Purpose:** To look at NT-proBNP and Echo requests in our health board to determine the number of inappropriate Echo requests in patients with NT-proBNP of less than 400 pg/ml.

**Method:** We reviewed the NT pro-BNP requests in our Health Board for 12 consecutive months. The criterion of NT pro-BNP level of less than 400 pg/ml was set according to the NICE Guidelines(2) for diagnosing heart failure. Local echo database was used to determine echo requests and its findings.

**Results:** 370 NT pro-BNP were requested during the study period. 300 (81%) and 274 (75%) requests with NT-proBNP level of less than 400 pg/ml and less than 300 pg/ml were done respectively. However, 137 and 121 echo requests were generated for assessment of left ventricular function, respectively, despite of these results. These echo requests are inappropriate and equates to around 35 echo sessions per year in the department. The estimated cost for these echo requests was €13500 (£10,275). The cost of BNP testing is around €13-18 (£10-15) per assay. Using BNP guided echo request to rule out heart failure will potentially save €10500 (£8000) per year and 35 echo sessions for our department. More importantly, all patients with NT pro BNP of less than 400pg/ml and without cardiac history, the echo findings for left ventricular function were normal.

**Conclusion:** Using BNP guided Echo request according to the NICE guideline(2) and ESC guidelines 2012(1) to rule out heart failure is cost effective and this retrospective analysis also showed that BNP of less than 400pg/ml essentially ruled out heart failure and thus can be used as a 'rule-out' test. Reference 1. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012 2 NICE Guidelines for Chronic heart failure 2010.

Table 1

NT proBNP levels	<300pg/ml	> 300pg/ml	<400 pg/ml	> 400pg/ml
Numbers of assays	278 /370	92/370	300/370	70/370
No. of Echo requests	121/278	69	137/300	51
% of inappropriate echo requests	43.5%		45.6%	

Table showing number of NT-proBNP assays ordered and number of echo requested. The inappropriate echo requests are in bold and underlined.

**P2033**

**Prognostic value of serial b-type natriuretic peptide in hospitalized heart failure patients and mortality**

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**Background:** B-type natriuretic peptide (BNP) has prognostic significance in HF, and reduction of BNP level may be predicts clinical improvement or good clinical results. However, there is a limited data about role of follow-up BNP level. The aim of this study was to evaluate the prognostic impact of short-term follow up BNP and development of clinical outcome in heart failure patients.

**Methods:** We analyzed 733 hospitalized HF patients in the Wonju Christian Hospital Heart Failure Registry from April 2011 to December 2013. Among them 284 patients (age=72.8 ± 12.2 years, Male=118, 41.5%) with concomitant measuring of BNP on admission and short-term follow-up period (within 2 month). We compared for the incidence of all-cause of mortality during the clinical follow-up (mean 764 days) according to the BNP quartiles on admission as an initial and short term follow up period

**Results:** The mean initial BNP was 1189.92 ± 1022.83 pg/ml and mean follow up BNP was 690.76 ± 884.06 pg/ml and mean follow up duration was (23.5 ± 16.8) days. Multivariate analysis demonstrated a positive linear association between the risk of death and the BNP quartile. The patient with the highest quartile of follow up BNP (HR=4.360, Pvalue < 0.0001) was significantly associated with higher risk of the all cause mortality, compared to the patients with the lowest quartile of follow-up BNP level. However, the initial BNP was not significantly associated with all cause mortality. A multivariate Cox proportional hazards model analysis showed that follow up BNP was an independent association of all cause mortality after adjustment of covariates (HR=4.224, 95%CI 2.057-7.059). The Kaplan Meier curves also showed significant differences in the incidence of the primary endpoint between the 4 quartile groups according to fBNP (Log rank p = < 0.001). Additionally (%) changes of BNP was also significantly associated with mortality.

**Conclusions:** Short-term follow up plasma BNP and also the percent changes of BNP level, not initial BNP level is a significant prognostic marker of heart failure and it's clinically useful to evaluate the clinical outcome

## NURSING

### P2034

#### Embedding a specialist heart failure nurse into the general medicine teams to improve outcomes for patients with chronic heart failure

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**Introduction:** Chronic heart failure remains a major public health issue with care costs estimated at \$1 billion per annum, mostly due to hospital admission and re-admission. Older patients are presenting to hospital with multiple comorbidities that impact on delivery of evidence-based treatment strategies.

**Purpose:** By embedding a specialist heart failure (HF) nurse within General Medicine, we aimed to streamline the patient journey, promote adherence to evidenced-based treatments, improve patient knowledge and reduce re-admission rates.

**Method:** Baseline demographic, treatment and clinical outcome data was collected between May and September 2014. Between March and September 2015, all patients admitted with a diagnosis of Acute Decompensated Heart Failure (ADHF) were prospectively identified. Throughout their hospital stay, a specialist HF nurse was involved in patient management and early follow up arranged. Outcomes post intervention were compared with baseline data.

**Results:** 124 consecutive patients were included at baseline and 215 post intervention. Mean age was 76 years and 54% were male. Post-intervention, 153 patients (71%) were admitted under General Medicine and 113 patients (53%) had a left ventricular ejection fraction <50% (HFREF). Overall the mean HF knowledge score improved from 5.9 during at baseline to 8.2 on a 10-item survey of self-care behaviour. 30-day readmission rate was reduced from 37% to 21% ( $p < 0.001$ ).

**Conclusion:** Hospitalised HF patients are elderly with a high prevalence of HFpEF. Unlike HFREF, pharmacological strategies remain uncertain. However, symptomatic treatment, patient education and early review to detect signs of fluid retention appear to help keep these patients at home. Specialist HF nurse involvement in the care of patients admitted with ADHF can improve patient knowledge and self-management. A strategy including early review post-discharge either in clinic or the patient's local area results in reduced 30 day readmission rates.

### P2035

#### A delphi study to update cardiac nursing core competencies.

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**Introduction:** Following recent developments, such as the new health challenges due to the aging of the population, and the rapid scientific and technological advances of the last few years, cardiac nurses in Italy need to update and re-define their competencies and set new standards in line with the best international practices.

**Purpose:** The aim of this project is to elicit a national and international consensus around new core cardiac nursing competencies.

**Methods:** The Delphi technique - the main premise of which is based on the assumption that group opinion is more valid than individual opinion - was chosen to elicit national and international consensus around the core cardiac nursing competencies. In the present Delphi study, three rounds will be employed, during which questionnaires to elicit consensus on the core cardiac nursing competencies will be sent out to a panel of national and international cardiac nursing experts.

**Results:** Based on the most recent literature on cardiac nursing competencies and following preliminary debates with a panel of national and international experts, a prioritized list of 10 items has been produced and which, at the end of the three rounds of this Delphi study, will be presented at the conference with their significance and likely impact on the quality of cardiac nursing.

**Conclusions:** Important steps recently taken at a European level to identify a core curriculum that offers a European perspective for cardiovascular nursing education based in current health challenges. A broader perspective of cardiovascular competencies with a greater emphasis not only on stroke, peripheral vascular disease, but also prevention, and rehabilitation can support single countries to fulfil country-specific health care priorities. The results of the present study

will be used to develop a program for the self-assessment of cardiac nursing competencies.

### P2036

#### Retrospective profile research of the patients evaluated for the inclusion on the cardiac transplant queue of a period of fifteen years.

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**Introduction:** The cardiac transplant (CT) is a therapy indicated on the treatment of cardiac insufficiency (CI) when the drug therapy is not efficient. The selection and evaluation of the candidates to the transplant considers the stratification of prognostic variables and the comorbidities, as well as factors that could contraindicate or compromise the transplantation protocol.

**Objectives:** Analyse the patients' profile that were evaluated for the inclusion on the cardiac transplantation queue by the nurse. Variables: Gender, age, ethnicity, etiology of the disease, nationality, caregiver, education, family income, tabagism, alcohol and illicit drugs use, body mass index and co-morbidities such as hypertension, diabetes and dyslipidemia.

**Methods:** In the period 2000-2015 analyzed 1071 patients evaluated by nurses for inclusion cardiac transplant (CT) orthotopic, heterotopic retransplantation through in electronic medical records and physical consultation and nursing assessment forms filed with the heart failure unit.

**Results:** 63% of the patients evaluated were not included on the CT queue and 37% were included; 12% underwent a priority transplantation; 70% male, 71% white, 15% black, 13% mulattos, 1% yellow. Considering the etiology: 21.5% ischemic, 33% chagasic, 26% idiopathic, 4% valve, 0.5% restrictive, 1% vascular disease graft, 3% hypertensive, 2% hypertrophic cardiomyopathy, 0.2% congenital, 1.2% viral, 2% periparturient, 0.5% graft dysfunction, 5% other. Nationality: 38% from São Paulo, 62% other states; Originally from: 80% São Paulo, 20% other states; Caregiver: 52% spouse, 9% siblings, 13% children, 18% parents, 5% other relatives, 1% contracted, 2% without any caregiver; Education: 51% first grade, 21% high school, 14% higher education, 11% elementary school, 3% illiterate; Average family income between 700 ± 660 dollars; BMI: 24 ± 4 Kg/m<sup>2</sup>; Diabetes: 27%, Diabetes / insulin dependent: 51%; Dyslipidemia: 22%; High blood pressure: 43%; Alcohol use: 22% active, 19% abstemic, smoking: 7% active, 46% abstemic; Illicit drugs: 1% active, 3% abstemic; BMI: 24 ± 4 Kg/m<sup>2</sup>; re-transplant: 1% with a survival rate of 13.5%; heterotopic transplantation: 1% with survival rate of 12.5%; Double transplant (heart and kidney): 0.5% with survival rate of 20%.

**Conclusion:** The stratification criteria used for the patients inclusion on the CT queue are rigorous, which can be demonstrated by the number of patients evaluated and included on the queue. It was also observed that from the patients included on the queue, just a little percentage of them really underwent the transplant, due to the high morbi-mortality resulted by the CI. This study also demonstrates the high incidence of chagasic cardiomyopathy transplant indication. We obtained a high rate of patients with primary education level associated with a low family income. The vast majority of the population evaluated was insulin-dependent diabetic patients.

### P2037

#### Adherence to heart failure treatment is generalizable across behaviors

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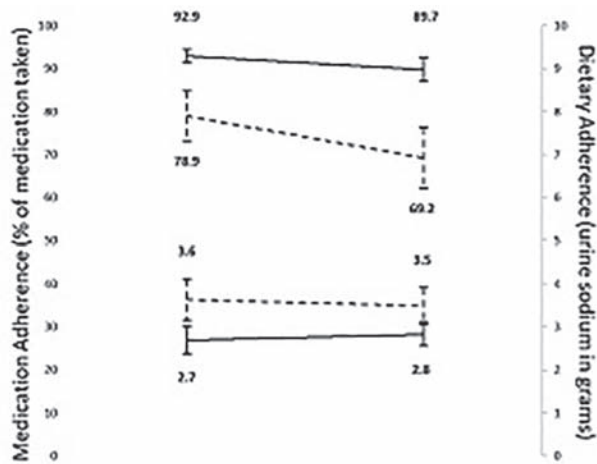
Objective measurement of heart failure (HF) treatment adherence requires a variety of measures to obtain a full picture of behavior. Many of these measures are expensive, time-consuming, and burdensome to patients.

**Purpose:** We sought to identify the best objective means of quantifying adherence in HF by comparing adherence to medications and diet.

**Methods:** A sample of 280 adults with chronic HF was enrolled from three U.S. out-patient centers and followed for six months. We performed a secondary analysis of data collected at baseline on medication (by electronic monitoring) and dietary adherence (by 24hour urine sodium (Na)). Growth mixture modeling was used to cluster and compare medication adherence and dietary adherence.

**Results:** We observed two distinct patterns of HF adherence (entropy = 0.86; probabilities ≥ 95%;  $p < 0.001$  for all comparisons) (Figure). 57% of patients ( $n = 159$ ) had HF medication adherence rates of approximately 90% and had urine Na levels <3g/day throughout 6 months of study (solid line = good adherence). The remaining 43% ( $n = 121$ ) had HF medication adherence rates in the range of 70% and had 24hour urine Na level consistently ≥ 3.5g/day (dashed line = poor adherence).

**Conclusion:** Patients with HF are either adherent to both prescribed medications and dietary sodium restriction or they are nonadherent. Objectively measuring adherence to both behaviors provides redundant information.



## P2038

## Rasch analysis of a heart failure self-care screening tool (Heart-FaST)

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**Background:** Screening heart failure (HF) patients for self-care ability is advocated before applying education and support strategies. The Heart Failure Screening Tool (Heart-FaST) was developed specifically to assist nurses to identify patient barriers that impede engagement in self-care in three distinct domains: risk factors, cognitive and emotional functioning.

**Purpose:** To ascertain whether a total score, derived from the three domains of Heart-FaST, can be used as a valid measure of the overall construct of capacity to engage in self-care.

**Methods:** Heart-FaST was administered to 135 HF patients (X-age = 69, SD = 12; 40 females) enrolled in a multidisciplinary heart failure management program. A Rasch analysis examined fit to the Rasch model, rating scale performance, internal-consistency reliability, targeting, differential item functioning, local independence and unidimensionality.

**Results:** Components of the Hands and Numbers criteria of the Clock Drawing Task were amalgamated to circumvent the effect of local dependence. The Serial Sevens rating scale was reduced from three to five categories while the rating scale of the Emotional Functioning items was reduced from seven to two categories following evidence of threshold disorder. The fit of data to the Rasch model was acceptable following these modifications, after removing two items due to misfit and differential item functioning. Confirmation of the unidimensional nature of Heart-FaST was achieved via a test of unidimensionality that identified only 4% to 12% of participants with multidimensional response patterns. The final scale consisting of 22 items (scores range from 0 to 28; higher scores indicate higher risk for poor self-care) had adequate internal-consistency reliability ( $\alpha = 0.64$ ).

**Conclusions:** Results provisionally support the use of Heart-FaST as an ordinal scale that is capable of differentiating two participant groups (low versus high risk) with respect to their capacity to engage in heart failure self-care.

## P2039

## Patient with heart failure and relatives attitudes towards using reflection cards during educational program.

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**Background:** Chronic heart failure requires a complex treatment regime on a life-long basis. Medication, self-monitoring, diet and social isolation are challenging patient and resulting in readmissions. Educational program for patients with heart failure is individual and contains consultations with cardiologist, specialized trained nurse and if needed referred to physiotherapy, dietician, social worker and psychologist. A multidisciplinary group program, established in 2012., added to the individual program. To retain knowledge and support reflection on "daily knowledge and daily activity" is playing cards based on a formerly French heart failure game used in the group program.

**Purpose:** This study aims to evaluate patients and relatives attitudes towards using

reflection cards, during educational group program in the heart failure clinic in a Danish hospital.

**Methods:** This study is a cross-sectional study conducted October 2012 - June 2015(16 groups) and based on a formerly questionnaire by Hibbard et.al Patients referred to the heart clinic for the first time, is during the individual program offered to participate in the group program. Participants play once facilitated by a specialized trained nurse. Questionnaire answered, at final session. Respectively responded 96% (110/114) patients and 90% (38/42) relatives. Data presented using descriptive statistics.

**Results:** 96% (142/156) of participants agree or very much agree to the education giving knowledge and understandable. 92% agree or very much agree in being confident in following and understanding lifestyles changes. 77% (114/148) scores the reflection cards to 6-10 (score 1 = poor and 10 = excellent). 50% (74/142) added effect as: new learning, check understanding, giving more dialog and personal involvement. Score 2-6 given by 23% (34/148) with statements, the game is not as important. The group program with all 3 session rates to 6-10 by 95%(152/156) of the participants.

**Conclusion:** We find Patients attitudes towards the reflection cards very positively and several expressed that it leads to understanding and learning. The group program seems to facilitate reflection and understanding in lifestyle changes. Patient seem to have less contact to the clinic when both being in individual and group program but it calls for further investigation.

## P2040

## Socio-demographic and clinical determinants of poor self-care in patients with heart failure and diabetes mellitus

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**Background:** Patients with both Heart Failure (HF) and Diabetes Mellitus (DM) are at risk of severe adverse outcomes. Self-care is vital in both conditions. The effect of DM on HF self-care is unclear and determinants of poor self-care in HF-DM patients are unknown.

**Objectives:** To compare self-care of HF patients with and without DM; to estimate the effect of DM on self-care of HF patients; to identify socio-demographic and clinical determinants of self-care in HF-DM patients.

**Methods:** A multicentre cross-sectional observational study was conducted. 1192 adults with confirmed diagnosis of HF were enrolled. Socio-demographic and clinical data were collected from medical records. Self-care maintenance, management and confidence were measured by the Self-Care of Heart Failure Index (scores range 0-100; higher scores=better self-care). Self-care of HF-DM patients versus HF without DM was compared by linear regression. Multiple linear regressions were performed to estimate the effect of DM on self-care of HF patients and to identify determinants of self-care in HF-DM patients.

**Results:** 379 HF patients (31.8%) were affected by DM. Self-care was sub-optimal in HF patients with and without DM (means range from 53.2 to 55.6). Self-care maintenance ( $p = 0.13$ ), management ( $p = 0.21$ ) and confidence ( $p = 0.51$ ) were not statistically different between HF patients with versus without DM. No statistically significant associations were found between the presence of DM and self-care maintenance ( $p = 0.12$ ), management ( $p = 0.21$ ) or confidence ( $p = 0.51$ ) of HF patients. Number of medications ( $p = 0.04$ ), cognitive status ( $p = 0.04$ ), New York Heart Association (NYHA) functional class ( $p = 0.01$ ) and self-confidence ( $p < 0.01$ ) were determinants of self-care maintenance in HF-DM patients. Number of medications ( $p = 0.02$ ), cognitive status ( $p = 0.01$ ) and self-care confidence ( $p < 0.01$ ) were determinants of self-care management. Number of medications ( $p = 0.01$ ), cognitive status ( $p < 0.01$ ) and family income ( $p = 0.01$ ) were determinants of self-care confidence.

**Conclusions:** Self-care of HF-DM patients is poor but no worse than the self-care of HF patients without DM. HF-DM patients taking fewer medications, having low income, low self-care confidence, limited cognitive function and worse NYHA class are at higher risk of poor self-care. Future studies are needed to describe DM self-care in HF-DM patients, to develop and test interventions, and to evaluate the effect of DM self-care on HF-DM patients' outcomes.

## P2041

## Assessing the relationship between frailty syndrome and self-care in chronic heart failure

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**Introduction:** Frailty syndrome frequently co-occurs with heart failure (HF), adversely affecting the course of the disease in various ways, such as restricting the patient's active participation in the treatment process. The optimization



of treatment and of patients' quality of life requires a methodical identification of predictors of decreased self-control and self-care capabilities in heart failure.

**Purpose:** The purpose of the study was to assess the correlation between two variables, frailty syndrome and self-care, in a group of chronic heart failure patients.

**Material and methods:** The study included 330 patients (148 female, 182 male; mean age  $\pm$  SD: 72.08  $\pm$  7.92) with clinically confirmed chronic heart failure, hospitalized in the Cardiology Department. To obtain research material, the authors used two standardized research instruments: the Tilburg Frailty Indicator (TFI) for frailty syndrome assessment and The European Heart Failure Self-care Behavior Scale (EHFScBS) to evaluate self-care in HF. Correlations and differences at  $p < 0.05$  were considered statistically significant.

**Results:** Frailty syndrome was identified in 86.67% of patients. Mean TFI score in the study group was  $M \pm SD = 7.22 \pm 2.72$  points. Mean score in the physical component of the TFI was  $M \pm SD = 4.12 \pm 1.82$  points, mean psychological component score was  $M \pm SD = 1.79 \pm 0.98$  points; mean social component score was  $M \pm SD = 1.30 \pm 0.93$  points. Mean self-care score was  $M \pm SD = 37.93 \pm 7.34$  points. Multiple regression analysis showed that the score in the physical component of the TFI was a significant predictor for decreased self-care capabilities in HF ( $\beta = -0.178$ ;  $p = 0.01$ ).

**Conclusions:** 1. Lower scores in the physical component of the TFI are correlated with better self-care in heart failure. 2. The physical domain of the TFI is an independent predictor of self-care in heart failure.

## P2042

### Differential associations of somatic and cognitive depressive symptoms with vitamin D deficiency and cardiac event-free survival in patients with heart failure

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**Background:** Depressive symptoms and vitamin D deficiency independently predict shorter cardiac event-free survival in patients with heart failure (HF). There has been limited evidence on the differential association of specific symptoms of depression with cardiac events. However, whether specific symptoms of depression are associated with vitamin D deficiency and cardiac event-free survival in HF patients has not been examined.

**Purpose:** We hypothesized that somatic symptoms of depression would have higher risk for vitamin D deficiency and cardiac events compared to cognitive symptoms of depression.

**Methods:** A total of 204 patients with HF (age 63  $\pm$  11 years, 33% female) completed the Patient Health Questionnaire-9 (PHQ-9) to assess depressive symptoms. Nutritional Analysis program were used to determine average daily intake of vitamin D through a 3-day food diary. Patients with >80% probability of deficiency were defined as having a diet deficient in vitamin D. Patients were followed for 1 year to determine time to first event of hospitalization due to cardiac problems or cardiac death. Covariate data on age, gender, body mass index, New York Heart Association class, ejection fraction, comorbidities, and prescribed medications including anti-depressants were obtained from patient interview and review of medical records. Hypotheses were tested by hierarchical logistic and Cox proportional hazard regressions.

**Results:** The mean score  $\pm$  SD on somatic depressive symptoms of the PHQ-9 was 4.5  $\pm$  3.3; on cognitive depressive symptoms, it was 2.6  $\pm$  2.8. Sixty patients (29.4%) had depressive symptoms indicating  $\geq 10$  of total PHQ-9 score. The average intake of vitamin D was 3.8  $\pm$  2.7 mcg/day and 122 patients (59.8%) had vitamin D deficiency. During 1-year follow-up period, 11 patients (5.4%) died and 46 patients (22.5%) were hospitalized due to cardiac problems. After controlling for all covariates, somatic depressive symptoms (HR=1.10, 95% CI=1.01-1.19,  $p = .025$ ) and vitamin D deficiency (HR=1.88, 95% CI=1.09-3.25,  $p = .023$ ) predicted shorter cardiac event-free survival, but cognitive depressive symptoms (HR=1.10, 95% CI=0.99-1.21,  $p = .064$ ) did not. In hierarchical logistic regression, somatic depressive symptoms ( $\beta = 1.14$ ,  $p = .036$ ) were associated with vitamin D deficiency, while there was no significant association of cognitive depressive symptoms ( $\beta = 0.94$ ,  $p = .388$ ) with vitamin D deficiency after controlling for all covariates.

**Conclusions:** In patients with HF, somatic depressive symptoms independently predicted shorter cardiac event-free survival, whereas cognitive depressive symptoms did not. This findings show that inadequate intake vitamin D is one possible mechanism to explain how somatic depressive symptoms contributed to adverse health outcomes for patients with HF. Future study is required to determine whether vitamin D adequacy could play a protective role in the impact of somatic depressive symptoms on cardiac events in patients with HF.

## P2043

### The effects of discharge planning on self-care ability in patients undergoing percutaneous transluminal coronary angioplasty in Iran.

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**Introduction:** Angioplasty is one of the most common methods for treatment coronary artery diseases. On the other hand one of the major issues in improving quality of care is patient participation in the treatment and self-care which can, in most cases, including for patients coronary angioplasty treatment, especially for continuity of care after discharge considered.

**Material and Method:** Intervention group patients in the period of one month after discharge according to required two home visits are. One month after discharge demographic information questionnaire and the self-care ability by two groups of patients completed. Data analysis with software SPSS version 22 and using descriptive statistics done.

**Results:** The study was difference significant statistics there is no control and intervention groups ( $P = 0.181$ ). Comparison averages of the self-care ability before and after the intervention in two group showed statistically significant differences ( $p = 0.0001$ ). As a result of paired t-test showed that statistically significant differences in the control group ( $P = 0.001$ ) and the intervention group ( $P = 0.0001$ ) during one month after discharge to admission. However, the difference between the means of the scores obtained at the time of admission and one month after discharge is much greater in the intervention group than the control group.

**Conclusion:** Recommended health care providers and nurses by strengthening their self-care on discharge planning, improve the ability of self-care and reduce its complications in patients in coronary angioplasty.

## POPULATION STUDIES / EPIDEMIOLOGY

## P2044

### Appropriateness of heart failure therapy in Bulgaria

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**Objective:** Heart failure (HF) is a leading health and socio-economic problem worldwide. Guideline-recommended therapy could significantly improve morbidity and mortality in HF patients. It is not known, however, to what extent cardiologists are keeping with the guidelines regarding HF therapy. We aimed to evaluate the appropriateness of medical therapy in HF patients in Bulgaria with respect to current guidelines.

**Methods:** From October to November 2015 Bulgarian cardiologists filled anonymously and voluntary a questionnaire, describing medical therapy of HF patients in their practice. 475 ambulatory patients were included in the registry. Mean age was 70  $\pm$  10 years, 54% were male, concomitant diseases were as follows: arterial hypertension - 340 patients (72%), diabetes - 118 (5%), coronary artery disease - 305 (64%), cerebro-vascular disease - 91 (19%), atrial fibrillation - 135 (28%).

**Results:** Most of the patients (81%) were in functional class III, and the majority had pulmonary (58%) and peripheral (61%) congestion. 176 patients (37%) were prescribed an angiotensin-converting enzyme inhibitor (ACEi), 150 (32%) - angiotensin-receptor blocker (ARB), 299 (63%) - beta-blocker (BB) and 38 (8%) - aldosterone-receptor antagonist (ARA).

The dosages of most commonly prescribed HF medications were as follows (mg): enalapril - 18  $\pm$  4, perindopril - 8  $\pm$  4, ramipril - 7  $\pm$  3, valsartan - 166  $\pm$  54, candesartan - 17  $\pm$  16, olmesartan - 28  $\pm$  11, telmisartan - 69  $\pm$  20, bisoprolol 6  $\pm$  5, metoprolol - 61  $\pm$  31, carvedilol - 16  $\pm$  12, spironolacton 26  $\pm$  9.

**Conclusions:** A significant part of HF patients in Bulgaria do not receive appropriate and guideline-recommended medical therapy. Those who are prescribed ACEis, ARBs, BBs and ARAs are far from reaching the target dosages.

## P2045

### Characteristics of police patients with heart failure.

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**Intro:** It's well known high prevalence in cardiovascular disease, and so in heart failure. At the police hospital, we saw this evolution in our patients (p). We make our own data base to analyse their characteristics.

**Objectives:** To define characteristics in p with decompensate heart failure (DHF) in our population.

**Method:** It is a prospective analysis of 370 p admitted for DHF, consecutively, in our Cardiology Service, from June 2012 to November 2015, with a median follow-up of 23 months (Q1 13 - Q3 33). Quantitative variables with normal distribution were expressed with medium and with standard deviation (analysed by Fisher's Test);

those with not normal distribution, were expressed with median (m) and quartiles (analysed by Mann Whitney's Test). Dichotomous variables were analysed by Chi2.

**Results:** We saw population with a m of 71 years old (Q1 62 - Q3 80), were predominately males (65.5%). In cardiovascular risk factors (CRF), we found 79.5% hypertension, 32.5% diabetics, 46.9% smokers, 35.9% dislipemics. Predominant etiology was ischemic one (36.1%). At admission 39.7% p had history of severe ventricular dysfunction; more frequent cause of decompensation was lack of treatment or non-compliance (30.3%), progression of underlying disease and arrhythmias were in 2° place (15.1% and 15.4%, respectively). With the echo, we found dilated ventricles (m diameters in diastole 56.3 mm, in systole 42 mm), m ejection fraction (EF) of 37% (35.1% p had EF < 35%, 49.5% EF < 45%), mild mitral regurgitation were observed in 45% p (31.7% moderate, 8.3% severe). 20.5% had history of myocardial infarction, 10% any device (pacemaker 9.2%). At labs, the m were abnormal values in glycemia (126 mg/ml), glomerular filtration rate (by MDRD 56.2 ml/min/1.73 m2 and by creatinine clearance in 24 hours 52 ml/min/1.73 m2), albumin (3.3 g/g). We remark that 68.7% p increased their seric creatinine during admission. At EKG, 55.7% had sinus rhythm, 37.2% had atrial fibrillation or flutter; QRS width had a m value of 100 msec; 25.5% showed LBBB. About pre hospital treatment, 59.9% received ACE inhibitors or ARB, 59% beta blockers, 17% aldosterone antagonists, 20.5% amiodarone, 49% diuretics. Mortality during admission was 4.6%, at the following-up was 35.2%. Readmissions were 25.6%.

**Conclusions:** We have an aged population, with high prevalence of CRF. Even known HF history, they have poor adherence to treatment. They have severe dysfunction, however have few p with devices. Most important co morbidity is renal dysfunction. We can improve the ambulatory treatment. We have no great differences in mortality and readmissions with international records.

**P2046**  
**Changing trends in heart failure hospitalizations 2010-2015 for patients with HFpEF and HFrEF**

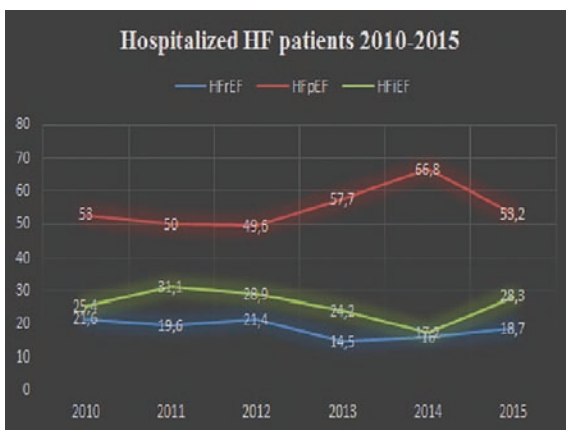
B Branimir Kanazirev<sup>1</sup>; MSD Dimova<sup>1</sup>; VZZ Zlateva<sup>1</sup>; AAK Kirkorova<sup>1</sup>; JDK Kashlov<sup>1</sup>  
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**Materials and methods:** In 1615 hospitalized patients ejection fraction, mean age and percentage female gender were calculated during a period of six year from 2010 to 2015. Ejection fraction above 50% was considered preserved, below 40 % was considered reduced and in between was estimated as intermediate.

**Results:** Trends in hospitalization of patients with heart failure were observed with increase of mean age and increase of the percentage of hospitalized female gender. Concomitantly a tendency of increasing the percentage of patients with heart failure with preserved ejection fraction (HFpEF) and a decrease of the percentage of patients with heart failure with reduced ejection fraction(HFrEF) was noted. Patients with HF with intermediate EF also showed some variation during the years.

**Conclusions:** Although these changes did not reach statistical significance tendencies of changing trends in hospitalized patients are observed even in a relatively short period of time.

Mean Age and percentage of females admit						
	2010	2011	2012	2013	2014	2015
Age	70,1	71,1	73,1	72,4	72,0	72,8
Females %	52	54	46	50	57,4	57,2



Hospitalized HF patients 2010-2015

**P2047**  
**Risk factor differences by geography, income level and ethnicity among patients with heart failure from eleven Asian regions (the asian-hf registry)**

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**Background:** Rapid epidemiological transition has contributed to a surge in cardiovascular diseases, including heart failure (HF), in Asia.

**Aim:** To determine differences in risk factors based on geographic region, stage of economic development and ethnicity among Asian patients with HF

**Methods:** ASIAN-HF is a multicentre prospective registry of 5276 patients with HF with reduced ejection fraction (≤40%) from 11 Asian regions (China, Hong Kong, India, Indonesia, Japan, Korea, Malaysia, Philippines, Singapore, Taiwan, Thailand). We compared 3 key risk factors: ischaemic heart disease (IHD), hypertension (HTN) and diabetes mellitus (DM) by geographic region (by United Nations), income level (by WHO: Lower – Indonesia, Philippines, India; Middle – China, Thailand, Malaysia; Higher – Singapore, Hong Kong, Taiwan, South Korea, Japan) and ethnicity (Chinese [29.6%], Indian [31.3%], Malay [15.4%], Japanese [10.3%], Korean [6.0%], Thai [3.6%] and Indigenous South-East [SE] Asians [2.5%]).

**Results:** Mean age of Asian patients was strikingly low (60±13 years), with two-thirds <65 years old, yet 64% had 2 or more comorbidities. Patients from East Asia and higher income countries were older while Malays were the youngest ethnic group. IHD was prevalent in 58% overall; with highest prevalence in SE Asia (70%), and lowest in East Asia (44%). Prevalence was not related to income level, but strongly influenced by ethnicity (Indian [OR=3.1]; Malay [OR=1.6] and Thai [OR=1.7] vs Chinese). HTN was prevalent in 52% overall; with higher prevalence in higher income regions (OR=1.9 vs lower income). Malays (62%) and Chinese (58%) had the highest prevalence; but these ethnic differences were influenced by geography: Indians and Chinese from SE Asia had higher prevalence compared to Indians from South Asia (73% vs 38%) and Chinese from East Asia (67% vs 48%); all p = 0.001. DM was prevalent in 40% overall; with strikingly higher prevalence in higher income regions (OR=2.7 vs lower income), as well as geographic regions of SE Asia (46%) and South Asia (37%). Median duration of diabetes was 8 years (IQR 4-14). Indians (OR =3.1) and Malays (OR =1.67) had the highest adjusted odds of diabetes compared with Chinese, whereas Koreans had the lowest (OR = 0.67).

**Conclusions:** These first prospective multinational data demonstrate significant heterogeneity among Asian patients with HF, depending on geographic region, socioeconomic status, and ethnicity. These findings carry implications for managing the HF epidemic in Asia, and suggest that lifestyle, genetic and environmental factors are important considerations.

**P2048**  
**Pharmacotherapy for heart failure in adult patients with congenital heart disease: initial results from challenge registry**

Hellenic Cardiological Society  
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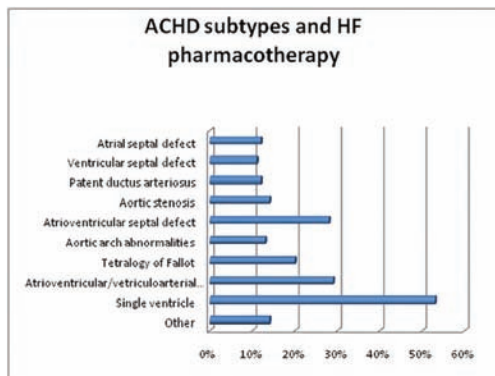
**Introduction:** As adult congenital heart disease (ACHD) population ages, prevalence of heart failure (HF) rises in these patients.

**Purpose:** We aimed to highlight the characteristics of ACHD patients who are under medical therapy for HF.

**Methods:** Data from February 2012 until October 2015 were collected from the national registry of ACHD in Greece (CHALLENGE). For severity of ACHD subtypes, Bethesda classification was used.

**Results:** A total of 1705 ACHD population were included in CHALLENGE registry, of which 286 (16.8%) were under HF medical treatment. Physicians were more likely to prescribe HF pharmacotherapy in ACHD patients with single ventricle (SV) (53%), followed by atrioventricular/ventriculoarterial (AV/VA) abnormal connections (29%), atrioventricular septal defect (AVSD) (28%) and tetralogy of Fallot (TOF) (20%). Regarding the elderly (> 60 years old) with CHD (n = 182), 76 patients (42%) were under HF treatment. Patients under medical treatment were older (45.2 vs 34.7 years,  $p < 0.001$ ), more frequently males (52.8% vs 45.8%,  $p < 0.001$ ), had more severe CHD (27.3% vs 10.3%,  $p < 0.001$ ), were more symptomatic (NYHA III/IV 27.3% vs 4.5%,  $p < 0.001$ ), underwent multiple ( $\geq 2$ ) surgeries (34.6% vs 16.1%,  $p < 0.001$ ) and were more frequently under antiarrhythmic medical therapy (40.2% vs 10.9%,  $p < 0.001$ ).

**Conclusion:** In Greece, the most common forms of ACHD that required HF treatment were SV, AV/VA abnormal connections, AVSD and TOF. Patients with advanced age, male gender and more advanced disease were prone to be under HF medical therapy.



ACHD subtypes and HF pharmacotherapy

## PSYCHOSOCIAL / ETHICAL CONCEPTS / EDUCATION

### P2049

#### Heart failure awareness: a cross-sectional study on misconceptions and educational opportunities

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**Background:** Heart failure (HF) is a growing cause of morbidity and mortality. The vast majority of HF patients lack basic comprehension of HF and self-care, which manifests itself in suboptimal outcomes in such patients.

**Purpose:** This study targeted at establishing the preexisting level of knowledge on HF in Lithuania and evaluating the effects of a single lecture on such knowledge.

**Methods:** A cross sectional survey study using an anonymous questionnaire designed by the German Competence Network Heart Failure (CNHF), provided to the participants prior to and after a standardized lecture on HF. The survey was conducted at five hospitals and two shopping malls, during public events. The CNHF questionnaire consisted of two sets of questions focusing on individual characteristics of the respondent and HF-related knowledge. A completion of the questionnaire was followed by a 20-minute standardized lecture on HF. The participants were given the opportunity to pose questions. After the lecture, the same questionnaire was completed for the second time. The gathered data was verified by a standardized procedure in Germany, and then transferred into a databank.

**Results:** A total of 1025 Lithuanian respondents, including patients, hospital employees, and shopping malls' visitors, participated in survey. The majority (60%) of the respondents were female. The rate of the participants with occupational experience in the medical field was 15%. The majority (79%) of the study population had heard about HF previously. Overall pre-existing HF-knowledge was insufficient. Only 44% of the respondents recognized the grim prognosis of HF once the patient needs hospitalization for HF. Evaluation of pre-existing knowledge also revealed that a whopping 58% of subjects who had worked in the medical field mistakenly perceived exercise as harmful for those with HF. Male participants were more prone to falsely attributing HF to normal process of ageing than their female counterparts

(58% and 42%, respectively,  $p < 0.001$ ). The lecture significantly increased the rate of correct answers in most of the questions. Particularly notable gains were observed in those without prior medical experience.

**Conclusions:** The HF-knowledge in the mixed study population was lacking. The standardized lecture successfully improved theoretical HF-knowledge short-term. Long-lasting impact, however, remains unclear.

### P2050

#### Differences of psychological features in patients with HF: results of a CAPS-LOCK HF (Complex Assessment of Psychological Status Located in Heart Failure) study

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**Background:** It is likely that the psychological reaction towards heart failure (HF) differs between males and females, which may determine sex-oriented and aetiology-oriented treatment and recommendations.

**Purpose:** the aim of the study was to assess the psychological state of patients with HF with a reduced ejection fraction (HFrEF) with regard to gender and aetiology.

**Methods:** 758 patients with HFrEF (mean age – 64 ± 11 years, men – 79%, NYHA class III-IV – 40%, ischemic aetiology – 61%) were included in a prospective Polish multicenter Caps-Lock-HF study. Scores on five different self-report inventories: CISS (Coping Styles in Stressful Situations), MHLCC (Multidimensional Health Locus of Control), GSES (Generalised Self-efficacy scale), BDI (Beck Depression Inventory) and a modified Mini-MAC (adjusted to HF) were compared between the sexes taking into account the aetiology of HFrEF.

**Results:** There were differences in the CISS scale and BDI score between the genders – women had higher scales of both the CISS (emotion- and avoidance-oriented) and BDI scores (general score – 14.2 ± 8.7 vs 12.3 ± 8.6,  $p < 0.05$ ; subscale – somatic score – 7.3 ± 3.7 vs 6.1 ± 3.7,  $p < 0.05$ ). In the ischemic subpopulation, women had higher BDI scores (general score and subscales – somatic and affective) than men. In the non-ischemic subpopulation the differences between genders were limited to the CISS avoidance-oriented subscale (women – 17.2 ± 3.8 vs men – 16.2 ± 3.4,  $p < 0.05$ ). In a multivariable analysis with demographic and clinical data as the dependent variables, female sex, NYHA class, atrial fibrillation and diabetes mellitus determined the BDI score. Similarly, in the ischemic subpopulation, the female sex, NYHA class and atrial fibrillation determined the BDI score, while in the non-ischemic population NYHA class was the only factor that influenced the BDI score. Adding the psychological data made a significant additional contribution to the prediction of depression status. The final model, which included the demographic, clinical and psychological data, correctly predicted the BDI score in 42.9% of the cases.

**Conclusions:** There are distinct differences in psychological features with regard to gender in patients with HFrEF. Women demonstrate less favourable psychological characteristics in the CISS and BDI scores. Gender-related differences in the BDI score are especially explicit in patients with an ischemic aetiology of HF. The BDI score is related to psychological predisposition.

### P2051

#### Heart failure videos on a famous video-sharing website - the good, the bad, and the ugly: a study on the utility and education value for patients, healthcare practitioners and learners

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**Introduction:** Heart failure is a major international health issue, with over 23 million people worldwide living with heart failure, and a global economic cost of up to \$108 billion per annum. Patient education in heart failure is essential, as therapies become more complex and patient self-care becomes more important. A video-sharing website can be a source of resources on heart failure for both patient and medical education purposes.

**Purpose:** To investigate and characterize heart failure videos on this video-sharing website in terms of content and target audience, and to determine their use for patients, healthcare practitioners and learners.



**Methods:** On October 1st, 2015, it was queried for the search terms "congestive heart failure" and "heart failure." The first 10 pages of results were analyzed, each including 20 videos per page. Videos were analyzed by the authors for their source, target audience, utility for patients, relevance, number of views, advertisements, and content.

**Results:** A total of 200 videos were analyzed, the total views were 4,858,591 (average 24,293 views per video), and 159 videos were found to be relevant to medicine. Individuals of unknown credentials were the source of 32% of the videos, whereas educational companies and hospitals were the source of 16.5% and 11.5%, respectively. Healthcare practitioners and learners were the target audience of 71.7% of the relevant videos, whereas patients were the target audience in only 36.5%. Only 5% of the videos were misleading with endorsement of alternative treatments or treatments lacking evidence, and 16.5% of the videos contained advertisements.

**Conclusion:** This site is a popular video-sharing platform with many videos on heart failure. Most videos are relevant to medicine, but surprisingly the majority are intended for healthcare professionals and learners that may be too advanced for patients. Healthcare practitioners should be aware that users with unknown credentials upload a significant number of heart failure videos. The lack of a commonly agreed upon peer-review process and the lack of a proper rating system raise concerns with the accuracy of information being accessed by heart failure patients on the platform. A more objective and independent peer-reviewed guide on health-related videos would be extremely useful for the public and health professionals.

## P2052

### Right ventricular dysfunction and depressive symptoms in patients with chronic heart failure: clinical and pathophysiological implications

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**Introduction-Purpose:** Depression is a common condition in chronic heart failure (CHF) and has been independently associated with an adverse prognosis. This study investigates the relationship of depressive symptomatology [estimated by Zung self-rating depression scale (Zung SDS)] with echocardiographic indices of right ventricular dysfunction in patients with CHF.

**Methods:** Zung SDS, functional questionnaires [Kansas City Cardiomyopathy Questionnaire (KCCQ) and Minnesota Living with Heart Failure Questionnaire (MLHFQ)], BNP, 6-minute walk test (6MWT) and a comprehensive echocardiographic study were assessed in 70 CHF patients. Thirty-three percent of patients had preserved left ventricular ejection fraction LVEF $\geq$ 50% (HFPEF).

**Results:** Twenty-four patients (34%) were found to have symptoms of mild to severe depression (Zung SDS $\geq$ 44). These patients were older (73.4 $\pm$ 9.2 vs. 68.3 $\pm$ 7.2yrs,  $p=0.014$ ), with significantly higher early mitral inflow velocity to early diastolic mitral annulus TDI velocity ratio (E/e') (14.9 $\pm$ 3.1 vs. 10.2 $\pm$ 2.5,  $p<0.001$ ) and greater left atrial volume (63.6 $\pm$ 12.2 vs. 54.8 $\pm$ 10.7ml,  $p=0.003$ ) compared to those without depression. Moreover, they had greater right ventricular diameter (40.7 $\pm$ 2.6 vs. 36.9 $\pm$ 3.4mm,  $p<0.001$ ), higher systolic pulmonary artery pressure (PASP) (45.1 $\pm$ 6.7 vs. 37.1 $\pm$ 6.1mmHg,  $p<0.001$ ), lower systolic tricuspid annular TDI velocity (sRV) (8.2 $\pm$ 1.1 vs. 11.2 $\pm$ 1.7cm/sec,  $p<0.001$ ), lower early diastolic tricuspid annular TDI velocity (eRV) (7.1 $\pm$ 2.1 vs. 8.7 $\pm$ 2.4cm/sec,  $p=0.013$ ) and greater inferior vena cava diameter at end-expiration (22.1 $\pm$ 2.9 vs. 17.7 $\pm$ 3.2mm,  $p<0.001$ ) compared to HF patients without depression. They also exhibited worse overall summary KCCQ (28.3 $\pm$ 6.1 vs. 47.9 $\pm$ 15.9,  $p<0.001$ ), higher total score MLHFQ (62.0 $\pm$ 12.2 vs. 39.0 $\pm$ 9.4,  $p<0.001$ ), decreased 6MWD (257.1 $\pm$ 78.00 vs. 397.7 $\pm$ 84.2m,  $p<0.001$ ) and increased BNP (713.5 $\pm$ 221.3 vs. 418.9 $\pm$ 223.4pg/ml,  $p<0.001$ ). In multiple linear regression analysis, PASP (B: 0.389, 95%CI: 0.130-0.648,  $P=0.004$ ) and sRV (B: -1.556, 95%CI: -2.399 to -0.713,  $p=0.001$ ) were independent predictors of Zung SDS after adjusting for age and gender. ROC analysis revealed that a PASP cut-off value of 37.5mmHg (91.7% sensitivity and 60.9% specificity,  $p<0.001$ ) and sRV cut-off value of 9.5cm/sec (80.0% sensitivity and 87.5% specificity,  $p<0.001$ ) discriminated CHF patients with depression vs. those without.

**Conclusion:** RV dysfunction seems to play a role in the pathophysiology of depressive status in CHF. Echocardiographic indices of RV dysfunction are independent predictors of depressive symptomatology in these patients.

## P2053

### Factors related to the psychological changings in elderly patients suffering from chronic heart failure

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**Introduction:** Chronic diseases lead to restrictions in all areas of everyday life of patients, especially among elderly. This restrictions due to special conditions can become even more important than symptoms of an illness to a person. Moreover, serious health problems of a relative lead to essential changings in his family. Permanent therapy, frequent appeal for help and hospitalizations affect not only patient's psychological state, but his close surrounding's too. Relatives often don't understand the seriousness of the clinical state and life prognosis of the patient which form barrier to the relations. The purpose of the study was to assess the psychological changings of elderly patient suffering from chronic heart failure (CHF) and its associated factors.

**Methods:** Elderly outpatients (16 M, 26 F, aged 60-88 years), suffering from CHF II-IV functional class NYHA, completed validated questionnaires regarding their quality of life and emotional health. Due to the answer to the question 'Did your heart failure prevent you from living as you wanted during the past month (4 weeks) by making you feel you are a burden to your family or friends?' patients were divided in to two groups. Group 1 – patients with positive answer to the question, group 2 - patients with negative answer to the question. Statistical analysis was made using software packages SPSS 16.0.

**Results:** Patients of group 1 had higher education level ( $n=12$ , 92,3%), compared to patients of group 2 ( $n=15$ , 51,7%),  $p=0,011$ , and more severe symptoms of CHF ( $=0,019$ ). QoL among patients of group 1 was 38,8 $\pm$ 8,4 points compared to patients of group 2 (27,2 $\pm$ 14,8 points),  $=0,036$ . Depression score was 9,0 $\pm$ 2,9 among patients of group 1 and 5,7 $\pm$ 2,9 – of group 2,  $=0,008$ . We found that depression state correlated with QoL worsening ( $=0,007$ ,  $r=0,43$ ). Feeling of burden for close surrounding correlated positively with higher level of education ( $=0,014$ ,  $r=2,56$ ), QoL worsening ( $=0,034$ ,  $r=0,34$ ), depression ( $=0,005$ ,  $r=0,44$ ), severe clinical status ( $=0,029$ ,  $r=2,26$ ); negatively – supporting from family ( $=0,029$ ,  $r=-2,20$ ). Feeling of burden increased by loneliness ( $=0,029$ ,  $r=-0,47$ ), depression ( $=0,017$ ,  $r=0,47$ ) and CHF duration ( $=0,036$ ,  $r=0,43$ ) among women, and only by education level – among man ( $=0,037$ ,  $r=0,52$ ).

**Conclusion:** 31% of elderly patients with CHF experienced feeling of burden for relatives which happened due to QoL worsening, depression, severe clinical status and lack of understanding of the close surrounding. Thus, the early psychological consulting of this patients, especially in the elderly, should be directed to the solution of family problems and saving of favorable climate for the patient, which will help him to stay positive and to prevent progress of depression.

## P2054

### Social support in patients with congestive heart failure after percutaneous coronary intervention

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**Purpose:** To assess the relationship between social support and clinical characteristics in patients with congestive heart failure (CHF) after percutaneous coronary intervention (PCI).

**Methods:** A total of 659 patients after PCI (520 males and 139 females, 78.9% vs 21.1%, respectively, mean age 58.0 $\pm$ 8.8 years) were included in the study. Multi-dimensional Scale of Perceived Social Support (MSPSS) was used for measuring of social support level. Based on CHF severity assessed by NYHA all patients were divided into two groups: group 1 consisted of 520 patients with NYHA functional class I-II and group 2 included 139 patients with NYHA functional class III-IV.

**Results:** The mean values of the MSPSS were 70.9 $\pm$ 11.2 scores for group 1 compared to 68.5 $\pm$ 13.5 scores for group 2 ( $=0.03$ ). Group 1 reported low social support level in 4.3%, moderate in 28.1% and high in 67.6% of patients, whereas in group 2 low, moderate and high social support levels were observed in 7.2%, 38.8% and 54.0% of patients, respectively ( $=0.01$ ).

Multiple logistic regression analysis for confounding factors such as age, gender, smoking status, alcohol abuse, diabetes mellitus, arterial hypertension, office systolic and diastolic blood pressure, total cholesterol, left ventricular ejection fraction and severity of coronary lesions by SYNTAX score showed the independent association of CHF with social support levels (OR = 0.47; 95% CI 0.23-0.98).

**Conclusion:** Patients with CHF functional class III-IV more frequently had low and moderate social support levels, whereas high level was detected more frequently in patients with CHF functional class I-II. Severity of CHF was independently associated with social support levels.

## P2055

### How men with heart failure perceive male and female faces?

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The perception of face is particularly important for social functioning.

As health status may affect the perception of other people (and also their faces), we investigated if middle-aged men with heart failure (HF) evaluate facial and non-facial stimuli in a different way as compared to healthy, age-matched controls.

65 men with clinically confirmed HF (NYHA II, age:  $58 \pm 11$  years) and 143 healthy men (age:  $51 \pm 14$  years) evaluated the aesthetics of photographs using a 7-point scale (where 1 = the lowest score, 7 = the highest score). The set included 15 photographs (9x13 cm) of 10 adult faces (en-face or half-profiles; 5 women, 5 men) and 5 non-facial pictures (landscapes and animals taken from the Internet). Scores were averaged separately for men's faces, women's faces and non-facial stimuli in order to reflect how a particular individual perceive the aesthetics of men, women and non-facial stimuli presented in the photographs.

Comparing to healthy controls, HF patients rated the pictures presenting men and women using significantly higher scores:  $4.29 \pm 0.12$  vs.  $3.52 \pm 0.07$  ( $p < 0.0001$ ) for pictures of men and  $5.52 \pm 0.10$  vs.  $4.82 \pm 0.06$  ( $p = 0.0002$ ) for pictures of women. However, this effect did not occur for non-facial stimuli ( $5.27 \pm 0.12$  vs.  $4.87 \pm 0.08$ ,  $p = 0.16$ ).

The observed differences in perception between healthy men and HF patients seem to be face-specific.

It may suggest that the range of non-somatic psychoconsequences of HF is very wide and it affects features important for patients' psycho-social functioning, essential for adequate social support and proper quality of life.

## EXERCISE TESTING & TRAINING

### P2056

#### prediction of exercise training effect of cardiac rehabilitation using rate pressure product, and peak METs and heart rate recovery on post revascularized patients

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**Background:** Training effect using rate-pressure product at a 5-metabolic equivalent workload (RPP5), and the change in estimated peak MET (METPK) during treadmill testing baseline fitness were found to be the best predictors of change in exercise tolerance after training. Heart rate recovery (HRR) and RPP5 are also measurable tools that can be used as an outcomes parameter.

**Methods:** Resting heart rate, systolic blood pressure and computed HRR, RPP5, and METPK during treadmill stress test (TST) at baseline and after completion phase II Cardiac rehabilitation were determined.

**Results:** A total of 41 patients were enrolled in the study. 61% were revascularized with percutaneous coronary angioplasty while 39% underwent coronary artery bypass graft. A significant improvement in exercise capacity in terms of METSpk was seen in the baseline TST compared with exit TST. Similarly there was an improvement trend in RPP and HRR at baseline TST compared with exit TST but was not statistically significant.

**Conclusion:** The significant improvement in terms of METpk is consistent with findings from previous studies that cardiac rehabilitation improves exercise tolerance. However baseline fitness appears to play a role in low training effect in patients under the NIH protocol. Similarly the comparison of the HRR and RPP in the baseline and exit TST showed an improvement trend.

Patient Demographics	
Table 1 Profile of Patients	
Age (years), mean + SD	54.9 ± 11.4
Gender, n, %	
Male	39 (95.1)
Female	2 (4.9)
Diagnosis, n, %	
CAD	21 (51.2)
CAD 2-V	1 (2.4)
CAD 3-V	4 (9.8)
NSTEMI	10 (24.4)
STEMI	5 (12.2)
Intervention, n, %	
CABG	16 (39.0)
PCI	25 (61.0)

### P2057

#### A novel cardiopulmonary exercise testing prognosticating algorithm for heart failure patients with reduced and preserved ejection fraction

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**Objectives:** cardiopulmonary exercise testing (CPET) is a well known prognostic tool in chronic heart failure (CHF) but multitude of parameters impedes the interpretation of CPET in common practice. The aim of the study was to create a simple algorithm for predicting cardiovascular mortality (CVM) using CPET indices in optimally treated CHF patients with reduced and preserved left ventricular ejection fraction.

**Methods:** 111 optimally treated patients (83 men, 28 women, mean age  $60.6 \pm 12.8$  years,) with CHF NYHA class I-III of various etiologies were enrolled in the study. 30,6% had preserved LVEF. After performing CPET the patients were followed up for  $25.1 \pm 9.7$  months in average. Cardiovascular mortality (CVM) was considered the primary end-point. Using the method of classification and regression trees (C&RT) we analyzed the prognostic value of peak oxygen consumption (VO<sub>2</sub>peak) and its derivatives (Weber class, % from predicted VO<sub>2</sub>peak, oxygen uptake efficiency slope), ventilatory equivalent for carbon dioxide (VE/VCO<sub>2</sub>), ventilatory class derived from VE/VCO<sub>2</sub>, partial pressure of end-tidal carbon dioxide (PetCO<sub>2</sub>) at rest and at the peak load, presence of exercise oscillatory ventilation, blood pressure (BP) and ECG response to exercise, heart rate (HR) recovery in 1 minute after test termination and the reason for test termination. Heart Failure Survival Score (HFSS) model combining VO<sub>2</sub> peak with LVEF, mean BP, serum sodium, presence of coronary heart disease, QRS width and resting HR was also included into analysis.

**Results:** CVM due to sudden cardiac death (n=7) and progression of HF (n=13) amounted 18,0%. According to C&RT analysis combination of HFSS and ventilatory class allowed to work out an algorithm accurately predicting CVM in 87,4% of cases. In patients with HFSS ≤ 6,61 probability of cardiovascular death within 2 years amounted 72,7%, and with HFSS > 6,61 - 12,0%. Addition of ventilatory class specified the prognosis in patients with HFSS > 6,61 predicting CVM with probability of 7,7% in I-III ventilatory class and of 55,6% in IV ventilatory class. Addition of other CPET indices didn't adjust the prognosis.

**Conclusions:** In patients with CHF with both reduced and preserved LVEF combination of Heart Failure Survival Score based on VO<sub>2</sub> peak and ventilatory class provides a useful algorithm for predicting cardiovascular mortality.

### P2058

#### The pattern of oscillatory ventilation during exercise and recovery in CPET is associated with the severity of chronic heart failure

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**Background/Introduction:** Oscillatory ventilation (OV) in chronic heart failure (CHF) is described by the amplitude and the length of cyclic fluctuations in breathing. The clinical significance of the pattern of this phenomenon during exercise and during recovery has not been investigated yet.

**Purpose:** To investigate the relationship between OV characteristics during exercise and recovery phase of CPET with indices of CHF severity.

**Methods:** Ninety one consecutive patients with systolic CHF were analyzed (age:  $55 \pm 11$  years, VO<sub>2</sub>peak:  $18 \pm 6$  ml/kg/min). All patients underwent a CPET. Cyclic fluctuations in ventilation with an amplitude during exercise greater than 15% of the average resting amplitude that lasted longer than 60% of total exercise duration, were considered as exercise OV. The same criteria applied for the recovery phase lasting 3 min. Length was also measured for each fluctuation. The average length (λ<sub>aver</sub>) of exercise OV of each patient was used in the analysis. The median value of λ<sub>aver</sub> (39.5 sec) of all exercise OV patients was used as cut off to define two groups [λ<sub>aver</sub>(1) ≤ 39.5 sec, λ<sub>aver</sub>(2) > 39.5 sec]. Also, the average amplitude (haver) was similarly studied [median value: 6.1 L/min, haver(1) ≤, haver(2) >]. Parameters of CPET compared in each group were: VO<sub>2</sub>peak, %VO<sub>2</sub>peak predicted, VO<sub>2</sub> at anaerobic threshold (VO<sub>2</sub>AT), ventilatory equivalent for CO<sub>2</sub> (VE/VCO<sub>2</sub>slope), maximum ventilation (V<sub>E</sub>peak), partial pressure of end-tidal carbon dioxide at anaerobic threshold (PetCO<sub>2</sub>AT) and at maximal exertion (PetCO<sub>2</sub>peak), maximum respiratory rate (RR<sub>max</sub>), the first degree slope of VO<sub>2</sub> (VO<sub>2</sub>/tslope) and heart rate (HRR) at the first minute of recovery. Values are expressed as means ± SD.

**Results:** Fifty six patients exhibited exercise OV (62% of CHF). λ<sub>aver</sub> groups differed on % VO<sub>2</sub>peak predicted ( $62.8 \pm 15.4$  vs  $41.5 \pm 6.5$  %,  $p = 0.01$ ), VO<sub>2</sub>AT ( $12.6 \pm 4.5$  vs  $7.5 \pm 3.3$  mL/kg/min,  $p = 0.04$ ), VE/VCO<sub>2</sub>slope ( $34.1 \pm 6.6$  vs  $49.2 \pm 6.9$ ,  $p < 0.01$ ), PetCO<sub>2</sub>AT ( $33.5 \pm 4.0$  vs  $26.7 \pm 4.3$  mmHg,  $p < 0.01$ ), PetCO<sub>2</sub>peak ( $31.5 \pm 4.6$  vs  $18.3 \pm 2.9$  mmHg,  $p < 0.01$ ) and on LVEF ( $33 \pm 9$  vs  $22 \pm 6$  %,  $p = 0.02$ ) comparing

$\lambda_{aver(1)}$  vs  $\lambda_{aver(2)}$ , respectively. haver groups were different in terms of VE<sub>peak</sub>, RR<sub>max</sub> and PetCO<sub>2</sub>peak in favor of haver(1) ( $p < 0.05$ ). Thirty eight out of 56 exercise OV patients exhibited OV during exercise and recovery (42% of CHF, 68% of exercise OV).

**Conclusions:** Average length and amplitude of ventilatory oscillations seem to be significant parameters of exercise OV pattern related to the severity of CHF. Oscillatory ventilation is also present during the recovery phase. These results encourage further prospective studies in larger sample of patients.

## P2059

### A comparison of the effect of outpatient cardiac rehabilitation between acute heart failure and acute myocardial infarction

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**Background:** Cardiac rehabilitation (CR) is a comprehensive management of cardiac disease. Previous studies demonstrated CR improved functional capacity, but improvement rate of functional capacity in acute heart failure and acute myocardial infarction patients (pts) have not been well documented.

**Purpose:** The purpose of this study is to identify the characteristics of population to which CR is more beneficial.

**Method:** We have enrolled 152 pts with cardiopulmonary exercise testing (CPX). We compared the CPX variables between acute heart failure pts (AHF, n = 73) and acute myocardial infarction pts (AMI, n = 79), and with or without CR after 3 and 6 months.

**Result:** The pts with AHF were older than those with AMI ( $70.0 \pm 11.9$  vs.  $66.6 \pm 10.0$  years old;  $p < 0.01$ ) and had lower BMI ( $22.8 \pm 3.6$  vs.  $24.0 \pm 3.4$  kg/m<sup>2</sup>;  $p = 0.02$ ). They were more likely to have more co-morbidities; atrial fibrillation (44.3% vs. 39.0%;  $p < 0.01$ ) and chronic kidney disease (45.3% vs. 22.8%;  $p < 0.01$ ). There was no significant difference in gender of male, the prevalence of hypertension and diabetes between AHF and AMI pts (78.0% vs. 81.0%;  $p = 0.59$ , 69.8% vs. 74.5%;  $p = 0.46$ , 33.0% vs. 29.4%;  $p = 0.58$ , respectively). In pts with AHF, peak VO<sub>2</sub>, VO<sub>2</sub>/pulse and ejection fraction were lower at baseline ( $15.7 \pm 4.3$  vs.  $18.2 \pm 5.0$  ml/kg/min;  $p < 0.01$ ,  $8.4 \pm 2.7$  vs.  $9.6 \pm 3.4$  ml/bpm;  $p < 0.01$ ,  $48.2 \pm 17.4$  vs.  $60.2 \pm 10.0$ %;  $p < 0.01$ , respectively). After 3 months, in pts with AHF, the improvement rate of peak VO<sub>2</sub> was higher in pts with CR than those without CR ( $18.5 \pm 22.0$  vs.  $0.0 \pm 15.9$  % of improving;  $p < 0.01$ ), but in patients with AMI, there was no significant improvement rate of peak VO<sub>2</sub> ( $12.2 \pm 17.1$  vs.  $13.4 \pm 20.3$  % of improving;  $p = 0.82$ ). These trend of improvement were sustained in 6 months (with AHF;  $23.0 \pm 26.7$  vs.  $3.7 \pm 15.4$ % of improving;  $p < 0.01$ , with AMI;  $17.4 \pm 15.2$  vs.  $16.5 \pm 19.9$  % of improving;  $p = 0.86$ ). After the adjustment by age and gender in multiple logistic regression models, CR was independently associated with higher improvement rate in the pts with AHF after 3 and 6 months (20.0% of improving; 95% confidence interval 9.6-30.4,  $p < 0.01$ , 17.7% of improving; 95% confidence interval 4.0-31.4%,  $p = 0.01$ , respectively).

**Conclusion:** The pts with AHF had lower functional capacity, but higher improvement rate with CR than those with AMI after 3 and 6 months. CR was independently associated with higher improvement rate in the pts with AHF.

## P2060

### Non invasive cardiac output measurement in 500 healthy volunteers: validation of new normal values

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**Background:** Cardiac output (CO) is a key parameter in the assessment of cardiac function, and its determination is critical to the diagnosis, treatment and prognostic evaluation of all heart diseases. In clinical practice, the determination of CO is limited by the fact that the validated techniques are invasive, expensive, and mainly performed at rest. Little information is available about CO during exercise.

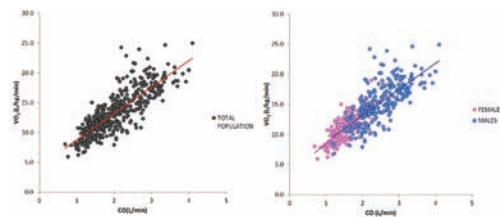
**Purpose:** To assess the behavior of CO during maximal exercise in a large cohort of healthy subjects and to validate normal values.

**Methods:** 500 healthy subjects (age  $44.9 \pm 13.4$ , range 18-77 years, 261 males, 239 females) were enrolled, and they underwent cardiopulmonary exercise testing with non-invasive measurement of cardiac output by inert gas rebreathing technique (Innocor).

**Results:** CO increased from  $5.4 \pm 1.5$ l/min at rest to  $13.2 \pm 3.5$ l/min at peak exercise in the total population, from  $5.9 \pm 1.5$  to  $15.3 \pm 3.3$ l/min in men and from  $4.8 \pm 1.2$  to  $11.0 \pm 2.0$ l/min in women.

**Conclusions:** the simultaneous measurement of CO and oxygen consumption (VO<sub>2</sub>) at peak exercise in a large sample of healthy subjects resulted in an equation predictive of normal reference values of peak exercise cardiac output:

- total population:  $CO = 4.4 \times \text{peak } VO_2 + 4.3$  ( $R^2 = 0.7$ )
- men:  $CO = 4.9 \times \text{peak } VO_2 + 3.6$  ( $R^2 = 0.5$ )
- women:  $CO = 4.3 \times \text{peak } VO_2 + 4.5$  ( $R^2 = 0.5$ )



## P2061

### The impact 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.

**Purpose:** The aim of this study was to evaluate the impact of aerobic exercise training with vascular occlusion in patients with CHF.

**Methods:** Forty 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=20) or a control exercise group (CG, n=20). Exercise was performed at an intensity of 40 to 60% of maximum Peak VO<sub>2</sub>/W (PVO<sub>2</sub>) 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 50-80 mmHg to the systolic pressure ( $209.5 \pm 7.6$ mmHg). We evaluated safety and effect of the intervention on exercise capacity, serum levels of brain natriuretic peptide (BNP) and thigh circumference (15cm above the patella).

**Results:** There were no differences between two groups at study entry (Age:  $61.7 \pm 11.2$  vs.  $61.7 \pm 10.3$  years; Height:  $166.7 \pm 7.4$  vs.  $167.1 \pm 5.8$  cm; Weight:  $68.8 \pm 10.1$  vs.  $69.8 \pm 11.3$  kg; Ejection Fraction:  $48.6 \pm 16.1$  vs.  $52.9 \pm 16.2$  %; PVO<sub>2</sub>:  $17.1 \pm 3.8$  vs.  $15.9 \pm 3.5$  ml/kg/min; BNP:  $128.5 \pm 112.8$  vs.  $142.6 \pm 183.3$  pg/ml; Circumference of right thigh:  $47.7 \pm 6.0$  vs.  $47.9 \pm 4.9$  cm; Circumference of left thigh:  $48.2 \pm 6.1$  vs.  $47.8 \pm 4.9$  cm). Change of PVO<sub>2</sub> was significantly larger in IG than in CG (30.4% vs 16.5%,  $p < 0.05$ ). Change of serum levels of BNP was significantly larger in IG than in CG ( $-58.9 \pm 7.5$  vs.  $7.7 \pm 7.0$  pg/ml,  $p < 0.05$ ). Change of circumference of right thigh was significantly larger in IG than in CG ( $1.9 \pm 1.7$  vs.  $-0.2 \pm 1.2$  cm,  $p < 0.05$ ). Change of circumference of left thigh was significantly larger in IG than in CG ( $2.0 \pm 1.6$  vs.  $-0.1 \pm 1.3$  cm,  $p < 0.05$ ).

**Conclusion:** These results suggest that aerobic exercise training with vascular occlusion can improve, without serious adverse events, exercise capacity, BNP and thigh circumference in patients with CHF.

## PROGNOSIS

## P2062

### Neutrophil gelatinase-associated lipocalin in prediction of in-hospital heart failure and mortality in patients with acute myocardial infarction

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**Background:** Neutrophil Gelatinase-Associated Lipocalin (NGAL) is a sensitive marker of acute kidney injury. It is considered as a novel biomarker for progressive inflammatory process in patients with coronary artery disease and from a pathophysiological perspective in many ways affects the prognosis after myocardial infarction.

**Purpose:** The aim of this study was to evaluate the role of NGAL in prediction of in-hospital heart failure and mortality in patients with ST-segment elevation myocardial infarction treated with fibrinolytic therapy.

**Methods:** We included 42 consecutive ST-segment elevation myocardial infarction patients treated with fibrinolytic therapy (alteplase). The median follow-up time was 7 days (interquartile range, 6 to 8 days). Blood samples were drawn immediately after admission prior to fibrinolytic administration. The end points were in-hospital heart failure (n 19) and all-cause mortality (n 9).

**Results:** Patients with high NGAL ( $\geq 134.05$   $\mu$ g/l; 75th percentile) had significantly increased risk of in-hospital heart failure and all-cause mortality compared to



patients with low NGAL ( $\leq 134.05 \mu\text{g/l}$ ; 75th percentile),  $p = 0.002$ ;  $p = 0.001$ , respectively.

High NGAL was an independent predictor of in-hospital heart failure and all-cause mortality (hazard ratio 2.88; 95% confidence interval: 1.6552-5.0112;  $p = 0.0002$  and hazard ratio 6.45; 95% confidence interval: 1.9466-21.0147;  $p = 0.0002$ , respectively).

**Conclusion:** High plasma NGAL is significant independent predictor of in-hospital heart failure and all-cause mortality in ST-segment elevation myocardial infarction patients treated with fibrinolytic therapy.

## P2063

### Predictors of very short term (< 72 hours) hospital admission or death in patients with decompensation of heart failure attended in primary care setting

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**Background:** Information about prognostic factors related to the heart failure patients attended in primary care is scarce.

**Purpose:** To identify predictive variables (easily measurable at primary care setting) related to a very short term (<72 hours) hospital admission or death in patients with decompensation of heart failure attended in primary care setting.

**Methodology:** HEFESTOS is a cohort study aimed at knowing the main triggers and the prognosis of some factors related to the heart failure decompensations attended in primary care setting Heart failure patients attended as a consequence of an episode of decompensation from 1st, March to 31st December 2015 were included. The following variables were collected: age, sex, heart rate, blood pressure, NYHA class, days since the onset of symptoms, oxygen saturation, diuretic dose, crackles, ankle oedemas, paroxysmal dyspnea, pathological weight gain, orthopnea, hospital admission in the last year, causative factor of decompensation, comorbidity and ejection fraction. Logistic regression adjusting by age and sex were performed.

**Results:** a total of 177 consecutive patients were recruited (50.6% women), mean (SD) age was 81.4 (8.55) years. During the first 72 hours after the visit, 42 patients were hospitalized or died. Paroxysmal dyspnea (OR 3.6, 95% confidence interval 1.36-6.61), weight gain (OR 3.0, 95% confidence interval 1.36-6.69), heart rate > 100 beat/min (OR 3.35, 95% confidence interval 1.18-9.47) and breathing frequency > 25 breath/min (OR 2.36 95% confidence interval 1.08- 5.18) were associated with a higher risk of very short term (<72 hours) hospital admission or death.

**Conclusions:** A small number of variables, easily measurable at primary care setting, may identify those patients who will be more probably to be hospitalized or death.

## P2064

### Factors influencing the occurrence of adverse cardiac events in patients with chronic heart failure

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**Background:** Knowledge of factors influencing the occurrence of adverse cardiac events in patients with chronic heart failure helps to identify those, which should be covered with special care, educational programs and social support. The aim of this study was to determine the factors affecting the prognosis of patients with chronic heart failure, including the degree of compliance by patients with medical recommendations and treatment options used.

**Patients and Methods:** The study included 84 consecutive patients diagnosed with chronic heart failure, hospitalized in the Department of Cardiology in order diagnostic tests or due to decompensation of heart failure. The average age of the study population was 56,  $7 \pm 10.9$  years, the majority of respondents were male (77.4%). Participants were mainly in the III and IV NYHA functional class (56%, 25%) and mean left ventricular ejection fraction was 31, 6%. In univariate and multivariate assessment of risk of death and serious cardiovascular events (MACE) during the annual observation included demographic characteristics, laboratory, clinical, treatment adherence by patients and therapeutic methods used in the course of hospitalization.

**Results:** During the follow-up 15 patients died (17.9%) and 36 (42.9%) experienced MACE. In the study population 39.3% of patients were treated pharmacologically and in 60.7% additional methods of invasive treatment were used. Patients were characterized by a high degree of adherence of pharmacological (94%) and non-pharmacological recommendations, ie physical activity, limiting sodium and fluid intake in the diet, and recommendations related to self-control such as weight control did not achieve a satisfactory result (respectively 50%, 56.5%, 80%, 64.7%). Among patients in whom an improvement in NYHA class after 12 months occur significantly more frequently surgical treatment were used. Risk factors for death were functional class IV NYHA, renal failure, low left ventricular ejection fraction, free marital status and low degree of acceptance rate of the disease. Risk factors for a serious cardiovascular event were: IV NYHA functional class, presence of peripheral edema,

low left ventricular ejection fraction, reduced systolic blood pressure, increased heart rate, urgent admission to hospital, patient age, a free marital state and low physical activity.

**Conclusion:** Patients with chronic heart failure are saddled with a high risk of death or other serious cardiovascular event. The majority of patients comply with the recommendations of pharmacology, while the smaller exhibit discipline in complying with the recommendations for dealing with drug-free. Factors influencing the prognosis is mainly clinical and demographic parameters. Adverse prognostic factor for failure to follow recommendations include lack of regular physical activity.

## P2065

### Alcohol consumption and heart failure in patients with previous revascularization; a substudy of the POP-HF study

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The prognosis of patients (pts) after coronary artery bypass surgery (CABS) has been noted in many studies, but there were no studies which analyzed prognosis of light-to-moderate alcohol consumers with heart failure (HF) after prior CABS. This substudy of POP-HF study (PostOperative Prognosis-Heart Failure study), aimed to evaluating the influence of light-to-moderate alcohol consumption on the HF expression in patients after prior CABS.

**Methods:** The effect of light-to-moderate alcohol consumption was assessed in 124 pts with HF after prior CABS (post bypass group) and control group of 560 pts with HF and without prior CABS, who were followed from April 1988 to December 2015.

**Results:** At baseline post bypass group was slightly younger ( $p = 0.0442$ ), with more men ( $p = 0.4320$ ) and with more pts with previous angina ( $p = 0.0422$ ) and previous AMI ( $p = 0.0399$ ). Control group of pts had more hyperlipidemia ( $p = 0.0422$ ). Other baseline characteristics were similar in both groups of patients. After adjustment for cardiovascular risk factors by logistic regression, alcohol consumption displayed a protective effect against HF in post bypass group of patients, but not in control group of pts.

**Conclusions:** The effect of light-to-moderate alcohol consumption is associated with decreasing risk of HF in pts with prior CABS, but not in pts without prior CABS. This effect of light-to-moderate alcohol consumption is probably because of decreasing of cholesterol, triglycerides and fibrinogen, as well as physiological changes in coronary arteries and decreasing in sympathetic nervous system activity.

## P2066

### Transient loss of consciousness assessment in a University Hospital: from diagnosis to prognosis.

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**Introduction and objectives:** Transient loss of consciousness is a symptom that has several differential etiologic diagnosis, causes significant morbidity and mortality and has a significant impact on quality of life. The purpose of this study was to access the diagnosis and prognosis of these patients admitted in a university hospital.

**Methods:** The study included 125 patients admitted in the emergency room and admitted to the hospital during the year 2013 with transient loss of consciousness. Patients were contacted by phone to evaluate the follow-up to 18 months from the date of admission for each patient.

**Results:** The cardiogenic syncope etiology was the most common cause of transient loss of consciousness (39.2%). The 18-month total mortality was 11.2% but 27.8% of patients with unexplained cause of transient loss of consciousness at discharge died ( $p = 0.031$ ); 20% of patients had recurrent episodes of transient loss of consciousness, moreover 35.3% of patients with reflex syncope had recurrence ( $p = 0.023$ ). 60% of patients who recurred had injuries and/or accidents. 20% of patients with recurrences gave up driving ( $p = 0.019$ ).

**Conclusion:** Transient loss of consciousness results in significant morbidity and mortality, so the diagnosis should be done in a correct and timely manner, following standardized guidelines such as the European Society of Cardiology.

## P2067

### Prognostic factors and outcomes of Extracorporeal membrane oxygenation support in patients who suffered from cardiogenic shock.

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**Purpose:** Extracorporeal oxygenation support(ECMO) has been employed as rescue therapy in patients with hemodynamic failure which were caused by cardiac problems. But mortality of the patients on ECMO remains high. So we investigated the predictors of mortality and outcomes in patients with cardiogenic shock who underwent ECMO.

**Methods:** The records of patients with refractory cardiogenic shock who had applied Extracorporeal oxygenation support were analyzed from may 1,2006 to October 31, 2015 at Kyung Hee University Hospital at Gandong. Refractory cardiogenic shock was defined as sustained hypotension with ongoing tissue hypoperfusion despite of optimal fluid, vasopressor and inotropic therapy.

**Results:** A total of 40 patients with cardiogenic shock required ECMO during study period. Among these, 47.5% of patients (19/40) had successfully been weaned from the ECMO, and survival rate after the application of EMCO was 40.0% (16/40). The proportion of patients who received cardiopulmonary resuscitation was lower in survivor group compared to non-survivor group. (37.5% vs. 70.8%,  $p=0.037$ ) Patients with cardiogenic shock caused by acute coronary syndrome showed poor survival rate compared to those with cardiogenic shock due to other origin such as valvular heart disease, cardiomyopathy and myocarditis. (31.2% vs. 66.7%,  $p=0.028$ ) Serum lactic acid level at the time of initiation of ECMO was higher in non-survivors than survivors. ( $6.67 \pm 7.09$  vs.  $11.44 \pm 6.04$  mg/dL,  $p=0.003$ ) Finally, the peak levels of creatinine kinase-MB and troponin I during ECMO were higher in non-survivors than survivors despite of little differences of initial levels. ( $182.88 \pm 119.71$  vs.  $97.08 \pm 109.94$ ,  $p=0.048$  and  $48.06 \pm 51.70$  vs.  $9.47 \pm 14.58$ ,  $p=0.017$ , respectively)

**Conclusion:** High serum lactate level, high peak level of serum troponin and creatinine kinase-MB isoenzyme, existence of cardiopulmonary resuscitation events had significant impact on mortality of patients with cardiogenic shock. The patients with cardiogenic shock caused by acute coronary syndrome had poor prognosis compared to those with cardiogenic shock due to other cardiac disease, such as valvular heart disease, cardiomyopathy, myocarditis.

Clinical characteristics and parameters			
	Survivor (n = 16)	Non-survivor (n = 24)	p
Lactic acid (mg/dL)	6.67 ± 7.09	11.44 ± 6.04	0.003
CPR events (%)	6 (37.5)	17 (70.8)	0.037
CK-MB (peak, mg/dL)	97.08 ± 109.94	182.88 ± 119.71	0.048
Troponin-I (peak, ng/mL)	9.47 ± 14.58	48.06 ± 51.70	0.017
Etiology (acute coronary syndrome, %)	5 (31.2)	16 (66.7)	0.028

**P2068**

**Validation of the Seattle Heart Failure Model (SHFM) for mortality risk prediction in a portuguese population**

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**Introduction:** Annual mortality rate in heart failure (HF) patients can range between 5 and 75%. The Seattle Heart Failure Model (SHFM) is a multivariate risk prediction model for mortality. It incorporates clinical, laboratory and therapeutic variables, widely available in clinical practice.

**Purpose:** To assess the performance of the SHFM in predicting mortality in a real-world cohort of Portuguese patients with HF.

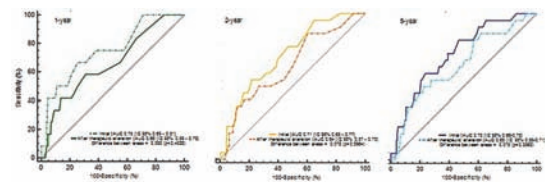
**Methods:** Retrospective cohort study of ambulatory patients with chronic HF. The SHFM was applied in the first visit, using the online calculator (<http://depts.washington.edu/shfm>). In case of adding medications or devices to a patient's therapeutic regimen until a year after the first visit, the SHFM was calculated again according to those changes. Endpoint was all-cause mortality. Kaplan-Meier method estimated observed survival. Discrimination and calibration were assessed respectively by the area under the receiver-operating characteristic (ROC) curve and the Hosmer-Lemeshow (H-L) goodness-of-fit test and graph.

**Results:** During a median follow-up period of 24 months, 58 (26%) patients died. All variables used in the SHFM were analysed in groups with and without endpoint. The SHFM had adequate discrimination throughout the 5-year period (figure). Observed and predicted mortality were similar (table). The H-L chi-square statistic was 7.58 ( $p=0.27$ ), 14.51 ( $p=0.07$ ), 4.61 ( $p=0.80$ ) at 1-,2- and 5-year, respectively.

**Conclusion:** The SHFM was reliable in predicting mortality among Portuguese patients with HF. However absolute risk was overestimated at 1- and 2-year follow-up. Adding therapeutic changes until one year after the first visit decreased SHFM predicted mortality but had no statistically significance improvement in the discriminative capacity of the SHFM.

Performance of the SHFM		
Time	Predicted mortality [SHFM]	Observed mortality (CI 95%)
1-year	6.5 %	5.4 % (2.8% - 9.4%)
1-year (after therapeutic alterations)	6.2 %	
2-year	15.9 %	9.2 % (6.1% - 14.9%)
2-year (after therapeutic alterations)	11.6 %	
5-year	28.1 %	27.3 % (21.2% - 35.4%)
5-year (after therapeutic alterations)	28.0%	

Performance of the SHFM in predicting mortality at 1-, 2- and 5-year in the first visit and after therapeutic alterations done until a year later. SHFM: Seattle Heart Failure Model. CI: Confidence interval.



Discriminative capacity of the SHFM

**P2069**

**Prognostic significance of the echocardiographic assessment of inferior vena cava in chronic heart failure.**

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**Purpose:** Diameter of the inferior vena cava (IVC) and the degree of its inspiratory collapse are used as echocardiographic indices of right atrial pressure. The aim of the study was to assess the relation between IVC diameter and late outcome in patients with chronic heart failure(CHF) with reduced left ventricular ejection fraction (EF) defined as EF<40%.

**Methods:** 225 patients were enrolled in the study (median age: 68 years, female 44%). Clinical data, biochemical markers, and echocardiographic parameters were analysed. All patients underwent echocardiography with assessment of IVC diameter and the degree of its inspiratory collapse. The primary composite endpoint was cardiovascular death and rehospitalizations for acute heart failure decompensation.

**Results:** Patients with CHF in the highest tertile of IVC diameter had lower body mass index, were more likely to be in higher NYHA functional class, to have ischemic heart disease, atrial fibrillation, renal insufficiency, mitral and tricuspid regurgitation, right ventricular dysfunction, larger left and right atrial volumes, higher estimated pulmonary pressure and plasma NTproBNP blood level and were treated with higher doses of diuretics. There was a positive association between IVC diameter and NTproBNP ( $r=0.68$ ;  $p<0,05$ ). 34% of patients reached a primary endpoint at one year follow-up. In a multivariable regression model, higher NYHA functional class, right ventricular dysfunction and larger IVC diameter independently predicted poor outcome. A cut off value of an IVC diameter greater  $\geq 22$  mm predicted MACE with a sensitivity of 86% and a specificity of 72%

**Conclusion:** In patients with CHF with reduced EF, larger IVC diameter identifies patients with worse outcome.

**P2070**

**Comparative analysis of three prognostic scores in heart failure with reduced ejection fraction**

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**Background:** Despite optimal treatment (drugs and devices) for heart failure, many patients continue to show disease progression, ultimately leading to death or cardiac transplantation. We evaluated and compared three scores for prognostic assessment of patients with heart failure and reduced ejection fraction (HF-REF).

**Methods:** We identified 200 HF-REF patients (EF <40% at any point during medical follow-up) who underwent a cardiopulmonary exercise test (CPET) between 2003 and 2013 in a single center. For each patient, we calculated three scores (Heart Failure Survival Score – HFSS; Seattle Heart Failure Score – SHFS; Metabolic

Exercise Cardiac Kidney Indexes – MECKI) using data at the time of the CPET. ROC curve analyses were performed to evaluate and compare the prognostic accuracy of each score for the prediction of all-cause death or cardiac transplantation at 2-years after CPET (study endpoint).

**Results:** Mean age was  $55.1 \pm 10.7$  years and 79.5% were male. The most common heart failure etiology was ischemic heart disease (45%). Median ejection fraction was 30% (interquartile range: 25%-35%). Sixty-six percent had implanted a device with defibrillator capability. During the 2-year follow-up after CPET, 18 patients died and 25 underwent cardiac transplantation. The MECKI score showed the best discriminative power for the study endpoint (see figure). The best cut-off value for the MECKI score was 14.46% (sensitivity 88.37%; specificity 86.62%; NPV 96.5%; PPV 64.4%).

**Conclusion:** In a contemporary population of patients with HF-REF, the MECKI score showed superior prognostic accuracy compared to the HFSS or the SHFS. The present study supports the use of the MECKI score when evaluating HF-REF patients for transplant candidacy.

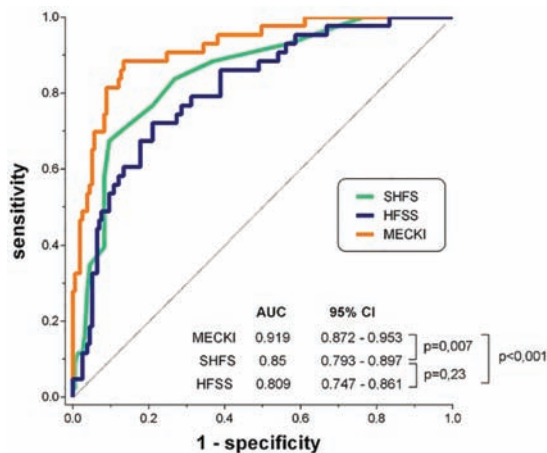


Figure 1 - ROC curve analysis

## P2071

### One year prognostic value of Jung variable for acute heart failure in patients with acute ST elevation myocardial infarction treated invasively

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**Background:** Jung variable is a simple clinical risk index combining age, systolic blood pressure and heart rate. It is designed to be calculated quickly at first medical contact, and all potential subsequent risk stratifications points.

**Aim:** To determine the prognostic accuracy of Jung variable and established risk scores for one year acute heart failure in STEMI patients treated with percutaneous coronary intervention (pPCI), and to validate it in independent STEMI patients population.

**Methods:** Primary and validation prospective studies of consecutive patients were conducted in two tertiary hospitals. One-year acute heart failure (AHF) was assessed as end point of study. The Jung variable was calculated using the equation:  $\text{systolic blood}/(\text{heart rate} \times \text{age}) \times 100$ . The predictive value of Jung variable and TIMI, PAMI, and Zwolle scores were evaluated with Cox regression analysis, calibration of scores with Hosmer-Lemeshow test and the diagnostic accuracy of the scores was assessed using receiver operating characteristic curves, while scores were compared using the DeLong method.

**Results:** Out of 647 patients 70 (10.8%) died and 42 (6.5%) had AHF in primary, while out of 418 patients 33 (7.9%) died and 52 (12.4%) had AHF in validation study. In primary study Jung variable was univariate predictor of AHF, but PAMI score was independent predictor of AHF (1.207 (1.118-1.304);  $p < 0.01$ ), while in validation study Jung variable was independent predictor of AHF (7.911 (3.910-16.005);  $p < 0.01$ ). In a primary study, C-statistic and 95% confidence intervals of PAMI score was the biggest (0.690 (0.600-0.780)), but comparable to Jung variable (0.676 (0.58-0.766)), TIMI and Zwolle risk score ( $p > 0.05$ ). C-statistic for predicting AHF in a validation study was the biggest for Zwolle score (0.876 (0.826-0.925)). C-statistic for Jung variable was well (0.732 (0.655-0.809)), but lower than AUC for other risk scores ( $p < 0.05$ ). Hosmer-Lemeshow test of Jung variable in both studies was nonsignificant ( $p > 0.05$ ).

**Conclusion:** Jung variable, simple, quickly determined at first medical contact, was predictor of one year AHF in primary and validation studies with STEMI patients treated with pPCI. Discriminatory capacity and calibration for Jung variable in both studies was good, comparable to TIMI, PAMI and Zwolle risk scores in primary study.

## P2072

### Hand-carried ultrasound assessment of the inferior vena cava at discharge for predicting readmission and mortality after hospitalization for acute decompensated heart failure

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**Introduction:** Congestion is one of the hallmarks of acute heart failure (HF) and can be measured by inferior vena cava (IVC) ultrasound study, that correlates well with right auricle pressures. IVC collapse at discharge after acute decompensated HF may be of use to predict patients' evolution.

**Purpose:** The aim of our study was to evaluate IVC collapse as mortality and readmission predictor in patients admitted with acute heart failure.

**Methods:** We performed prospective descriptive study with patients with acute HF as main diagnosis who required admission in a university hospital from July 2014 to February 2015. We performed IVC ultrasound at discharge and patients were classified as having IVC collapse  $>$  or  $\leq 50\%$ . Anthropometric, clinical and analytical parameters were collected. We analyzed readmission and mortality as primary outcomes at 30 and 90 days.

**Results:** IVC ultrasound was performed in 145 patients during the study period, with a mean age of  $85.5 \pm 7$  years, 40% males, and 84% with preserved systolic function. The most frequent comorbidities were hypertension (95%), diabetes (38%), atrial fibrillation (68%) and chronic kidney disease (38.6%). Mean follow-up period was 176 days (18-360 days). Readmission rates at 30 days and 90 days were 17% and 32% respectively, 61,5% due to HF. Mortality rates at 30 days and 90 days were 12 patients (8%) and 39 patients (27%), respectively, 15 of them because of HF. 44 patients had IVC collapse  $\leq 50\%$  at discharge and had more HF readmissions than those patients with IVC collapse  $> 50\%$  at 30 days (8 patients-21% vs 7 patients-7%;  $p=0,06$ ) and 90 days (14 patients-42% vs 15 patients-18%;  $p=0,009$ ), respectively. Mortality due to HF was higher among patients with IVC collapse  $\leq 50\%$  both at 30 days (6 patients-14% vs 0,  $p < 0.0001$ ) and 90 days (11 patients-28% vs 1 patient-1%;  $p < 0.0001$ ).

**Conclusions:** IVC collapse at discharge after HF decompensation is a good predictor of death and HF readmission both at 30 and 90 days.

## P2073

### Gender-related risk of dying in patient after cardiac resynchronization

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**Introduction:** Risk of dying significantly increase in heart failure population qualified for cardiac resynchronization, there is a need to evaluate it.

**Methods:** 108 patients (20W; aged  $74.9 \pm 6.3$ ) with advanced heart failure (NYHA II, III, IV ambulatory, left bundle branch block, QRS  $> 120$  ms.) qualified for cardiac resynchronization device implantation were included into study. Patients were divided into groups depending on the type of implanted device. In all patients were assessed 1 and 3-year risk of dying with the use of the Heart Failure Risk Calculator – Maggic (Meta-Analysis Global Group in Chronic Heart Failure).

**Results:** Risk of dying within 1 year in all included patients was  $21,4\% \pm 9,6\%$  and 3-years risk was  $45,2\% \pm 15,7\%$ . Risk of dying within 1 year for women was  $16,2\% \pm 7,1\%$  compared to  $22,5\% \pm 9,7\%$  for men;  $p=0,010$ . Risk of dying within 3 years in women was  $22,5\% \pm 9,7\%$  compared to men  $47,05\% \pm 15,67\%$ ;  $p=0,000$ . Average risks of dying according the type of CRT (pacemaker only versus cardioverter-defibrillator) are presented in the table below. In CRT-pacemaker men had significantly higher risk of dying within 1 year ( $p=0,012$ ) and 3 years ( $p=0,008$ ) compare to women. This relation was not observed for ICD-CRT.

**Conclusion:** Gender-related risk of dying for men is significantly higher if compare to the women. Type of CRT device do not influence risk of death

Risks of dying according type of CRT			
Score	CRT-pacemaker	ICD-CRT	p
Integer score [%]	$26,88 \pm 5,41$	$27,49 \pm 5,48$	0,626
1 years score [%]	$20,66 \pm 9,14$	$21,68 \pm 9,74$	0,639
3 years score [%]	$43,88 \pm 15,58$	$45,65 \pm 15,8$	0,621



## P2074

**Clinical impact of gender in mortality after transcatheter aortic valve implantation for severe aortic stenosis**

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**Background:** Transcatheter Aortic Valve Implantation (TAVI) is an effective alternative to surgical valve replacement in symptomatic patients with severe aortic stenosis at high or extreme surgical risk, but the impact of sex on outcomes remains unclear. The aim of this study was to examine sex differences in outcome after TAVI.

**Methods:** A total of 500 consecutive patients undergoing TAVI were evaluated. Differences in all-cause mortality were examined and the safety endpoints (vascular complications, stroke, myocardial infarction, acute kidney injury) according to the Valve Academic Research Consortium criteria.

**Results:** 295 patients (59%) were female. The prevalence of comorbidities was higher in men compared with women, including coronary artery disease, chronic obstructive pulmonary disease, chronic renal failure (55.6% vs. 34.2%,  $p < 0.001$ , 45.9% vs. 24.1%,  $p = 0.001$  and 31.2% vs. 15.3%,  $p = 0.001$ , respectively). There were not significant differences in complications after TAVI, in-hospital mortality 4.4% for men vs. 3.1% for women,  $p = 0.290$ , vascular complications 2.9% vs. 6.8%,  $p = 0.056$ , stroke 3.4% vs. 3.4%,  $p = 0.988$ . After follow-up of  $34.36 \pm 23$  months, the total mortality was similar in both sex, 25.9% vs. 21%,  $p = 0.206$ . Survival at 1, 2, 3, 4 y 5 years were slightly lower in men 87.6% vs. 91.64%, 81.4% vs. 86.4%, 76.9% vs. 81.7%, 70.4% vs. 79.2%, 64.8% vs. 73.5%, log Rank 2.3,  $p = 0.126$ . There was most total mortality in men 23.2% vs. 15.2%, [OR = 1.688 (95% CI 1.04-2.742),  $p = 0.023$ ] and this results persisted for 2 years, [HR = 1.576 (1.019-2.438),  $p = 0.042$ ].

**Conclusions:** Male sex is associated with worse comorbidities, but the results of procedure and long-term survival were similar in both sex

## P2075

**Predictive value of the shock index on long term mortality in patients treated with successful primary percutaneous coronary intervention**

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**Purpose:** Early identification of patients with ST-elevation myocardial infarction (STEMI) who are at risk for developing cardiogenic shock will allow more aggressive treatment strategy and approach. Preprocedural shock index (SI) measured invasively before primary percutaneous coronary intervention (pPCI) is a strong independent predictor of on in-hospital and medium-term mortality. The aim of this study is to analyse the predictive value of the SI at hospital admission on long-term mortality in patients treated with successful pPCI.

**Method:** We analysed 1619 consecutive STEMI patients who were treated with successful pPCI (postprocedural flow TIMI=3). SI was calculated at hospital admission, before pPCI (SI=heart rate/systolic blood pressure). A positive SI was defined as being above 1. The follow-up period was 5 years.

**Results:** Among analysed patients 1193 (74.1%) were male and 418 (25.9%) were female; the mean age of analysed patients was 58 years (IQR 51, 68). Positive SI at admission was identified in 80 (4.9%) patients. Patients with positive SI had significantly higher 5-year mortality as compared with patients with SI < 1 - 25% vs 4.89%,  $p < 0.001$ . In Cox regression model positive SI was an independent predictor of 5-year mortality: HR 2.76 (95%CI 1.32-6.21),  $p = 0.003$ . Positive SI remained an independent predictor of long-term mortality after excluding 38 (2.35%) patients who died during hospitalization - HR 2.29, 95%CI 1.21-3.96,  $p = 0.014$ . Other independent predictors of 5-year mortality were: ejection fraction < 40% (HR 2.58, 95%CI 1.65-4.96,  $p = 0.001$ ), age > 65 years (HR 2.19, 95%CI 1.41-3.38,  $p = 0.001$ ) and 3-vessel disease (HR 1.56, 95%CI 1.02-2.39,  $p = 0.040$ ).

**Conclusion:** Positive shock index at hospital admission was the strongest independent predictor of 5-year mortality in STEMI patients treated with successful pPCI. This simple parameter may be used in everyday clinical practice for risk stratification during first contact with patients.

## PATHOPHYSIOLOGY

## P2076

**Meta-analysis about the effects of transcatheter closure of patent foramen ovale for secondary prevention of stroke or transient ischemic attack**

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**Background:** In recent years, a potential relationship between stroke, and patent foramen ovale (PFO) has emerged. Thus we decided to investigate the role of transcatheter closure of PFO on the recurrence of stroke.

**Methods:** PubMed and Embase databases were systematically searched from January 2000 to November 2015 for pertinent clinical studies. For inclusion in the meta-analysis, we decided to consider only randomized controlled trials (RCTs), that had compared transcatheter PFO closure with medical therapy in patients with previous cryptogenic stroke. The primary end-point was the composite of stroke and transient ischemic attack (TIA), and adverse cardiovascular events. Data were independently extracted on trial conduct quality, baseline characteristics, and efficacy and safety endpoints from published articles and appendices.

**Results:** After excluding 437 citations, we finally included a total of three RCTs of 2298 subjects with previous cryptogenic stroke or TIA, or systemic arterial embolism. PFO closure did not significantly reduce the risk of recurrent stroke/TIA (3.4% vs 5%; OR = 0.75; 95% CI: 0.53-1.12;  $p = 0.13$ ); however, an increased risk of incident atrial fibrillation/flutter was detected (3.9% vs 1.2%; OR = 3.55; 95% CI: 1.85-6.75;  $p < 0.0001$ ).

**Conclusions:** In this meta-analysis of RCTs performed in patients with PFO and previous cryptogenic stroke, transcatheter PFO closure did not significantly reduce the short-term incidence of recurrent stroke or TIA events compared with antithrombotic therapy.

## P2077

**Thromboembolic findings in heart failure patients submitted to necropsy**

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**Introduction:** Thromboembolic events carry/represent a significant portion of the morbidity of Heart Failure (HF). However, few studies have evaluated the occurrence of thrombotic and embolic events in patients with heart failure submitted to necropsy.

**Methods:** We analyzed 1241 autopsies performed from January 2000 through May 2005 in our hospital and selected 500 patients with diagnosis of heart failure, cardiogenic shock, or cardiomyopathy at autopsy. Patients with congenital heart diseases, pericardial diseases and postoperative shock were excluded. Clinical and autopsy diagnoses were confronted and discrepancies were categorized in classes I-IV in decreasing order of importance regarding therapy and prognosis; the causes of death according to specific clinical scenarios were explored.

**Result:** We studied 500 autopsies and found 250 patients with thromboembolic events at necropsy. Mean age of this group was  $73.5 \pm 10.6$  years; 152 (60.8%) patients were male and 98 (39.2%) female. According to the analysis, 80 (32%) out 250 patients had a thromboembolic event as specific cause of death: acute myocardial infarction was present in 53 (66.3%) patients, pulmonary embolism in 18 (22.5%) patients and systemic embolism in 6 (7.5%). A number of 180 thromboembolic events considered related to the cause of death were found in 119 patients. These main events were: 59 (32.7%) intracardiac thrombosis, 35 (19.4%) pulmonary embolism, 32 (17.7%) systemic embolism and 31 (17.2%) acute myocardial infarction; 51 (20.4%) thromboembolic events were unrelated to death. Further analysis of 232 patients with retrievable clinical data found discrepancies between in vivo and post-mortem diagnoses in 191 (82.3%): class I discrepancies occurred in 56 (24.1%) patients, class II in 35 (15.1%), class III in 38 (16.4%) and class IV in 62 (26.7%). Pulmonary embolism was the cause of death of 24 (42.9%) patients with a class I discrepancy.

**Conclusion:** Thromboembolic events are frequently associated to death process in patients with heart failure. Pulmonary embolism is a major source of discrepancy between in vivo and post mortem diagnosis.

## P2078

**Serum activity of selenium in various phenotypes of heart failure: clinical and pathophysiologic implications**

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**Introduction - Purpose:** Emerging evidence suggests that promotion of adverse remodeling and clinical deterioration is possibly induced by micronutrient dyshomeostasis in heart failure (HF). Selenium (Se) is an essential trace element required for antioxidant defense, oxidative metabolism, regulation of gene expression and

thyroid hormones metabolism. The aim of this study was to assess serum Se concentrations in patients with HF.

**Methods:** We studied 69 patients, 75% male, aged  $68 \pm 11$  years, 28% with preserved left ventricular ejection fraction (LVEF  $\geq 40\%$ ), including 50 with acute HF (AHF) and 19 with chronic HF (CHF). Se concentration was assessed by atomic absorption spectrometer with the Graphite Tube Atomizer.

**Results:** Serum Se concentrations were  $74.93 \pm 6.91 \mu\text{g/L}$ . Serum Se did not differ between acute HF and chronic HF patients ( $74.88 \pm 7.10$  vs.  $75.05 \pm 6.55 \mu\text{g/L}$ ,  $p = 0.927$ ) and across different NYHA classes ( $p = 0.971$ ). Serum Se was significantly lower in HF patients with reduced LVEF compared to those with preserved LVEF ( $73.61 \pm 7.52$  vs.  $77.71 \pm 4.90 \mu\text{g/L}$ ,  $p = 0.042$ ). In multiple linear regression analysis, only LVEF (B: 0.469, 95%CI: 0.153 – 0.785,  $p = 0.005$ ) and myocardial injury biomarker troponin C (B: -3.246, 95%CI: -6.202 to -0.290,  $p = 0.032$ ) were independently associated with serum Se after adjusting for age and sex.

**Conclusion:** Serum Se was significantly lower in HF patients with reduced LVEF in comparison to those with preserved LVEF. Systolic dysfunction and ongoing myocardial injury seems to be closely related with serum concentrations of Se in HF patients.

## HYPERTENSION / LV HYPERTROPHY/ RENAL DENERVATION

### P2079

#### 24-hour patterns of central and peripheral systolic blood pressure in the very elderly with heart failure with preserved ejection fraction

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Circadian profile of central blood pressure (BP) and its relationship to peripheral diurnal rhythm of BP had not been investigated in the elderly population to the moment. The aim of current study was to investigate and compare 24-hour profiles of central and peripheral blood pressures in the very elderly via their simultaneous ambulatory monitoring Parallel 24-h ambulatory aortic and brachial blood pressure monitoring was performed in 67 treated hypertensive subjects older than 80 years (mean age  $84.1 \pm 3.1$  years, 25.5% male, mean clinic brachial SBP  $134.8 \pm 23.2$  mm Hg) with HFpEF. We used oscillometric cuff-based device BPLab Vasotens. Patients with EF < 40%, atrial fibrillation and severe comorbidities were not included. 24-h, awake and sleep-time systolic, diastolic and pulse blood pressure in aorta and brachial artery were compared in subgroups divided according to the diurnal pattern of brachial systolic blood pressure (SBP). Dipper pattern was defined as relative decrease of mean SBP values of 10 to 20% at night, nondipper – less than 10% and reverse-dipper – as absent of nocturnal SBP reduction. The diurnal profiles of central systolic and pulse BPs run in parallel with those of peripheral BPs in patients with all types of dipping pattern and SBP amplification at night did not change significantly comparing to day-time values. Non-dipping or reverse-dipping SBP patterns appeared to be typical and were observed in 82.1% patients, while 50.7% participants had inadequate DBP dip < 10%. The proportionality of night-time SBP and DBP changes varied in different types of SBP diurnal profile. SBP and DBP decreased proportionally in dippers (ratio of DBP/SBP night-time reduction was 1,18) and disproportionately in non-dippers (the ratio was 2,6). In those patients with reverse-dipping pattern SBP and DBP changed in opposite directions at night. This disproportion in SBP and DBP night-time changes resulted in different intensity of PP night-time rise that was most evident in reverse-dippers. Relative nocturnal reduction of PP was  $9.3 \pm 4.72\%$  in dippers, whereas non-dippers and reverse-dippers had relative PP increase of  $6.2 \pm 8.6$  and  $22.9 \pm 12.3\%$ , respectively. The diurnal patterns of central and brachial BPs observed in very elderly treated hypertensives with HFpEF were almost parallel. PP amplification is similar in the day- and nighttime and this finding is different from previously observed PP amplification diurnal behavior in younger subjects. Proportionality of SBP and DBP sleep-time changes depends on dipping status and results in nocturnal PP increase in non- and reverse-dippers.

### P2080

#### No association is observed between long- and short-term blood pressure variability in patients with controlled arterial hypertension without heart failure

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**Background:** Visit-to-visit blood pressure variability (BPV) is associated with cardiovascular disease risk. In view of the inconvenience of obtaining blood pressure at multiple visits to calculate visit-to-visit BPV, substituting BP variability from calculating short-term variability (intra-visit and 24-hours) may be a practical alternative. The aim of the study was to evaluate the associations between long-term (visit-to-visit) and short-term (intra-visit and 24-hours) BPV in patients with uncomplicated controlled arterial hypertension (AH).

**Methods:** 52 pts (20 men, age  $58.9 \pm 9.0$  yrs; 4 smokers; 6 diabetics) with AH without HF were treated to target BP < 140/90 mmHg with combination of RAAS-inhibitor

and amlodipine for 14 months. Visit-to-visit BPV was calculated as SD for 5 visits during 8 months after target BP achievement. Intra-visit BPV was calculated as SD of 3 BP values at each visit. ABPM was performed before treatment and at the end of the study.  $p < 0.05$  was considered significant.

**Results:** Baseline BP was  $163.4 \pm 8.1/100.9 \pm 4.2$  mmHg; achieved- $123.7 \pm 9.7/76.8 \pm 6.7$  mmHg. Intra-visit systolic BPV varied from 0.8 to 7.0 mmHg (mean  $3.1 \pm 1.1$  mmHg), diastolic BPV – from 0.8 to 4.2 mmHg (mean  $2.3 \pm 0.7$  mmHg). Daytime systolic BPV varied from 6 to 29 mmHg, daytime diastolic BPV varied from 5 to 31 mmHg. Nighttime systolic BPV varied from 5 to 18 mmHg, nighttime diastolic BPV – from 4 to 23 mmHg. Visit-to-visit systolic BPV after achievement of target BP varied from 1.79 mmHg to 16.79 mmHg (mean  $7.2 \pm 3.6$  mmHg); (tertile I < 5.38; II 5.38 – 7.78; III > 7.78 mmHg). The groups were similar by age (I  $56.6 \pm 8.94$ , II  $59.4 \pm 9$ , III  $60.7 \pm 9.1$  yrs,  $p > 0.05$ ), gender, metabolic risk factors, baseline and achieved BP. Groups were also similar by intra-visit systolic BPV ( $3.0 \pm 1.0$  vs  $3.4 \pm 1.2$  vs  $3.0 \pm 1.2$  mmHg, respectively), intra-visit diastolic BPV ( $2.1 \pm 0.8$  vs  $2.1 \pm 0.4$  vs  $2.5 \pm 0.9$  mmHg, respectively); daytime systolic BPV ( $13.5 \pm 3.8$  vs  $15.6 \pm 2.9$  vs  $14.9 \pm 5.1$  mmHg), daytime diastolic BPV ( $14.0 \pm 6.1$  vs  $13.6 \pm 3.3$  vs  $12.3 \pm 4.7$  mmHg), nighttime systolic BPV ( $10.7 \pm 2.9$  vs  $11.6 \pm 3.1$  vs  $11.4 \pm 3.1$  mmHg) and nighttime diastolic BPV ( $8.2 \pm 2.5$  vs  $10.2 \pm 3.5$  vs  $9.9 \pm 4.0$  mmHg). No correlation was found between visit-to-visit and short-term blood pressure variability.

**Conclusion:** Absence of association between visit-to-visit blood pressure variability and short-term variability underlines the importance of its separate calculation in patients with uncomplicated controlled AH without HF.

### P2081

#### Effect of treatment bisoprolol and verapamil on left ventricular diastolic function, arterial stiffness and cardiovascular coupling.

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The purpose of the study was to compare the effect of treatment  $\beta$ - blocker bisoprolol and calcium antagonist verapamil on left ventricular diastolic function (DFLV), arterial stiffness and cardiovascular coupling (CVC) of patients with hypertension.

**Materials and Methods:** Included 60 patients (mean age  $55 \pm 12$  years), 29 men, 31 women with hypertension I- IIst. and heart rate  $\geq 75$  beat/min. Blood pressure (BP), resting heart rate (HR), pulse wave velocity on carotid- femoral (PWVcf), DFLV and CVC were evaluated at baseline and after 3 months of therapy with bisoprolol and verapamil.

**Results:** Both type of therapy significantly decreased SBP, DBP, HR. The changes of CVC and DFLV were not significant. PWVcf (-11.5%) was significantly decreased in the bisoprolol group. Bisoprolol showed antistiffening effect that was better than verapamil. Multivariate analysis showed a decrease in PWVcf is determined only by the type of therapy, but not the dynamics of systolic BP and HR.

**Conclusion:** Both drugs showed a comparable reduction in the blood pressure and HR. In direct comparison with bisoprolol showed a more pronounced effect on “surrogate” prognosis marker PWVcf compared with verapamil. CVC and DFLV dynamics were not found on both groups.

### P2082

#### Study of association of vitamin D and hypertension in a South Asian cohort

nil

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**Background:** Hypertension continues to be a public health menace with substantial morbidity & mortality. The antihypertensive effect of vitamin D is attributed to its negative regulation of Renin angiotensin aldosterone system (RAAS), anti-oxidant and anti-angiogenic effects. Data regarding role of Vitamin D in Asian Indian population is meager.

**Methods:** One hundred two subjects with Essential hypertension who were Vitamin D naïve were enrolled from outpatient department. Ninety nine Healthy age and sex matched non hypertensive controls were also taken for comparison. Serum Vitamin D level estimation was done in both groups via immunoabsorbant assay and deficiency defined as values < 20 ng/ml.

**Results:** Vitamin D deficiency was more prevalent among cases in comparison to controls (80.4% vs 67.7%,  $p = 0.01$ ). The mean 25-OH vitamin D levels among cases was  $15.15 \pm 12.51$  ng/ml versus a corresponding value of  $33.59 \pm 16.69$  ng/ml among controls ( $p = 0.0001$ ). We observed an inverse association between vitamin D levels and systolic blood pressure ( $p$  value = 0.01).

**Conclusion:** Vitamin D deficiency is linked to hypertension and may serve as cheap and efficient measure to cut down elevated BP and its complications.

## P2083

**Factors associated with left ventricle diastolic function in patients with arterial hypertension and mildly reduced kidney function**

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It has been shown that renal function impairment may potentiate left ventricle stiffening that may influence its diastolic function. We examined 52 patients with essential AH stage 2 (mean SBP 158,04±2,24 mmHg, mean DBP 92,19±2,15 mmHg; eGFR 86,2±1,8; age 51,29±2,24), 25 men and 27 women. We performed Doppler echocardiography according to local full protocol, LV diastolic function was determined by measuring velocity of the peak E and peak A of transmitral flow with determination of E/A, velocity of peak E' by tissue Doppler with determination of E/E', deceleration time (Dt) and isovolumic relaxation time (IVRT) measurement. eGFR was estimated using CKD-EPI formula. Also we used hematology and biochemical blood testing, urine analysis, microalbuminuria and urine creatinine excretion with albumin to creatinine excretion ratio (A/C). To assess the relationship between these values we used Spearman correlation analysis. The mean values were E/A 1,04±0,06, E/E' 7,58±0,44, Dt 253,9±12,6 msec, IVRT 92,6±3,9 msec. We found that E/E' was correlated with A/C (r=0,38 p=0,046), serum sodium (r=0,341 p=0,038) and with the quantity of leucocytes (Leu) in the urine portion (r=0,396 p=0,037). E/A was associated with serum potassium (r=0,385 p=0,035), eGFR (r=0,376 p=0,017), uric acid (r=-0,675 p=0,005), the quantity of Leu in hematology (r=-0,436 p=0,033) and urine (r=-0,456 p=0,013) samples. Dt was associated with urine specific density (r=0,313 p=0,039), eGFR (r=0,693 p=0,034), erythrocyte sedimentation rate (r=0,410 p=0,046), quantity of Leu (r=0,0576 p=0,001) and erythrocytes (r=0,387 p=0,042) in urine portion. IVRT correlated with serum sodium (r=0,374 p=0,019) and potassium (r=0,383 p=0,04) concentration, eGFR (r=0,412 p=0,011) and blood hemoglobin concentration (r=0,485 p=0,16). In patients with arterial hypertension and started renal function impairment all the predictors found could be useful for the prognosis of the development of LV diastolic dysfunction.

## P2084

**Benefit of forty-eight-hour ambulatory blood pressure monitoring in hemodialysis population**

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**Introduction:** Hypertension (HTN) is the second leading cause of end-stage renal disease (ESRD), and it present in up to 90% of ESRD patients irrespective of the etiology of kidney disease. Blood Pressure (BP) exhibits continuous variation during the day and the night, as a result of complex interactions between environmental, behavioral, and endogenous factors. Data derived from ambulatory BP monitoring (ABPM) allow better characterization of BP during everyday activities and sleep, and most importantly, better correlate with target organ damage, cardiovascular disease (CVD) risk, and long term patient prognosis than clinic BP.

**Purpose:** The aim of our work is to define the role of ABPM in hemodialysis (HD) patients and assess correlation of the results with the echocardiographic data.

**Methods:** The study has a cross-sectional design. We enrolled 17 patients from a single HD unit undergoing thrice weekly HD. We performed ABPM for 48 hours (day of dialysis (D1), day followin dialysis (D2)) in all patients. using an appropriately sized cuff, ABPM was recorded every 20 min during the day (6 a.m. to 10 p.m.) and every 30 min during the night (10 p.m. to 6 a.m.); using a BRAVO 24 HRABP SUN TECH MEDICAL MODEL 222-B properly calibrated and validated; in the non access arm. Dialysis unit BP recordings measured by the dialysis unit staff before and after dialysis were collected prospectively at the time of the patient visit. Two-dimensionnal- guided M-mode echocardiograms were performed 30 min before and 30 min after HD.

**Conclusion(s):** Our study confirms the high prevalence of BP abnormalities at the ABPM in HD population. Not only ABPM helps in the diagnosis and categorization of HTN, but can also provide prognostic. We suggest that ABPM should become the norm for the diagnosis of HTN and prognostic evaluation in chronic HD population.

**Results:** According to the collected BP before HD, 4 (23.5%) patients had HTN, against 10 (58.8%) according to the measure taken after HD. According to ABPM, we defined 4 categories of BP: 5 (29.4%) patients were normotensive, 4 (23.5%) were with sustained HTN, 4 (23.5%) with masked HTN and 4 (23.5%) with white-coat- HTN. Systolic BP of 48 H correlated significantly with pre and post dialysis BP (p<0.05). Pulse pressure (PP) of 48 H correlated significantly with pre and post dialysis BP (p<0.01). The study of the variation of nocturnal BP objectified a dipper profile in 3 cases (17.6%), non-dipper in 12 cases (70.6%), inverted-dipper in 2 cases (11.8%). No cases of hyper-dipper was identified. Three patients (17.6%)

had echocardiographic left ventricle after HD from 318.41 g/m<sup>2</sup>±71.21 to 261.95 g/m<sup>2</sup>±86.56 (p=0.002).

**HFpEF – HEART FAILURE WITH PRESERVED EJECTION FRACTION**

## P2085

**Association of Serum liver enzymes with E/Em ratio in patients with heart failure preserved ejection fraction (HFPEF)**

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**Background:** Prior studies have suggested the use of biomarkers that show diverse biological processes in systolic heart failure. Whether this can be applied for diastolic heart failure is unknown. In this prospective cross sectional study, we evaluated the relation of serum liver enzyme with echocardiography parameters in heart failure preserved ejection fraction (HFpEF)(EF≥45%) and being compared with reduced ejection fraction (HFrEF).

**Methods:** Serum alanine transferases, aspartate transaminase, total and direct bilirubin were measured in 100 patients with stable chronic heart failure. Mean age of patients was 59.82±14.35 (60% women, 48% HFpEF). There was no significant difference in liver function test in two groups. Transthoracic echocardiography was done in the same day. Association of a few echocardiographic systolic and diastolic indices with laboratory data was assessed.

**Results:** Similarly to past studies, we found significant relation between liver function test and echocardiography parameters in HFrEF (P value: 0.002). In HFpEF, while there was no significant relation of total and direct bilirubin to echocardiography parameters except we found significant correlation of serum transaminases with E/Em (P value: 0.02)

**Conclusion:** Liver dysfunction is not uncommon in HFrEF and is related to severity of systolic and diastolic dysfunction based on echocardiography findings. However, it is just E/Em ratio in significant relation to liver enzymes in HFpEF.

Table 1

	ESV(ml)	LVEDD(cm)	E/Em(ratio)	LAVI(ml/m <sup>2</sup> )
ALT	0.24	0.6	0.02	0.84
AST	0.28	0.6	0.05	0.37
T-Bili	0.31	0.7	0.47	0.18
D-Bili	0.27	0.83	0.72	0.75
Uric acid	0.06	0.41	0.44	0.62

Pearson correlation of echocardiographic parameters with liver enzymes in patients with heart failure preserved ejection fraction

## P2086

**The relationship between arterial stiffness and left ventricular ejection fraction in heart failure.**

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**Backgrounds:** Heart failure (HF) is pandemic with high morbidity and mortality, and also is becoming a worldwide economic burden. Although many studies has been conducted to identify characteristics of patients with HF with reduced ejection fraction (HFrEF), characteristics and pathophysiological features of patients with HF with preserved ejection fraction (HFpEF) remain unclear. Hypertension and diabetes mellitus are the most important risk factors for developing HFpEF, comprehensive risk factors are still lacking. Cardio-ankle vascular index (CAVI) has been widely applied to assess arterial stiffness in patients with known cardiovascular diseases. Therefore, we investigated the relationship between CAVI and several parameters of HFpEF.

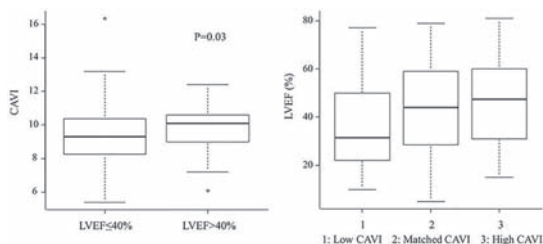
**Methods:** We enrolled consecutive 108 patients who were hospitalized for acute heart failure and examined CAVI from April 2013 to March 2015. We excluded patients with atrial fibrillation, aortic regurgitation and also excluded the patients whose ankle brachial index was less than 0.9, because these patients' CAVI are unreliable. We defined the patient whose left ventricular ejection fraction (LVEF) was less than 40 as HFrEF, and the patient whose LVEF was more than 40 as HFpEF. Since CAVI is influenced by age and sex, we calculated CAVI using by regression formula as follows, CAVI=5.43+0.053 x age for men, and CAVI=5.34+0.049 x age for women (J Atheroscler Thromb 2011; 18: 924-938). We divided CAVI into three groups as follows, measured CAVI minus calculated CAVI is less than -0.5 are low



CAVI, is between -0.5 and +0.5 are matched CAVI and more than 0.5 are high CAVI.

**Results:** There is no differences in age ( $73 \pm 11$ ,  $72 \pm 15$ ), sex (male: 57.4%, 74.5%), serum Creatinine ( $0.99 \pm 0.21$ ,  $1.12 \pm 1.6$ ), serum potassium ( $4.22 \pm 0.70$ ,  $4.35 \pm 0.59$ ) between HFpEF and HFrEF. Calculated CAVI was significantly higher in HFpEF compared with HFrEF ( $10.1[9.0-10.6]$ ,  $9.3[8.28-10.38]$ ,  $p=0.03$ ). There was statistically significant difference in LVEF between low CAVI and high CAVI ( $31.5\%[22.0-50.0]$ ,  $47.5\%[31.5-60.0]$ ,  $p=0.03$ ).

**Conclusion:** Thus, the present study demonstrated that CAVI was closely related to HFpEF, suggesting that arterial stiffness might be involved in the development of HFpEF.



Figure

## P2087

### Relationship between left ventricle geometry and disorders of glucose metabolism in patients with heart failure with preserved ejection fraction

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**Background:** There are four types of left ventricular (LV) geometry: normal, concentric remodeling, eccentric hypertrophy and concentric hypertrophy. It has been shown that abnormal LV geometry significantly increase the risk of cardiovascular events. The most unfavorable prognostic implications are associated with concentric hypertrophy. Diabetes and prediabetes are also important risk factors of cardiovascular disease. Little is known about the association between disorders of glucose metabolism and LV geometry changes in patients with heart failure with preserved ejection fraction (HFPEF).

**Purpose:** The aim of this study was to evaluate the relationship between LV geometry and incidence of diabetes (DM) and prediabetes (PD) in patients with HFPEF.

**Methods:** 443 consecutive pts were enrolled based on HFPEF diagnosis. The pts were divided into two groups depending on disorders of glucose metabolism diagnosis: group A – 175 pts with DM or PD (118 M, mean age  $64.3 \pm 11.0$  yrs), group B – 268 without DM or PD (189M, mean age  $61.8 \pm 10.9$  yrs). LV function and structure parameters were analyzed based on transthoracic echocardiography. LV mass (LVM) was calculated from Devereux-Reichek formula, and LV mass index (LVMI) was calculated as the LVM divided by height to the power of 2.7. LV relative wall thickness (RWT) was calculated as diastolic intraventricular septal dimension (IVD) divided by LV diastolic dimension, both measured in the parasternal long axis.

**Results:** We found that the groups A and B were significantly different in respect to interventricular septum diastolic dimension-IVD ( $12.5 \pm 2.5$  vs.  $11.6 \pm 2.3$  mm,  $p=0.0001$ ), LVM ( $279 \pm 101$  vs.  $257 \pm 80$  g,  $p=0.009$ ), LVMI ( $69 \pm 24$  vs.  $62 \pm 18$  g/m<sup>2.7</sup>,  $p=0.0007$ ) and RWT ratio ( $0.50 \pm 0.13$  vs.  $0.47 \pm 0.12$ ,  $p=0.005$ ), as well as BMI ( $29.9 \pm 4.7$  vs.  $26.9 \pm 3.8$  kg/m<sup>2</sup>,  $p < 0.0001$ ) and waist circumference ( $103 \pm 12$  vs.  $95 \pm 11$  cm,  $p < 0.0001$ ). Furthermore in the entire study population we found significant correlation between the level of blood glucose at admission and IVD ( $r=0.14$ ,  $p < 0.05$ ), LVMI ( $r=0.10$ ,  $p < 0.05$ ) and RWT ( $r=0.10$ ,  $p < 0.05$ ). There was also association between waist circumference and LVMI ( $r=0.28$ ,  $p < 0.001$ ).

**Conclusions:** The presence of glucose metabolism disorders in patients with HFPEF is associated with septal hypertrophy and increased LV mass and consequently may lead to LV concentric hypertrophy development.

## P2088

### Baseline hemodynamic characteristics of patients in the REDUCE elevated left atrial pressure in patients with heart failure trial

Corvia Medical Inc.

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**Introduction:** Treatment of patients with heart failure with preserved ejection fraction (HFpEF) is challenging since there are no effective evidence-based therapies. While the underlying pathophysiology is complex, multifactorial and potentially variable between patients, an elevated pulmonary capillary wedge pressure (PAWP), particularly during exercise, is considered a key contributor to morbidity and exercise intolerance in all patients with HFpEF. The REDUCE LAP-HF trial is investigating the safety and effects of an interatrial septal shunt device designed to reduce left atrial pressure.

**Purpose:** The purpose of this study was to characterize the hemodynamic responses to exercise at baseline in patients upon enrollment into the REDUCE LAP-HF trial, with particular emphasis on changes in PAWP, central venous pressure (CVP) and their difference; it is the PAWP-CVP difference that would be the driving force for flow through an interatrial device to reduce PAWP.

**Methods:** Patients with HFpEF, as defined by LV ejection fraction (EF)  $\geq 40\%$ , New York Heart Association (NYHA) class II-IV, PAWP  $\geq 15$  mmHg at rest or  $\geq 25$  during supine bike exercise, and CVP  $< 15$  mmHg at rest, were eligible for participation in this study. Pressures and cardiac outputs (CO, by thermodilution) were measured via standard right heart catheterization at rest and during symptom-limited supine bike exercise. All tests were read at a central core laboratory.

**Results:** 64 patients qualified for the study. Mean age was  $69 \pm 8.3$  years and 65% were female. Patients exercised for an average of  $7.3 \pm 3.1$  minutes to  $42.5 \pm 18.3$  Watts with an increase of heart rate from  $69.3 \pm 14.4$  to  $95.8 \pm 18.4$  bpm and an increase of CO from  $5.5 \pm 1.6$  to  $8.7 \pm 2.6$  L/min. CVP increased from  $9.0 \pm 3.6$  to  $17.6 \pm 5.8$  mmHg and PAWP from  $17.4 \pm 5.2$  to  $34.3 \pm 7.4$  mmHg. Consequently, the PAWP-CVP difference increased from  $8.3 \pm 4.1$  mmHg at rest to  $16.7 \pm 6.5$  mmHg at peak exercise. All differences listed above were significant at  $p < 0.001$ .

**Conclusion:** HFpEF patients qualified for the REDUCE LAP-HF study exhibited marked increases in both PAWP and CVP during supine bicycle exercise. PAWP increased approximately twice as much as CVP so that the PAWP-CVP pressure gradient (the driving force for flow through an interatrial shunt) increased significantly. This suggests that the hemodynamic impact of such a shunt device would be significantly greater during exercise than at rest. Results of repeat hemodynamic exercise testing 6 months following shunt implant in these patients will elucidate the degree of PAWP reduction by this approach as well as its impact on exercise tolerance and morbidity.

## GENE AND CELL THERAPY

## P2089

### Re-do cell base therapy in patients with chronic coronary artery disease

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**Background:** Cell base therapy is a promising strategy for treatment of non-operable patients with coronary artery disease. Little is known about re-do cell base therapy in patients with chronic heart disease.

**Purpose:** Assessment of repeated administration of bone marrow cells in patients with chronic coronary artery disease 3-5 years after the first procedure.

**Methods:** Within 2003-2013 years 215 patients with non-operable coronary artery disease received cell based therapy - intracoronary administration of bone marrow cells. 15 of them had received the same re-do procedure 4-5 years later. Clinical observation, echocardiography (Echo-CG), single photon emissive tomography (SPECT) investigation were performed during 3 years after re-do procedure. Quality of life was assessed by SF36.

**Results:** 2 pts died during follow up (1 year and 2 year later). Functional improvement (decreasing of angina pectoris) noted 60% of patients 3-9 months after re-do procedure. Transplantation of bone marrow cells was associated with increasing in myocardial perfusion by SPECT at 12-month of follow-up. Echo-CG parameters did not change significantly, but patients with low ejection fraction had tendency to improving them during follow up. Coronarography revealed stable atherosclerotic damages in coronary arteries and increasing collateral blood flow.

**Conclusion:** Re-do intracoronary administration of bone marrow stem cells may be useful procedure in patients with non-operable coronary artery disease.

## P2090

### Gene polymorphism of beta receptors in patients with chronic heart failure

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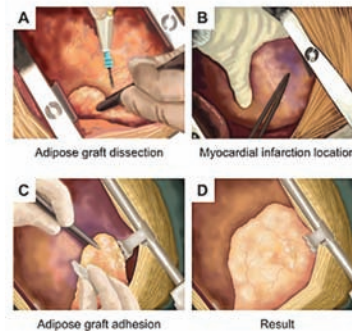
**Purpose:** To examine of adenylate cyclase activity and gene polymorphism of beta ( $\beta$ ) receptors in patients with chronic heart failure (CHF).

**Methods:** 72 male patients at the age of 40 to 55 years old with postinfarction cardio sclerosis (PICS) have been examined. All patients were divided into two groups: 1st group included 35 patients with CHF II FC and 2nd group included - 37 patients with CHF III FC by NYHA classification. Activity of adenylate cyclase erythrocytes was assessed by Solomon method (1979). Genetic typing was conducted by method of polymerase chain reaction (PCR).

**Results:** Initial density of erythrocytic beta2-adrenal receptors at patients with II FC CHF making up  $27.7 \pm 1.4$  conventional units, while at patients with III FC CHF this index making up  $30.8 \pm 1.3$  conventional units. ( $P < 0.001$ ). At patients with II FC CHF basal activity of adenylate cyclase made up  $4.15 \pm 0.14$  pmol/mg/min, with III FC CHF  $3.56 \pm 0.13$  pmol/mg/min against  $6.1 \pm 0.19$  pmol/mg/min of control group. At genetic typing it was noted that the most expressed reduce of basal activity was revealed in group Gly389 homozygote in comparison with group Arg389.

**Conclusions:** At CHF patients, in group of Gly389 homozygotes more expressed failures of adenylate cyclase system activity have been noticed.

Figure 2



Schematic illustration of the AGTP.

ISCHEMIA / REPERFUSION / PRECONDITIONING / POSTCONDITIONING

P2091

**First-in-man safety and efficacy of the adipose graft transposition procedure (AGTP) in patients with a myocardial scar.**

SAF2014-59892, JCI-2012-14025, Fundació La MARATÓ de TV3, Red TerCel (RD12/0019/0029), RIC (RD12/0042/0047), FIS PI14/01682, and FEDER. P Paloma Gastelurrutia<sup>1</sup>; A Bayes-Genis<sup>1</sup>; ML Camara<sup>2</sup>; A Teis<sup>2</sup>; J Lupon<sup>2</sup>; X Ruyra<sup>2</sup>;

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**Background:** The present study evaluates the safety and efficacy of the Adipose Graft Transposition Procedure (AGTP) as a biological regenerative innovation for patients with a chronic myocardial scar. The adipose tissue surrounding the heart and pericardium may serve as an autologous biological matrix for salvaging this injured myocardium, as experiments in porcine models have suggested.

**Methods:** This prospective, randomized single-centre controlled study included 10 patients with established chronic transmural myocardial scars. Candidates for myocardial revascularization were randomly allocated into two treatment groups. In the control arm (n=5), the revascularizable area was treated with CABG and the non-revascularizable area was left untouched. Patients in the AGTP-treated arm (n=5) were treated with CABG and the non-revascularizable area was covered by a biological adipose graft. The primary endpoint was the appearance of adverse effects derived from the procedure including hospital admissions and death, and 24-hour Holter monitoring arrhythmias at baseline, 1 week, and 3 and 12 months. Secondary endpoints of efficacy were assessed by cardiac MRI.

**Results:** No differences in safety were observed between groups in terms of clinical or arrhythmic events. On follow-up MRI testing, participants in the AGTP-treated arm showed a borderline smaller left ventricular end systolic volume (LVESV; p=0.09) and necrosis ratio (p=0.06). The AGTP-treated patient with the largest necrotic area and most dilated chambers experienced a noted improvement in necrotic mass size (-10.8%), and ventricular volumes (LVEDV:-55.2 mL and LVESV:-37.8mL at 1year follow-up) after inferior AGTP.

**Conclusions:** Our results indicate that AGTP is safe and may be efficacious in selected patients. Further studies are needed to confirm its clinical value. (NCT01473433, AdiFlap Trial). Legend: Pericardial adipose tissue dissected and transposed onto the infarct.

Table 1

	AGTP-treated	Control		AGTP-treated	Control	
	Baseline	3 mo.	12 mo.	Baseline	3 mo.	12 mo.
Necrosis mass, gr	33.9	32.9	30.0	21.3	21.6	17.6
Necrosis ratio, %	22.3	20.1	19.3	14.3	14.7	16.4
LVEF, %	41	43	47	42	47	46
LVESV, mL	139.6	131.9	114.9	127.8	99.2	104.6
LVEDV, mL	219.8	218.0	202.4	212.2	187.7	194.6
CO, L/min	5.0	5.5	5.8	5.1	5.9	5.5
SV, mL	80.2	87.3	87.5	84.4	88.5	90.1

Mean MRI values at baseline, three months and one year follow-up.

P2092

**Impact of regional wall motion abnormality on myocardial infarction with mild cardiac troponin elevation is different according to the degree of left ventricular dysfunction**

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**Background:** Echocardiographic evaluation of regional wall motion abnormality (RWMA) is frequently performed in routine practice especially when cardiac enzyme elevation is indeterminate. We aimed to investigate whether RWMA in this patients have an impact on clinical outcomes in this category of patients.

**Methods:** Between November 2005 and August 2013, a total of 2,124 patients (64.7 ± 12.2 years, 1,371 males) with non-ST-segment elevation myocardial infarction enrolled. Patients were divided into two groups according to regional wall motion score (RWMS) [Group I (n=598): RWMS ≥ 24, Group II (n=1,526): RWMS < 24]. Primary endpoint was composite of major adverse cardiac event (MACE) at 1 year. MACE was comprised of death, non-fatal myocardial infarction, stent thrombosis, target lesion revascularization, and target vessel revascularization. Cut off value of 24 points for MACE was defined by receiver operating characteristics (ROC) curve analysis (AUC: 0.586, p < 0.0001).

**Results:** There were no differences in baseline characteristics between the two groups except older age in group I (70.1 ± 12.2 vs. 66.3 ± 11.7, p < 0.0001) and more males in group II (59.7% vs. 66.2%, p = 0.005). Also medical histories such as hypertension, diabetes, and smoking showed no significant differences. However, left ventricular ejection fraction (LVEF) was significantly lower in group I than in group II (44.3 ± 11.3% vs. 56.7 ± 10.0%, p < 0.0001). Subgroup analysis was performed according to LVEF (EF ≥ 40% vs. EF < 40%). In-hospital mortality was different between groups regardless of LVEF (EF ≥ 40%: 2.0% vs. 1.1%, p < 0.0001, EF < 40%: 8.1% vs. 5.8%, p = 0.025). Group I showed significantly more 1-year MACE when LVEF ≥ 40% (7.7% vs. 6.4%, p = 0.001). When EF < 40%, however, there was no difference in MACE between Group I and II (16.9% vs. 15.1%, p = 0.228).

**Conclusion:** RWMA in NSTEMI patients with mild cardiac troponin elevation may predict higher in-hospital mortality regardless of LVEF, but could predict adverse long-term MACE only in preserved EF not in low EF.

P2093

**Myocardial mechanics within 24 hour after successful reperfusion in acute ST segment elevation myocardial infarction are still compromised even in normal left ventricular ejection fraction**

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**Purpose:** The necrotic phase of myocardial infarction, of which dominant pathologic processes are inflammation and necrosis, begins within a few hours and lasts for few days after ischemia. The myocardial mechanics during this critical period are still poorly understood. We aimed to evaluate myocardial mechanical alternation during necrotic phase of acute ST segment elevation myocardial infarction (STEMI) within 24 hour after successful primary percutaneous coronary intervention. (PCI)

**Methods:** Total 33 acute STEMI patients were enrolled [age=52 ± 17 years, 27 male (82%)] and compared with 28 normal control group of age and sex matched

[age=53 ± 12 years, 23 male (82%)]. Primary PCIs were done to all subjects within 90 minutes of emergency room (ER) arrival to balloon inflation times to culprit lesions. Myocardial mechanics were measured using speckle tracking image on transthoracic echocardiography (TTE) examination within 24 hours of successful primary PCIs and compared with normal subjects.

**Results:** Averaged time duration from onset of chest pain to ER arrival time was 313.4 ± 154.2 minutes and pain to balloon inflation time was 78.8 ± 42.1 minutes. Cardiovascular risk factors were hypertension (n = 18, 54.5%), diabetes mellitus (n = 6, 18.2%), smoking (n = 23, 69.7%) and family history (n = 6, 18.2%). Culprit coronary lesions were left main (n = 2), proximal left anterior descending (px LAD, n = 13), mid LAD (n = 7), px left circumflex artery (n = 2), px right coronary artery (px RCA, n = 4) and mid RCA (n = 5). On the TTE examination, mean left ventricular ejection fraction (EF) was 56.6 ± 18.2%. Left ventricular mechanics of global longitudinal strain (-16.2 vs. -23.2%, p < 0.001), global circumferential strain (-15.3 vs. -28.8%, p < 0.001), Basal rotation (13.2 vs. 35.5°, p < 0.001) and twist values (9.5 vs. 26.4°, p < 0.001) in peak systolic periods were significantly lower than normal subjects.

**Conclusion:** Myocardial mechanical deteriorations in acute stage STEMI were still compromised within 24 hours after successful PCIs even with normal LV EF. Necrotic phase of myocardial infarction might on-going even after successful reperfusion and measurement of myocardial mechanic would provide comprehensive myocardial performances in this critical stage.

## P2094

### The added assessment of combined administration of carperitide and nicorandil for acute myocardial infarction patients with successful percutaneous coronary intervention

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**Background:** There are reports about validity of additional administration of carperitide or nicorandil for acute myocardial infarction (AMI) patients with successful recanalization therapy. However, there are no reports about efficacy of combined administration of both drugs.

**Methods:** Among 895 patients who hospitalized due to first-time AMI in the period between July 2008 and February 2015, sequent 80 patients who confirmed TIMI III by percutaneous coronary intervention (PCI) and gave consent became the subject of this study. The patients were divided into four groups: control group, low-dose (0.0125-0.025 µg/kg/min) carperitide group, high-dose (0.05-0.2 mg/kg/h) nicorandil group, and low-dose carperitide and high-dose nicorandil combined administration group. Immediately following PCI, each drug was continuously administered for 72 hours and examined prospectively. We used left ventriculography to evaluate LVEF and LVEDVI, LVESVI at acute stage and at 6 months. Also we measured CPK at acute stage to proceed quantitative evaluation of myocardial infarction range.

**Results:** No significant difference was recognized in the time between onset of myocardial infarction and reperfusion, and the size of infarction in four studied groups. Also there were no significant differences in blood pressure and heart rate. Moreover, LVEF at chronic stage, LVEDVI and LVESVI were not significantly different between four groups.

**Conclusion:** There was no additional efficacy of combined administration of carperitide and nicorandil for AMI patients who succeeded revascularization by PCI at both acute and chronic stages.

## P2095

### Combined therapy of CAD accompanied by gastroduodenal pathology

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**Purpose:** To compare influence of gastroduodenal pathology therapy on clinical status of patients with angina pectoris stable.

**Methods:** 230 patients with angina pectoris stable, including 147 patients accompanied by gastroduodenal pathology H. pylori associated, were studied.

The patients were comparable according to age, sex and clinical status (p > 0.05). 67 (45.7%) patients of 147 has got duodenal ulcer, 29 (19.7%) - stomach ulcer, 51 (34.6%) - chronic gastritis, duodenitis.

The patients were divided in groups I, II or III.

Patients of group I (n = 74) received basic therapy of angina pectoris stable and omeprazol/clarithromycin/amoxicillin. Patients of group II (n = 63) - basic therapy and omeprazol. Patients of group III (n = 93) - basic therapy of angina pectoris stable.

**Results:** Patients with CAD and gastroduodenal pathology have lower efficacy of nitroglycerin on anginal pain (60.5% versus 100%, X<sup>2</sup>=5.13, = 0.024).

By the 24th week of treatment in group I the frequency of angina attacks decreased by 62.6 ± 4.2% (< 0.05). Weekly nitroglycerine consumption decreased by 70.4 ± 3.6% (p < 0.01).

In group II the frequency of angina attacks decreased by 30.7 ± 4.6% (< 0.05), weekly nitroglycerine consumption decreased by 21.2 ± 5.6% (< 0.05).

In group III the frequency of angina attacks decreased by 29.5 ± 3.8% (< 0.05), weekly nitroglycerine consumption decreased by 44.1 ± 5.8% (< 0.05).

According to exercise tolerance test exercise tolerance increased from 72.5 ± 3.1 to 105.1 ± 6.1 W (p < 0.01) (by 45.3 ± 3.2%, p < 0.01) in group I, from 70.3 ± 2.1 to 89.1 ± 3.4 W (p < 0.01) (by 26.5 ± 2.6%, p < 0.01) in group II, from 110.4 ± 5.5 to 124.5 ± 2.8 W (p < 0.001) (by 12.7 ± 3.8%, p < 0.01) in group III.

In group I H.pylori eradication effectiveness was 95.9%. In group II occurred spontaneous eradication in 3.4% patients.

The relapse rate of gastroduodenal pathology within 24 weeks of observation in group I was 5.4%, in group II - 39.7% (c<sup>2</sup>=20.41, < 0.001).

**Conclusions:** The inclusion of eradication therapy in treatment for CAD patients accompanied by gastroduodenal pathology, associated with Helicobacter pylori, provides a quick reduction of dyspeptic disorders and an angina syndrome stabilization.

## P2096

### Clinical expression of acute myocardial infarction with and without ST segment elevation in a specific population

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**Introduction:** Acute myocardial infarction (AMI) with and without ST segment elevation differs in clinical expression; these differences can be more prominent in some subgroups of patients.

**Aims:** Assess the differences between AMI with (STEMI) and without ST segment elevation (NSTEMI) in a specific population of women with an ejection fraction (EF) lesser than 40% (EF < 40%).

**Methods:** Retrospective study, including 533 women with AMI and an EF < 40%. The population was divided in two groups: A, including patients with NSTEMI (n = 251); B, including patients with STEMI (n = 282). Differences between groups were evaluated regarding the clinical profile.

**Results:** Group A was older than B, had more prevalence of comorbidities as hypertension, diabetes, dyslipidemia, chronic kidney disease and history of stroke (p < 0.05) and higher prevalence of previous history of AMI, percutaneous coronary intervention (PCI) and coronary artery bypass graft (CABG) (p < 0.001). Regarding reperfusion therapy (RT), CABG was more prevalent in group A and PCI in group B; the absence of RT was more prevalent in group A (p < 0.001). Group B had more complications during hospital stay, namely cardiogenic shock, ventricular tachycardia and hospital death (p < 0.05).

**Conclusions:** In this registry of patients with AMI and an EF < 40%, patients with NSTEMI were older, had more comorbidities and were less treated with RT, similar to general population. Despite the reduced EF of both groups, patients with STEMI had higher hospital complications and mortality. This shows that the intrinsic pathophysiological process of the two types of AMI persist even when considering subsets of patients with particular characteristics.

## P2097

### Revascularisation of patients with acute myocardial infarction without ST segment elevation and an ejection fraction lesser than 40%, without high or very high risk criteria

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**Introduction:** An ejection fraction (EF) lesser than 40% (EF < 40%) constitutes a criteria for invasive stratification of patients with acute myocardial infarction (AMI) without ST elevation (NSTEMI) within the first 72h after hospital admission, if there are no more severe criteria requiring urgent coronary angiography (CA).

**Aims:** 1) Characterize a population with NSTEMI and an EF < 40% in relation to the time interval to CA; 2) compare groups regarding their characteristics and prognosis.

**Methods:** Retrospective study, including 220 patients with NSTEMI and an EF < 40%, without high or very high risk criteria for invasive stratification. The population was divided in three groups: A, patients that didn't perform CA (16.4%); B, patients who underwent CA in the first 72h of hospital admission (78.6%); C, patients who underwent CA after the first 72h (5.0%). Groups were compared regarding their characteristics.

**Results:** Group A had more prevalence of previous history of AMI and percutaneous coronary intervention (p < 0.02). Group C had more signs of congestive heart failure (CHF), was treated with more diuretic therapy and non-invasive ventilation and had higher hospital duration of stay (p < 0.05). Group B corresponded to the majority of patients. They had similar characteristics to group C, but had lesser signs of CHF (p < 0.002). There weren't differences between groups regarding death.

**Conclusions:** The majority of patients with EF < 40% performed diagnostic CA within the first 72h recommended. Patients that didn't undergo CA had higher prevalence of known ischemic cardiomyopathy. The timing difference of CA between patients



who performed it was determined by the heart failure decompensation degree; however, this wasn't associated with differences in mortality.

**P2098**

**Predictors of mid-term clinical outcome of patients treated for acute coronary syndrome**

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Aim of the study was to identify frequency, type of events and predictors of mid-term outcome in patients treated for acute coronary syndrome (ACS).

**Methods:** patients with ACS, were subjected to analyze with variables as: age, gender, risk factors, SBP and HR during ACS, type of MI, location, CAD severity, LV function, type of treatment, in-hospital morbidity, medications post discharge, type and time to event. Statistical analyze: descriptive and comparative analyze, uni and multivariate regression analyze, Caplan-Meier event free survival analyze.

**Results:** 269 patients treated for ACS, at mean age 63,1 ± 11,1 y., 176(65,4%) males and 93(34,6%) females, were followed up for mean 20,1 ± 10,2 months. A total of 69 cardiac events (CE) in 68(25,3%) patients during the 269pts./446 y. follow up were registered, 8(3%) of which cardiac deaths (CD). Ischemic events were the most frequent (40-14,9%): angina-10(3,7%), scheduled revascularization after ACS because of multivessel CAD-19(7,1%), and acute ischemic event leading to re-revascularization-11(4,1%) pts. Symptomatic heart failure-13(4,8%) pts. leading to CD in 5, 3(1,1%), ischemic CVI with one fatal event, atrial arrhythmias in 6(2,2%) and malignant ventricular arrhythmias in 4(1,5%) pts. one with fatal ending, and one sudden CD. 42(61,7%) out of 68 events occurred during the first 6 months after the ACS. Univariate predictors were: DAPT(dual antiplatelet treatment) after ACS: beta -2,369, p=0,002, exp(B) 0,094; EF(%): beta -0,062, p=0,037; age: beta 0,036, p=0,022; NSTEMI: beta 2,360, p=0,005, exp(B) 10,385; anemia: beta 1,192, p=0,012, exp(B)3,293, and initial heart rate during ACS: beta 0,024, p=0,005. Multivariate analyze (logistic regression), identified four significant independent predictors: NSTEMI exp(B): 5,386, p=0,056; anemia: exp(B) 1,526, p=0,024; age: beta 0,040, p=0,052, and DAPT: beta -2,682, p=0,002, exp(B) 0,068;

**Conclusion:** being at advanced age, having NSTEMI MI and anemia during ACS, are independent negative predictors, while DAPT treatment was positive predictor of mid-term outcome after ACS. In terms of type of event, ischemic events predominated, especially in the first 6 month, leaving symptomatic heart failure fare behind.

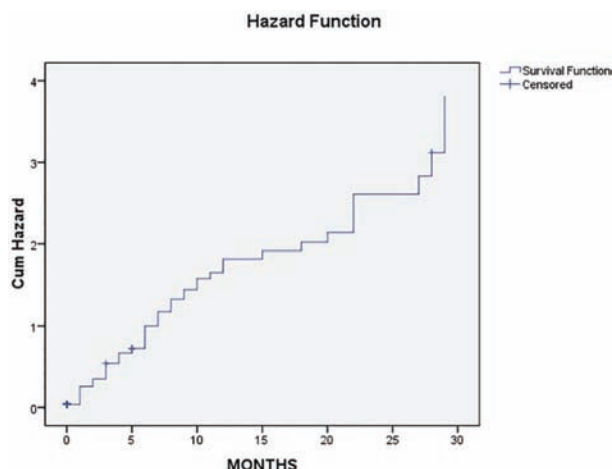


Figure 1. Caplan-Meier cumulative hazard

**P2099**

**Acute coronary dissection in a woman, due to emotional stress, presenting initially with a normal electrocardiogram and minimal elevation of troponin and causing an acute coronary syndrome.**

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**Introduction:** Our case-report discerns an acute coronary syndrome after emotional stress, with no predisposing factors for coronary artery disease (CAD) and with subtle initial laboratory findings. The acute coronary syndrome turned out to be due to coronary dissection.

**Purpose:** Our report aims to show that low initial probability of CAD and subtle laboratory findings should not be the only clues to be evaluated when deciding about the hospitalization of a patient and subsequently the procession to coronary angiography.

**Methods:** The patient was a woman 65 years old, which presented with intense chest pain and dyspnea after a strong emotional stress. She had a normal electrocardiogram, a normal echocardiogram and a minimal troponin elevation in the grey zone area. She was hospitalized in the cardiac intensive care unit and antiischemic treatment was initiated. The symptoms had a clinical remission for three days and the troponin was stable for these days. But afterwards she had again intense chest pain and dyspnea with profound electrocardiographic changes, significant elevation of troponin, elevation of BNP and mild hypokinesia of the lateral wall. The patient underwent an urgent coronary angiography.

**Results:** Coronary angiography has shown acute coronary dissection at the circumflex coronary artery (at a distal site). No significant coronary artery stenosis was observed. No other intervention was undertaken and the patient was managed conservatively and stabilized. Nitrates, b-blockers, double antiplatelet treatment and mild diuresis was the mainstay of treatment. Tests for autoimmune diseases (arteritis etc) were negative. There were not indications for connective tissue metabolism disorders. Finally, the patient was discharged with a directive for frequent cardiologic evaluation, antiischemic treatment, and avoidance of emotional and physical stress.

**Conclusions:** The clinical picture and triggering factors, and not only the initial probability of CAD and laboratory findings, should be evaluated when deciding about hospitalization. The severity of symptoms should prompt us to careful and thorough follow up. Subtle initial laboratory findings may be due to small initial expansion of the dissection which subsequently became larger. It also should be noted that circumflex coronary artery ischemia, if distal, may not give electrocardiographic findings. Emotional stress causes not only tako-tsubo cardiomyopathy but also coronary artery dissection. Acute coronary dissection is a rare entity but should always be in our diagnostic armamentarium even after emotional stress.

**MOLECULAR BIOLOGY / GENETICS**

**P2100**

**Preamplified real-time RT-PCR analyses of endomyocardial biopsies by T-PreAmp**

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**Background:** Low RNA amounts and low expression of certain target genes limit conventional real-time RT-PCR analyses of endomyocardial biopsies (EMB). A novel T-preamplification technique (T-PreAmp) enables a robust PreAmp of multiple target genes (> 92 gene assays), by a mean Ct improvement around 7 cycles, and with a low inter- and intra-assay variance (<5%), with multiple advantages compared to the SSRT (sequence specific reverse transcription) preamplification technique.

**Purpose:** Systematic evaluation of publications on the establishment and application of T-PreAmp in EMB.

**Results:** Our literature survey identified 19 publications applying the T-PreAmp protocol. The T-PreAmp has been applied to cell cultures, blood cells, snap frozen and paraffin embedded tissues. In EMB, CDKN1B was ascertained as a novel housekeeping gene for myocardial tissues. T-PreAmp in EMB revealed a significant association between the immunohistological proof of DCMi and the expression of CD3d, CD3z and of the constant T-cell receptor beta region (TRBC). The criterion of significantly increased TRBC or CD3d expression was associated with differential expression of several T-cell related genes, cytokines, and genes involved in extracellular matrix (ECM). The quantification of functional T-cell markers revealed significantly increased expression of Th1- and CTL-specific genes, while genes indicating regulatory and anergic T-cells were not differentially expressed. Differential TRBV dominances in human DCMi have been associated to the PCR proof of various viral genomes. In a patient presenting with acute myocarditis and parvovirus B19 (B19V) viremia, TRBV11 dominance was identified in the peripheral

blood monocytes (PBMC), with Th1- and CTL-characteristic functional T-cell markers (i.e. T-bet, IFN, Perforin), whereas markers of regulatory T-cells were not differentially expressed.

**Conclusions:** T-PreAmp is a powerful tool for preamplification and robust expansion of comprehensive target gene expression analyses of EMB (up to 92 target genes per preamplification reaction). In gene expression analyses of EMB, the T-PreAmp technique elucidated a novel housekeeping gene for myocardial tissues (CDKN1B), and confirmed differential expression of several T-cell related genes, diverse cytokines identifying a dominance of Th1- and CTL-polarized immunity, and of ECM related genes, in EMB from DCMi-patients, while a "counter-balance" of regulatory T-cells was not discernible. The finding of virus-associated TRBV-dominance in EMB and PBMC indicates virus-induced proliferation of peptide-reactive T-cell populations, driven by viral antigen challenge.

## P2101

### Role of mitochondria in intraventricular conduction delay: association between TOMM40 polymorphism and left branch bundle block.

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**Background:** TOMM40 gene polymorphism (translocase of outer mitochondrial membrane 40) plays a critical role in mitochondrial dysfunction in Alzheimer's disease and cardiac preconditioning, by both impairing mitochondrial Ca<sup>2+</sup> signaling and mtPTP (mitochondrial permeability transition pore) opening. At present only few investigations have explored polymorphism-related cardiac phenotype.

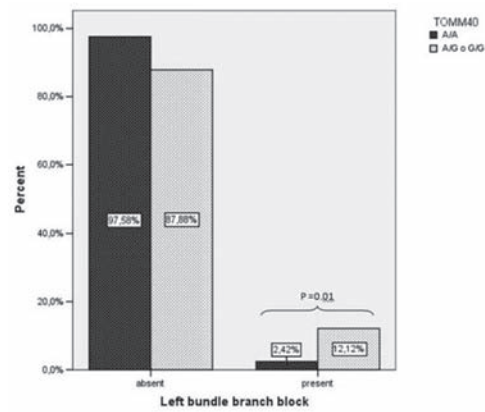
**Objectives:** The study aimed to examine the relationship between TOMM40 polymorphism and cardiac phenotype in patients affected by peripheral arterial disease.

**Methods:** TOMM40 polymorphism (rs2075650, AA and GX) were assessed in 198 consecutive patients, characterized for biochemical, electrocardiographic and echocardiographic parameters, traditional risk factors and history of myocardial infarction.

**Results:** We divided population in two groups, according to TOMM40 polymorphism (AA or GX), named AA group (165 pts) and GX group (33 pts). There was no difference between groups for the abovementioned factors, except for a greater prevalence of left bundle branch block (LBBB) in the GX group ( $\chi^2$  6.669,  $p=0.010$ ); this difference persists also after correction for confounding factors.

**Conclusions:** This study showed an association between TOMM40 polymorphism and left branch bundle block, suggesting a role of mitochondria in intramiocardial conduction delay.

Cardiac phenotype and comorbidity				
	Total (n 198)	AA (n 165)	GX (n 33)	P value
Age (yrs)	70.0 ± 7.7	70.0 ± 7.7	70.1 ± 8.2	ns
Men/women (n)	148/50	126/39	22/11	ns
Hypertension n (%)	179 (90)	148 (90)	31 (94)	ns
Dyslipidemia n (%)	187 (94)	154 (93)	33 (100)	ns
Type 2 diabetes n (%)	95 (48)	81 (49)	14 (42)	ns
Smoke n (%)	47 (24)	38 (23)	9 (27)	ns
Previous myocardial infarction n (%)	29 (15)	25 (15)	4 (12)	ns
Right bundle branch block (%)	13 (7)	9 (6)	4 (12)	ns
Left bundle branch block (%)	8 (4)	4 (2)	4 (12)	0.010
PR	164 ± 28	164 ± 29	162 ± 22	ns
QRS	101 ± 22	101 ± 22	103 ± 23	ns
QTc	407 ± 50	406 ± 50	415 ± 26	ns
Ejection Fraction (%)	58.7 ± 5.8	58.6 ± 6.0	59.0 ± 7.3	ns
Left ventricle end-diastolic diameter (mm)	45.8 ± 6.4	45.9 ± 6.4	45.5 ± 6.1	ns
Ventricular mass index (gr/m <sup>2</sup> )	76.4 ± 20.8	76.7 ± 21.0	74.8 ± 19.9	ns



Association between TOMM40 and LBBB

## P2102

### Polymorphism Glu298Asp NOS-3 gene in patients with chronic heart failure

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The purpose of the study is to study the features of polymorphism Glu298Asp NOS-3 gene in patients with chronic heart failure (CHF).

**Methods:** In patients with CHF 114 Uzbeks have been studied the genetic determinants of the development of endothelial dysfunction — alleles and genotypes Glu298Asp NOS-3 gene. The control group consisted of 75 healthy individuals — men of Uzbek nationality.

**Results:** Analysis of the distribution of genotypes Glu298Asp NOS-3 gene in patients with CHF showed: Glu/Glu — I in patients with CHF FC was 84.2% in patients with FC II — 70.4%, and FC III — 64.7% (Table 1). Glu/Asp genotype 3 patients met FC I — 15.3%, in 12 patients with FC II and —27.3% in 17 patients with FC III CHF —33.7%. In the group of healthy individuals Glu/Glu genotype occurred in 92%, Glu/Asp at 6.7%. Patients in the control group allele Glu was — 95.3%, and Alel Asp — 4.7%. Patients frequency vstechaemosti Glu — allele was distributed as follows: 92.1% in patients with CHF FC I, 84.1% in patients with class II and 81.4% in patients with FC III CHF.

**Conclusions:** Thus, the study of the distribution of alleles and genotypes Glu298Asp NOS-3 gene in patients with heart failure showed the progression of CHF depends on the polymorphism of this gene and gene Glu298Asp NOS-3 is effective prognostic markers.

## VASCULAR BIOLOGY

## P2103

### Association of adrenomedullin and atrial natriuretic peptide with endothelial function and peripheral vascular resistance in heart failure subjects

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**Background:** Adrenomedullin (ADM) is involved in vascular homeostasis and endothelial function. A-type natriuretic peptide (ANP) has potent diuretic, and vasodilating actions. Mid regional epitopes of these peptides (MR-proANP and MR-proADM) present increased plasma stability.

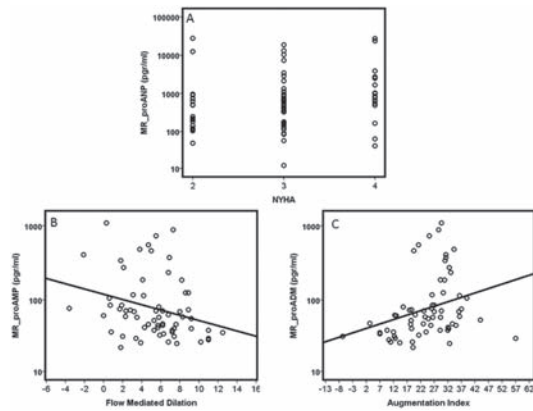
**Purpose:** To examine the association of MR-proANP and MR-proADM with indices of systolic and diastolic dysfunction in patients with chronic stable heart failure.

**Methods:** In this cohort study we enrolled 69 consecutive patients with stable chronic systolic heart failure in NYHA class 2 to 4. Endothelial function was evaluated by flow-mediated dilatation (FMD). Augmentation index (AIx) was measured as an index of arterial wave reflections. Serum levels of MR-proANP and MR-proADM were measured with ELISA.

**Results:** The mean age of the participant was 68 ± 10 years. In our study population there was no association between MR-proANP and MR-proADM with ejection fraction, while MR-proANP was associated with NYHA class ( $\rho=0.24$ ,  $p=0.04$ ). Importantly, we observe that MR-proADM was inversely associated with FMD ( $r=-0.315$ ,  $p=0.01$ ) and positively with AIx ( $r=0.398$ ,  $p=0.001$ ). However, MR-proANP was not associated neither with FMD ( $r=0.03$ ,  $p=0.8$ ) nor with AIx ( $r=0.08$ ,  $p=0.05$ ).

**Conclusion:** These findings confirm the different mechanisms involved in MR-proANP and MR-proADM secretion and revealed that MR-proADM is strongly associated not only with heart failure and ventricular filling pressures but also with endothelial function and peripheral vascular resistance.

**Conclusion:** These findings confirm the different mechanisms involved in MR-proANP and MR-proADM secretion and revealed that MR-proADM is strongly associated not only with heart failure and ventricular filling pressures but also with endothelial function and peripheral vascular resistance.



**Introduction:** Cardiac type-2 ryanodine receptors (RyR2) play a pivotal role during excitation-contraction coupling. There is considerable evidence that abnormal, increased RyR2-mediated diastolic SR-Ca<sup>2+</sup> release is linked to heart failure (HF) and arrhythmias such as atrial fibrillation (AF). Dantrolene (Dan), known as a drug for malignant hyperthermia, has been discussed to stabilize the cardiac RyR2. We thus aimed to investigate the effects of Dan on arrhythmogenic triggers and contractile function in human AF and HF myocardium.

**Methods/Results:** Human atrial cardiomyocytes (CM) were isolated from 7 patients with AF and left ventricular (LV) CM from 7 patients with end-stage HF. Functional measurements of SR Ca<sup>2+</sup> leak were performed by confocal microscopy using Fluo-3 AM. In LV HF CM Dan (10 μM) caused a reduction of spark-frequency by 33 ± 16% (p < 0.05, n = 83 cells / 6 patients Dan vs. 94 cells / 6 patients control) leading to a reduction of the calculated diastolic SR-Ca<sup>2+</sup>-leak (frequency x width x duration x amplitude) by 76 ± 21% (p < 0.05, n = 83/6 vs. 94/6). Moreover, Dan decreased the frequency of Ca<sup>2+</sup>-waves and spontaneous Ca<sup>2+</sup>-transients by 52 ± 24% (p < 0.05, n = 102/6 vs. 109/6). The reduction of the arrhythmogenic diastolic SR-Ca<sup>2+</sup>-leak was further reproducible in atrial CM from patients with AF. Dan treatment in AF reduced the spark-frequency by 50 ± 19% (p < 0.05, n = 122/7 vs. 120/7) and the diastolic SR-Ca<sup>2+</sup>-leak by 56 ± 21% (p < 0.05, 122/7 vs. 120/7). Patch clamp experiments revealed that Dan abolishes cellular arrhythmogenic triggers (DADs and spontaneous APs) significantly in HF (p < 0.05 n = 16/7 vs. 19/7) and in AF (p < 0.05 n = 12/6 vs. 14/6). Importantly, Dan had no effect on action potential duration compared to control in AF and HF. The investigation of the effect of Dan on isometrically twitching muscle strips showed no significant alterations of systolic and diastolic force. Mean data of systolic force after drug-incubation was 5.6 ± 1.7 vs. 6.4 ± 2.8 mN/mm<sup>2</sup> for Dan and vehicle control, respectively (n.s., n = 5 each).

**Conclusion:** Dan beneficially altered calcium homeostasis in human HF and AF CM. Arrhythmogenic SR Ca<sup>2+</sup> leak due to destabilized RyR2 was significantly decreased by Dan, and cellular arrhythmogenic triggers could be abolished. APD and contractility were not affected by Dan. Thus, Dantrolene as an already approved compound for malignant hyperthermia in men might be a potential antiarrhythmic compound for patients with AF and HF and merits clinical investigation.

**P2104**

**Mediterranean diet and erectile dysfunction**

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**Introduction:** Mediterranean Diet represents a way of life which combines longevity and a high quality of health. As far as the physiology of vessels is concerned, the application of this diet has shown that it can improve the good operation of the endothelium. The endothelial dysfunction is the main pathophysiological mechanism of the erectile dysfunction which influences dramatically the quality of life.

**Purpose:** We have studied the correlation between the Mediterranean Diet with the presence and rate of Erectile Dysfunction.

**Methods:** We studied 100 patients with Erectile Dysfunction without any history of cardiovascular disease (aged 52 ± 15 years) and 100 people without Erectile Dysfunction (test group), similar to age and danger factors. Erectile Dysfunction was evaluated based on the international questionnaire of sexual health (International Index of Erectile Dysfunction, IIEF). Low IIEF score shows severe Erectile Dysfunction. The degree of application of the Mediterranean Diet was found according to a special score (MED-DIET score, with a theoretic variation 0-55). High prices of this score show a great devotion to this kind of diet.

**Results:** Compared to the test group the patients with Erectile Dysfunction had considerably lower MED-DIET score (P < 0.05). All facts considered, MED-DIET score was positively related to erectile efficiency as this was expressed through IIEF score (P < 0.01). The relation of MED-DIET score with the IIEF score remained important as the age, the danger factors and the testosterone levels (P < 0.05) were examined.

**Conclusion:** This study showed that a poor, long-term application of the Mediterranean Diet has unfavorable effects on Erectile Dysfunction without taking into consideration the classic danger factors. A diet rich in fruit, pulses, vegetables, dried fruit and mainly olive oil combined with medium consumption of alcohol, especially between meals can be proven useful as far as the improvement of the vessels' functionality is concerned and also the erectile cardiovascular efficiency.

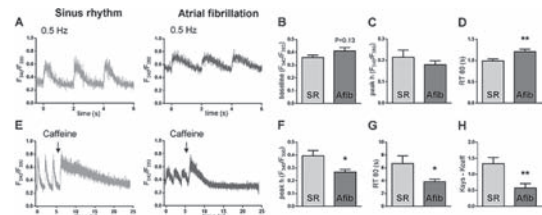
**BASIC SCIENCE: ATRIAL FIBRILLATION**

**P2107**

**Effects of atrial fibrillation on ventricular calcium cycling in human myocardium**

German Research Foundation SFB 1002, Deutsche Herzstiftung e.V.  
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Atrial fibrillation (Afib) is the most common sustained arrhythmia, causing significant morbidity and mortality. In the atria it is associated with profound changes of cellular electrophysiology and Ca-handling. However, little is known about the effects of irregular heart rhythm itself on EC-coupling in the ventricle. This is of great relevance with regard to pathophysiological understanding and clinical treatment strategies. We isolated ventricular cardiomyocytes from patients with compensated cardiac hypertrophy (aortic stenosis) showing sinus rhythm (SiR) or persistent Afib (n = 4/4). Ca-cycling properties were investigated by epifluorescence microscopy (Fura2-AM). To our knowledge, these are the first measurements in this regard in human cells. Afib exhibited a tendency towards higher diastolic Ca-levels compared to SiR (B, n = 18/23, P = 0.13). The amplitude of systolic transients (0.5 Hz) was not altered (C, n = 18/23, P = 0.41), but elimination kinetics were slowed (D, RT 80, n = 17/22, P < 0.01) and the height of caffeine-induced Ca-transients was reduced in Afib (F, n = 12/12, P < 0.05) indicating a lower SR Ca-load. Elimination-kinetics of caffeine-induced Ca-transients were accelerated in Afib vs. SiR (G, RT80, n = 12/12, P < 0.05) suggesting increased NCX-activity. Conclusively, calculated SERCA2a-activity was diminished in Afib (H, n = 10/12, P < 0.01). Our findings have clear relevance as reduced SR Ca-load, SERCA2a-activity and increased NCX-activity are key-features of heart failure, but can obviously already be observed in patients with cardiac hypertrophy and Afib despite a still preserved ejection fraction. It may therefore be hypothesized that irregular ventricular excitation promotes pathologic alterations of Ca-homeostasis paving the way for contractile dysfunction and electric instability.



**BASIC SCIENCE: ARRHYTHMIAS AND TREATMENT**

**P2106**

**Dantrolene reduces cellular arrhythmogenic triggers in human atrial fibrillation and heart failure**

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**P2108****Pitx2 modulates atrial membrane potential, rendering atrial cells susceptible to antiarrhythmic drug treatment with sodium channel blockers**

EUTRAF to PK, BHF to PK, Leducq Foundation to PK, PSIBS of UoB for TY to LF, DFG, and BIF fellowship to SMK  
SM Kuhlmann<sup>1</sup>; AP Holmes<sup>1</sup>; F Syeda<sup>1</sup>; TY Yu<sup>1</sup>; S Tull<sup>1</sup>; D Pavlovic<sup>1</sup>; L Fabritz<sup>1</sup>; P Kirchhof<sup>1</sup>

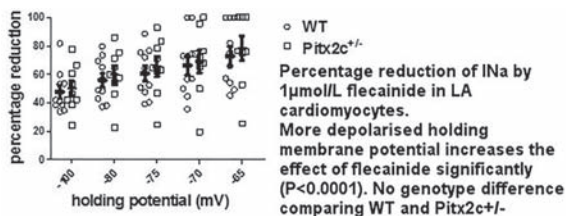
<sup>1</sup>University of Birmingham, Birmingham, United Kingdom

**Purpose:** Atrial fibrillation (AF) is common in heart failure patients and contributes to its morbidity and mortality, e.g. in tachycardia-induced cardiomyopathy. Common gene variants on chromosome 4q25, close to the PITX2 gene, predispose to AF, modify the response to antiarrhythmic drug (AAD) therapy, and alter left atrial PITX2 mRNA levels. We therefore studied how PITX2 modifies atrial electrophysiology and the response to AADs, making use of PITX2-deficient (Pitx2c+/-) mice.

**Methods:** We assessed arrhythmias in isolated, perfused hearts, sharp electrode action potentials in superfused left atria, and sodium (INa) and potassium currents (Ito, IK1, IKACH) by whole-cell patch-clamp in isolated LA cells.

**Results:** Pitx2c+/- left atria had shorter action potentials and a more positive resting membrane potential than WT (P < 0.05 (WT: -70.1 ± 0.7 mV, n = 30 cells. Pitx2c+/-: -67.8 ± 0.7 mV; n = 31 cells)). Flecainide, but not sotalolol, fully suppressed atrial arrhythmias in Pitx2c+/- atria but not in WT, increasing post-repolarization refractoriness. INa amplitude or Nav1.5 channel expression were not different between genotypes. Different holding potentials affected INa equally in both genotypes at baseline and with flecainide (1 μM), irrespective of genotype (Figure). Ito, IK1, or IKACH were not different in WT and Pitx2c+/- LA (all P > 0.2). A comparable effect of LA holding potential (RMP) on the effect of flecainide was replicated in HEK cells expressing human Nav1.5 channels.

**Conclusions:** We identified a more depolarised resting membrane potential in mice with reduced PITX2c expression that markedly modulates the effects of sodium channel blockers. Our findings identify an altered resting membrane potential as an important modulator of antiarrhythmic drug efficacy.

**P2109****The relation of atrial fibrillation to the severity of dyspnea in patients presenting to the emergency room**

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**Background/Introduction:** Dyspnea is one of the most common symptoms presented by patients in the cardiac emergency rooms. As the etiology of dyspnea is multifactorial, from psychogenic causes to serious heart conditions, and the treatment stands upon eliminating the causing factor, various aspects should be considered when performing the differential diagnosis.

**Purpose:** We aimed to determine if the presence of atrial fibrillation (AF) is associated with the severity of dyspnea.

**Methods:** 151 consecutive patients admitted to the cardiac emergency room were included in the study. The inclusion criterion was dyspnea. Exploratory groups were defined based on cardiac rhythm at the time of admission: AF group and non-AF group and two subgroups regarding their heart rate (HR): moderate heart rate (MHR) group (HR < 90 beats per minute (bpm)) in AF group as well as in non-AF group and high heart rate (HHR) group (HR ≥ 90 bpm) accordingly in AF and non-AF groups. Patients were asked to fulfill the numerical and visual Borg dyspnea test charts in a scale from 1 to 10 points. Data was analysed using SPSS v23 statistical package. Independent samples T-test was used to compare the results amongst patient groups.

**Results:** Of 151 examined patients 68 (45%) were female and 83 (55%) male. 75 (49.7%) patients presented atrial fibrillation (tested by 12-lead electrocardiogram) at the time of admission, while 76 (50.3%) did not. Mean HR in AF group was 95.32 bpm while in non-AF group – 84.72 bpm. Study did not find a statistically significant difference between mean dyspnea points in AF (mean of dyspnea points – 6.4) and non-AF (6.56) patient groups, male (6.18) and female (6.63) groups as well as between two MHR (6 in MHR – non-AF, 7.13 in MHR – AF) and HHR (5.97 in HHR – non-AF, 6.82 in HHR – AF) subgroups – for both numerical and visual evaluations (p > 0.05).

**Conclusion:** Atrial fibrillation does not influence the subjective severity of dyspnea.

**BASIC SCIENCE: VALVULAR HEART DISEASE (DIAGNOSIS, MANAGEMENT AND INTERVENTIONAL THERAPIES)****P2110****The value of exosomal miRNAs to predict clinical outcome in patients undergoing percutaneous mitral valve repair using MitraClip system**

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**Aims:** Long-standing mitral regurgitation (MR) causes chronic volume overload eventually leading to left ventricular (LV) remodeling and heart failure. In the present study we aimed to assess the potential of a panel of echocardiographic parameters and miRNA biomarkers to predict clinical outcome and functional recovery after percutaneous mitral valve repair (PMVR) using the MitraClip system.

**Methods:** 67 patients (76 ± 6 y, 53% w) with heart failure symptoms (NYHA > 2) and moderate-to-severe MR (> 2) underwent PMVR. We performed conventional 2D echocardiography, including speckle tracking analysis before the procedure (BL) and at six-months follow-up (FU). Circulating exosomal miRNA abundance was determined after enrichment of exosomal microparticles from serum followed by Taqman PCR for quantification of specific miRNAs.

**Results:** Mitral valve repair resulted in increased effective stroke volume (SV) despite unchanged LV ejection fraction (EF), indicating recovery of overall cardiac performance. LV global longitudinal strain (GLS) revealed differing potential for recovery of contractility. Patient clinical recovery (defined NYHA class improvement) significantly correlated with exosomal miR-enc-1, miR-enc-2, and miR-enc-5; whereas post-procedural pulmonary artery pressure (PAP) with miR-enc-6 and miR-enc-7.

**Conclusions:** Possible predictive value of exosomal miRNAs regarding myocardial recovery requires further evaluation of candidate miRNAs in validation cohorts. Distinct exosomal miRNA profiles may differentiate functional disturbances in left ventricle vs. left atrium and pulmonary circulation vs. right ventricle, and thus progression of heart failure through different phases until the transition to irreversible myocardial damage. Clinical application of confirmed predictive miRNAs would enable further individualization of treatment decision based on a patient's likely individual response to therapy

**P2111****Permanent pacemaker implantation in patients undergoing trans-catheter aortic valve implantation: 1st year single center experience**

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**Background:** Transcatheter aortic valve implantation (TAVI) has been established as a treatment option for patients with symptomatic aortic valve stenosis who are not considered candidates for open surgery. However, the proximity of the aortic valve annulus to the conduction system is a known risk of conduction disturbances that requires monitoring and, in some cases, permanent cardiac pacing. The aim of this study was to assess the incidence rate of conduction disorders and the predictors of permanent pacemaker implantation in patients undergoing TAVI.

**Methods:** We conducted a retrospective observational study that included consecutive patients treated with TAVI in a single tertiary centre between November 2014 and November 2015. Baseline parameters, procedural characteristics as well as twelve-lead surface ECG before and shortly after TAVI were evaluated. A comparison between patients that required pacemaker with those who did not was done using a univariate analysis.

**Results:** A total of 41 patients (41.5 % male), 80 ± 7.4 years successfully underwent TAVI, 66% implanted the third-generation percutaneous self-expanding CoreValve. A permanent pacemaker was implanted in 9 (22%) of the patients, dual chamber in 89% of cases. The pacemaker was implanted on average at 7 ± 3 days following TAVI (range 3 to 12 days). When comparing patients who required pacemaker versus those who didn't, we found a higher prevalence of new auriculoventricular conduction disturbance after implantation of TAVI (67% vs. 19 %, p = 0.011). No other baseline electrocardiographic parameters or clinical characteristics associated with the need of permanent cardiac pacing (namely age, sex, intraventricular delay conduction disturbances previous or after TAVI) were found.

**Conclusion:** Cardiac conduction disturbances are common after TAVI and are associated with an increased risk of permanent pacemaker. Careful ECG monitoring may be necessary for as long as one week after TAVI due to a risk of atrioventricular conduction disturbances of more late onset. In our small group of patients only new-onset auriculoventricular conduction disturbances was found to be associated with permanent pacemaker requirement. Future research and registries with larger

groups of patients will allow to find independent predictors for pacemaker implantation.

## BASIC SCIENCE: DEVICES / CRT / ICD

### P2112

#### Different response to cardiac resynchronization therapy in patients with congestive heart failure

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**The aim:** The aim of the study was to evaluate clinical, morphological and functional features and mortality in patients with chronic heart failure (CHF) in patients with different time of the best response to cardiac resynchronization therapy (CRT).

**Materials and methods:** 122 patients (82.8% men) with CHF NYHA functional class III-IV (mean age 54.8±9.6 years). At baseline, 1 months, 3 months and each 6 months after implantation we evaluated clinical and echocardiographic parameters. In 28 patients the best decrease of left ventricular end-systolic volume (LVESV) was achieved up to 3 months (1.1±0.9 months, I group – ‘early’ response) and in 94 patients – after 3 month (22.6±14.9 months, II group – ‘late’ response). Groups did not differ in clinical characteristics, NYHA functional class, QRS duration and parameters of mechanical dyssynchrony.

**Results:** In the II group responders (decrease in LVESV ≥15%) were identified significantly more frequently (90.4% vs. 60.7%; p=0.001), all patients with decrease of LVESV ≥30% (superresponders) had ‘late’ response. During follow-up period (33.2±16.7 months) increase in left ventricular ejection fraction (LVEF) and decrease in LVESV were more evident in patients with ‘late’ response. In Kaplan-Meier analysis mortality in II group was significantly lower (3.2% vs 28.6%; p=0.001). Cox regression showed that LVESV (HR 1.012; 95% CI 1.004–1.021; P=0.005) and the time of response (HR 0.131; 95% CI 0.032–0.530; P=0.004) were associated with long-term mortality.

**Conclusion:** Patients with ‘early’ response to CRT show significantly lower improvement in LVEF and LVESV compared to patients with ‘late’ CRT response. ‘Early’ response and greater LVESV are associated with higher mortality rate.

### P2113

#### The effect of biventricular stimulation in patients with chronic heart failure with moderate clinical manifestations

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**Objective:** to assess the effectiveness of CRT (cardiac resynchronisation therapy) implantation in patients with chronic heart failure NYHA functional class II.

**Methods:** 50 patients (pts) with ischemic (23 pts) or dilated cardiomyopathy(27 pts) complicated by CHF NYHA functional class (FC) II, LV EF below 35%, QRS duration 150 msec and more and with ECHO confirmed mechanic myocardial dyssynchrony were examined. All patients underwent the LV end-diastolic volume (LVEDV), LV end-systolic volume (LVESV), LV end-systolic diameter (LVESD) LVEF, LV end-diastolic diameter (LVEDD), interventricular delay, dyssynchrony index (TS-DS), ), all segments max delay were estimated by ECHO. The levels of BNP, the six-minute walk test (6MWT) and life quality (LQ) were measured initially and at 6 months after CRT implantation.

**Results:** At 6 months, LVEDV significantly decreased from 318,41±15,8 ml to 252,7±22,1ml (<0,05), LVESV decreased from 241,41±12,9 to 166,8±20,4 (<0,05), LVEF increased evidently from 24,17±0,85% to 35,5±2,3% (<0,05). Intracardiac hemodynamic changes were accompanied by decreased mechanic dyssynchrony event rate - there was trend to the evident decrease of inter-ventricular delay from 67,7±4,2 to 38,15±7,3 msec. (<0,05 ), TS-DS- from 65,5±5,1 to 56,3±6,2 msec. (<0,05 ), all segments max delay from 183,5±11,5 to 151,7±17,8 msec. (<0,05 ); improved LQ of patients: LQ evidently decreased from 59,9±1,67 scores to 37,1±2,5 scores (<0,05); 6 MWT increased from 393,8,2±15,07 m to 479,1±17,06 m; NT-proBNP decreased from 1442,4±277,8 to 627,37±301,5(<0,05).

**Conclusions:** At 6 months biventricular heart stimulation evidently enhances heart haemodynamic and the clinical conditions of pts, improving exercise tolerance in pts with chronic heart failure NYHA functional class II.

### P2114

#### Measurement of left ventricular ejection fraction in candidates to implantable cardioverter-defibrillator: echocardiography versus radionuclide ventriculography in 67 patients

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<sup>1</sup>Osp. Civile Macerata, AV3 Asur Marche, SC Cardiologia, Macerata, Italy

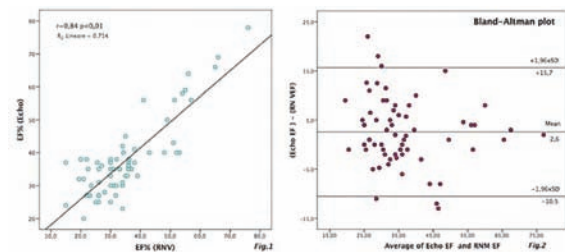
**Background:** conflicting results have been reported in the measurement of left ventricular ejection fraction (LVEF) by different techniques. That is of paramount importance when dealing with chronic heart failure (CHF) patients who may be candidates to implantable cardioverter-defibrillator (ICD).

**Aim of the study:** to assess the difference in measurement of LVEF derived either by echocardiography (Echo) or by radionuclide ventriculography (RNV) in the same CHF patients candidates to ICD implant.

**Materials and methods:** in the period between 2010 to 2014, 67 CHF patients (age 26-87 years, average 76 years, 54 males and 13 females), NYHA functional class III or IV were admitted in our department of cardiology and studied before ICD implant. LVEF was assessed using both techniques (Echo and RNV) during the same hospitalization; measurements were taken in the same day or in consecutive days without changes in clinical status or in drugs administration.

**Results:** the man value of LVEF obtained by Echo was 37.61±11.5% (range 20-78%). The man value of LVEF obtained by RNV was 35±12.5% (range 15-76%). The mean difference (Echo LVEF – RNV LVEF) was 2.6±6.7% (range 13-22%). The statistical analysis showed a linear correlation, statistically significant, between the LVEF measurements obtained by the two techniques (Figure 1); on the contrary the difference between the two means was not significant. depicts; When analysing data by a different statistical way, the Bland-Altman plot (Figure 2), we observed that values included in the confidence interval were far from the mean (15.7% and -10.5% respectively), despite a mild mean difference.

**Conclusions:** the present study showed a strong linear correlation between the values of LVEF obtained with the two techniques (Echo / RNV) as well as a trivial mean difference, therefore confirming the clinical usefulness of both. However, the wide range (26.2%) of mean differences found in our CHF patients, suggests to be cautious when deciding the appropriateness of ICD implant on the value of LVEF obtained only by one technique.



Figure

### P2115

#### Endothelial dysfunction with continuous flow left ventricular assist device support: effects on the number and function of endothelial progenitor cells

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**Background:** Contemporary continuous flow left ventricular assist devices (Cf-LVADs) support non-pulsatile physiology. This was associated with impaired endothelial function and the common occurrence of vascular complications. The mechanism of endothelial dysfunction in patients on Cf-LVAD support has not been determined.

**Methods:** In this prospective observational study patients in stage D heart failure (HF) were evaluated before and at 1 and 3 months after Cf-LVAD implantation. We measured reactive hyperemia index (RHI) for endothelial function using peripheral arterial tonometry. Circulating endothelial progenitor cells (EPC) were identified using flow cytometry and represented as the proportion of mononuclear cells expressing VEGFR-2/CD133, or VEGFR-2/CD34. Functional aspects of EPCs were evaluated after 7 days of culture by identification of colony forming units and the MTT assay for viability of cells.

**Results:** Twenty-one patients supported with Cf-LVAD for more than 3 months were included. Patients were 62±7 years old, 18(86%) males and 14(67%) had ischemic etiology. Twelve (57%) were implanted with HeartMate II (Thoratec) and 9 (43%) received an HVAD (Heartware) LVAD. RHI and EPC results are shown in the table. At 3 months early EPCs (VEGFR-2/CD133) and MTT significantly increased. RHI at

3 months strongly correlated with EPCs at 1 month (spearman's  $-0.8$ ,  $p < 0.001$  for both). Pre and post LVAD EPCs did not form colonies in culture.

**Conclusion:** While pre-operative endothelial dysfunction persists after surgery, EPCs increase in number but remain dysfunctional, suggesting possible damage caused by the Cf-LVAD circulation. Newer LVADs with maintained pulsatility may be more protective of endothelial physiology.

Variable	Pre-LVAD	1mo after LVAD	3mo after LVAD
RHI	1.46 ± 0.41	1.38 ± 0.25 (n = 13)	1.41 ± 0.31 (n = 18)
VEGFR-2/CD133%	3(1;7)	2(1;9) (n = 17)	7(2;17) (n = 18)*
VEGFR-2/CD34%	3(1;4)	4(2;9) (n = 17)	4(2;11) (n = 18)
MTT 570nm	0.4 ± 0.3 (n = 20)	0.4 ± 0.3 (n = 17)	0.6 ± 0.4 (n = 17)§

mean ± SD or median (IQR). \* $p < 0.04$ ; § $p = 0.01$  versus pre-LVAD using Wilcoxon signed rank test.

## P2116

### A novel implantable counterpulsation assist device optimizes left ventricular mechanoenergetics and improves myocardial perfusion in a porcine model of acute heart failure

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**Background:** We have developed a novel implantable counterpulsation LVAD, the Pressure-Unloading Left Ventricular Assist Device (PULVAD), designed to provide LV pressure unloading and diastolic aortic augmentation.

**Purpose:** To investigate the effects of PULVAD support on LV and myocardial perfusion in a porcine model of acute heart failure (AHF).

**Methods:** PULVAD comprises a pneumatically-driven pumping chamber implanted in the thoracic cavity and connected to the ascending aorta. The pump is ECG-synchronized to operate 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). Seven farm pigs were instrumented with Millar catheter, sonomicrometry crystals and a Doppler flow probe placed around the left anterior descending artery (LAD). Pigs underwent induction of AHF by LAD ligation for 60 minutes, followed by reperfusion. PULVAD was implanted in the thoracic cavity and connected to the ascending aorta. PULVAD was driven by the Arrow Autocath 2 Wave system console (a conventional intra-aortic balloon pump console) and was ECG-synchronized to provide LV pressure unloading along with aortic diastolic pressure augmentation. Traditional hemodynamics, indices of LV energy consumption, indices of LV mechanical performance and LAD blood flow were measured without and after brief (30-60 seconds) PULVAD support during reperfusion.

**Results:** PULVAD support induced a profound reduction in LV afterload, manifested as a significant decrease in systolic aortic pressure (from  $99.2 \pm 23.1$  to  $80.3 \pm 24.6$  mmHg,  $p < 0.05$ ) and in end-diastolic aortic pressure (from  $82.1 \pm 24.4$  to  $59.9 \pm 28.6$  mmHg,  $p < 0.05$ ). PULVAD support reduced LV energy consumption, manifested as a significant decrease in LV stroke work (from  $2974 \pm 1816$  to  $2406 \pm 1686$  mmHg\*ml,  $p < 0.05$ ), while concurrently improving LV mechanical performance (relative increase in ejection fraction:  $27.4 \pm 42.1\%$ ; relative increase in stroke volume  $23.5 \pm 39.0\%$ ,  $p < 0.05$ ). PULVAD support significantly increased mean LAD blood flow (from  $50.77 \pm 23.44$  to  $64.64 \pm 24.22$  ml/min,  $p < 0.05$ ), mainly by producing a dramatic augmentation in diastolic LAD blood flow ( $62.40 \pm 31.45$  ml/min to  $98.28 \pm 36.30$  ml/min,  $p < 0.05$ )

**Conclusions:** PULVAD, a novel implantable counterpulsation LVAD, optimizes LV energetic performance (decreases energy consumption and concurrently improves mechanical performance) by LV unloading and augmentation of myocardial blood flow.

## BASIC SCIENCE: HEART FAILURE IMAGING

## P2117

### Limited increase of cardiac index and myocardial perfusion during dobutamine-stress in a porcine model of early HFpEF: a cardiac magnetic resonance imaging study.

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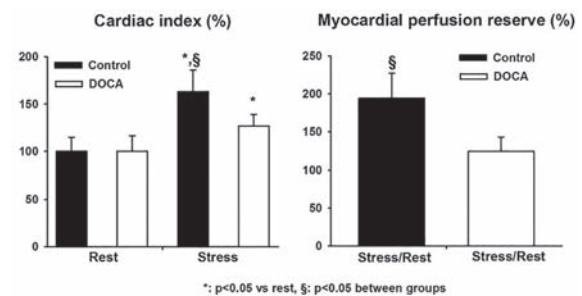
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**Introduction:** Heart failure with preserved ejection fraction (HFpEF) evolves by accumulation of risk factors over time and still lacks a guideline therapy, in part due to the complex pathophysiology. An increased left ventricular stiffness at rest is the hemodynamic hallmark of the disease. However, most patients become symptomatic preferably during exercise, and a limited myocardial perfusion and contractility reserve may play a role. We therefore investigated left ventricular (LV) function and perfusion during dobutamine-stress in a previously established porcine model of hypertensive heart disease/early-stage HFpEF.

**Methods and Materials:** Five anesthetized deoxycorticosterone-acetate (DOCA)-salt induced early-stage HFpEF pigs and seven weight-matched controls underwent cardiac magnetic resonance imaging at rest and during dobutamine stress (heart-rate increase:  $21 \pm 7\%$ ). Indices of left ventricular (LV) function were evaluated from cine short-axis images. Early-diastolic tissue velocity (E'), transmural velocity (E), and coronary sinus net-forward blood volume (CSV) were acquired from 4D phase-contrast measurements and evaluated by prototype software (4D-Flow). Global myocardial perfusion (GMP) and perfusion reserve (MPR) were estimated from rest/stress CSV and LV mass. Rest, stress, and rest-to-stress differences (in %) of parameters in DOCA and control animals were compared by t-test.

**Results:** Dobutamine increased LV ejection-fraction and decreased LV end-systolic volume in both groups ( $p > 0.05$ ). E' was lower in DOCA at rest ( $p = 0.019$ ) and during stress ( $p = 0.025$ ), yielding higher E/E' at rest and stress ( $4.4 \pm 0.9$  vs  $3.0 \pm 0.5$  and  $4.6 \pm 0.3$  vs  $3.6 \pm 0.8$ , all  $p < 0.05$ ), indicating higher LV filling pressures in DOCA. Cardiac index increased less in DOCA pigs (graph), and the LV end-diastolic volume index decreased during dobutamine in DOCA (DOCA,  $-20 \pm 11\%$ ; controls,  $-5 \pm 11\%$ ;  $p = 0.042$ ). GMP did not differ between groups at rest ( $p = 0.538$ ), but increased less in DOCA-pigs during dobutamine, resulting in a reduced MPR (graph).

**Conclusion:** In a preclinical model of early-stage HFpEF, an impaired increase of cardiac index during dobutamine-stress was paralleled by a reduced myocardial perfusion reserve. Exercise induced myocardial ischemia may be a contributor to LV dysfunction in HFpEF.



## P2118

### Native myocardial T1 times are not necessarily increased with myocardial collagen: a preclinical study in hypertensive hypertrophic heart disease.

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**Introduction:** Heart failure with preserved ejection fraction (HFpEF) evolves by accumulation of risk factors over time and still lacks a guideline therapy, in part due to the complex pathophysiology. Myocardial fibrosis is one of the major contributors of left ventricular diastolic dysfunction, the classical hallmark of the disease. T1 mapping is a cardiac magnetic resonance technique that allows the detection of myocardial fibrosis. However, the accuracy of this technique in detecting increased interstitial collagen in the setting of early left ventricular (LV) remodelling needs to be further elucidated. We therefore aimed to investigate whether native left ventricular (LV) T1-times are increased with myocardial collagen in a previously established porcine model of hypertensive heart disease/early-stage HFpEF.

**Methods and Materials:** Five anesthetized deoxycorticosterone-acetate (DOCA)-salt induced hypertensive, hypertrophic pigs and three healthy animals underwent ECG-gated 3T magnetic resonance imaging, including assessment of LV mass and native myocardial T1-times (MOLLI protocol 5(5)5(5)5). After in-vivo measurements, animals were sacrificed and transmural biopsies were collected for stereological analysis. T1-maps were evaluated by manual segmentation according to the AHA 17-segment model. LV T1-times were calculated as averages from



segmental values. Stereological evaluation included myocardial volume fractions of interstitium (Vint/LV) and collagen (Vcoll/LV), as well as collagen volume related to the interstitium (Vcoll/int). Parameter means of DOCA and control animals were compared by t-test; relationships between parameters were analyzed with correlation analysis.

**Results:** LV mass was higher in DOCA pigs (DOCA,  $134 \pm 21$ g; controls,  $88 \pm 2$ g;  $p < 0.001$ ). LV T1-times did not differ between groups (DOCA,  $1161 \pm 21$ ms; controls,  $1195 \pm 36$ ms;  $p = 0.094$ ). Vcoll/int showed higher levels in DOCA (DOCA,  $17 \pm 4\%$ ; controls,  $8 \pm 3\%$ ;  $p = 0.032$ ). Related to LV mass, Vint/LV (DOCA,  $17 \pm 5\%$ ; controls,  $21 \pm 2\%$ ;  $p = 0.202$ ) and Vcoll/LV (DOCA,  $2.7 \pm 0.8\%$ ; controls,  $1.7 \pm 0.5\%$ ;  $p = 0.109$ ) were not significantly different. Whereas myocardial T1-times did not correlate significantly with Vint/LV and Vcoll/int, the negative correlation with Vcoll/LV was significant ( $r = -0.71$ ,  $p = 0.047$ ).

**Conclusion:** Although interstitial collagen content is elevated in our large-animal model of early-stage HFpEF, LV T1-times did not differ. The effect of cardiomyocyte hypertrophy (decreased interstitial space) dominates native T1-times in a voxel rather than increased myocardial collagen content.

## P2119

### Challenging diagnosis in constrictive pericarditis

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**Background:** Perhaps no cardiac disorder is as elusive as constrictive pericarditis (CP) mimicking diseases as divergent as MI to cirrhosis. The penalty for incorrect decision is direr, needless sternotomy vs. continued undiagnosed symptoms.

**Methods:** 65 years old patient with persistent atrial fibrillation, without notable medical history, with signs of right failure despite maximal treatment. Echocardiography with signs of pulmonary hypertension, normal left ventricular systolic function, bia-rial dilatation, define the diagnostic of rhythmic cardiopathy. For the patient sent for ablation to our center, a cardiac scanner was used before ablation.

**Results:** Cardiac CT highlights the evidence of extensive pericardial calcification associated with increasing of pericardial thickness, diagnosing the constrictive pericarditis. CMR evaluation revealed the presence of ventricular interdependence and tagged cine CMR showing no tethering and no adhesion of the thickened pericardium to the myocardium, making feasible the pericardectomy. Partial pericardectomy was performed. Anatomic pathological images revealed an idiopathic chronic calcified pericarditis.

**Conclusions:** Given the ability to define all segments of pericardium and its physiologic interaction of with the heart, CMR associated cardiac CT may as well be the new 'gold standard' of diagnosis.

## P2120

### Left ventricular remodeling in patients with type 2 diabetes mellitus

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**Background:** Many studies have emphasized the architectural changes and left ventricular (LV) remodeling as a result of myocardial chronic stress factors such as hypertension and diabetes, as well as the risk of progression to heart failure.

**Purpose:** To study the LV geometrical remodeling in patients with type 2 diabetes mellitus (T2DM) with or without hypertension (HT), without coronary artery disease, asymptomatic for heart failure, with normal ejection fraction (LV EF > 55 %).

**Methods:** 337 patients with T2DM (175 male, age 38-77 years) and 100 age-matched normal subjects (52 male) as a control group underwent echocardiography for the evaluation of LV dimensions, mass and remodeling. They were divided in three groups: control group – 100 normal subjects; T2DM alone group – 213 patients; T2DM + HT group – 124 patients.

**Results:** 37.1 % (79/213) of patients with T2DM versus 76.61% (95/124) of patients with T2DM+HT had an abnormal LV geometry ( $p < 0.001$ ). A concentric remodeling was found in 17.84% (38/213) of patients with T2DM versus 17.74% (22/124) of patients with HT+T2DM ( $p = ns$ ). 12.68% (27/213) of patients with T2DM versus 29.84% (37/124) of patients with T2DM+HT showed concentric hypertrophy ( $p = 0.05$ ), whereas 6.57% (14/213) of patients with T2DM versus 29.03 % (36/124) of patients with HT+T2DM showed eccentric LV hypertrophy. ( $p = 0.001$ ). An important statistical significance was noticed between the presence of T2DM and LV remodeling ( $r = 0.49$ ;  $p < 0.001$ ), as well as a strong relationship between the presence of T2DM+HT and LV remodeling ( $r = 0.75$ ;  $p < 0.001$ ).

**Conclusions:** Diabetes mellitus is an important factor on the LV geometrical remodeling. When only DM is present the most common remodeling type is the concentric remodeling, whereas when DM coexists with HT both concentric and eccentric hypertrophic models are similarly expressed.

## P2121

### Imaging cardiac hydatid cysts: 10 cases.

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**Introduction and Purpose:** Cardiac hydatid disease is rare. Rupture of a cardiac cyst is a serious complication. Diagnosis of cardiac hydatid cysts is often made using transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) provides details of the cysts. We report 10 cases of cardiac hydatidosis, review the modes of diagnosis, and stress the contribution of modern imaging techniques

**Methods:** we have collected ten cases of CH between 1990 and 2014. The average age of patients was 33 years and sex ratio = 0.3. We assessed retrospectively the clinical and echocardiography features of CH in consecutive Patients.

**Results:** symptom consisted on atypical chest pain in six patients, dyspnea in two cases and dizzy spell was noted in one case. One patient was asymptomatic. Electrocardiogram showed a disturbance of repolarization in six cases, conduction disorder in one case and pseudo-aspect of necrosis in two patients. Trans thoracic echocardiography coupled to trans esophageal way allowed diagnosis in all patients by showing uni-vesicular cyst in six cases, multi-vesicular cyst in three cases and calcified in one patient.. The cyst site was within the left ventricular wall in seven cases, pericardium in one patient and right ventricle in two cases. The Chest CT scan our MRI performed in four patients confirmed the echocardiography data. Serology for primitive CH was positive only in 5 cases. All patients underwent surgery with good immediate results. Echocardiograph findings correlated well with surgical findings. Echocardiography Follow up (Mean 50 months) eliminated recurrence of CH.

**Conclusion:** Transthoracic echocardiography suggests the initial diagnosis. CT and MRI provide details of the location and extension of the cardiac hydatidosis.

## BASIC SCIENCE: EXERCISE TESTING & TRAINING

## P2122

### Effect of cardiac rehabilitation on progenitor endothelial cells in patients with heart failure

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**Background:** Alterations in the matrix metalloproteinases levels (MMPs) and in the number of endothelial progenitor cells (EPCs) have been observed in chronic heart failure (CHF) patients. Design: We investigated the effect of a three-week cardiac rehabilitation (CR) program on the number of circulating CD34/KDR+ cells and on serum levels of MMPs in 21 CHF patients. In addition, we studied the effect of patients serum on colony forming units-endothelial cells (CFU-ECs) proliferation.

**Methods:** Peripheral blood and serum were obtained from patients with CHF undergoing CR at admission and at discharge. We measured CD34/KDR+ cells and serum levels of MMP-1 and tissue inhibitor of metalloproteinases (TIMP)-1 by ELISA. Moreover the function and number of CFU-EC colonies were evaluated in cultures performed with serum obtained before and after CR. Exercise tolerance before and after CR was assessed by 6-minute-walking-test (6MWT).

**Results:** At discharge, 6MWT distance and percentage of circulating CD34/KDR+ cells increase ( $0.35 \pm 0.03$  to  $0.58 \pm 0.04$ ;  $p < 0.05$  and  $154 \pm 27$  to  $233 \pm 48$ ;  $p < 0.0001$ , respectively). Conversely, serum concentrations of MMP-1 and TIMP-1 ( $11.4 \pm 2.4$  vs.  $6.3 \pm 1.1$  ng/ml,  $p < 0.01$  and  $320.4 \pm 41.2$  vs.  $167.2 \pm 12.6$  ng/ml,  $p < 0.01$ , respectively) decrease. Interestingly, we found an increase of CFU-EC proliferation in cultures performed with serum obtained at discharge.

**Conclusions:** In CHF patients, three-weeks CR increases the number of circulating EPCs, decreases serum levels of enzymes involved in matrix remodeling and increases serum ability to sustain CFU-EC proliferation. These findings support the hypothesis that CR positively affects the activity of factors involved in cardiovascular repair.

## P2123

### Effect of a cardiac rehabilitation program on circulating CD34/CD117 cells, their proliferation and, metalloproteinases profile in patients with heart failure

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**Aims:** Circulating adult stem cells are thought to exert beneficial effects on re-endothelialization after endothelial injury. Aim of this study was to assess the effect of a cardiac rehabilitation program on mobilization of CD34/CD117 positive cells in the peripheral blood, changes in serum levels of Matrix Metallo Proteinases (MMP-1, MMP-2 and MMP-9), Tissue Inhibitor of Metallo Proteinase-1 (TIMP-1) and TNF- $\alpha$  and on the effect of patient's serum on EPC maturation in culture in patients with mild heart failure.

**Methods:** Blood and serum were collected from 14 patients with NYHA class II heart failure, undergoing an in-patient cycle of cardiac rehabilitation. PBMC were analysed by flow cytometry at admission and at discharge for CD34, KDR, CD117 and CXCR4 markers. Serum levels of MMP-1, MMP-2, MMP-9, TIMP-1 and TNF- $\alpha$  were detected by ELISA before and after rehabilitation. Culture of EPCs from healthy donors were performed with serum obtained from patients at admission and at discharge.

**Results:** Compared to baseline an increase in the percentage of CD34/CD117 positive cells was found at discharge. At discharge, all patients showed a significant decrease in serum concentrations of MMP-1 and TIMP-1. EPCs cultures showed a significant increase in CFU number in EPCs cultivated with serum from patients at discharge. We also found an inverse correlation between TNF- $\alpha$  plasma levels and CD34/KDR positive cells number in blood and between TNF- $\alpha$  and number of EPCs that adhere to activated HUVECs.

**Conclusions:** Physical training in patients with HF induces mobilization of bone marrow stem cells and modifies serum concentrations of TIMP-1 and MMP-1 that may favour vascular repair and inhibit left ventricular remodelling. Moreover functional assays as CFU number analysis, showed that proliferation of cells is influenced by factors that are modified in the serum of patients after rehabilitation. These results underlie new exercise-related beneficial effects in patients with heart failure.

#### P2124

##### Effect of exercise training on serum capacity to induce endothelial cell death in patients with chronic heart failure

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Serum from patients with cardiovascular diseases increases apoptosis in human endothelial cells suggesting the importance of humoral factors in the progression of the disease. Aim of this study was to evaluate whether an in-hospital exercise training program (3 weeks) may influence the apoptotic capacity of sera from patients with chronic heart failure. HUVECs were incubated with a medium containing 20% serum from 39 patients with HF (NYHA II) obtained before and after either a three week exercise training program or at baseline and after three months in patients receiving standard care, and compared to 10 age-matched healthy donors (HD). Sera from CHF patients showed enhanced proapoptotic capacity compared to sera from HD as assessed by Cell Death Assay (HFA 67  $\pm$  5.4% and HFA-E 70  $\pm$  5.6% vs HD 23  $\pm$  5.8% ; p < 0,001). In addition, the capacity of sera to trigger endothelial cells apoptosis in vitro was significantly reduced after physical activity (HFA-E 70  $\pm$  5.6% vs HFD-E 41  $\pm$  4.5%, p < 0,001). Apoptosis assessment performed by intracellular PI staining confirmed both the increased capacity of pre-training CHF sera to trigger programmed cell death compared to the healthy donors (HFA-E 42,14  $\pm$  1,9% vs HD 14,2  $\pm$  0,7% p < 0,001), as well as the ability of physical training to markedly reduce such activity (HFA-E 42,14%  $\pm$  1,9 vs HFD-E 31,9%  $\pm$  1,4%, p < 0,001). The reduction of DNA fragmentation after exercise training correlated with the improvement in functional capacity of patients. Moreover the expression of positive regulators of apoptosis proteins Bax and cleaved Caspase-3 was significantly reduced in HUVECs exposed to sera collected after rehabilitation. Likewise, circulating TNF- $\alpha$ , MMP1, TIMP1 and of the MMP-9/TIMP-1 ratio levels were significantly reduced after exercise training.

In conclusion, in-hospital supervised cardiovascular training program reduces the ability of serum-derived factors to induce endothelial cell death in patient with CHF.

#### P2125

##### Reference equations for the six-minute walk test in heart failure patients

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**Background:** The six-minute walking test (6-MWT) is the most common exercise test, used to evaluate functional capacity and effects of therapeutic interventions on heart failure (HF) patients enrolled in cardiac rehabilitation (CR) programmes.

**Purpose:** The purpose of this study was to establish a reference equation to predict 6-MWT performance in HF population.

**Methods:** 80 HF patients (85% males; mean age 78  $\pm$  7 years), enrolled in a chronic disease assessment programme completed the 6-MWT. Baseline clinical assessment took place prior to testing and included stature, body mass, BMI, medical and pharmacological history, ventricular function and New York Heart Association (NYHA) functional class. Multinomial logistic regression was used to determine the factors associated with poor performance ( $\leq$ 300 m) in the 6-MWT. Threshold values were identified for dependent (total distance 300 m) and independent variables (age > / < 75; stature > / < 172 cm; BMI > / < 25 kg · m<sup>-2</sup>; step length > / < 0.63 m; walking pace index > / < 50%; resting heart rate > / < 80 beats min<sup>-1</sup>; LVEF > / < 45%). Odds ratios with 95 per cent confidence intervals (CI) were calculated.

**Results:** Mean 6MWT distance was 310  $\pm$  20 m. Age and stature were the only

variables which correlated significantly with test performance. In regression analysis, 42% of variance in 6MWT performance was accounted for by age, but stature was no longer a significant predictor: 6MWT distance (m) = 765 - (6  $\times$  age), m. Multinomial logistic regression analysis showed that independent predictors of poor performance were: BMI  $\geq$  25 kg·m<sup>-2</sup> (OR = 13.1, 95% CI = 1.48 - 110) and age  $\geq$  75 years (OR = 5.1, 95% CI = 1.31 - 18.79).

**Conclusions:** Clinical variables such as ventricular function are unrelated to 6 minute walk test performance in heart failure patients. Old age and high BMI are, however, independent predictors of poor performance and should be accounted for when the test is used to categorise patients according to prognostic cut points. Test performance may be better expressed as a percentage of normal population values which account for age and BMI.

## BASIC SCIENCE: PROGNOSIS

#### P2126

##### Differences between overweight/obese patients and normal weight patients with stable heart failure. A Possible link to survival benefit

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**Background:** Chronic heart failure (CHF) patients with increased body mass index (BMI) (overweight and obese) have better survival rates than their normal weight counterparts. It is not known what factors related to increased BMI underlie this benefit.

**Objective:** We aimed to assess how body composition, diet, exercise levels and functional capacity differed between obese/overweight and normal weight patients.

**Methods:** 106 patients with chronic stable heart failure were categorized according to their BMI. Anthropometric measurements, body composition (Tanita), fat mass and free fat mass, dietary 3 day records and functional assessments including 6 minute walk test, 3 day FitBit records and NYHA class were recorded.

**Results:** There were no differences in daily energy, fat, or carbohydrate consumption or activity levels between the groups. However, overweight and obese CHF patients have significantly increased fat mass, % fat, free fat mass and consumed more protein. Mean age 66.8  $\pm$  12.7. 72.2% (n = 78) were male and 27.8% (n = 30) were female.

**Conclusion:** Our study highlights that energy intake and activity levels do not differ significantly between overweight/obese and normal weight patients. However, the higher fat free mass and protein intake suggests differences in protein metabolism may be relevant to the survival benefit with higher BMI.

	Normal weight	Overweight	Obese	p-value
No. pts (n)	23	38	45	
Age (years $\pm$ SD)	67.1 $\pm$ 2.7	67.9 $\pm$ 2.1	65.8 $\pm$ 1.9	0.716
Fat Mass	15.7 $\pm$ 1.3	24.2 $\pm$ 1.5	37.4 $\pm$ 0.97	$\leq$ 0.0001†
Free Fat Mass	47.0 $\pm$ 2.0	57.0 $\pm$ 1.5	59.9 $\pm$ 1.4	$\leq$ 0.0001†
%Body Fat	24.8 $\pm$ 1.5	30.1 $\pm$ 1.1	38.4 $\pm$ 1.0	$\leq$ 0.0001†
Waist circumference(cm)	84.0 $\pm$ 1.8	97.7 $\pm$ 1.4	110.5 $\pm$ 1.3	$\leq$ 0.0001†
Functional Measurements				
NYHA	1.25 $\pm$ 0.11	1.33 $\pm$ 0.09	1.27 $\pm$ 0.08	0.840
6min walk (m)	394.0 $\pm$ 31.0	403.6 $\pm$ 24.7	387.6 $\pm$ 22.7	0.889
Activity (Mean no. of steps per day)	5120.1 $\pm$ 924.8	5839 $\pm$ 713.1	5564 $\pm$ 661.5	n 0.819
Mean Daily Dietary Intake				
Energy (kcal)	1641.1 $\pm$ 108.3	1716.1 $\pm$ 87.2	1844.0 $\pm$ 81.3	0.292
Proteins(g)	69.3 $\pm$ 4.9	76.4 $\pm$ 3.9	85.3 $\pm$ 3.6	0.03†
Fat(g)	66.4 $\pm$ 5.7	66.3 $\pm$ 4.6	74.1 $\pm$ 4.3	0.384
Carbohydrate (g)	196.5 $\pm$ 13.7	206.2 $\pm$ 11.0	204.4 $\pm$ 10.3	0.292

## BASIC SCIENCE: LEFT VENTRICULAR FUNCTION

#### P2127

##### Left ventricular function in asymptomatic scleroderma patients about 25 cases

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**Introduction and Purpose:** Scleroderma has been associated with an increases risk of cardiovascular diseases. The aim of this study is to assess the systolic and diastolic function of the left ventricular (LV) in asymptomatic scleroderma patients.

**Methods:** We included 25 scleroderma patients without symptoms or signs of heart failure or angina (groupe I) and 25 healthy subjects ( groupe II) ;The two groups had similar mean age ,sex ratio ,mean blood pressure and body mass index. All included subjects had no evidence of diabetes mellitus ,valvular or ischemic heart diseases. we used standard echocardiography and tissue Doppler imaging(TDI)

**Results:** LV diastolic diameter and LV ejection fraction were similar in both group ,however we observed lower mitral annulus systolic velocities measured by TDI in scleroderma patients ( $5.2 \pm 0.7$ cm/s vs  $8.6 \pm 0.9$ cm/s,  $p < 0.01$ ) reflecting subclinical LV systolic dysfunction. there was not significant difference in the ratio of early to late diastolic mitral filling velocities E/A and in deceleration time of E between the 2 groups. However mitral annulus early diastolic velocities Ea measured by TDI were markedly reduced in scleroderma patients ( $7.0 \pm 1.1$ cm/s vs.  $12.5 \pm 1.4$  cm/s,  $p < 0,01$ ) WITH function. diastolic impaired suggesting  $p < 0,01$ )  $\pm 1.7$ ;  $7.1 \pm 1.9$  vs ( $13.1$  velocities Ea E of ratio higher.

**Conclusion:** This study shows the presence of systolic and diastolic dysfunction in asymptomatic scleroderma patient's. Tissue Doppler imaging may provide a useful tool to monitor the disease process and treatment response of this subclinical myocardial dysfunction.

## P2128

### Platelet function parameters assessment by Multiplate aggregometry and leucocyte count in patients with acute coronary syndrome and lower ejection fraction

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**Background:** Acute coronary syndrome ( ACS) is common and affects a significant number of people annually. Death occurs due to either arrhythmia or heart failure.

As leucocytosis is a hallmark of inflammatory reactions in patients with ACS, we investigated the relationship between leucocytosis on admission and left ventricular ejection fraction (LVEF) in patients with ACS. Platelets play a pivotal role in atherogenesis and its thrombotic complications such as those occurring in patients with ACS which is a platelet-driven process.

**Purpose:** To study platelet function parameters assessment by Multiplate aggregometry and leucocyte count in patients with ACS and lower ejection fraction.

**Methods:** A total of 82 patients with acute coronary syndrome (ACS) were considered for entry into the study. Leucocyte count was measured on Sysmex kx21n. Platelet function parameters-response to acetylsalicylic acid(ASPI test), clopidogrel(ADP test) and thrombin receptor activating peptide(TRAP test) were assessed by the Multiplate platelet function analyzer. Brain natriuretic peptide levels (BNP) were measured using a Triage meter pro biosite. Value of ejection fraction was measured by echocardiography.

**Results:** 82 patients were entered into the study (54 males, 28 females). In this group were 17 patients with left ventricular ejection fraction (LVEF) <40%-group I and 65 patients with LVEF >40%-group II. Mean age of patients in group I was  $70.94 \pm 10.09$ , while in group II was  $64.72 \pm 10.55$ . ( $P < 0.05$ ). Mean leucocyte count in group I was  $10.31 \pm 4.40 \times 10^9/l$ , in group II was  $8.10 \pm 2.81 \times 10^9/l$ . ( $P < 0.05$ ). Mean BNP in group I was  $609.43 \pm 396.14$  pg/ml, in group II was  $218.55 \pm 279.95$  pg/ml ( $P < 0.05$ ). In I group value of ASPI test was  $472.50 \pm 303.34$  AU\*min, in II group ASPI test was  $391.60 \pm 256.83$  AU\*min. (NS). In I group value of ADP test was  $659.43 \pm 181.17$  AU\*min, in II group it was  $533.63 \pm 182.11$  AU\*min. ( $P < 0.05$ ). In I group value of TRAP test was  $1163.39 \pm 284.94$  AU\*min, but in II group it was  $1019.12 \pm 266.98$  AU\*min. ( $P < 0.05$ ).

**Conclusion:** Patients with ACS and LVEF <40% were older than patients with ACS and LVEF >40%. Patients with ACS and LVEF <40% had higher leucocyte count, BNP levels and higher values of ASPI, ADP and TRAP test than patients with ACS and LVEF >40%.